UNIVERSITY OF STIRLING

HEALTH-RELATED QUALITY OF LIFE, SYMPTOMS EXPERIENCE AND PERCEIVED SOCIAL SUPPORT AMONG PATIENTS WITH LIVER CIRRHOSIS: A CROSS-SECTIONAL STUDY IN EGYPT

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DECLARATION

I declare that this thesis is my own work except where otherwise stated.

Naglaa Youssef
April 2013

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BRIEF BACKGROUND ABOUT THE AUTHOR

Naglaa Fathy Afifi Youssef graduated in the Faculty of Nursing, Cairo University, Egypt with Bachelor of Nursing Sciences. Following that, Youssef was awarded the Master of Nursing Sciences with an “Excellent” level degree in the same University. From 1999 to 2006 Youssef joined the Department of Medical-Surgical Nursing (Adult Nursing), Faculty of Nursing, Cairo University as a clinical instructor. In 2006, she was promoted to be assistant lecturer in the same University.

In 2009, she got a competitive governmental scholarship from the Ministry of Higher Education to study her PhD. From September 2009 till 2013 conducted her PhD in the School of Nursing, Midwifery and Health, University of Stirling, Scotland, UK under the supervision of Doctor Josie Evans, Doctor Ashley Shepherd and Professor Sally Wyke. After finishing her PhD, Youssef will return to her Faculty in Cairo University as a lecturer.

PUBLICATIONS, CONFERENCES PRESENTATIONS AND AWARD

Publications

YOUSSEF, N.F.A., SHEPHERD, A., EVANS, J.M.M. and WYKE, S., 2012. Translating and testing the Liver Disease Symptom Index 2.0 for administration to people with liver cirrhosis in Egypt. *International Journal of Nursing Practice,* **18**(4), pp. 406-416.

Conferences presentations

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Long-Term Conditions: Building Bridges between Researchers, Practitioners and Service Users”, Hilton Hotel Dundee, Scotland, UK, (Poster).

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LIST OF ABBREVIATIONS

ALD:	Alcoholic liver disease
ASSIA:	Applied Social Sciences Index and Abstracts
BP:	Bodily pain
CASP:	Critical Appraisal Skills Program
CDYCDLR:	Centre Doctor Yassin Abdel Ghaffar Charity for Diseases of the Liver and Research
CINAHL:	Cumulative Index to Nursing and Allied Health Literature
CLDQ:	Chronic Liver Disease Questionnaire,
CRO:	Clinical reported outcomes
DLA:	Dutch Liver Association
DREC:	Department of Nursing and Midwifery Research Ethics Committee
NHTMRI:	Research Ethics Committee Board of the National Hepatology and Tropical Medicine Research Institute
e.g.	Exempli gratia: Latin expression means for instance
ECAQ:	Executive Committee for Accreditation and Quality
et al:	et alia: Latin expression means and other
etc.:	et cetera: Latin expression means "and other things" or "and so on
GH:	General health
HBV:	Hepatitis B virus
HCV:	Hepatitis C virus
HQOL-v_2:	Hepatitis Quality of Life Questionnaire Version 2,
HRQOL:	Health-Related Quality of Life
HUI:	Health Utilities Index
HUI-II:	Health Utilities Index-Mark II,
HUI-III:	Health Utilities Index-Mark III,
i.e: id est:	Latin expression means that is to say
IQOLA :	International Quality of Life Assessment
LDQOL 1.0:	Liver Disease Quality Of Life 1.0,
LDSI-2.0:	Liver Disease Symptom Index 2.0,
LDSI-2.0:	Liver Disease Symptom Index-2.0
MCS:	Mental component summary score
MELD:	Model of End-Stage Liver Disease
MFI-20:	Multidimensional Fatigue Index-20
MFMER:	Mayo Foundation for Medical Education and Research
MH:	Mental health
MSPSS:	Multidimensional Scale of Perceived Social Support
NA: Not	available
NAFLD:	Non-alcoholic fatty liver disease
NBS:	Norm-Based Score
NHP:	Nottingham Health Profile,
NHS:	National Health Service
p.	page
PAT:	Parenteral Antischistosomal Therapy
PBC:	Primary Biliary Cirrhosis
PCS:	Physical component summary score
PF:	Physical functioning
PGWBI:	Psychological General Well-Being Index,

PhD:	Doctor of Philosophy
PRO:	patient reported outcomes
QOL:	Quality of Life
QOLI:	Quality Of Life Index,
RE:	Role limitations due to emotional problems
RP:	Role limitations due to physical health problems
SF:	Social functioning
SF-12:	Short Form 12,
SF-36:	Short Form-36
SIGN:	Scottish Intercollegiate Guidelines Network
UK:	United Kingdom
US:	United States
USA:	United States of America
VT:	Vitality
WHO:	World Health Organisation
WHOQOL-G:	World Health Organisation Quality of Life-Group

ABSTRACT

Background: Liver cirrhosis is a global health problem and a national health problem in Egypt. There is a lack of literature on Health-Related Quality of Life (HRQOL) and symptoms experience of liver disease and cirrhotic patients in Middle East, particularly in Egypt. **Aims:** This PhD had three major aims: First aim: To describe HRQOL of Egyptian liver cirrhotic patients and to identify and evaluate the factors associated with (HRQOL) physical and mental health domains. Second aim: To explore and describe experienced symptoms (prevalence, severity and hindrance) in Egyptian cirrhotic patients and to identify and evaluate factors associated with symptoms severity and symptoms hindrance (distress). Third aim: To explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to identify and evaluate factors associated with general perceived social support. **Method:** A cross-sectional study with a convenience sample of 401 patients from three hospitals in Cairo, Egypt, was conducted between June and August 2011. Patients were interviewed to complete a background data sheet, Short Form-36v$_2$ (SF-36), the Liver Disease Symptom Index (LDSI)-2.0 and the Multidimensional Scale of Perceived Social Support (MSPSS).

Results:

Findings for first aim: The findings showed that all domains and component summary scores [Physical component summary score (PCS) and mental component summary score (MCS)] of the generic SF-36 were below the norm (cut-off score 50), suggesting that patients with liver cirrhosis in Egypt have poor HRQOL. About 87.2% of the patients rated their general health as poor or fair, which means the majority of these patients have low perceived general health. Many socio-demographic and medial factors were shown to be significantly associated with perceived HRQOL. Women, illiterate and unemployed people, and patients with frequent hospitalisation had poor PCS and MCS, while patients with advanced disease stage, increasing number of comorbidities and complications and those admitted to inpatients had significantly poorer PCS only. Perceived social support from a spouse had a statistically significant positive association with PCS and MCS, while perceived social support from family and friends had a statistically significant positive association with MCS only. Also, severity and hindrance of symptoms significantly correlated with PCS and MCS.

Using stepwise multiple linear regression analysis, two models were developed to identify factors associated with PCS (Model 1) and MCS (Model 2) health. Model 1 could significantly explain 19% of the variation in PCS (R^2 = 0.190, R^2_{adj} = 0.180, p = 0.0005), and four factors (symptoms severity, disease stage, comorbidities and employment status) were significantly ($p \leq 0.02$) associated with PCS. Model 2 could significantly explain 31.7% of the variation in MCS (R^2 = 0.317, R^2_{adj} = 0.308, p = 0.0005), and four factors (symptoms severity, employment status, perceived spouse support and perceived family support) were associated ($p \leq 0.04$) with MCS. The key findings of this study were that severity of symptoms and social support from spouse and family were associated with HRQOL. Where patients with high symptoms severity were likely to report poor PCS and MCS; and patients with

low perceived social support were likely to report poor MCS. Symptoms severity contributed significantly in explaining 28.7% of the variation in PCS and 43.6% of the variation in MCS.

Findings for second aim: This study found that the majority of patients had one or more of a wide range of symptoms and social problems. Two-thirds of patients reported joint pain (78.3%), decreased appetite (75.6%) and memory problems (77.3%). Joint pain and depression were reported to have the biggest impact on daily life. Symptoms severity and distress were significantly higher among patients who were: female, illiterate, unemployed, and who had advanced cirrhosis with more complications and comorbidities ($p \le 0.006$). Symptoms severity ($r=-0.206$) and symptoms distress ($r=-0.205$) were negatively associated with perceived social support ($p=0.005$). Stepwise regression analysis showed that the regression model could significantly explain 19.6% of the variation in symptoms severity ($R^2 = 0.196$, $R^2_{adj} = 0.180$, $p = 0.0005$), and 14% of the variation in hindrance of symptoms ($R^2 = 0.140$, $R^2_{adj} = 0.132$, $p = 0.0005$). Being female, having an increasing number of liver disease complications, and having low perceived support from spouse were significantly associated with high-perceived symptoms severity and hindrance ($p \le 0.01$).

Findings for third aim: This study found that social support score was relatively high among patients with cirrhosis in Egypt (total score mean of MSPSS was 2.02± standard deviation (0.537), while perceived support from spouse was the highest source of support. 67.5% of the patients felt their spouse is around when they need him/her and 71.7% of them share their joys and sorrows with their spouse. Likewise, 64.9% of married people feel their spouse cares about their feelings. In relation to the perception of adequacy of family support, it was observed that 52.6% felt that their families do not really try to help them. At the same time, 52.1% reported that they got the emotional help and support that they needed from their families. Regarding perceived support from friends, more than half of the patients reported that their friends do not really try to help them (57.9%), they cannot count on their friends when things go wrong (65.6%) and they cannot talk about their problems with their friends (56.4%). There was a significantly positive association between the perception of social support and general health perception (GHP), suggesting that when social support decreases GHP also decreases or and vice versa ($r= 0.208$, $p = 0.0005$). Stepwise regression analysis showed that the regression model could significantly explain 10.9% of the variation in perceived social support ($R^2 = 0.109$, $R^2_{adj} = 0.100$, $p = 0.0005$). Marital status, gender, age and employment status were significantly associated with general perceived social support ($p \le 0.01$), while unmarried, females, unemployed and elderly cirrhotic patients were vulnerable groups that were likely to perceive low social support.

Overall discussion and conclusion: This is the first study to investigate HRQOL, symptoms experience and perceived social support in patients with liver cirrhosis in Egypt. All aspects of HRQOL of Egyptian cirrhotic patients were poor, and they were experiencing various symptoms that can affect their daily life. However, social support was found to be related to perceived symptoms severity and perceived poor mental health. Hence, social support may alleviate suffering for certain cirrhotic patients. Nurses have a responsibility to assess and treat symptoms that cirrhotic patients experience, particularly such treatable symptoms as depression, pain and decreased appetite. Also, nurses should involve the patient’s family in any

plan of care. Future intervention studies that aim to develop programs to relieve treatable symptoms and enhance social support are also recommended.

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1 CHAPTER 1- INTRODUCTION TO THE THESIS

1.1 INTRODUCTION

This chapter briefly states my rationale for selection of this area of study and summarises its major aims and research questions. It then outlines the overall organisation of the thesis.

1.2 PERSONAL RATIONALE TO CONDUCT THIS STUDY

Until coming to the United Kingdoms (UK) to undertake the PhD research here, I worked as a clinical instructor for six years and as an assistant lecturer for three years in the Faculty of Nursing, Cairo University in Egypt and my major task was to teach and train undergraduate students in nursing care for adults in medical and surgical departments. In this role, I observed the problems faced by many patients with different chronic conditions, but was aware that in the medically dominated world of healthcare, which focuses on a traditional medical model, patients received little advice on how to manage the symptoms they had or how to decrease their suffering by satisfying their psychosocial needs. As a nurse educator and from my experience with the patients, I am aware that a little information and psychological support can decrease patients' suffering and improve their Health-Related Quality of Life (HRQOL). With my belief that chronic disease is not a bad experience in itself, but it can be a bad or good experience based on the quality of the supportive healthcare resources as well as quality of the supportive social environment. I know it is essential to care well for patients and to teach them how to care for themselves in order to improve their HRQOL. This personal belief and experience drove the topic of my research.

My long-term aim is to develop a self-care programme for patients with liver cirrhosis in Egypt that would help to decrease their suffering by providing the knowledge that they need to care for themselves and to help them improve their HRQOL. I started to search the literature to find existing research to get the basic knowledge and evidence that can answer these questions: what is the HRQOL of liver cirrhotic patients in Egypt? What are their biopsychosocial needs? What are the factors that influence their HRQOL? What symptoms do these patients experience? in order to use these studies as evidence to develop the self-care programme. There was no identified study could answer these questions.

Assessing patients' needs is the key principle of developing educational or self-care programmes. Moreover, developing a programme has to be based on existing research explaining what the needs of these patients are and what will help them to improve their HRQOL. My observation and experience only are not enough to justify why I need to develop this programme and test its impact, without previous research to describe what their HRQOL and their needs actually are. Therefore, I decided to conduct the current study and based on its findings, the self-care programme will be developed (see section 3.10 definition of self-care), and its impact will be tested by developing other research in the future.

1.3 AIMS OF THE STUDY AND RESEARCH QUESTIONS

This study has three general aims and several research questions:

The first aim is to describe Health-Related Quality of Life (HRQOL) of Egyptian liver cirrhotic patients and to identify and evaluate factors associated with (HRQOL) physical and mental health domains.

Research questions to achieve aim 1

1.1. How do patients with liver cirrhosis in Egypt perceive their (HRQOL) physical and mental health?
1.2. How do patients with liver cirrhosis perceive their general health?
1.3. What is the relationship between individual characteristics (socio-demographic characteristics) and perceived physical and mental health?
1.4. What is the relationship between biophysical variables (medical data and disease stage) and perceived physical and mental health?
1.5. Does symptoms severity influence physical and mental health?
1.6. Does perceived social support influence physical and mental health?
1.7. Do disease stage, symptoms experience (severity and hindrance), perceived social support, socio-demographic factors and medical data explain the perception of the physical health of patients with liver cirrhosis?
1.8. Do disease stage, symptoms experience (severity and hindrance), perceived social support, socio-demographic factors and medical data explain the perception of the mental health of patients with liver cirrhosis?

The second aim is to explore and describe experienced symptoms (prevalence, severity and hindrance) in Egyptian cirrhotic patients and to identify and evaluate factors associated with symptoms severity and symptoms hindrance (distress).

Research questions to achieve aim 2

2.1. What symptoms do patients with liver cirrhosis experience?
2.2. Which of the reported symptoms limit the daily activities of patients with cirrhosis?
2.3. What is the association between individual characteristics and symptoms experience (severity and hindrance of symptoms)?
2.4. What is the association between biophysical variables and symptoms experience?
2.5. What is the association between general health perception and symptoms experience?

2.6. Does perception of social support influence perception of symptoms experience?
2.7. What are factors associate with symptoms experience among cirrhotic patients in Egypt?

The third aim is to explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to identify and evaluate factors associated with general perceived social support.

Research questions to achieve aim 3

3.1 How do patients with liver cirrhosis in Egypt perceive the available social support?
3.2 Do patients with liver cirrhosis perceive social support from spouse, family and friends to be adequate?
3.3 Do patients' socio-demographic characteristics and disease stage influence perceived adequacy of social support?
3.4 What is the relationship between perception of general health and perception of social support among patients with liver cirrhosis?
3.5 What are the factors associated with perceived adequacy of social support among liver cirrhotic patients in Egypt?

1.4 STRUCTURE OF THE THESIS

This thesis consists of eight chapters following this Introduction:

Chapter 2

The second chapter provides a background to liver cirrhosis epidemiology, a review of the literature on the concepts of Quality of Life (QOL), and HRQOL and social support and its relationship with health.

Chapter 3

This chapter clarifies the search strategy that was used to find the relevant literature. Then it provides a review of the literature in three sections on HRQOL, symptoms experience and perceived social support among patients with liver cirrhosis.

Chapter 4

This chapter describes the philosophical paradigm and methodological approach that were adopted in this study, followed by illustrating and discussing the theoretical model of HRQOL outcomes that was used in this study. The research design, the population and sampling, and clinical settings are clarified as well as the data collection procedures. Finally, ethical approval and ethical considerations are discussed.

Chapter 5

This chapter provides details of the pilot study that was conducted before the main study. The results of the pilot study are presented in two sections: Section I describes the translation process findings and section II describes the pilot study findings.

Chapter 6

This chapter presents the findings from the main study analysis in three sections. Section I describes participant characteristics and the HRQOL of people with liver cirrhosis in Egypt. Section II presents factors associated with HRQOL using bivariate analysis. Section III presents factors associated with HRQOL using multivariate (stepwise multiple linear regression) analysis.

Chapter 7

This chapter presents results related to the second and the third aims of the main study in two sections. Section I describes and analyse the symptoms experience of people with liver cirrhosis, how these symptoms affect their daily activities, and associated factors of overall symptoms severity and symptoms hindrance (distress). Section II presents how patients with liver cirrhosis in Egypt perceived available social support and factors associated with perceived social support.

Chapter 8

This chapter examines the psychometric properties of the three measures used in patients with liver cirrhosis: Liver Disease Symptom Index-2.0 (LDSI-2.0), Multidimensional Scale of Perceived Social Support (MSPSS) and Short Form-36v$_2$ (SF-36v$_2$) using the main study data.

Chapter 9

The final chapter discusses the key findings of the study in relation to previous studies in three sections. Section I discusses HRQOL and its associated factors. Section II discusses symptoms experience and its associated factors. Section III discusses social support and its associated factors. The implications of the study findings in terms of theory, practice and research are outlined. Recommendations for improving the healthcare system in Egypt and for further research are stated. The strengths and weaknesses of the study are also acknowledged.

2 CHAPTER 2- LITERATURE REVIEW PART-1

This chapter is presented in two sections. Section I considers liver cirrhosis; its epidemiology, causes and the epidemic of the hepatitis C virus (HCV) in Egypt and finally, complications and challenges of treating patients with cirrhosis.

Section II addresses the nature of Quality of Life (QOL) in more detail, beginning with defining Quality of Life (QOL), then discussing the relationship between QOL and health. An examination of Health-Related Quality of Life (HRQOL) then follows relating to its definition, domains and the importance of measuring HRQOL. Finally, the relationship between HRQOL and social support is discussed.

2.1 SECTION I: LIVER CIRRHOSIS

2.1.1 Epidemiology of Liver Cirrhosis

Liver cirrhosis is a serious disease associated with significant morbidity and mortality (Bosetti et al. 2007; Gutteling et al. 2007); it is considered one of the leading causes of death worldwide (Mathers 2008; Kochanek et al. 2011) and is the seventh leading cause of death in Egypt 2002 (World Health Organisation (WHO) 2006). Cirrhosis can affect any individual; young and old, males and females (WHO 2006; Bosetti et al. 2007).

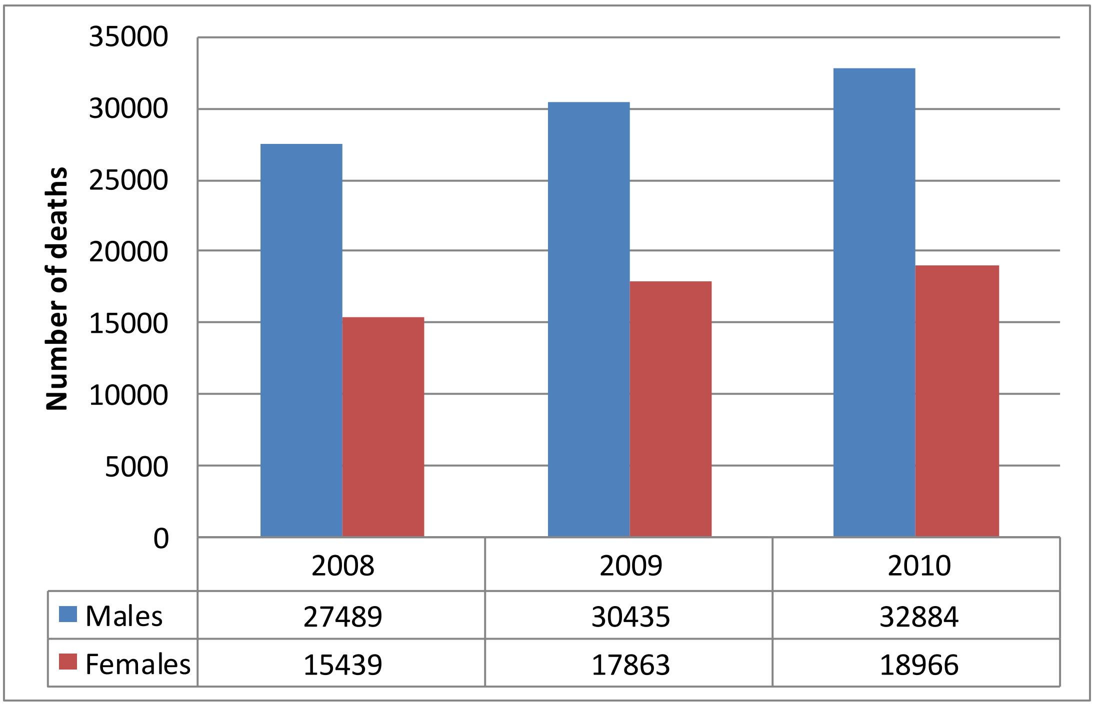
Liver disease and cirrhosis remains a major cause of death worldwide and a national problem in Egypt (WHO 2013). An estimated 800,000 deaths each year are attributed worldwide to cirrhosis (WHO 2006). However, Egypt has the highest prevalence of deaths due to liver disease and cirrhosis worldwide. For instance, the number deaths due to liver disease in 2007-2008 was 8908 in the United

Kingdoms (UK), 38964 in the United States of America (USA), 67 in Kuwait, and 24 in Qatar, 165 in Jordan and 566 in Morocco, and in Egypt it was 42928 (WHO 2012c).

Mortality due to liver disease is still increasing in Egypt (WHO 2012c) (Figure 2-1). The total number of deaths due to liver disease and cirrhosis in 2010 was 51850. The majority of deaths was among those aged 55 to 74 (n = 29477); mortality among men was higher than among women (32884 vs. 18966 respectively) (WHO 2012c) (Figures 2-1, 2-2). Figure 2-2 shows the number of deaths due to liver disease and cirrhosis in Egypt between years 2008 and 2010 among all ages group. The number of deaths rose steadily until age 35-54; then increased sharply until it reached a peak at age 55-74, and then it declined gradually. Although women and men had the same trend, the actual number of deaths is higher among males (WHO 2012c).

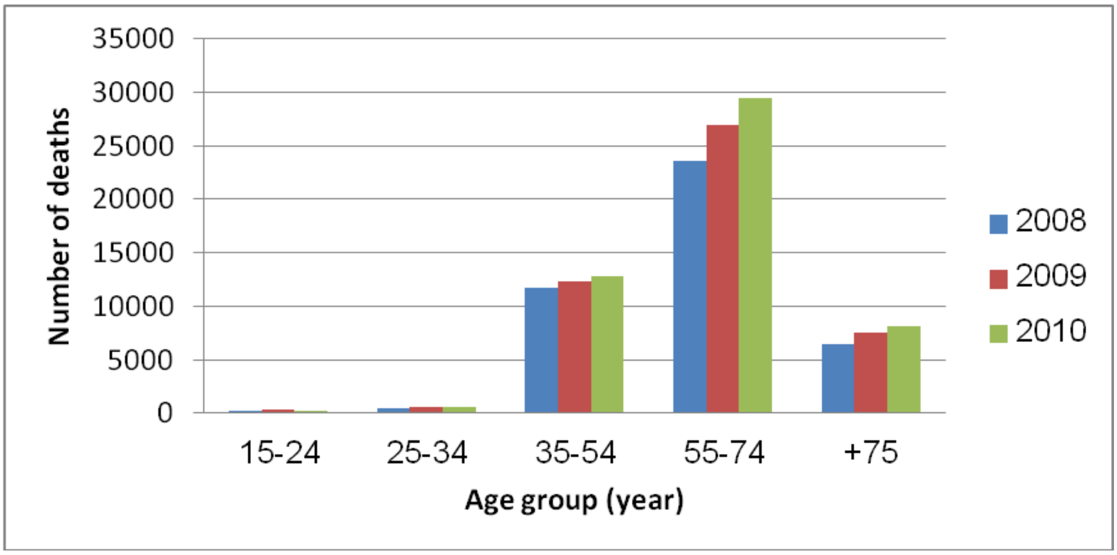
It was estimated that three per cent of patients with chronic liver disease in Egypt die every year because of liver cirrhosis complications (Strickland et al. 2002). Hepatic dysfunction, oesophageal varices bleeding, ascites, and liver cancer are the most serious complications and are often fatal (Fujimoto and Kaneda 1999). Once complications of cirrhosis develop, the morbidity and mortality rates increase steeply (Dong and Saab 2009).

Figure 2-1: Trends of deaths due to liver disease, by gender group, in Egypt from 2008 to 2010, (WHO 2012c)



	2008	2009	2010
🟦 Males	27489	30435	32884
🟥 Females	15439	17863	18966

Figure 2-2: Number of deaths due to liver disease, by age group, in Egypt from 2008 to 2010, (WHO 2012c)



2.1.2 International and National Causes of Liver Cirrhosis

The common causes of chronic liver disease and liver cirrhosis worldwide are hepatitis B and/or C (HBV, HCV) virus infection. Approximately 240 million people worldwide are chronically infected with HBV (WHO 2012); and up to 170 million people (3% of the global population) are chronically infected with HCV (WHO 2010). It was estimated that about 3 to 4 million persons get infected each year with HCV (WHO 2012a). Up to 50% of people infected with HCV develop liver cirrhosis, liver failure and hepatocellular carcinoma (WHO 2010). In Western countries, the most common cause of liver cirrhosis is chronic alcohol abuse (Ramstedt 2001; Mandayam et al. 2004; Schuppan and Afdhal 2008), while in Egypt it is HCV (Darwish et al. 2001; Wasfi and Sadek 2011).

2.1.3 Epidemic of Hepatitis C in Egypt from Past to Present

Egypt has the highest prevalence of HCV worldwide (WHO 2006; Sievert et al. 2011; WHO 2012a). Egypt also has higher rates of HCV infection than neighbouring countries and other countries in the world with comparable socio-economic conditions and hygienic standards for invasive medical, dental, or paramedical procedures (Frank et al. 2000; Rao et al. 2002; WHO 2006). A systematic review conducted by Sievert et al. in 2011 shows that Egypt has a higher prevalence of HCV than other countries in Asia and Australia, e.g. Syria, Pakistan and China.

Lehman and Wilson (2009) conducted a systematic review (using community-based studies conducted in Egypt from 1990 to 2004) to calculate the fluctuating sources of HBV and HCV. They found that the HCV prevalence was 21.8% in 1990-1994, then declined dramatically between 1995 and 1999 to 12.5%, then rose slightly from 1999 to 2004 to 13.5%. Recently, El-Zanaty and Way (2009) conducted a Demographic and Health Survey (DHS) in 2008 on behalf of the Egyptian Health Ministry. They found that of the 11,126 respondents aged 15-59, 10% had the active HCV. Accordingly, it seems that the rate of HCV infections declined from 13.5% to 10 % respectively in the period 2004 to 2008.

Egypt has a history with the epidemic of Schistosomiasis (bilharziasis). It is a parasitic infection carried by snails living in the Nile River. A mass campaign providing intravenous therapy against Schistosomiasis in the period between 1960s and 1970s was conducted (Dalglish 2008). El Gohary (1995); Frank (2000); Rao et al. (2002) and Lehman and Wilson (2009) showed that Parenteral Antischistosomal Therapy (PAT) was the main cause for spreading the HCV among the Egyptian people, because contaminated syringes were used. Thus, there is a higher prevalence of HCV in people aged over 44 years than in younger ones (Sievert et al. 2011).

Although the major cause for transmitting the HCV (PAT campaign) was abolished many decades ago, a strategy for preventing the spread of HCV by screening blood donations, sterilization techniques and avoiding unnecessary injections was implemented (Sievert et al. 2011). However, it seems that HCV continues to be transmitted in Egypt (Lehman and Wilson 2009). This may be due to the increase in infected people with the HCV, especially in geographical areas close to the Nile Delta, where there is a higher prevalence of infections than in Upper Egypt. Also, it seems there are other factors that may cause continuity of spreading HCV in Egypt. For example, household transmissions (spouse, father-offspring, sibling transmission), unsterilized equipment or techniques during surgery, blood transfusions, tattoos, circumcision, acupuncture, public shaving by the village barber, ear piercings and drug injections may be important causes of spreading the HCV (Darwish et al. 2001; Sievert et al. 2011,).

In a recent study, El Feki et al. (2013) investigated the prevalence of HCV and its risk factors among a randomly selected sample of 400 participants from a rural area and 165 from an urban area in Egypt. They found that the prevalence of HCV was higher in the rural area than the urban area (36% versus 18.2%), with the number of the HCV positive patients in the rural area higher than the urban area (94% versus 63.3%). A significant risk factor for HCV infection in rural and urban areas among young people (≤30 years) was informal circumcision in rural areas, and blood transfusion in rural and urban areas. While a significant risk factor among older people (>30 years) were bilharziasis and endoscopy in rural area, and blood transfusion and parenteral treatment for bilharziasis in rural and urban areas (El Feki et al. 2013). Therefore, it seems that infected blood transfusion is the major risk factor for the increasing prevalence of HCV in different regions in Egypt.

2.1.4 Complications of Liver Cirrhosis and Challenges of Management

There is a clinical spectrum of liver cirrhosis; at one end, there are no obvious signs or complications (known as compensatory cirrhosis stage) and at the other end, there are severe signs and complications (known as decompensatory cirrhosis stage) (Everson 2005). Patients with decompensated cirrhosis are at risk of death from cirrhosis complications (Everson 2005) such as variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, hepatic renal syndrome or/and hepatic carcinoma (Everson 2005; Dong and Saab 2009; Bjornsson et al. 2009; Porth and Matfin 2009; Alazawi et al. 2010).

Patients with cirrhosis are the group most difficult to treat; particularly those with HCV genotype 4 (the genetic structure of HCV). The standard medical therapies for HCV are Interferon and Ribavirin. However, according to the recent systematic literature review the overall response rate of cirrhotic patients who were treated with antivirus therapy did not exceed 33.3% for all genotypes and 21% for genotype 1 and 4 (Bota et al. 2011). Therefore, effective treatment for patients with liver cirrhosis (Alazawi et al. 2010) especially those infected with HCV genotype 4 (Bota et al. 2011) is not proven. In Egypt Genotype 4 is the most common type of HCV (93%) (Kamal and Nasser 2008; Sievert et al. 2011). Thus, people with chronically infected HCV will progress to liver cirrhosis, which will lead to an increasing number of people with liver cirrhosis in the future.

Nowadays, medical intervention for patients with compensated cirrhosis has two dimensions. The first is to treat HCV infected people to clear the virus. Secondly, to temporarily control progression of cirrhosis complications among patients who do not respond effectively to antiviral therapy (Everson 2005). Once patients develop complications of cirrhosis the aim of any medical treatment is to treat these complications so they recover from the critical condition and their health status is stabilised (Everson 2005).

Management of cirrhosis is still aimed at treating causative factors, such as stopping alcohol consumption, or managing complications according to type to alleviate any disabling or life-threatening problems (Dong and Saab 2009; Mayo Foundation for Medical Education and Research (MFMER) 2013). Also, periodic check-ups of the patients are essential for detecting early signs of hepatic encephalopathy or hepatic carcinoma (Heidelbaugh and Sherboundy 2006;

Cheney et al. 2012). A liver transplantation is the only available medical intervention for end-stage liver cirrhosis. However, this is impossible for many patients because either there are insufficient resources such as money or an appropriate donor (Allam et al.2010) or they are not eligible for this intervention.

Patients with liver cirrhosis experience different complications with different signs and symptoms, which can affect their daily activities negatively. Studies conducted in Western countries where medical services of high quality are provided, found that patients with cirrhosis have a lower Health-Related Quality of Life (HRQOL) than the average population (Gutteling et al. 2006). They also experience a lower mental state of health than patients with other chronic diseases such as congestive heart failure and chronic obstructive pulmonary disease (Younossi et al. 2001). Patients with chronic diseases such as liver cirrhosis may need not only physiological treatment but also psychosocial support to improve their HRQOL (discussed in the next section)

2.2 SECTION II: QUALITY OF LIFE AND HEALTH-RELATED QUALITY OF LIFE

Many terms are utilized interchangeably with the term Quality of Life (QOL), and it is essential to differentiate between them (Haas 2007). One of these terms is HRQOL. There is indeed considerable overlap between QOL and HRQOL. The two terms have been used in previous research interchangeably, but they are not equivalent. Therefore, this section focuses on clarifying the following terms: What does QOL mean? What is the relationship between QOL and health? How was HRQOL generated? What are the definition and domains of HRQOL? Why is it important to measure HRQOL? Finally, the theoretical associations between social support and HRQOL are discussed.

2.2.1 Quality of Life

The term *'Quality of Life'* existed many centuries ago' when Aristotle (384-322 BC) philosophically asked the questions “what does life mean” and “what is the best way of life” in order to explain the association between happiness, ‘well-being’ and a good life (Chung et al. 1997). According to Aristotle, happiness is developing a life goal and focusing one’s activities to achieve this goal (Chung et al. 1997). At the same time, happiness means different things to different people at different times, for example, when an individual falls sick he thinks health is happiness, but when he is poor, he thinks money is happiness. Due to this subjectivity, there have been long debates among researchers about the conceptualization and operationalization of QOL. There is also a difference of opinion as to whether QOL should have a valid place in reality, especially in health practice. Therefore, it is important to explore the relationship between health, ill health and QOL.

2.2.1.1 Definition of Quality of Life

Over the past two decades, numerous but not similar definitions of QOL have been provided. For example, the World Health Organisation QOL Group (WHOQOL-G) defined QOL as the *'individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, values and concerns'* (1998, p. 551). WHOQOL-G acknowledges that peoples’ perceptions about their life are subjective, shaped by their cultural background, life experiences, preferences and personal objectives. Therefore, QOL is a dynamic concept because values and evaluations of life are influenced by the individuals' reactions, emotions, physical health status and/or their experiences (Carr et al. 2003). It is also a multidimensional term that reflects the individual’s overall lives (Bowling 2001).

QOL can be divided into subjective and objective areas (Bowling 2001). A subjective perception of QOL reflects the individuals' sense of well-being, which involves happiness and satisfaction with their overall life (Anderson and Burckhardt 1999; Bowling 2001; Haas 2007), satisfaction with spirituality (Krupski et al. 2006) job, income, and feeling healthy, having happy social relationships and social support (Phillips 2006). Objective QOL measures what an individual is able to do (functional status) (Haas 2007); and materialistic objects (Fallowfield 1990) such as economic status (Shek 2005); although these are less common in health research (Haas 2007).

The above discussion reflects that despite the inconsistency and complexity of defining QOL, there is a general agreement that QOL is a multidimensional concept (Bowling 2001; Bowling 2005; Haas 2007). It is a difficult and complex concept to define or to measure because there are cultural, ethical, and religious beliefs that influence an individual's perceptions about QOL and its consequences (Zhan 1992).

2.2.1.2 The Relationship between Quality of Life and Health

In 1948, the World Health Organisation (WHO) defined health as a *'state of complete physical, mental and social well-being and not merely the absence of infirmity and disease'.* Thus, health can be considered in a multidimensional way, including physical, psychological and social health status and well-being in the context of disease (Fairclough 2002; Carr et al. 2003; Sirgy et al. 2006). As a result, the feeling of 'good health' may be with or without disease. For example, an individual may have a disease but as s/he is able to cope with difficult situations, s/he may still report a feeling of good health. Additionally, if this person has strong social support s/he may be psychologically healthy (Bowling 2005). Therefore, satisfaction and happiness may be experienced not only with health but also with disease.

Helman (2007) added that health is a state of physical and psychological balance of the individual with himself and with others. Therefore, a decline in any health domain is considered an illness mainly if this decline hampers the patients' daily activities and social contacts (Helman 2007). Accordingly, health is a vital domain of overall QOL (Taylor 2000; Bowling 2001). Other domains include employment status, adequate income, education, housing and social relationships (Taylor, 2000; Bowling 2001). Thus, the WHO definition of health is considered to be the most basic definition that reflects the relationship between QOL and health (Fairclough 2002; Carr et al. 2003), although it is complicated because it is difficult to distinguish between the terms QOL and health status (Haas 2007) sometimes in the literature. As a result, health researchers developed the term HRQOL to make it easier to measure QOL within the health domain (Sirgy et al. 2006; Gutteling et al. 2007) and to discriminate between QOL as a general sense of well-being and HRQOL as a satisfaction with health status (Fayers and Machin 2007).

2.2.2 Health-Related Quality of Life

The HRQOL term was coined in 1980s by psychological and sociological researchers to help measure the health domains that influence an individual's physical and mental health status and to avoid overlap with the broad term of QOL and its domains (McHorney 1999; Bowling 2001; Gutteling et al. 2007). Bowling (2001) confirmed that the term HRQOL is more limited than QOL, and relates to a patient's subjective satisfaction with his/her health status, with medical intervention and/or the impact of any biopsychosocial changes on the patient's health status.

2.2.3 Importance of measuring QOL in Health (HRQOL)

The advancement in medical diagnostic procedures as well as medical and surgical interventions have given many patients a chance of survival and/or have increased their life expectancy (Fallowfield 1990; Sirgy et al. 2006; Haas 2007), particularly among patients with liver cirrhosis. Although a complete cure of liver cirrhosis is not yet possible, the available medical interventions can save patients’ lives and improve their longevity. However, a chronic disease can suddenly cause life threatening complications, e.g. bleeding, which can affect the patients' QOL negatively. It is therefore important to assess their QOL. Bowling (2005) maintained that a medical model is no longer enough; particularly in cases of chronic or life threatening diseases.

Until recently, the medical model dominated the assessment of health conditions and the treatment outcome (Bowling 2005), e.g. a successful medical intervention was measured in terms of quantity of survival, mortality, morbidity, complications, biological tests, physical conditions, neglecting the quality of that survival, i.e. 'HRQOL' (Fallowfield 1990; Bowling 2005; Phillips 2006). Using only clinical data to treat patients can be considered dehumanising, because healthcare providers forget to ask patients about their feelings of 'well-being' (Fallowfield 1990). Bowling (2005, p. 1) declares that ‘*What matters is how the patient feels; rather than how professionals think they feel’.* For example, feelings of pain and discomfort or perceptions of change in daily physical functioning or emotions are indicators of ill health, not only pathological abnormalities (Bowling 2005). Thus, the traditional medical model that focuses on a clinical outcome becomes insufficient to understand the patients' health problems because *'there are multiple influences upon patient outcome, and these require a broad model of health to incorporate them'* (Bowling 2005, p. 1).

Therefore, health researchers have started to shift their philosophy of treatment from just quantity of life to both quality and quantity of life. So, QOL measurements are used to assess the successful outcome of a medical intervention and as well as to investigate patients' satisfaction with their health or with the medical intervention (Fallowfield 1990).

The measurement of QOL has become vital in healthcare, especially as a method of evaluating diseases and outcomes of interventions and their impact on the patient's life (Moore et al. 2005). Evaluating QOL helps to determine the individuals who perceive their health negatively to develop supported intervention programs to improve the health conditions of these individuals and to avoid complications (Taylor 2000) e.g. reducing symptoms, increasing functional performance and improving health perceptions, which will enhance their QOL (Anderson and Burckhardt 1999). The perceptions of patients related to their QOL has become essential to evaluate the effectiveness of rehabilitation programs; as patients are the best guides for healthcare providers to modify and improve their programmes (Fayers and Machin 2000; Bottomley 2002). Thus, QOL measurements are crucial to collect data about the problems that affect patients and to understand the impact of the illness and the side effects of treatment.

Assessing how patients feel relating to their state of health will help healthcare providers to enhance the patients' QOL (Fayers and Machin 2000; Bottomley

2002). Measuring HRQOL can provide unique data for tracking individuals' physical and psychological health over time, and for identifying unmet health needs to improve their biopsychosocial health (Taylor 2000). Szende et al. (2003) argue that *'Assessment of health-related QOL has become a recognized and important part of the evaluation of the health status of patients with chronic diseases' (*p. 679).

2.2.4 Definition and Domains of HRQOL

There are numerous but similar definitions of HRQOL. For example, Anderson and Burckhardt in 1999 have stated that HRQOL is the patients' subjective perception of the impact of their disease and/or its treatment on their daily life, and their physical, psychological and social functioning. Also, Bowling (2001) defined HRQOL as *'an optimum level of mental, physical, role (e.g. work, parent, career, etc.) and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being. It should also include some assessment of the patient's level of satisfaction with treatment, outcome and health status and with future prospects' (*p. 6). Both these definitions clearly acknowledge that HRQOL is a multidimensional concept. It is theoretically based on the WHO definition of health, which integrates physical, psychological, social functioning and well-being (Bowling 2001) as well as the individuals' subjective perceptions about their health status, capacity and performance.

Fayers and Machin (2000) added that the dimensions of HRQOL are physical health and symptoms, psychological and cognitive status, social role and social well-being or sexuality status. Helman (2007) argues that health is a holistic concept, which includes physical, psychological, social and spiritual health. Considering these various definitions, the common consistently shared domains of

HRQOL are physical, psychological and social health, although there may be other specific domains that differ from study to study based on its aims (Fayers and Machin 2000), such as sexual health.

Different terms are used in HRQOL such as health status, functional status, well-being and QOL, which are sometimes used interchangeably (Sirgy et al. 2006). QOL should not be used as a synonym for HRQOL because QOL is broader than HRQOL (Sirgy et al. 2006). However, there is considerable agreement that HRQOL and health status are similar. For example, health status consists of (1) functional capacity and (2) functional performance (Leidy 1994; Anderson and Burckhardt 1999); and HRQOL consists of (1) the ability to perform daily life activities and (2) satisfaction with functioning levels (Fayers and Machin 2000). As a result, assessing the HRQOL reflects the individual's health status as well as well-being. Hence, both concepts: HRQOL and health status are used interchangeably in this thesis.

2.3 SOCIAL SUPPORT

2.3.1 Definition of Social Support

Social support is a broad term that does not have a consistent or exact definition (Helgeson 2003; Lyyra and Heikkinen 2006) and this lack of agreement has resulted in a lack of consistency and comparability in research studies (Williams et al. 2004). As Hupcey (1998) states *'social support is a multi-faceted concept that has been difficult to conceptualise, define and measure. Although this concept has been extensively studied, there is little agreement among theoreticians and researchers as to its theoretical and operational definition. As a result, the concept remains fuzzy and almost anything that infers a social interaction may be* *considered social support'* (p. 1231). Thus, the definitions of social support that do exist fall into five theoretical categories: (1) type of support; (2) behaviour of provider of support; (3) reciprocity or exchange of resources between provider and recipient of support; (4) social network; and (5) perception of recipient of support (Hupcey 1998).

Perceived social support reflects the individual's general expectations of available support (Tijhuis et al. 1995). Hlebec et al. (2009) define perceived social support as a *'subjective evaluative assessment of support resources and behaviours'* (p. 156) and states that *'perceived support is a person's belief that some social support is available if needed'*. Lakey and Cohen (2000) state that perceived social support is commonly measured by asking the respondent to evaluate the quality or availability different types of support. It was argued that an individual's evaluation of social support is one of the indicators of the effectiveness of interpersonal relationships (Hlebec et al. 2009).

2.3.2 Types of Social Support

Social support is a tool that describes the nature of the social environment or people surrounding the individual (Helgeson 2003). Social support itself requires the existence of social relationships to provide supportive resources which include emotional, instrumental, informational (Williams et al. 2004) and companionship support (Wills and Shinar 2000). These types of support have been defined by Wills and Shinar (2000) as following: emotional support means availability of person who listens sympathetically and expresses caring, concern, love, and interest, especially during times of stress. Instrumental support means providing practical help such as helping with transportation, household duties and looking after children and/or lending money. Informational support means helping in solving problems by providing required information such as information about available services and resources, and providing guidance during a specific action. Finally, companionship support means availability of persons with whom to participate in cultural, social and recreational activities.

2.3.3 Source of Social Support

Different sources of support have been found related to health outcomes including primary relationship (partner, families and friends) and professional or therapeutic relationship (nurses and doctors) (Wills and Shinar 2000). However, effectiveness of social support depends on the stressor demand (Lakey and Cohen 2000) and the provider of the support (Hlebec et al. 2009). Lakey and Cohen (2000) argue that according to the stress-support matching hypothesis, each stressor event requires a specific type of social support (demands of the stressor) that will be effective in promoting coping and reducing stress effect. For example, emotional support is helpful no matter where it comes from, including family, friends or healthcare providers (Helgeson 2003), particularly during illness. For example, DuPertuis et al. (2001) investigated the relationships between types, sources of support and frequency of contact from family and friends and perceived physical and mental health in 1,386 older men (median age = 62.7 years). They found that people with high perceived support from family and friends had better physical health and lower depression than people with low perceived support from family and friends. However, frequency of contact was not significantly associated with physical health.

Conversely, informational support should come from a specific source, like a professional person to be most effective (Helgeson 2003). For example, disease severity was perceived to be lower among patients with chronic HCV who reported hepatologists as a source of information than patients who reported other sources such as significant others, internet, television…etc. (Constant et al. 2005).

2.3.4 Underlying Mechanism of Social Support

The mechanism of relationship between social support and health outcomes is not completely understood and is still under empirical investigation. For instance, Cohen and Wills (1985); Tijhuis et al. (1995); Hlebec et al. (2009) state two possible hypotheses to describe the mechanism of social support in general: the *'main-effect'* hypothesis and the *'buffering-effect'* hypothesis.

The *'main-effect'* hypothesis states that support influences behaviour and well-being under normal situations. For example, the main-effect hypothesis indicates that social support has a positive influence at all times even if the individual is not under stress (Cohen and Wills 1985; Tijhuis et al. 1995). Thus, the main-effect hypothesis addresses the association between social support and QOL as a linear relation, which means more social support directly can lead to better QOL. Therefore, according to this model, the integration of an individual, for example, into social networks can decrease the susceptibility to psychological or physical problems (Cohen and Wills 1985).

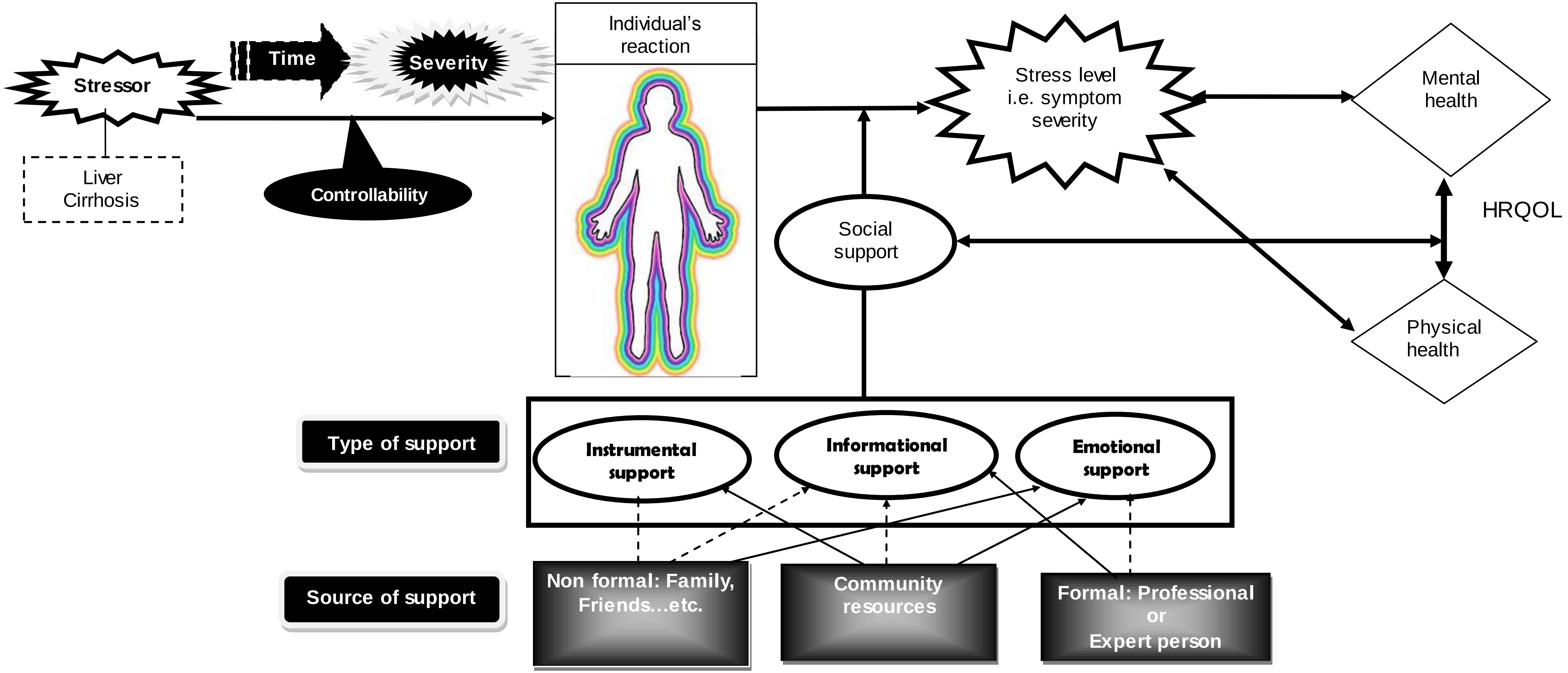
The *'buffering-effect'* of social support states that social support is effective only during stressful situations like during illness. Thus supporting individuals during stressful situations can protect them from the diverse effects of that stress (Cohen and Wills 1985; Wills and Shinar 2000). Accordingly, the buffer-effect will occur when a stressor to be buffered is present (Tijhuis et al. 1995; Wills and Shinar 2000). The association between social support and health in the presence of a stressor (such as liver cirrhosis) was studied based on the buffer-effect hypothesis; see Diagram 2-1 that was proposed to illustrate this relationship. Accordingly, sufficient support can decrease or prevent a stress reaction that might result in a physiological or psychological illness (Cohen and Wills 1985), (Diagram 2-1). For example, providing support such as informational support from a healthcare provider can prevent a disease being perceived as highly severe (stressful) (Constant et al. 2005). Social support can enhance an individual's perception in terms of his/her ability to cope by providing information that can lead to solving the problem and therefore decrease its significance (Cohen and Wills 1985). Thus, to support an individual coping with a stressful event, such as during disease, the appropriate resources from the surrounding people need to be provided in order to decrease the individual's stress level, particularly with highly stressful events (Helgeson 2003).

2.3.5 The Relationship between Social Support and HRQOL

Several research studies have assessed the association between social support and HRQOL among patients with different chronic conditions. Social support has been found to be a vital factor in improving HRQOL among patients with chronic diseases, particularly mental health. For example, Arestedt et al. (2012) found that there was a significant positive association between perceived social support after controlling for age and gender among elderly patients with chronic heart disease and HRQOL. Social support was associated specifically with mental health but not associated with physical health. Furthermore, Karnell et al. (2007) showed that with increasing social support there was a decline in symptoms of depression and improvements in mental health but there was no significant difference in the physical health of patients with head and neck cancer. Therefore, it appears that social support may be an important factor in perceived mental health in patients with chronic illness.

The linkage between social support and survival rate has been investigated in numerous longitudinal studies, which showed that social support, especially perceived emotional support, is significantly related to improved psychological and physical health outcomes as well as a decrease in the mortality rate (Brummett et al. 2005; Lyyra and Heikkinen 2006). Cohen and Wills (1985) illustrate that lack of social support can cause psychological symptoms such as anxiety or depression, which may have a negative influence on an individual’s health status. Perceived social support has a significant effect on the HRQOL in patients with coronary artery disease, especially in female patients (Staniute et al. 2011). Therefore, when planning cardiac rehabilitation programs, special attention should be paid to patients with little social support (Staniute et al. 2011). However, little is known about perceived social support from different sources and its association with perceived physical and mental health in liver cirrhotic patients (more details in Chapter 3, section 3.5.2.3).

Diagram 2-1: Suggested theoretical framework of the association between stressor, social support and health status according to the buffer effect



2.3.6 Paradigms of Measuring Social Support

Social support, particularly functional social support, can be assessed by two different methods; perceived support and received support. Perceived support is examined by asking individuals to what extent they perceive the people surrounding them are available to support them (Helgeson 2003; Sherbourne and Hays 1990). While received support is assessed by examining whether the people surrounding them are actually available and do provide the individual with the required support and coping skills (Helgeson 2003; Hlebec et al. 2009). Although both perceived and received support are measured through an individual's perception (Helgeson 2003), the received support may be confused with the individual's needs and cannot reflect exactly the available amount of support (Sherbourne and Hays 1990). For that reason, the perceived availability of support is considered the most important aspect of measuring the adequacy of functional support (Sherbourne and Hays 1990). Also, assessing perceived support may be more feasible in research studies than assessing received support that requires direct observation, which may be difficult.

Various measurements can be used to investigate social support. Structural instruments describe the existence of relationships e.g. marital status and network size. Functional instruments examine the quality of these relationships (Cohen and Wills 1985). Cohen and Syme (1985) suggest that for selecting the appropriate social support measurement to evaluate the perceived support it is essential to know whether a social support measurement examines a specific type of support (structure or function) or combines both, also whether it covers all or just some types of functional support. Therefore, these factors have to be considered when selecting a tool to investigate perceived adequacy of provided support.

2.4 CONCLUSION

The literature has indicated that liver cirrhosis remains a leading cause of death worldwide and in Egypt in particular. Viral hepatitis C is the most common cause of cirrhosis in Egypt. There is significant evidence that liver cirrhosis is a chronic irreversible disease causing various complications, which can have negative effects on the patients' health as well as their overall QOL. Although medical management of liver cirrhosis has advanced and can positively affect the patients' longevity, morbidity has increased. There is also an expectation that the number of people with liver cirrhosis in the future will rise.

Nowadays, the medical management of patients with liver cirrhosis is based on taking prescription drugs to avoid developing complications, continuous check-ups and a change in life style to decrease signs and symptoms in order to improve the patients' HRQOL.

Measuring HRQOL and the factors that influence it, such as symptom severity or perceived social support, has become an important area of health research in different populations with or without disease. Assessing HRQOL can be valuable in determining significant problems among a specific group of patients. This knowledge can be used to develop appropriate policies or programs of interventions to improve the population's HRQOL.

There has been a major effort in assessing HRQOL among patients with chronic liver disease or cirrhosis in Western countries, showing that patients with cirrhosis have a poorer HRQOL than the general population, and patients with other chronic diseases. Therefore, the next chapter will review previous studies that have described HRQOL, symptom experience and social support and evaluated their associated factors among patients with liver cirrhosis.

3 CHAPTER 3- LITERATURE REVIEW PART 2

This chapter aims to present the search strategy that was used to find relevant literature, and analyse and discuss the literature related to Health-Related Quality of Life (HRQOL), symptoms experience and perceived social support in liver disease patients. This literature review is structured in three sections. Section I describes HRQOL and aims to: (1) find the currently used HRQOL measurements in liver disease studies, (2) explore the HRQOL of liver disease patients compared with healthy people, (3) determine whether liver disease stage is related to perceived HRQOL, and (4) determine factors contributing to the understanding of HRQOL in cirrhotic patients. Section II describes symptoms experience and aims to identify: (1) instruments used to assess symptoms experience, (2) symptoms experience in cirrhotic patients and (3) self-care in cirrhotic patients. Section III explains social support, and aims to analyse the literature to find: (1) how liver disease patients perceived provided social support and (2) sources of support for liver disease patients. Finally, a summary is provided with an outline of the current study's aims.

3.1 SEARCH STRATEGY AND SELECTING RELEVANT PAPERS

3.1.1 Search Strategy

Systematic searching of electronic databases [MEDLINE, CINAHL, PsychINFO and ASSIA] was conducted. Google scholar was also accessed as a public site for research. The search was not limited to publishing time or study design in order to find all the relevant papers up to April 2012. The following Medical Subject Headings (MeSH) and appropriate keywords were used separately and in combination based on “AND” and “OR” terms: health-related quality of life’, ‘quality of life’, ‘well-being’, ‘functional status’, ‘health status’, ‘symptom, 'depression', 'psychological status', 'fatigue', 'pain', ‘social support', 'social network', 'psychosocial support', 'support system', 'perceived social support', 'liver disease', 'liver cirrhosis', and 'hepatitis'. Appendix 3-1 details the search strategies used. Specific inclusion and exclusion criteria were used to find relevant paper (Table 3-1).

Table 3-1: Literature review inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
1. Studied patients with liver cirrhosis, 2. The study was written in English, 3. The study reported a research-based study (no restriction on design), 4. The study used HRQOL as a dependent variable, 5. The study examined any symptom as a dependent or independent variable, 6. The study examined social support, 7. Psychometric studies that reported relevant data	1. A paper was excluded if any of these inclusion criteria was not met (1, 2 & 3). 2. Participants with only primary biliary or alcoholic cirrhosis or fatty liver results, pre-post transplantation, hepatic carcinoma, advanced hepatic encephalopathy, receiving interferon therapy, 3. Clinical trials that only examined the impact of medical treatment or surgical procedure on QOL, HRQOL or symptom, 4. Commentary, letter to editor or other papers not reporting original research results

3.1.2 Database Search Results

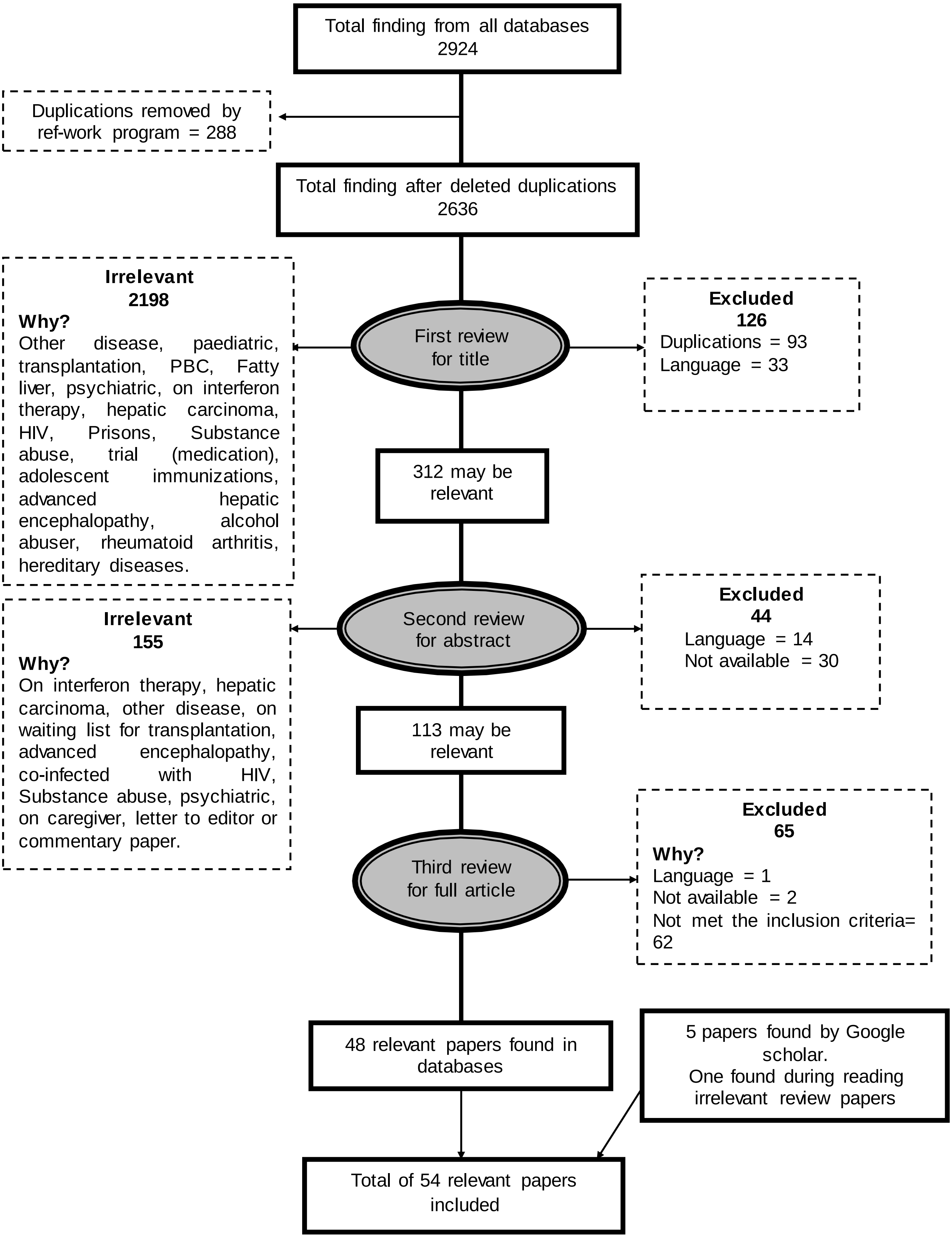
The database search yielded a total of 2924 publications (Diagram 3-1). 2636 remained after removing duplicates. A further three screening stages took place: (1) The titles of the 2636 articles were screened; 2324 were excluded because they were irrelevant, duplicated or not written in English. (2) Abstracts of the remaining 1312 articles were screened, of which 113 appeared to be relevant. (3) The full-text of the 113 papers was then reviewed to identify the papers that met the inclusion criteria. Forty-eight papers met the inclusion criteria.

3.1.3 Results of Google Scholar Search and Sites in Egypt

The aim of this search was to find any relevant Egyptian studies that were not found in the searched databases. Google scholar was searched twice, limiting the timeframe to 1990-2012 and to studies in English. The first search was conducted to find papers that investigated HRQOL using the keywords: 'quality of life' AND 'chronic liver disease' OR 'hepatitis C' in “Egypt” as commonly used terms in research studies. The search yielded a total of 4340 publications. Only the first 200 papers were reviewed, because the remaining papers seemed irrelevant. The titles and abstracts of these 200 papers were read to identify those that met the inclusion criteria. If the title and abstract appeared to be relevant, the whole paper was read to decide if it met the inclusion criteria. Eight papers were reviewed but only five papers were relevant. One of these five papers had already been found in another database; therefore, only four new papers were included in the review.

The second search was carried out using the key terms: 'fatigue' OR 'pain' OR 'depression' AND 'chronic liver disease' OR 'hepatitis C' in 'Egypt', to find papers that investigated symptoms. The search yielded a total of 973 publications, but only the first 200 papers were reviewed as with the first search in Google scholar. One paper appeared to be relevant based on the title and abstract, and was reviewed fully. Another paper was found during reading irrelevant papers of literature and it was also reviewed. Additionally, a manual search was carried out in Egypt at the Libraries of the Faculty of Medicine, Faculty of Nursing, and Central Library in Cairo University, National Liver Institute, Academy of Scientific Research and Technology and Arab Journal of Gastroenterology. The search did not yield any new studies.

Diagram 3-1: Flow diagram of literature screening process



3.1.4 Summary of Search and Quality Appraisal

A final total of 54 papers met the inclusion criteria and are included in this review. Forty-one papers studied HRQOL and QOL as the main outcome (Section I), and 13 papers studied symptoms as the main outcome (Section II). The quality of the reviewed studies was assessed using the quality appraisal form (Appendix 3-2) that was developed based on the Critical Appraisal Skills Program (CASP) criteria and a checklist for assessment of methodological quality (Downs and Black 1998). All papers that met the inclusion criteria were used and no study was excluded due to its quality. The results of all studies are reported in tabular form based on data extraction tables using criteria suggested by Garrard (2007) for developing a research matrix. Data were extracted using the following headings: Author, year of publication, country, design, sampling method, measurements and key results.

SECTION I: HEALTH-RELATED QUALITY OF LIFE (HRQOL)

3.2 CHARACTERISTICS OF REVIEWED PAPERS THAT STUDIED HRQOL

3.2.1 Publishing Year and Place

Forty-one papers were all in English and published over 15 years period between 1997 and 2012, see appendix 3-3 for methodological characteristics of 41 studies. Twenty-five of them were conducted in Europe from 2001-2011, with the Netherlands producing the highest number of studies: four in total. In Asia, six studies were conducted from 2005-2012; and 14 studies were conducted in America from 1997-2010, with the United States (US) producing the highest number of studies: 10 in total. In Africa, two studies were conducted in Egypt from 2004-2011. This suggests that there is a growing interest worldwide in assessing HRQOL or QOL in patients with chronic liver disease and cirrhosis. Europe and

America have produced the highest number of these studies while in the Middle East it seems that studying HRQOL or QOL in people with liver disease or cirrhosis is uncommon. In 2007, Gutteling et al. argued that due to an increasing number of people with chronic disease in developed countries, assessing patients’ physical, psychological and social well-being (HRQOL) has become an important outcome measure.

3.2.2 Methodological Limitations of Reviewed Papers that Studied HRQOL

There are some important methodological limitations of studies identified in this review. First, there is often a lack of a theoretical basis in liver disease research, which can build a bridge between theory and practice, with none of the 41 studies using a theoretical model for the research. Secondly, there is a lack of consistency in the definitions of HRQOL or QOL, which results in overlapping between the two terms, as well as with other concepts such as functioning health (see section 3.3.3). Third, there is a lack of consistency in categorising liver disease according to cause (see section 3.5.3.1). Finally, there is a lack of consistency in the use of standardised measures to classify liver disease according to disease severity (stage) (see section 3.4.2). Despite these limitations, because of the shortage of liver disease research in the area of HRQOL, particularly in the Middle East, no study was excluded due to its quality.

3.2.2.1 Design of Studies

Of the 41 studies, 21 were observational, cross-sectional or survey studies, five were database cohort study or retrospective, two were prospective (Singh et al. 1997; Taliani et al. 2007) and one was a quasi-experimental study (Zandi et al. 2005). However, ten studies did not explicitly mention the study design.

Furthermore, two mentioned a prospective design (Haage et al. 2008; Svirtlih et al. 2008). However, these 12 studies all seemed cross-sectional in nature. The only randomised controlled trial investigated the effects of a self-care program on cirrhotic Iranian patients' HRQOL. Of the two prospective studies, one USA study had duration of 100 days for all participants and 18 months for patients after transplantations (Singh et al. 1997), and one Italian study aimed to assess and compare the change in HRQOL from baseline to 6 months among HCV patients treated with interferon and ribavirin therapy (Taliani et al. 2007).

The survey, particularly the cross-sectional design, is therefore the most commonly used method in liver disease research. This limits the ability of studies to identify causal relationships between the studied variables and HRQOL.

3.2.2.2 Studied Population

The study sample sizes varied between 30 and 1175 patients in the 41 studies. Twenty-five studies had ≤ 200 patients (30-200 patients), and 16 studies had more than 200 patients (200-1175 patients); while three of these studies used the same sample in three separate papers (van der Plas et al. 2003; van der Plas et al. 2004; Gutteling et al. 2006). The liver disease causes and stages varied, with most studies focused on chronic liver disease due to various causes (n = 25), and only a few focused on cirrhosis stage (n = 13). Recruiting a low sample size (≤ 200) (e.g. Hauser et al. 2004; Karaivazoglou et al. 2010), studying a non-representative sample of liver disease or cirrhotic patients (e.g. Arguedas et al. 2003; van der Plas et al. 2004), recruiting participants from the community (e.g. van der Plas et al. 2004) or outpatients' clinic (e.g. Haag et al. 2008) made it difficult to generalise results from the studies to all liver cirrhotic patients, especially in clinical settings.

Using a convenience, retrospective or consecutive sampling method to recruit the participants (n= 26 studies) also limited generalisability of some results. Therefore, the findings from the reviewed 41 studies should be treated with caution.

3.3 TOOLS USED TO ASSESS HRQOL IN LIVER DISEASE PATIENTS

Out of the 41, 37 studies examined HRQOL and four studies examined QOL (Table 3-2). These 37 studies were used to identify the commonly used HRQOL questionnaires. Several generic and liver disease specific HRQOL questionnaires were found, but generic tools were more commonly used (Figure 3-1).

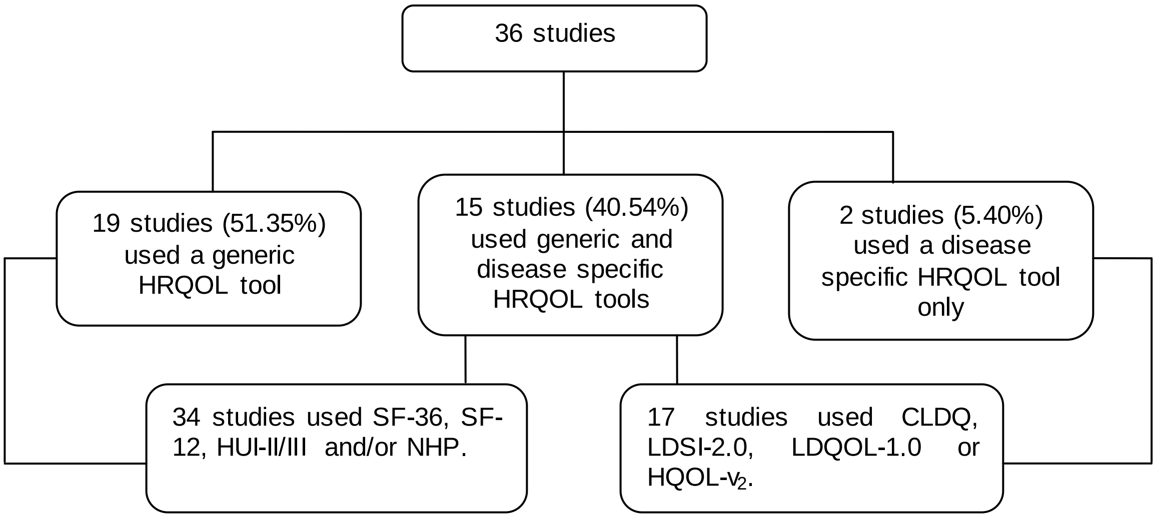
Table 3-2: Tools used to investigate HRQOL and QOL in liver disease patients

Authors	**Country**	**HRQOL and QOL tools**	
		Generic tools	**Liver disease specific tools**
1. Afendy et al. 2009	USA	SF-36	
2. Arguedas et al. 2003	USA	SF-36	
3. Bailey et al. 2009	USA	Cantril's Ladder for measuring QOL.	
4. Bao et al. 2007	China	SF-36	CLDQ
5. Basal et al. 2011	Egypt	SF-36	
6. Bianchi et al. 2005	Italy	PGWBI	
7. Bondini et al. 2007	USA	SF-36, HUI-II and HUI-III	CLDQ
8. Dan et al. 2008	USA	SF-6D, HUI-II	
9. Fritz and Hammer 2009	Austria	SF-12	
10. Girgrah et al. 2003	Canada	SF-36	
11. Gutteling et al. 2006	Netherlands	SF-12	LDSI-2.0
12. Haag et al. 2008	Germany	SF-36	
13. Hauser et al. 2004	Germany	SF-36	CLDQ
14. Hilsabeck et al. 2005	USA	SF-36	
15. Hsu et al. 2009	Canada	SF-36, SF-12, HUI-II	HQLO-v_2
16. Jover et al. 2005	Spain	SF-36	CLDQ
17. Kalaitzakis et al. 2006	Sweden	SF-36	
18. Kalaitzakis et al. 2008	Sweden	SF-36	
19. Karaivazoglou et al. 2010	Greece	SF-36	
20. Kim et al. 2006	Korea	QOLI	
21. Les et al. 2010	Spain	SF-36	CLDQ
22. Liu et al. 2012	Japan	SF-12	
23. Marchesini et al. 2001	Italy	SF-36, NHP	
24. Moyer et al. 2003	USA	SF-36	
25. Schwarzinger et al. 2004	Egypt	SF-12	
26. Singh et al. 1997	USA	Self-assessed Rating of	

Authors	Country	HRQOL and QOL tools	
		Generic tools	Liver disease specific tools
		Perceived QOL	
27. Sobhonslidsuk et al. 2006	Thailand	SF-36	CLDQ
28. Sumskiene et al. 2006	Lithuania		CLDQ
29. Svirthlih et al. 2008	Serbia	SF-12	
30. Taliani et al. 2007	Italy	SF-36, WHOQOL-BREF	CLDQ
31. Teixeira et al. 2005	Brazil	SF-36 part from LDQOL 1.0	LDQOL 1.0
32. Teixeira et al. 2006	Brazil	SF-36	
33. Teuber et al. 2008	Germany	SF-36	
34. Toda et al. 2005	Japan	SF-36	
35. van der Plas et al. 2003	Netherlands	SF-36	LDSI-2.0
36. van der Plas et al. 2004	Netherlands	SF-36	LDSI-2.0
37. van der Plas et al. 2007	Netherlands	SF-36	LDSI-2.0
38. Wilson et al. 2010	USA	SF-36	
39. Wunsch et al. 2011	Poland	SF-36	CLDQ
40. Younossi et al. 2001	USA	SF-36	CLDQ
41. Zandi et al. 2005	Iran		CLDQ

SF-36: Short Form 36,
NHP: Nottingham Health Profile,
LDSI-2.0: Liver Disease Symptom Index 2.0,
CLDQ: Chronic Liver Disease Questionnaire,
LDQOL 1.0: Liver Disease Quality Of Life 1.0,
PGWBI: Psychological General Well-Being Index,
SF-12: Short Form 12,
QOLI: Quality Of Life Index,
HUI-II: Health Utilities Index-Mark II,
HUI-III: Health Utilities Index-Mark III,
HQOL-v_2: Hepatitis Quality of Life Questionnaire Version 2,
QOL: Quality Of Life,

Figure 3-1: Studies using HRQOL tools



3.3.1 Generic HRQOL Questionnaire

Four generic HRQOL questionnaires were identified: Short-Form 36 (SF-36) was used in 29 studies; Short-Form 12 (SF-12) was used in six studies; Nottingham Health Profile (NHP) was used in one study and Health Utilities Index (HUI) [Mark II and Mark III] was used in three studies. Table 3-3 summarises the generic HRQOL tools and their components.

The Short-Form (SF)-36 measures eight domains that commonly represent health status: physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health (GH), vitality (VT) (i.e. fatigue and energy), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH) (i.e. psychological well-being) (Ware 2000). The eight domains in the SF-36 can be integrated to form a physical component summary (PCS) score that indicates physical health, and a mental component summary (MCS) score that indicates mental health. The SF-36 scores from 0 to 100 where a lower score indicates a poorer health status. It also has a cut-off score of 50±10, meaning that scores lower than 50 indicate health below the mean. The cut-off score is used to make cross-cultural comparisons of HRQOL possible and when a normal comparative group is not available. Similarly, the SF-12 is a generic questionnaire that was developed to be a shorter alternative to the SF-36. It contains six domains of the SF-36: PF, BP, VT, SF, MH, and role limitations but without specifying whether role limitations are due to emotional or physical problems.

Table 3-3: Summary of generic HRQOL tools and their components

Generic tools	**Tool components**									
SF-36	**8 domains**								**Component summary scores**	
Domains	physical functioning	role limitations due to physical health problems	bodily pain	general health	vitality	social functioning	role limitations due to emotional problems	mental health	PCS	MCS

Generic tools	**Tool components**												
NHP	**Part I**						**Part II**						
Domains	physical mobility	pain	Social isolation	emotional reactions	energy	sleep	Paid employment	Jobs around the home	Social life	Family relationships	Sex life	Interests and hobbies	Holidays

Generic tools	**Tool components**													
HUI	**HUI-II**							**HUI-III**						
Domains	sensation	cognition	mobility	emotion	self-care	fertility	pain	hearing	vision	emotion	speech	pain	cognition	ambulation	dexterity

The NHP is a generic HRQOL questionnaire that is used to investigate aspects of physical, emotional, and social health, and is divided into two parts. Part I involves six domains: physical mobility, pain, social isolation, emotional reactions, energy, and sleep. Part II assesses seven aspects of life that are most affected by health status (using Yes/No answers); NHP scores range from 0 to 100 where a lower score indicates a better health (Hunt et al. 1985).

HUI-Mark II and Mark-III are preference-based generic HRQOL questionnaires that are used to investigate patients' preferences for a specific health state over a one-week period. HUI contains 15 constructs, seven attributes form part of HUI-Mark II: sensation, cognition, mobility, emotion, self-care, fertility and pain, and eight attributes form part of HUI-Mark III: hearing, vision, emotion, speech, pain, cognition, ambulation and dexterity. HUI scores range from 0-1 where a score of 1 means a healthy state (Feeny et al. 2002).

There is therefore some inconsistency in conceptualization of HRQOL where different tools contain different domains that measure different aspects of health (Table 3-2) making it difficult to compare the findings of different studies systematically or to find evidence sometimes about the impaired domains of HRQOL. For example, the two generic HRQOL tools, SF-36 and NHP, were used in the study with Italian cirrhotic patients (Marchesini et al. 2001). Both tools indicated a significantly lower HRQOL of cirrhotic patients than the normal population. However, the SF-36 found that the largest differences were in the domains of role limitations, due to emotional and physical health problems, general health and bodily pain. The NHP found the largest differences in physical mobility and energy but no difference in pain between cirrhotic and healthy people.

Therefore, Marchesini et al. (2001) acknowledge that the SF-36 may be more sensitive than the NHP in finding differences between liver disease patients and healthy people.

3.3.2 Liver Disease Specific HRQOL Questionnaires

It has been argued that the generic HRQOL measures may not be sensitive to detect disease-related changes such as symptoms (Younossi et al. 1999; van der Plas et al. 2004). Therefore, liver disease specific HRQOL questionnaires have been developed and are used alone (Arguedas et al. 2003; Afendy et al. 2009; Fritz and Hammer 2009) or combined with generic HRQOL tools to capture sensitive disease issues (Hauser et al. 2004; Jover et al. 2005; Gutteling et al. 2006; Bao et al. 2007; Hsu et al. 2009).

Four disease specific HRQOL questionnaires are used in included studies among liver disease patients to assess their health status: chronic liver disease questionnaire (CLDQ), Liver Disease Symptom Index 2.0 (LDSI-2.0), Liver Disease Quality Of Life 1.0 (LDQOL 1.0) and Hepatitis Quality of Life Questionnaire version 2 (HQOL-v_2). The CLDQ was used in 11 studies, LDSI-2.0 was used in four studies, LDQOL 1.0 was used in one study and HQOL-v_2 was used in one study. However, while some are too narrowly focused (i.e. HQOL-v_2), which focuses on patients with HCV, others are too long and do not address the extent to which symptoms affect patients' quality of life (i.e. LDQOL 1.0 and CLDQ)

CLDQ was developed in the USA by Younossi et al. (1999) to evaluate the influence of liver disease on liver disease patients' health status. It contains 29 items that produce six domain scores: abdominal symptoms, fatigue, systemic symptoms, activity, emotional function and worry. It can also give an overall summary score. It was validated in patients with different types, causes and at different stages of liver disease, and it has adequate internal reliability (Younossi et al., 1999). Its validity and reliability have been established in several languages (Hauser et al. 2004; Sobhonslidsuk et al. 2004; Jover et al. 2005 Bao et al. 2007) but not in Arabic.

LDSI-2.0 is the second most commonly used disease specific HRQOL tool that was developed in the Netherlands by van der Plas et al. (2004) to assess the symptom severity and impact of this symptom on daily life and social activities of liver disease patients due to different causes. It contains 24 items divided into two subscales: symptom severity and limitation of daily life due to symptoms (see more details about LDSI-2.0 and other liver disease specific HRQOL in Chapter 5). It was validated in patients with different types, causes and at different stages of liver disease, and it has adequate internal reliability (Unal et al. 2001; van der Plas et al. 2004). Its validity and reliability have been established in English, Dutch (Hauser et al. 2004; Sobhonslidsuk et al. 2004; Jover et al. 2005 Bao et al. 2007) and Arabic (Youssef et al. 2012). The other measures (i.e. HQOL-v_2 and LDQOL 1.0) are less commonly used. The HQLQ-v_2 was developed in the USA by Bayliss et al. (1998). It contains 69 items combining the generic SF-36 domains with three additional generic scales and two hepatitis specific domains. It was validated in patients with viral hepatitis (Bayliss et al. 1998). It is available is several languages but not Arabic. However, it may have several disadvantages: (i) It is long, therefore it may be a problem with critically ill patients or to use with other questionnaires, and (ii) it was developed for patients with HCV, thus it may be not suitable for patients with different causes of disease. The LDQOL 1.0 was developed in the USA by Gralnek et al. (2000). It consists of 75 items combining the generic (SF-36) and disease-specific (12 items) scales. The LDQOL 1.0 is available in several languages such as Spanish and Brazilian Portuguese (Teixeira et al. 2005) but not in Arabic. However, it is very long.

In conclusion, various HRQOL questionnaires such as generic, disease specific and patient-preference tools were used in liver disease studies. However, generic tools were the most commonly used to evaluate different aspects of health: physical, psychological and social as well as perceived well-being, with the SF-36 the most commonly used. It is available in several languages such as English, German, Dutch and Arabic. Although there are several well developed and valid liver disease HRQOL tools, none were available prior to my pilot study in Arabic. There is, therefore, a need to develop a valid and reliable liver disease HRQOL questionnaire to investigate the impact of liver disease on Egyptian patients' lives. Details of the translation and psychometric properties of LDSI-2.0 are in Chapter 5.

3.3.3 Theoretical and Operational Definitions of HRQOL

None of the previous 37 studies used a theoretical framework to guide their study. Thirty-one (83.78%) of the 37 studies did not provide a definition of HRQOL, and only six (16.21%) attempted to define HRQOL. However, there was no consensus in these definitions. For instance, two studies used the WHO 1948 definition of health to define HRQOL (Sobhonslidsuk et al. 2006; Sumskiene et al. 2006) (Chapter 2, section 2.2.1.2: definition of health). Svirtlih et al. (2008) defined HRQOL as the patients’ subjective assessments of their physical, mental and social well-being. Gutteling et al. (2006) defined HRQOL as the impact of the disease and/or medical treatment on the patient’s physical, emotional and social functioning; Haag et al (2008) as an impairment of the physical and mental functional status; and Hauser et al. (2004) as the assessment of symptoms, and the impact of the health status on psychological functioning and sense of well-being.

Although, these definitions share some aspects of HRQOL (physical, psychological and social) there is an inconsistency as to whether HRQOL refers to functional status, health status or well-being. There are also some overlaps in the theoretical definition of health and HRQOL. Sobhonslidsuk et al. (2006) and Sumskiene et al. (2006) used the WHO definition of health to define HRQOL, although the WHO definition is commonly known as a general definition of health itself. It appears that there is no agreement about what HRQOL in liver disease research means with a lack of theoretical and operational understanding of this concept. There was also inconsistency in using various generic and disease specific questionnaires to investigate HRQOL. Therefore, a conceptualization of HRQOL in liver disease research is recommended for future research to avoid its overlapping with other concepts such as well-being and functional status and to give a consistent interpretation of the study's findings.

3.4 LIVER DISEASE PATIENTS' HRQOL

This section aims to explain HRQOL among patients with liver cirrhosis and the factors associated with HRQOL using the 37 relevant studies (Table 3-2). The extent to which these studies focused on HRQOL of cirrhotic patients depended on the study's aim, disease stage and whether the authors investigated generic and/or disease specific HRQOL.

Generally, patients with liver disease have been found to suffer from disease related stress that can influence their physical and mental health status. Liver disease was perceived to be more stressful than diabetes and hypertension by patients with chronic HCV (Castera, et al. 2006). Some studies found that patients with chronic liver disease, particularly resulting from a viral infections had disease related worries about their family situation (van der Plas et al. 2004, Hauser et al. 2004), depression and anxiety (Blasiole et al. 2006), fear of disease complications (van der Plas et al. 2004) and psychological distress (Kim et al. 2006). Cirrhotic patients due to viral hepatitis who had poor mental health were liable to experience social impairments such as poor emotional reaction (Marchesini et al. 2001), social isolation (Marchesini et al. 2001; Blasiole et al. 2006), limitations in their social functioning (Blasiole et al. 2006) and financial affairs (van der Plas et al. 2004).

3.4.1 HRQOL of Liver Disease Patients Compared with Healthy People

Evidence from observational studies found a significant difference in HRQOL between patients with liver disease and healthy people. For instance, in the US, patients with liver disease as a result of various causes (viral, cholestatic and hepatocelluer) and at different stages of liver diseases had a poorer HRQOL than the healthy population in domains of mental (MCS) and physical health (PCS) using SF-36 (Younossi et al. 2001). Similarly, Hauser et al. (2004) found that patients with chronic HCV had a poorer physical and mental health domains (SF-36) (PCS: 40.94±12.06 and MCS: 43.21±11.98 respectively) than the healthy German population.

Additionally, liver disease patients, particularly at the cirrhotic stage, had a significantly lower HRQOL in all domains of SF-36 than healthy Italian people. The largest differences were observed in role limitations due to physical and emotional problems (39% and 31% respectively), perceived general health (24%) and bodily pain (6%) (Marchesini et al. 2001). Similarly, HRQOL in all domains of SF-36 was poorer in viral liver disease patients due to HCV and HBV than in the healthy Greek population (Karaivazoglou et al. 2010). The greatest impairments were in the domains of role limitation due to emotional problems (41.7%), perceived general health (67.9%) and mental health (52.4%) (Karaivazoglou et al. 2010). Girgrah et al. (2003) showed that cirrhotic patients in Canada had significant impairment ($p \leq 0.01$) in all domains and component summary scores (SF-36) except in the domain of bodily pain. It may be that the experience of physical pain may be low in liver disease patients, although the relatively small sample size may have contributed to the lack of finding a significant difference between liver disease patients and healthy people in the domain of bodily pain.

Most of the reviewed studies from Western and Eastern countries, which used the validated generic HRQOL tool (SF-36), found significant differences in the HRQOL of liver disease patients and healthy controls people. Patients with liver disease had a poorer physical; psychological, social and well-being state than people without liver disease. These are the results of liver disease studies in developed countries with sufficient resources and a well-developed health system, what about results in developing countries, particularly Egypt?

In Egyptian community-based study, 146 chronically infected people with HCV were compared with 1,140 non-infected people. Using the multivariable analysis, adjusting for confounding factors (such as age, gender, education and healthcare related risks), unexpectedly found that there was no significant difference in all domains and component summary scores of SF-12 (score from 0-100), supporting that the infected and non-infected people had the same HRQOL ($p > 0.05$) (Schwarzinger et al. 2004).

Many reasons may cause this contradiction in findings. First, the Western studies were conducted with liver disease patients who were aware of their disease, while in this Egyptian study the people did not know about their serological status. It may be that peoples' awareness is a factor in their perceived health status. Further research is needed to find the association between serological awareness and perceived HRQOL.

Secondly, the Western studies investigated patients at mixed stages of disease, who attended tertiary or referral hospitals (such as Younossi et al. 2001; Hauser et al. 2004) or were members of a liver disease group (van der Plas et al. 2007). In the Egyptian study, the researchers investigated a community-based population who might be asymptomatic of liver disease, as symptoms experience maybe a factor in the perceived HRQOL (Wilson and Cleary 1995).

Third, the normal comparative group in the Egyptian study may not have been representative of Egyptian healthy people, as they were from rural areas and therefore likely to suffer from poverty and illiteracy which may be factors in perceived HRQOL. For instance, when Schwarzinger et al. (2004) compared the HRQOL of healthy rural people in Egypt with healthy people (norm-based sample) in the US; there was a significant deterioration in the physical and mental health domains ($p < 0.0001$) of rural Egyptian non-infected people compared to healthy US people (Schwarzinger et al. 2004).

Fourth, although the researcher gave the background for the translation process of the SF-12 into Arabic, the SF-12 psychometric properties are unclear and questionable in the Schwarzinger et al. (2004) study that might affect the tool sensitivity in finding a significant difference. On the other hand, a study was undertaken in three University Hospitals in Egypt to investigate HRQOL of 200 chronic liver disease patients with HCV (Basal et al. 2011). They used the norm-based cut-off score of SF-36 (50±10). The results showed that chronically infected patients with HCV without advanced decompensated cirrhosis (Child-A and B) had poor physical and mental health, with a mean PCS of 38.01 ± 15.78 and MCS of 39.03 ± 15.05 (Basal et al. 2011).

In general, literature found that patients with chronic liver disease had poorer HRQOL than healthy people. However, there is a difference between countries as to which domains of HRQOL patients perceived as worse. Additionally, little is known about the HRQOL of liver disease patients in Egypt.

3.4.2 Criteria of Classifying Liver Disease into Stages

There was inconsistency in classifying liver disease into stages across all 54 studies. Figure 3-2 and Table 3-4 summarise the studies that used/did not use disease stage criteria. The Child-Pugh score is the most commonly used method to categorize liver disease into stages A (mild), B (moderate) or C (worse) based on laboratory and clinical data, to determine disease severity. It is a tool incorporating five laboratory and clinical variables: ascites, encephalopathy, prothrombin time, serum levels of bilirubin and albumin (Cholongitas et al. 2005).

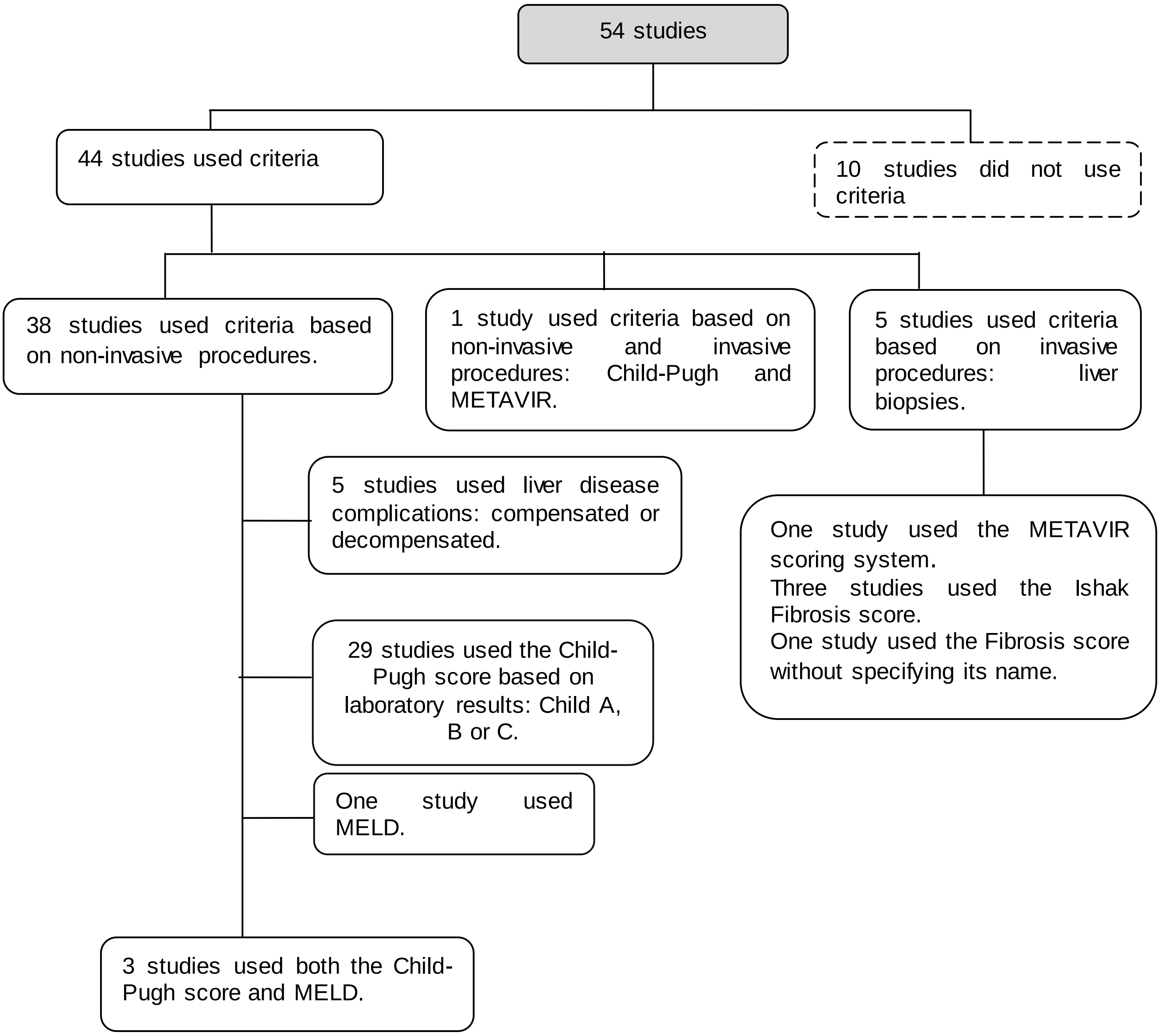
One study used only a Model of End-Stage Liver Disease (MELD) (Bajaj 2008). Three studies used both the Child-Pugh score and MELD to report disease severity (Kalaitzakis et al. 2006; Kalaitzakis et al. 2008; Wunsch et al. 2011). MELD is a tool that includes three laboratory variables: international normalized ratio, serum creatinine, and serum bilirubin. The Child-Pugh score and MELD are usually used to predict the survival rate in liver disease patients (Kamath and Kim 2007).

However, in a recent systematic review of the accuracy of MELD vs. Child-Pugh score in liver disease patients the results showed that MELD was not any more sensitive than the Child-Pugh score (Cholongitas et al. 2005).

Other studies categorized cirrhosis according to the presence of liver disease complications during the year of data collection, as in compensated and decompensated cirrhosis (van der Plas et al. 2003; van der Plas et al. 2004; Gutteling et al. 2006; van der Plas et al. 2007; Hsu et al. 2009). This method does not need recent laboratory data, which may not be available during a cross-sectional survey.

A few studies used criteria that are based on invasive procedures to categorize disease stages, for example, the Ishak Fibrosis score (Svirtlih et al. 2008). The Ishak Fibrosis score is based on liver biopsies to categorize liver disease from early fibrosis to cirrhosis. It ranges from 0–6, with 5-6 being the cirrhosis stage (Everhart et al. 2010). Similarly, the histological fibrosis score according to the METAVIR scoring system (Constant et al. 2005; Hilsabeck et al. 2005) is also based on liver biopsies. However, 10 studies used no criteria to categorize liver disease into stages, and no explanations for this omission were given. Therefore, the discrepancy in the method made it difficult to compare the studies' findings.

Figure 3-2: Criteria for categorising liver disease into stages



In conclusion, the Child-Pugh score is the most commonly used criteria for classifying cirrhosis into three stages, where Child-Pugh A is considered compensated cirrhosis and Child-Pugh B/C is considered decompensated cirrhosis. Therefore, the Child-Pugh score is most appropriate if recent laboratory and clinical data are available. Otherwise, other criteria that classify disease according to recent liver disease complications through the year of data collection are available.

Table 3-4: Criteria for categorising liver disease into stages

Study	Non-invasive criteria			Invasive criteria		Criteria not available
	Child-Pugh score	Complications	MELD	Fibrosis score	METAVIR	
1. Afendy et al. 2009	√					
2. Arguedas et al. 2003	√					
3. Bailey et al. 2009						×
4. Bajaj 2008			√			
5. Bao et al. 2007	√					
6. Basal et al. 2011	√					
7. Bianchi et al. 2005	√					
8. Blasiole et al. 2006	√					
9. Bondini et al. 2007	√					
10. Constant et al. 2005					√	
11. Cordoba et al. 1998	√					
12. Dan et al. 2008	√					
13. Davis et al. 1998	√					
14. Dwight et al. 2000						×
15. Elshahawi et al. 2011	√					
16. Erim et al. 2010						×
17. Fritz and Hammer 2009	√					
18. Girgrah et al. 2003	√					
19. Gutteling et al. 2006		√				
20. Haag et al. 2008	√					
21. Hauser et al. 2004	√					
22. Hilsabeck et al. 2005	√				√	
23. Hsu et al. 2009		√				
24. Jover et al. 2005	√					
25. Kalaitzakis et al. 2006	√		√			
26. Kalaitzakis et al. 2008	√		√			
27. Karaivazoglou et al. 2007	√					
28. Karaivazoglou et al. 2010				Ishak Fibrosis		

Study	**Non-invasive criteria**			**Invasive criteria**		**Criteria not available**
	Child-Pugh score	Complications	MELD	Fibrosis score	METAVIR	
29. Kim et al. 2006	√					
30. Kim et al. 2006a	√					
31. Kraus et al. 2000						×
32. Les et al. 2010	√					
33. Liu et al. 2012						×
34. Marchesini et al. 2001	√					
35. Moyer et al. 2003						×
36. Rakoski et al. 2012						×
37. Schwarzinger et al. 2004						×
38. Singh et al. 1997	√					
39. Sobhonslidsuk et al. 2006	√					
40. Sumskiene et al. 2006	√					
41. Svirtlih et al. 2008				Ishak Fibrosis		
42. Taliani et al. 2007						×
43. Teixeira et al. 2005	√					
44. Teixeira et al. 2006						×
45. Teuber et al. 2008				Ishak Fibrosis		
46. Toda et al. 2005	√					
47. van der Plas et al. 2003		√				
48. van der Plas et al. 2004		√				
49. van der Plas et al. 2007		√				
50. Wilson et al. 2010				Fibrosis scale		
51. Wu et al. 2012	√					
52. Wunsch et al. 2011	√		√			
53. Younossi et al. 2001	√					
54. Zandi et al. 2005	√					
Total	33	5	4	4	2	10

3.4.3 Liver Disease Stage and Perceived HRQOL

A considerable reduction of HRQOL with advanced liver disease has been reported in several observational studies (22 in total) (Table 3-5).

The disease specific HRQOL questionnaire (LDSI-2.0) showed that cirrhotic (compensated and decompensated) patients had a higher probability of experiencing physical and psychosocial problems due to liver disease than non-cirrhotic patients (van der Plas et al. 2003). Cirrhotic patients (compensated and decompensated) were more likely than non-cirrhotic to report personality changes, memory problems, itch, jaundice and sleepiness ($p \leq 0.03$). However, with advanced stage of cirrhosis, particularly with decompensated cirrhosis, patients had a higher probability of reporting worry about family situation, right abdominal pain, decreased appetite, financial problems, fear of disease complications, and depression ($p \leq 0.01$) (van der Plas et al. 2003).

Furthermore, using the disease specific HRQOL tool (CLDQ), there was no significant difference in perceived disease specific HRQOL between Child-B and Child-C. Both had higher abdominal symptoms and fatigue compared to Child-A. However, Child-B had a higher worry compared to Child-A, while Child-C had higher systemic symptoms compared to Child-A ($p<0.05$) (Bao et al. 2007). This study contributed to the understanding of how patients with chronic liver disease perceived their generic and disease specific HRQOL according to disease stage. However, the discrepancy in findings caused difficulties to find the relevancy of disease stage to perceived fatigue between Child-B and Child-C cirrhosis. For example, the SF-36 found a significant reduction in vitality (i.e. increase in fatigue) with Child-C compared to Child-B, while CLDQ found a similar fatigue level.

However, using both tools, the results supported that with advanced stage of cirrhosis there was a reduction in physical health.

Significant deterioration in physical health only (PCS/SF-36) with advanced cirrhosis has been identified in several studies (Younossi et al. 2001; Arguedas et al. 2003; Haag et al. 2008; Hsu et al. 2009; Les et al. 2010). For instance, decompensated cirrhotic patients (Child-C) had significantly poorer physical health domains, with higher limitations due to physical problems, bodily pain, poor perceived general health, and poor social functioning ($p<0.04$) compared to patients with compensated cirrhosis (Child-A) (Arguedas et al. 2003). Using multivariate analysis, the Child-Pugh score was significantly associated with the majority of physical health domains: PF, RP and GH ($p<0.05$) (Sobhonslidsuk et al. 2006), and physical health (PCS ≤0.04), but it was not associated with mental health domains (MCS) (Kalaitzakis et al. 2006; Haag et al. 2008). It may be that disease stage influences physical health more than mental health in liver disease cirrhotic patients.

In a recent study, Afendy et al. (2009) compared US and Italian liver disease patients. There was a significant difference in the perceived HRQOL between Italian and American cirrhotic patients. Italian cirrhotic patients had a significantly better HRQOL in the domains of BP, VT and PCS, whereas US cirrhotic patients had better HRQOL in the domains of RE, MH and MCS. This suggests that cirrhotic Italian patients had better perceived physical health while US cirrhotic patients had better mental health. Thus, the cultural background of the patient may be a factor related to perceived HRQOL.

In the light of these findings, it appears that disease stage can influence HRQOL from different aspects, particularly physical health. However, these findings may not be applicable to Egyptian patients as the cultural and environmental context is obviously different. Also, there is no available knowledge that could contribute to gaining insight into how cirrhotic patients in Egypt perceive their HRQOL, and whether the disease stage influences their HRQOL.

The only identified study that examined HRQOL using SF-36 in liver disease patients in Egypt, Basal et al. (2011) showed opposite findings to the rest of the literature in terms of the association between disease stage and perceived physical and mental health. They found that there was no significant difference in HRQOL according to disease stage. However, these findings may be questionable, due to the relative sample size and the focus on the early stages of liver disease (Child-A and B). Therefore, this link between disease stage and perceived HRQOL of Egyptian liver disease patients, particularly with cirrhosis, needs to be investigated. It is important to find how patients with decompensated cirrhosis perceive their HRQOL compared to patients with compensated cirrhosis and compare them to normal population. Furthermore, the reviewed studies were observational studies with "snap shot" recruitment. Therefore, it is recommended to develop longitudinal studies with a reasonable sample size of cirrhotic patients, to find the evidence of any causal association between disease stage and perceived HRQOL.

Table 3-5: Studies investigating the influence of liver disease stage on HRQOL using SF-36 or SF-12

Author/Country	**Methodology**		**Key results**
	Sample size (for comparison: sample size per group)	**Criteria of classifying disease stage**	
Afendy et al. 2009 USA	1103 cohort sample-from databases of liver disease centres in US and Italy. Sample was divided into: Group (G)1: alcoholic =175, Group2: viral hepatitis =714, G3: autoimmune hepatitis =13, G4: cholestatic liver disease =119, G5: non-alcoholic fatty liver =67 (number of patients with cirrhosis =761/69%) Mean age for all samples (54.2±12.0). All non-alcoholic fatty liver disease was found in females.	Child-Pugh score	Cirrhotic patients had poorer HRQOL than non-cirrhotic in all domains and component summary scores of SF-36 (delta score=6.6-34, p<0.05). Patients with Child-A had better HRQOL in all domains and PCS than Child-B cirrhosis and they had better MCS than Child-C. No significant difference in domains of component summary scores of SF-36 between Child-B and Child-C. Regression test, presence of cirrhosis predicted PCS and MCS. Significant difference in perceived HRQOL between Italian and American cirrhotic patients. Italian cirrhotic patients had significantly better HRQOL in domains of BP, VT and PCS. American cirrhotic patients had better HRQOL in domains of RE, MH and MCS.
Bao et al. 2007 China	126: 20 chronic HBV, 28 Child-A, 78 Child-B/C	Child-Pugh score	Disease severity associated with impaired HRQOL in all domains of SF-36 in patients with Child-B/C compared to Child-A (p<0.01). Disease severity related to poor disease specific HRQOL (CLDQ) in these domains (p<0.05): Child-B had poorer abdominal symptom, fatigue and worry compared to Child-A. Child-C had poorer abdominal symptom, fatigue and systematic symptoms compared to Child-A. Child-C had poorer HRQOL than Child-B in these domains of SF-36: RP and VT (p<0.05).
Basal et al. 2011 Egypt	27 Child-A, 173 Child-B	Child-Pugh score	No significant difference in MCS and PCS between Child-A and Child-B cirrhosis.
Dan et al. 2008 USA	140 patients with mixed disease stage: 88 non-cirrhosis, 54 cirrhosis (28 Child A and 26 Child B/C), mean age 49.4±11.2, 42% females, 36%	Child-Pugh score	Cirrhotic patients had lower HRQOL in all domains than non-cirrhotic patients (p<0.05). Child B/C had poorer HRQOL than Child-A cirrhosis

Author/Country	Methodology		Key results
	Sample size (for comparison: sample size per group)	Criteria of classifying disease stage	
	HBV, 29% HCV, 24% had cholestatic liver disease.		
Teixeira et al. 2005 Brazil	103 patients (with liver cirrhosis) G1: 63 cirrhosis G2: 40 without cirrhosis, Cirrhotic group: mean age 46±9.2, 64.4% men. Child-A= 53.98%, B= 22.22%, C= 23.80%.	Child-Pugh score	Cirrhotic patients had lower QOL than non-cirrhotic patients especially patients in the end stage of cirrhosis (Child-C). Decompensated cirrhotic patients had higher severity of concentration and memory problems, higher problems in sexual function, sleep, liver disease effect, quality of social interaction, loneliness, hopelessness, health distress and liver disease stigma than compensated cirrhotic patients.
Fritz and Hammer 2009 Australia	75 cirrhotic patients Disease severity: 37 Child-A, 34 Child-B and 4 Child-C. Causes of cirrhosis: 68% alcohol, 10.7% viral B or C and 21.3% others. Mean age 57±1.4 (range 24-82), 56% males.	Child-Pugh score	Child-A had similar HRQOL (PCS and MCS) to healthy people. Child-B had lower PCS than Child-A (p=0.006), no significant difference in MCS.
Girgrah et al. 2003 Canada	30 patients with cirrhosis, Disease stages: Child-A=12, Child-B/C=18 Mean age 54.4±3.1, 93.3% males. Causes: 60% alcoholic, 30% HCV, 10% others.	Child-Pugh score	No significant correlation between disease severity (Child-Pugh score or laboratory results) and PCS or MCS. Patients with Child-B or C (decompensated cirrhosis) had lower PCS and PF than Child-A (compensated cirrhosis) (p<0.01). No significant difference in MCS according to disease stage.
Gutteling et al. 2006 Netherlands	1175 patients with mixed disease stages: Disease severity: 42.5% non-cirrhosis 34% compensated, 7.3% decompensated 16.2% liver transplant. Mean age 48±12, 42.3% males Causes: autoimmune 12.7% hepatitis, 24.6% HCV, 15.7% Primary Biliary Cirrhosis (PBC). and 16.6% liver transplantation.	Complications	Disease severity was strongly related to poor HRQOL among patients with HCV. With increasing disease severity there was more deterioration in HRQOL (Beta=-0.02, p<0.01).
Haag et al. 2008 Germany	204 patients with chronic liver disease and 181 patients with functional dyspepsia. Disease severity: 100 had cirrhosis (Child-A=39,	Child-Pugh score	Child-C cirrhosis had poorer PCS than Child-A and B (p=0.02). No significant difference in MCS according to disease severity. Disease severity associated with PCS (p=0.04) but not MCS.

Author/Country	Methodology		Key results
	Sample size (for comparison: sample size per group)	Criteria of classifying disease stage	
	B=28, C=33). Causes of liver disease: HCV & HBV=101, alcoholic= 63, autoimmune/PBC=12, idiopathic= 28. Chronic liver disease group: mean age 52.7±13.9, 49% women, Functional dyspepsia group: mean age 44.7±14 64% women.		
Hauser et al. 2004 Germany	88 patients with chronic HCV. Disease stage: 70.4% non-cirrhosis, 17.0% Child-A, 12.5% Child-B/C, 23.9% on interferon therapy. Mean age 48.6%±14.6, 50% females,	Child-Pugh score	Disease severity could not associate withPCS or MCS.
Hsu et al. 2009 Canada	271 patients with chronic HCV. Disease severity: G1:197 had non-cirrhosis, G2: 17 compensated and G3: 57 decompensated. Mean age 49.7±8.6, 62.4% males.	Complications	Non-cirrhotic group had better HRQOL compared to cirrhotic groups in domains of: PF, RE and RP (p<0.005). Decompensated cirrhosis had the lowest domains of GH and PCS compared to non-cirrhosis and compensated cirrhosis (p<0.005). Compensated cirrhosis had the lowest RE compared to non-cirrhosis and decompensated cirrhosis (p<0.005).
Kalaitzakis et al. 2006 Sweden	128 patients with cirrhosis Disease severity: 22% had Child-A cirrhosis and 78% Child-B or C. causes: 43% alcoholic or mixed cirrhosis, 17% viral cirrhosis, 40% other causes. 9% hepatic carcinoma, 23% hepatic encephalopathy. Mean age 57.2±11.5, 61% males,	Child-Pugh score, MELD	Child-Pugh score and MELD were significantly associated with PCS, but not with MCS (p<0.005). Child-Pugh score could associate withPCS, p<0.05), but not MCS.
Karaivazoglou et al. 2010 Greece	84 patients viral hepatitis, HBV=45 and HCV=39 (matched in socio-demographic and disease severity). Mean age 46±16.7, 65.5% men.	Fibrosis scale	Fibrosis stage was associated with PCS (p=0.02), but not with MCS in HBV group. No significant association between fibrosis stage and HRQOL (PCS and MCS) in HCV group.

Author/Country	**Methodology**		**Key results**
	Sample size (for comparison: sample size per group)	**Criteria of classifying disease stage**	
Les et al. 2010 Spain	212 sample with cirrhosis Causes: 30.5% alcohol, 16.5% mixed alcoholic and HCV, 11% others. Mean age 61.5±10.9, 74% males.	Child-Pugh score	All domains of HRQOL were significantly poor according to Child-Pugh except domains of general health and mental health.
Marchesini et al. 2001 Italy	544 patients with cirrhosis Stages: 38% Child-A, 62% Child-B/C. Causes: 64% HCV or HBV, 29% alcoholic, 2% PBC. Mean age 60±11 (17-91), 63.9% males.	Child-Pugh score	Using logistic regression: Child-Pugh score was associated with PCS but not with MCS.
Sobhonslidsuk et al. 2006 Thailand	250 patients with chronic liver disease. Stage: 23.6% Child-A, 22.4% Child-B/C. Causes: 58.8% viral hepatitis C or B, 17.2% alcoholic and 10.8% non-alcoholic fatty liver. Mean age 49.1±8.5, 64% males	Child-Pugh score	Perceived general health decreased with increasing disease severity. Increasing disease severity was significantly associated with poor HRQOL domains of: PF, RP, GH and RE. Severity of disease was positively predictive PF, RP, GH and RE.
Sumskiene et al. 2006 Lithuania	131 patients with cirrhosis. Stage: 24.6% Child-A, 75.4% B or C. Causes: 40.5% viral hepatitis, 38.2% alcoholic, and others. Age: 17.6% were <40years, 51.1% were 40-60 years, 31.3% were > 60 years, 51.9% men.	Child-Pugh score	Disease severity was associated significantly with HRQOL. HRQOL was poorer among patients with advanced cirrhosis (Child-C) than patients in early stage of cirrhosis (Child-A) (p<0.01).
Svirtlih et al. 2008 Serbia	227 patients with chronic liver disease. Stage: 184 had chronic hepatitis and 43 had cirrhosis. G1: 167 HCV, mean age 39±11 (16-66), G2: 60 HBV, age 42.5±12 (19-66).	Ishak Fibrosis score	Significant difference in PCS and MCS among patients with cirrhosis and patients without cirrhosis. Patients with cirrhosis had worse HRQOL. Cirrhosis predicted poor PCS and MCS (p=0.000).
Teuber et al. 2008 Germany	215 untreated patients with chronic hepatitis C . Stage of fibrosis: 19.5% without fibrosis, 42.3% mild fibrosis, 21.4 moderate, 16.7% severe	Ishak Fibrosis score	Fibrosis was significantly predictive of PCS (P=0.01), but not of MCS. Patients with severe fibrosis or cirrhosis lower PCS than patients at early stage of cirrhosis. No significant association

Author/Country	Methodology		Key results
	Sample size (for comparison: sample size per group)	Criteria of classifying disease stage	
	fibrosis or cirrhosis. Mean age 46.7±13.4 (19-79), 57% males		between histological activity of the disease and the HRQOL (PCS and MCS). The main affected domains due to disease severity were PF, PR, and GH (p≤0.001).
van der Plas et al. 2003 Netherlands	1175 cohort sample of patients with chronic liver disease. G1: 489 non-cirrhosis, mean age 48±12, 43.8% males. G2: 391 had compensated cirrhosis, mean age 49±14, 41.4% males. G3: 84 decompensated, mean age 50±12, 42.9% males. Viral hepatitis: G1: 36.3%, G2: 20.9%, G3: 30.3%, G4: 186 transplanted patients	Complications	Decompensated cirrhotic patients had lower HRQOL than non-cirrhotic patients. Fatigue was worse among decompensated cirrhotic patients.
Wunsch et al. 2011 Poland	77 patients with cirrhosis. 61% males Sample of patients with cirrhosis was divided into two groups: with and without minimal encephalopathy. There was no significant difference between 2 groups regarding to age, gender, education, cause or disease severity. Mean age 52.8±13.1, (22-84 years).	Child-Pugh score, MELD	Disease severity (using MELD score) was significantly associated with poor PCS and MCS (p≤0.03). Disease severity (using Child-Pugh score) was not significantly associated with poor HRQOL
Younossi et al. 2001 USA	353 patients with different causes of liver disease. G1: 133 viral disease, mean age 46±9, 64.7% males, Child-A=18.1%, Child-B/C = 24%. G2: 126 cholestatic liver disease (PBC and others), 35.5% Child-A, 25.6% Child-B/C, mean age 54±11, 30.2% males. G3: 94 hepatocellular disease (alcoholic, genetics and other), 43.6% Alcoholic, 35% Child-A, 61.6% Child-B/C, cirrhosis mean age 52±13, 59.6% males	Child-Pugh score	HRQOL decreased with increasing disease severity, cirrhotic had lower HRQOL than non-cirrhotic. Cirrhosis significantly affected many domains of HRQOL according to causes of cirrhosis. Cholestatic cirrhosis had significantly poorer PF, RF, RE, GH and SF and PCS than patients with cirrhosis due to hepatocellular disease (p<0.01).

3.4.4 HRQOL of Egyptian Cirrhotic Patients

Little is known about cirrhotic patients in the Middle East, particularly in Egypt. Out of the 37 identified studies, only two studies by Schwarzinger et al. (2004) and Basal et al. (2011) examined the HRQOL of Egyptian patients with chronic HCV. Basal et al. (2011) studied patients with chronic liver disease related to HCV at stage A and B according to the Child-Pugh score, but did not investigate the advanced stage of cirrhosis. Schwarzinger et al. (2004) investigated non-cirrhotic chronic liver disease related to HCV in people unaware of their serological status and in a rural community. Although these two Egyptian studies contributed to the understanding of perceived HRQOL of liver disease patients, the findings were inconclusive and may not be applicable to liver cirrhotic patients. The two studies investigated liver disease related to HCV and ignored other causes such as bilharzias and viral HBV, although the cause may lead to a different perception of HRQOL. Thus, there is a need to examine the HRQOL of patients with compensated and decompensated cirrhosis because of mixed causes in Egypt to find out how these people perceive their health status.

3.5 FACTORS CONTRIBUTING TO THE UNDERSTANDING OF HRQOL

Several studies examined factors associated with the HRQOL in liver disease patients. Most of these studies focused on patients with mixed chronic liver disease stages (van der Plas et al. 2004; Gutteling et al. 2006; Sobhonslidsuk et al. 2006; Afendy et al. 2009; Dan et al. 2008; Haag et al. 2008; Hsu et al. 2009; Liu et al. 2012) with relatively small samples of cirrhotic patients (Younossi et al. 2001; Hauser et al. 2004; Toda et al. 2005; Teixeira et al. 2006; Bondini et al. 2007; Taliani et al. 2007; Svirtlih et al. 2008; Teuber et al. 2008; Wilson et al. 2010) or without cirrhosis (Karaivazoglou et al. 2010). Other studies focused on investigating HRQOL and related factors only in patients with cirrhosis (11 in total). It is difficult to make comparisons of all the reviewed papers, because HRQOL is a multidimensional concept that can be measured by different tools. These tools involve different categories of domains, for example SF-36 and NHP. Thus, only the studies that (1) examined only patients with cirrhosis, (2) investigated perceived HRQOL as a main outcome and (3) used SF-36 or SF-12 were reviewed. However, other studies examining mixed disease stages were used to support the discussion about the association between independent variables and HRQOL, if they were relevant (Table 3-6 summarises these studies).

In these studies several factors contributed to the perceived HRQOL in patients with cirrhosis. These factors include: (1) demographic characteristics and economic status, (2) environmental factors: social support, (3) bio-physiological factors and (4) symptoms experience. All these factors were analysed and discussed separately. Diagram 3-2 summarises all factors correlated with HRQOL in patients with liver cirrhosis.

Table 3-6: Studies investigating factors related to HRQOL in chronic liver disease and cirrhotic patients

Author/Country	Methodology		Results
	Design, sample method	Sample size	
Afendy et al. 2009 USA	Cohort study, sample from databases	1103 from US and Italia, number of patients with cirrhosis=761/69%)	Factors: Age associated with domains of SF-36 even after controlling confounding factors (i.e. gender, presence of cirrhosis, ethnicity). Females had poorer HRQOL than males in (PF, RP, BP, GH, VT and MH). Italians had better HRQOL than Americans in domains of BP, VT, and PCS. Americans had better HRQOL than Italians in domains of RE, MH and MCS. Regression test: age, presence of cirrhosis, ethnicity, gender, and cause of disease predicted PCS. Ethnicity, gender, presence of cirrhosis, cause of disease predicted MCS.
Arguedas et al. 2003 USA	Cross-section, consecutive	160 patients with cirrhosis	Factors: PCS was significantly lower in patients with previous history of hospitalization due to hepatic encephalopathy and among patients with ascites. No significant difference in MCS according to disease severity, history of hospitalization and presence of ascites. Patients with grade 1 HE (overt) had significantly lower PCS and MCS than patients without encephalopathy. Patients with subclinical encephalopathy had lower MCS than patients without it. The most affected domains were RE, MH and SF. No significant difference in MCS and PCS according to age, gender, ethnicity and cause of cirrhosis.
Bao et al. 2007 China	NA (seems cross-section), NA	126 patients with chronic liver disease divided into 20 with HBV and 106 with cirrhosis	Factors: Disease severity associated positively with increasing impaired domains of HRQOL in both SF-36 and CLDQ. Patients with decompensated cirrhosis (Child-B or C) had similar HRQOL in disease specific and generic HRQOL, with the exception of VT and RP. Significant difference between patients with minimal encephalopathy and patients without it on SF-36, and only a significant difference the domain of abdominal symptoms in CLDQ.

Author/Country	Methodology		Results
	Design, sample method	**Sample size**	
Basal et al. 2011 Egypt	Descriptive cross-section, Convenient	200 patients with chronic liver disease, Child-A or Child-B	Factors: Age and level of education were significantly associated with PCS, comorbidity and occupations significantly associated with MCS. No significant association between gender, marital status, income, severity of disease and both PCS and MCS.
Dan et al. 2008 USA	Retrospective, cohort sample/from databases	140 patients with chronic liver disease (38% had cirrhosis).	Factors: Mental health was not significantly different in patients with cirrhosis and patients without. Cirrhotic patients had poor health utility and the worst domains were emotion, mobility, self-care and sensation. Domains of cognition and pain were not significantly different between cirrhotic and non-cirrhotic patients. Females had poorer HRQOL, cognition and mobility than males. Older people had poorer PF and sensation. Regression test: gender (female) and having HCV significantly predicted poor HRQOL (SF-6D). Age and disease stage (cirrhosis) did not significantly associate withHRQOL, although cirrhosis significantly predicted health utility.
Fritz and Hammer 2009 Australia	NA (seems cross-section), consecutive	75 patients with liver cirrhosis	Factors: Disease severity associated significantly with poor HRQOL. No significant difference between patients with cirrhosis and the normal population in PCS and MCS. There was a significant difference between Child-B and Child-A and the HRQOL of the normal population, decompensated cirrhosis had a worse HRQOL. The most significant difference according to disease stage was PCS; but there was no significant difference in MCS.
Girgrah et al. 2003 Canada	NA (seems cross-section),, NA	30 patients with cirrhosis	Factors: No significant correlation between disease severity (Child-Pugh score or laboratory results) and PCS or MCS. However, patients with Child-B or C (decompensated cirrhosis) had lower PCS and PF than Child-A (compensated cirrhosis).
Gutteling et al. 2006 Netherlands	NA (seems cross-section), cohort sample from databases	1175 patients in different liver disease stages. 42.5% non-cirrhosis 34% compensated, 7.3%	Significant association between experience of symptoms and HRQOL. Regression test: positive association between severity of symptoms (i.e. joint pain, depression, abdominal pain, decreased

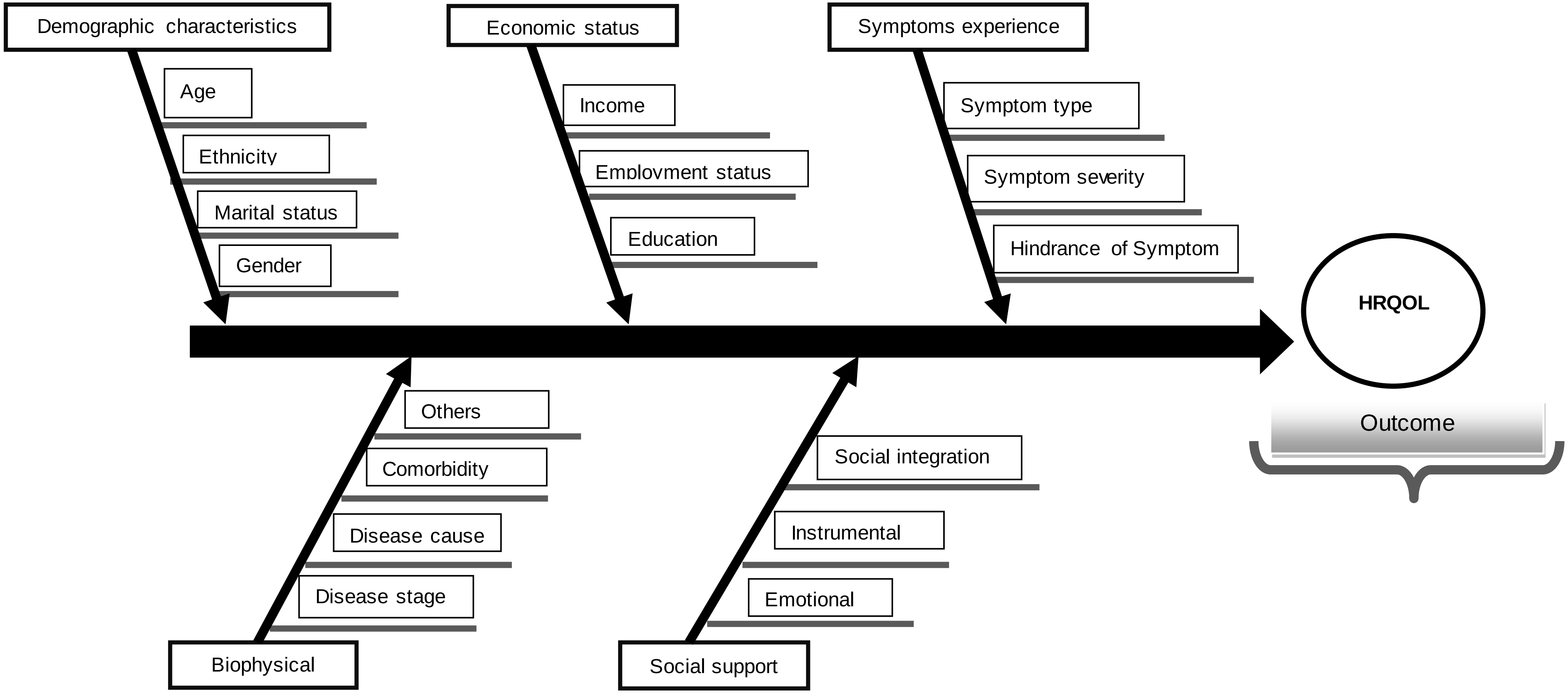
Author/Country	Methodology		Results
	Design, sample method	Sample size	
		decompensated 16.2% liver transplant.	appetite and fatigue) and HRQOL. With increasing disease severity there was more deterioration in HRQOL. Physical and psychosocial factors explained 53% of the variance in HRQOL. Demographic and medical factors explained 7% of the variance in HRQOL. A weaker significant association between daily time management, memory problems, change of personality, age and gender and HRQOL. Disease severity, depression, interferon therapy, fatigue, joint pain and limitations in financial affairs were strongly related to poor HRQOL among patients with HCV.
Haag et al. 2008 Germany	Prospective, consecutive	204 patients with chronic liver disease and 181 patients with functional dyspepsia (liver cirrhosis= 100).	Factors: Severity of depression and anxiety symptoms and age were associated with HRQOL. Age was not associated with HRQOL. Regression test: PCS could be explained by disease severity, anxiety and age. MCS could be explained by depression and anxiety.
Hsu et al. 2009 Canada	Cross-section/Comparative study, convenience	271 patients with chronic HCV. (liver cirrhosis= 74)	Factors: significant association between HRQOL and disease severity. Non-cirrhotic patients had lower hepatitis distress experiences than the cirrhotic patients. Married with a higher income had a better HRQOL. Female and older patients and those with history of substances abuse had lower MCS. Patients with comorbidities had lower HRQOL.
Kalaitzakis et al. 2006 Sweden	Cross-section, consecutive	128 patients with cirrhosis	Factors: Patients with minimal encephalopathy had lower PCS and MCS than patients without it. Child-Pugh score predicted PCS and MCS. Encephalopathy predicted PCS. Aetiology of cirrhosis was not associated with HRQOL.
Les et al. 2010 Spain	Cross-section, consecutive	212 patients with cirrhosis	Factors: Ascites, encephalopathy, low albumin level, prothrombin and haemoglobin, decreased mid-arm muscle circumference significantly correlated with disease specific HRQOL (CLDQ) and PCS. Beta-blockers, diuretics, spontaneous bacterial peritonitis, number of medications per day, low plasma, elevated levels of creatinine and bilirubin associated with PCS. Non-alcoholic

Author/Country	Methodology		Results
	Design, sample method	Sample size	
			related disease significantly correlated with disease specific HRQOL (CLDQ). Sex or age had no significant association with PCS or CLDQ. Regression test: female sex, non-alcoholic cause of cirrhosis, current ascites and decreased albumin level could associate withHRQOL (CLDQ). Encephalopathy, ascites, and decreased haemoglobin could associate withPCS. Decreased haemoglobin and non-alcoholic cause could associate withMCS.
Marchesini et al. 2001 Italy	Cross-sectional survey, Recruiting all patients who regularly are followed up in out-patient clinic through 6 months	544 patients with cirrhosis	Factors: No significant difference in HRQOL according to gender, cause of cirrhosis (alcoholic and non-alcoholic) and disease duration. Patients younger than 55 had poorer HRQOL. Recent admission to hospital, ascites, encephalopathy, daily therapy, diuretics, pruritus and muscle cramps correlated with poor PF. Muscle cramp and Pruritus associated with all domains of NHP (Sleep, energy, pain, emotional reaction, social isolation, physical mobility. Ascites, and muscle cramps associated with mental health. Hospitalization associated significantly with PF, BP, VT, and physical mobility.
Sobhonslidsuk et al. 2006 Thailand	Cross-section, NA (seems consecutive)	250 patients with chronic liver disease, (46% had cirrhosis)	Factors: significant association between increasing disease severity and poor HRQOL especially in these domains: PF, RP, GH, RE and in all domains of CLDQ. Regression test: severity of liver disease was predictive of CLDQ and PF, RP, GH and RE (SF-36). Financial burden associated negatively with most of SF-36 domains and CLDQ, and it predicted PF and RP. Perceived good health associated positively with all domains of (SF-36 and CLDQ). Cause of disease did not significantly associate with HRQOL. Female gender predicted poor PF, low education predicted low VT, type of work predicted RE, age predicted PF, RP and BP.
Jover et al. 2005	Cross-section,	46 patients with cirrhosis	Factors: Patients with extra-pyramidal signs had worse PCS and

Author/Country	Methodology		Results
	Design, sample method	Sample size	
Spain	consecutive		MCS and disease specific QOL.
Kalaitzakis et al. 2008 Sweden	Cross-section, consecutive	156 patients with cirrhosis	Factor: Child-Pugh score was associated with PCS and MCS. Aetiology of cirrhosis was not associated with HRQOL. Child-Pugh score and encephalopathy were associated with PCS.
Liu et al. 2012 Japan	Cohort study/ collected data from databases stratified random sample from the main data in databases.	306 patients with HCV	After matching groups: all HRQOL of patients with HCV were lower than matched healthy group. Work productivity loss and healthcare resources use outcomes were worse among patients with HCV than matched group. The main affected domains were MCS, bodily pain, general health, mental health. Other domains were not significantly different between control and HCV groups. When controlling comorbidities the HRQOL was still impaired among patients with HCV particularly in domains of MH, GH and MCS. Domain of pain becomes insignificantly different. Then comorbidities may be a factor that may enhance pain perception.
van der Plas et al. 2004 Netherlands	Survey, Consecutive	1175 patients with mix stages of liver disease in the main survey: Non-cirrhotic 42.5%, compensated cirrhosis 34%, decompensated 7.3%, liver transplant 16.2%. group of clinical patients with liver disease in pilot study=69	Significant positive association between symptoms experience (severity and hindrance) and HRQOL. Hindrance of symptom was strongly related to poor HRQOL more than the severity of symptoms.
Wunsch et al. 2011 Poland	NA, consecutive	77 patients with cirrhosis.	Factors: Disease severity using the model of end-stage liver disease (MELD score) correlated significantly with poor HRQOL in most of the SF-36 subscales, and only with activity subscale of CLDQ. No association between disease severity (using Child-Pugh score) and HRQOL.

NA: not available

Diagram 3-2: Summary of factors that may contribute to explain HRQOL in patients with liver cirrhosis



3.5.1 Demographic Characteristics

Several studies investigated the association between demographic characteristics and socio-economic status and HRQOL in cirrhotic patients. Table 3-7 summarises the studies that examined these variables in relation to HRQOL (i.e. physical and mental health) in cirrhotic patients.

The studies had conflicting findings about the association between age and gender and HRQOL (Table 3-7). For example, Afendy et al. (2009) and Basal et al. (2011) found that age was significantly associated with physical health domains (SF-36), with elderly people more likely to experience poor physical health. Dan et al. (2008), similarly, showed that older patients had poorer physical functioning and sensation than younger ones. However, age was not significantly associated with mental health domains (Afendy et al. 2009; Basal et al. 2011). Kim et al. (2006) investigated QOL and psychological distress in cirrhotic patients, finding that age was not associated with perceived QOL (Quality of Life Index) or psychological distress. Therefore, it seems that age is more likely to be associated with physical health and less likely with mental health domains in cirrhotic patients.

A few studies found that gender was related to perceived HRQOL in cirrhotic patients. Females were more likely than males to experience poor mental health domains (SF-36), and being female was associated with poor mental health domains (Afendy et al. 2009). However, in the Egyptian study, Basal et al. (2011) found that there was no significant different ($p \geq 0.2$) between males and females' physical and mental health domains (SF-36). On balance, it appears that there is an association between age and gender and perceived HRQOL, without knowing whether physical or mental health domains are more affected. However, further studies are needed to find the influence of gender and age on the HRQOL of cirrhotic patients.

3.5.1.1 Socio-economic Status

Employment status, occupation, level of education and income are the key indicators of socio-economic status. Although the association between socio-economic status and HRQOL was investigated in cirrhotic patients (Table 3-8), different indicators of socio-economic status were used that making comparison difficult. For example, one study in Egypt investigated many indicators (type of work, education and income level) of socio-economic status and its association with HRQOL (Basal et al. 2011). The results showed that type of work (i.e. housewives, officers, teachers and farmers) was significantly associated with mental health, but not with physical health (Basal et al. 2011). Educational level was also significantly associated with physical health, but not with mental health. Congruent with these findings, education in the study by Kim et al. (2006) was not associated with the overall QOL or psychological distress in patients with cirrhosis due to mixed causes. This suggests that education may be related to perceived physical heath, but not mental health. However, further studies are required to develop the evidence of this association.

Patients with decompensated cirrhosis had a higher probability of financial problems (van der Plas et al. 2003). About 33.3% of cirrhotic men reported that paid employment was the aspect most affected in their daily life (using NHP) (Marchesini et al. 2001). Also, 40% of patients less than 55 years old perceived their health status as a problem for employment (Marchesini et al. 2001). However, income was not significantly related to both physical and mental health domains

(Basal et al. 2011). This might be due to using invalid methods for assessing income, e.g. enough or not enough from the patients' perception.

Unemployed cirrhotic patients were more likely to have a poorer QOL than employed patients. Employment status (current work or not) was associated with QOL (Kim et al. 2006), suggesting that cirrhotic patients who were unable to work were more likely to experience depression than patients who were able to work. These results suggest that liver cirrhotic patients are more liable to have poor socio-economic status, which consequently affects their health status and overall QOL. However, further research is required to assess socio-economic status in cirrhotic patients using valid tools to measure the influence of socio-economic status on perceived HRQOL.

Table 3-7: Studies investigating the association between demographic characteristics, socio-economic status and HRQOL in cirrhotic patients

Study	Association between demographic variables and HRQOL								Association between economic status variables and HRQOL							
	Physical health				Mental health				Physical health				Mental health			
	Age	Gender	Marital status	Ethnicity	Age	Gender	Marital status	Ethnicity	Income	Employment status	Career type	Education	Income	Employment status	Career type	Education
Afendy et al. 2009	√	√	/	/	×	√	/	/	/	/	/	/	/	/	/	/
Arguedas et al. 2003	×	×	/	×	×	×	/	×	/	/	/	/	/	/	/	/
Bao et al. 2007	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Basal et al. 2011	√	×	×	/	×	×	×	/	×	/	×	√	×	/	√	×
Fritz and Hammer 2009	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Girgrah et al. 2003	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Jover et al. 2005	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Kalaitzakis et al. 2006	×	×	/	/	×	×	/	/	/	/	/	/	/	/	/	/
Kalaitzakis et al. 2008	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Les et al. 2010	×	×	/	/	×	×	/	/	/	/	/	/	/	/	/	/
Marchesini et al. 2001	√	√	/	/	×	×	/	/	/	/	/	/	/	/	/	/
Wunsch et	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Study	Association between demographic variables and HRQOL								Association between economic status variables and HRQOL							
	Physical health				Mental health				Physical health				Mental health			
	Age	Gender	Marital status	Ethnicity	Age	Gender	Marital status	Ethnicity	Income	Employment status	Career type	Education	Income	Employment status	Career type	Education
al. 2011																

√…significant association

×…not significantly associated

/….association was not studied

3.5.2 Environmental Characteristics

3.5.2.1 Ethnicity

Only two studies investigated the association between ethnic background and perceived HRQOL in cirrhotic patients (Arguedas et al. 2003; Afendy et al. 2009). For example, in the study by Arguedas et al. (2003) in 160 cirrhotic patients there was no significant difference in physical and mental health domains according to their ethnicity (Caucasian/African, American and other). However, the large cohort study (n = 1103) by Afendy et al. (2009) assessed HRQOL according to the country of origin (i.e. Italian and American). The results showed that Italians had a better HRQOL than Americans in the domains of BP, VT, and PF. In the domains of RE, MH and MCS were better among Americans than Italians.

Indeed, there were considerable discrepancies between these two studies to make them incomparable. For example, Afendy et al. (2009) studied patients in their own countries, while Arguedas et al. (2003) studied patients who were already living in the US. Therefore, it seems that the environment in terms of cultural and ethnic background may be a factor that can affect people’s perceptions about their health. Afendy et al.'s (2009) study contributed by showing the importance of cultural background and its relevance to specific domains of HRQOL.

3.5.2.2 Marital status

The association between marital status and perceived HRQOL is well documented in patients with other chronic diseases such as cardiac disease (Lee et al. 2005). However, little is known about this association in liver disease patients, particularly among cirrhotic patients. Few studies examined the association between marital status and HRQOL (Hsu et al. 2009; Basal et al. 2011) and QOL (Kim et al. 2006) However, it appears that a relationship between marital status and HRQOL or QOL is not supported; the studies involved relatively small sample sizes with different disease stage and used different tools. For example, Basal et al. (2011) showed that marital status was not associated with HRQOL, as there was no significant difference in domains of physical and mental health between married and single patients. Similarly, in a study including 129 cirrhotic patients due to different causes (i.e. viral hepatitis and alcoholic), Kim et al. (2006) showed that there was no significant difference in QOL according to marital status. However, in a study of 271 patients with mixed stages of HCV (without cirrhosis, compensated and decompensated cirrhosis) the results found that married people were more likely to have better physical and mental health, than singles (Hsu et al. 2009).

Theoretically, marital status has been classified as a type of structured social support, which describes the existence of a relationship (Cohen and Syme 1985) as discussed in Chapter 2, Marital status as a source of support can work directly as a buffer against stress, especially during illness. Consequently, it can influence perceived physical and mental health. In the theoretical framework of HRQOL outcomes (Diagram 4-2), social support has been considered as a mediation factor between disease symptoms and perceived HRQOL. Therefore, there is a need for more research to establish whether social support (functional support) and marital status (structure support) are significant factors in perceived HRQOL in patients with cirrhosis.

3.5.2.3 Perceived Social Support

Over the past years, the association between social support and HRQOL has been investigated among patients with different cardiac diseases (Bosworth et al. 2000; Kristofferzon et al. 2003; Graven and Grant 2012) and cancer (Lutgendorf et al. 2012; Trevino et al. 2013). A lack of social support was associated with low physical and mental health domains (SF-36), and depression. However, little is known about the association between the perceived availability of social support from informal sources and the perceived HRQOL among patients with liver cirrhosis. Only three studies investigating social support in liver disease patients were found (Blasiole et al. 2006; Erim et al. 2010; Wilson et al. 2010).

These studies aimed to assess mental health domains (SF-36) and depression (Wilson et al. 2010), coping and depression (Erim et al. 2010) and difficulties of social functioning and social support (Blasiole et al. 2006) as a mean outcome in patients with chronic HCV. Studies by Erim et al. (2010) and Wilson et al. (2010) included patients from outpatient clinics who were diagnosed with chronic HCV but not with cirrhosis (Erim et al. 2010; Wilson et al. 2010), while a study by Blasiole et al. (2006) included patients with HCV at various disease stages with a relatively small sample of cirrhotic patients (23.8%). The studies support the importance of social support for decreasing symptoms and improving social functioning. For example, patients with high social support had a high sense of coherence (i.e. coping with stressors), low depression and few anxiety symptoms (Erim et al. 2010). Using the SF-36, Wilson et al. (2010) also found that liver disease patients with high social functioning had better mental health and lower depression. Based on these findings it appears that there is an association between the perceived availability of social support and mental health.

3.5.3 Biophysical Factors [Medical History and Clinical Data]

Several biophysical variables were investigated in relation to HRQOL (using SF-36): (1) cause of liver disease, (2) comorbidities (medical or psychiatric), (3) hepatic encephalopathy and (4) other biophysical factors.

3.5.3.1 Cause of Liver Disease

A comparison of HRQOL according to the causes of cirrhosis was made in several studies (Marchesini et al. 2001; Arguedas et al. 2003; Dan et al. 2008; Kalaitzakis et al. 2008; Les et al. 2010). Inconsistencies in categorising disease causes made difficulties in drawing conclusions regarding the impact of the cause of cirrhosis on perceived HRQOL. For example, Afendy et al. (2009) investigated whether the cause of cirrhosis (i.e. alcoholic liver disease, autoimmune hepatitis, viral hepatitis, non-alcoholic fatty liver disease and cholestatic liver disease) associated with HRQOL. They used a mixed cohort of cirrhotic patients from Italy and the USA. The results showed that the factors associated with poor physical health were non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD). However, NAFLD, autoimmune hepatitis and cholestatic liver disease were associated with poor mental health domains (Afendy et al. 2009). These results suggest that patients with non-alcoholic fatty liver disease have a poorer physical and mental health domains than patients with viral hepatitis, or with alcoholic liver disease.

On the other hand, van der Plas et al. (2007) studied a large cohort of chronic liver disease patients with mixed stages and liver disease causes. The results showed that people with liver disease related to HCV had a poorer HRQOL and higher fatigue [Multidimensional Fatigue Index-20 (MFI-20)] than other causes (i.e. cholestatic, autoimmune, PBC, hemochromatosis, etc.) (van der Plas et al. 2007).

Viral hepatitis patients had a worse HRQOL, particularly in mental health, than other causes. They had more mental symptoms such as worry about the family situation, depression, and fear of liver disease complications. Patients with hemochromatosis had a poorer physical health, particularly bodily pain and role limitations due to emotional problems, and higher physical symptoms such as joint pain (ven der Plas et al. 2007). Having HCV was significantly associated with perceived poor HRQOL (SF-6D) (Dan et al. 2008).

In contrast, mental and physical health was not significantly different according to the cause of liver cirrhosis (hepatocellular, cholestatic, alcoholic and hepatitis C cirrhosis) in the study by Kalaitzakis et al. (2008). Also, Kim et al. (2006) found that there was no significant difference in cirrhotic patients' QOL according to cause of cirrhosis (HCV, HBV and alcohol). As the studies compared different causes using various disease categorisations it is difficult to draw general conclusions about the association between HRQOL and cause of cirrhosis.

Interestingly, Afendy et al. (2009) is the only study that investigated separately the association between cause of disease and HRQOL according to ethnicity (American and Italian patients) using regression methods. They found that in the American cohort, patients diagnosed with the NAFLD and ALD were more likely to report poor physical health, whilst those with NAFLD, PBC and primary sclerosing cholangitis were more likely to report poor mental health. In the Italian cohort, patients diagnosed with NAFLD were more likely to report poor physical health, however the causes of cirrhosis was not associated with mental health domains (Afendy et al. 2009). In Egypt, no study has investigated perceived HRQOL according to disease causes, only patients with liver disease due to HCV (Schwarzinger et al. 2004; Basal et al. 2011). Therefore, determining whether the cause of cirrhosis is related to the perceived HRQOL in Egyptian cirrhotic patients is needed.

3.5.3.2 Comorbidities

Comorbidities are common in cirrhotic patients, particularly medical comorbidities, such as diabetes mellitus, hypertension, respiratory problems…etc. (Marchesini et al. 2001; Kalaitzakis et al. 2006; Firtz and Hammer 2009; Les et al. 2010; Basal et al. 2011). The association between the presence of comorbidities and HRQOL was investigated among cirrhotic patients (Marchesini et al. 2001; Basal et al. 2011), and chronic liver disease patients (Hauser et al. 2004; Hsu et al. 2009). However, Fritz and Hammer (2009) considered it as a confounding factor when investigating the association between severity of gastrointestinal symptoms and HRQOL.

The relationship between the presence of comorbidities and HRQOL was inconsistent. For example, in a study by Hsu et al. (2009) into mixed disease stages, the number of present comorbidities (using index of Coexistent Disease) was strongly correlated with physical and mental health domains (SF-12). However, when Hsu et al. (2009) used another tool (Charlson Index) to assess comorbidities, there was a significant reduction in physical health but not in mental health. Similarly, Hauser et al. (2004) found that the number of medical comorbidities significantly predicted physical health but not mental health. However, in a recent Egyptian study by Basal et al. (2011), the HRQOL of patients with and without comorbidities were compared. Only the mental health domain was significantly reduced in patients with medical comorbidities (i.e. diabetes, peptic ulcer, hypertension and asthma) ($p = 0.02$). Interestingly, when using two generic HRQOL tools, the number of comorbidities was not significantly associated with HRQOL (using SF-36). Nevertheless, the number of comorbidities was significantly related to the domains of energy, emotional reaction, social isolation and physical mobility (using NHP) (Marchesini et al. 2001). Accordingly, it seems that the presence of comorbidities can influence HRQOL, but the effect may be more on physical health. Therefore, the association between the presence of comorbidities and perceived HRQOL needs further research.

3.5.3.3 Hepatic encephalopathy

Hepatic encephalopathy has been found to be a factor in perceived HRQOL. However, there is a contradiction over which aspect of health is more affected, mental or physical health. For example, in a study by Bao et al. (2007) hepatic encephalopathy in cirrhotic patients was comprehensively investigated using psychometric tests (i.e. Number Connection test-A and Symbol Digit Test) and an electroencephalogram. The results showed that eight domains of SF-36 were significantly poorer among patients with hepatic encephalopathy than in patients without ($p < 0.01$) (Bao et al. 2007). Even using another tool for diagnosing hepatic encephalopathy, (i.e. Retain Test) physical and mental health domains were lower in patients with encephalopathy ($p \leq 0.03$) (Arguedas et al. 2003). However, using the regression test, encephalopathy significantly predicted physical health but not mental health (Les et al. 2010). In other studies, however, there was no significant difference in either physical or mental health domains due to the presence of hepatic encephalopathy (diagnosed by psychometric hepatic encephalopathy score) (Wunsch et al. 2011). Although it seems there is a relationship between hepatic encephalopathy and impaired HRQOL, there is no evidence which aspect of health is affected. Therefore, future research should diagnose encephalopathy using a valid tool and investigate its effect on perceived HRQOL in cirrhotic patients.

3.5.3.4 Other Biomedical Factors

The reduction in HRQOL may be a result of other biomedical factors, including ascites, low albumen and haemoglobin levels, non-alcoholic cause (i.e. viral hepatitis) (Marchesini et al. 2001; Arguedas et al. 2003; Kalaitzakis et al. 2006; Les et al. 2010), type of medications (e.g. diuretics, beta blockers and lactulose) (Marchesini et al. 2001; Kalaitzakis et al. 2006; Les et al. 2010), number of daily medications (Marchesini et al. 2001; Les et al. 2010), spontaneous bacterial peritonitis (Les et al. 2010), neurological problems like extra pyramidal signs (i.e. tremor, difficulty to speak) (Jover et al. 2005), recent or previous hospitalizations (Marchesini et al. 2001; Arguedas et al. 2003) and a decrease in mid-arm muscle circumference (Les et al. 2010). These factors should be considered in future research of cirrhotic patients as well for the improvement of their HRQOL.

3.5.4 Symptoms Experience

Several studies of symptoms relating to liver disease were reviewed (Tables 3-6 and 3-8). In these studies, various symptoms were examined in liver disease patients at different stages of the disease but few of them focused on cirrhotic patients. In addition, few of the symptoms were examined in relation to the HRQOL of cirrhotic patients (Table 3-6). The studies for the literature review were selected because they showed an association between symptoms and HRQOL of chronic liver disease patients at mixed stages, and in cirrhotic patients. However, the studies used cross-sectional designs, compared different symptoms, and were inconsistent in their measurements (Table 3-6). It is therefore difficult to draw conclusions about the influence of general symptoms experience on HRQOL.

The evidence from the observational studies suggests that symptoms such as depression, anxiety (Girgrah et al. 2003; Hauser et al. 2004; Haag et al. 2008; Fritz and Hammer 2009), erectile dysfunction, sexual interest, sexual activity (Toda et al. 2005), fatigue (Girgrah et al. 2003; Teuber et al. 2008), gastrointestinal symptoms (Kalaitzakis et al. 2006; Fritz and Hammer 2009), pruritus, muscle cramps (Marchesini et al. 2001), overall symptom severity (van der Plas et al. 2004; Gutteling et al. 2006) and hindrances in daily life due to the presence of symptoms (van der Plas et al. 2004) may influence the HRQOL of patients with liver disease and cirrhosis.

Fritz and Hammer (2009) studied the association between the number of experienced gastrointestinal symptoms and HRQOL in 128 patients with liver cirrhosis. They found that mental and physical health (SF-36) decreased significantly with an increasing number of gastrointestinal symptoms. Also, patients with high levels of gastrointestinal symptoms had poor HRQOL. This association remained significant even after controlling for age, gender and comorbidities. Similarly, Kalaitzakis et al. (2006) found that the severity of gastrointestinal symptoms associated significantly with both physical and mental health domains (SF-36).

Gutteling et al. (2006) investigated physical and psychosocial factors using LDSI-2.0 (15 items of symptom severity) in 1175 patients at different stages of liver disease (i.e. non-cirrhotic, compensated, decompensated and post transplanted). The authors controlled demographic (age, gender) and medical (use of antiviral therapy, disease stage) variables to test the predictive ability of physical and psychosocial factors to HRQOL. Regression analysis identified that with increasing joint pain, depression, abdominal pain, fatigue, memory problems, change of personality and decreased appetite there was a strong reduction in HRQOL (SF-12) ($p < 0.05$). Additionally, the majority of patients (49/53) reported they had erectile dysfunction (Toda et al. 2005). Erectile dysfunction was also identified among patients who had poor PF, SF and RP. Although the correlation supported the relationship between erectile dysfunction and HRQOL, this relationship disappeared with regression analysis. The authors considered erectile dysfunction as the main outcome, and HRQOL as an independent factor. Therefore, cirrhotic patients' sexuality problems need further research to investigate this influence on their HRQOL.

Psychological symptoms such as depression and anxiety may be shaped by patients' perceptions and disease stage as well as physiological symptoms. Kim et al. (2006) studied overall symptoms experience in liver cirrhotic patients, but in relation to QOL. The results found that psychological distress was associated with disease severity (Child-Pugh score). Patients with decompensated cirrhosis were more anxious and depressed than patients with compensated cirrhosis. Depression is strongly associated with decreased vitality (Fatigue Assessment Inventory) ($r = 0.55$, $p < 0.001$) (Girgrah et al. 2003), and sleep disorder (Bianchi et al. 2005) in cirrhotic patients. Depression and anxiety were significantly associated with mental (SF-36) (Hauser et al. 2004; Haag et al. 2008) and physical health (Hauser et al. 2004) in liver disease and cirrhotic patients. Gutteling et al. (2006) found that physical and psychological factors could explain 53% of the variance in HRQOL, while the demographic and medical variables could only explain 7%.

Furthermore, symptom status has been investigated using the LDSI-2.0 which can be divided into two subscales, symptom severity and hindrance of daily life due to symptoms (van der Plas et al. 2004). The results showed that symptom severity and hindrance of symptoms were significantly associated with HRQOL. However, a reduction of HRQOL was more likely to occur with increasing hindrance of daily life due to symptoms than with increasing severity of symptoms. For example, hindrance of daily life due to symptoms of joint pain, depression, abdominal pain, decreased appetite, worry about family and sleepiness during the day were strongly associated with domains of PF, RP, BP, GH, SF, RE and MH. However, the severity of these symptoms affected HRQOL less (van der Plas et al. 2004). Therefore, it appears that the limitations of daily life due to the presence of symptoms are more important in predicting HRQOL than the severity of the symptoms themselves. No studies were found that examined symptoms experience and its influence on perceived HRQOL in liver disease and cirrhotic patients in Egypt.

SECTION II: SYMPTOMS EXPERIENCE

As seen in previous sections of this literature review, chronic liver disease and cirrhosis are a major cause of morbidity and mortality worldwide. Patients with liver cirrhosis may suffer from various physical and psychological symptoms that can affect their daily activities. Therefore, this section aims to review studies that assess the symptoms of patients with chronic liver disease and cirrhosis.

3.6 CHARACTERISTICS OF REVIEWED PAPERS THAT STUDIED SYMPTOMS

Out of 54 papers, 31 papers investigated symptoms in liver disease and cirrhotic patients and were found to be mostly descriptive and cross-sectional in nature. Table 3-8 presents a summary of these studies. Of the 31 studies, 13 were conducted in Europe, with Germany conducting the highest number of studies: five in total, and one study was conducted in Australia. In Asia, six studies were conducted and 10 studies were conducted in America, where US conducted the highest number of the studies. In Africa, one study was conducted in Egypt in 2011. This suggests that there is a growing interest worldwide in assessing symptoms in liver disease patients. In Egypt, studying symptoms in liver disease patients is still uncommon.

Most of the studies focused on patients with chronic liver disease at mixed stages (16 studies in total) (van der Plas et al. 2003, 2004 and 2007), with a relatively small sample of cirrhotic patients (Hauser et al. 2004; Teixeira et al. 2005) or without decompensated cirrhosis (Constant et al. 2005; Elshahawi et al. 2011). Other studies focused on investigating symptoms in cirrhotic patients only (13 in total)

Table 3-8: Studies investigating symptoms in liver disease patients

Author	Methodology			Studied symptoms	Results
	Design/sampling method	**Size and characteristic of sample**	**Tools**		
Bailey et al. 2009 USA	Cross-section, convenience	126 patients with chronic HCV, mean age 53 (27-78 years), 50.8% females	Revised Piper Fatigue Scale (RPFS), Body pain was measured by using the SF-36 (domain of pain). Centre for Epidemiology Studies Depression Scale (CES-D)	Pain, depression, fatigue	Patients had a moderate level of uncertainty-related liver disease, mild level of fatigue, mild level of discomfort/pain, not depressed. **Regression test:** Ambiguity subscale associated significantly with depression, QOL, pain and fatigue. Complexity subscale associated significantly with pain and fatigue. Unpredictability subscale associated significantly with pain. Education, age or gender did not associate with any of subscales of uncertainty.
Bajaj 2008 USA	Cross-section, consecutive	104 cirrhotic patients, 70% of them males and their caregivers.	**For patients:** Cognitive test battery MacArthur foundation socio-demographic questionnaire, specific financial questions **For caregivers:** Perceived caregivers burden (PCB), Zarit Burden Interview (ZBI)-short form, Beck	Depression among caregivers	63% had financial affair problems after diagnosis with liver cirrhosis. 57% had work problems (i.e. decreasing work hours and income or losing work), 56% are still working after diagnosed with cirrhosis. 53% decreased their work time. 57% saw their work as an important source of support. White-collar workers significantly perceived their financial affairs better than blue-collar workers. **Effect of medical expenses due to cirrhosis on the patients' medical adherence (i.e. appointment, medications and procedures) for the previous year:** 36% lost insurance,

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
			Depression Inventory, Beck Anxiety Inventory and Interpersonal Support evaluation List-Short Form (ISEL-SF)		26% missed medical appointments, 12% do not take medications, 10% do not take all the prescribed medications and 5% do not adhere to procedures. **Effect of medical expenses due to cirrhosis on the family’s daily activities for the previous 3 years:** 56% stopped saving, 46% in debt, 16% no education, 15% late on paying bills, 11% no food (skip food) and 10% need to leave their home for a cheaper one. Family of cirrhotic patients had high score of perceived caregivers burden and Zarit Burden Interview. Family had personal health, schedule and financial problems. Severity of perceived burden in caregivers was higher among spouses than other caregivers. Spouses had a higher disruption of schedule, personal health, entrapment, but not financial nor abandonment. 23% of caregivers had mild to moderate depression, 5% had severe depression, 34% had mild-moderate anxiety and 5% had severe anxiety. **Factors:** Severity of cirrhosis, previous hepatic encephalopathy and patients' cognitive profiles correlated positively with burden of the caregivers.
Bianchi et al. 2005 Italy	Prospective cross-section, consecutive	165 cirrhotic patients, 43 % females, age median 65 (37-87)	Beck depression inventory (BDI), State Trait Anxiety	Muscle cramp, somatic and psychological	58% had muscle cramps in the last month. 56.7% had depression 40.7% mild-moderate depression, 10%

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
			Inventory (STAI) *No specific tool for muscle cramp or sleeping symptoms*	depression, anxiety	moderate to severe depression, and 6% severe to extremely severe depression. Median of depression was 11 (normal range 0-37). No significant association between socio-demographic characteristics and depression. Depression associated positively with encephalopathy, disease severity, sleep disorders, number of daily therapy. Domain of somatic depression associated with ascites, disease severity, sleep disorders, daily therapy. Depression (as measured by Well-being scale), global, somatic and psychological depression (as measured by BDI) were significantly higher among alcohol drinkers than abstaining. Somatic symptoms (i.e. sleep disorders, fatigue, loss of appetite and weight, body image, loss of libido and inability to work) were worse than psychological depression. **Factors**: disease severity associated with domains of self-control, general health, vitality and psychological well-being (PGWBI) and with depression (BDI) and somatic depression subscale (BDI). Sleep disorders associated with anxiety, depression, self-control, vitality and general psychological well-being (PGWBI) and depression and somatic depression (BDI). Muscle cramps

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					associated with vitality and general psychological well-being (PGWBI). **<u>Regression test:</u>** sleep was associated with psychological well-being, and disease severity was related to poor psychological well-being and depression.
Constant et al. 2005 France	NA, consecutive	185 patients with chronic HCV (17% compensated cirrhosis stage). mean age 45±11 years, 60% males,	Spielberger State-Trait Anxiety Inventory (range 22-80) Visual analogue scale for perceived severity of liver disease (0-100). Attention coping: Monitoring-Blunting Questionnaire.	Trait anxiety	Patients perceived HCV as a severe illness (mean score=74±19). Mild anxiety (mean score=45±11) was similar to the community people. They were more likely to ask for information than ignoring (coping style). Factors using regression: age, hepatologist as a source of information and coping style predicted the variance in perceived HCV severity. Disease severity predicted perceived disease severity.
Cordoba et al. 1998 USA	Prospective, cross-section, Study 1: consecutive, study 2: randomly selected,	44 cirrhotic patients, 50% males, mean age 51±2 y (37-69).	A sleep questionnaire (Sleep clinic at North Western Memorial Hospital), Horn and Ostberg's questionnaire, Beck Depression Inventory (BDI), State Trait Anxiety Inventory (STAI)	Sleep quality, depression and anxiety	47.7% of cirrhotic patients had sleep disturbance and 38.6% of patients with chronic renal failure (CRF) had sleep disturbance. 4.5% of healthy people had sleep disturbance. Night time sleep: short sleep time night, difficulties falling asleep and more frequent nocturnal awakening were higher among two groups of patients than healthy group. Daytime activities were affected by higher episodes of undesired sleepiness and prolonged napping time. No significant difference in cognitive

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					functioning, medical and demographic characteristics between cirrhotic patients who reported satisfactory sleep and cirrhotic who reported unsatisfactory sleep. 26% of cirrhotic had moderate depression and 20% of CRF had depression. Anxiety and depression were higher among patients who had unsatisfactory sleep than who had satisfactory sleep.
Davis et al. 1998 Israel	Descriptive study, NA	80 patients with compensated cirrhosis or chronic liver disease, mean age 45.9±13.9, 51.25% male	Brief Symptom Inventory (BSI) Impact Event Scale (IES) assesses intrusive thinking (unwanted, recurrent and disturbing thoughts)	Irritability, depression, aggression, fear, sensitivity, physical symptoms, appetite, concentration, anxiety and others by using the Brief Symptom Inventory (BSI).	21.25% of patients stopped working because of liver disease. 50% of patients did not have severity of symptoms, 35% of patients had mild-moderate severity of symptoms and 15% of patients had severe symptoms experience. **Factors:** no significant difference in score of depression and Impact Event Scale according to gender, age, marital status, liver diseases duration and medical treatment. Significant association between depression and intrusive thinking. Depression and intrusive thinking were significantly higher among patients who stopped working due to liver disease than patients who were still working. Patients who stopped working due to liver disease were more likely to perceive high symptom severity compared to patients who were still

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					working. Significant negative association between educational level and depression. Basic education had significantly higher levels of avoidance thought compared to highly educated patients.
Teixeira et al. 2005 Brazil	Cross-section, NA	103 cirrhotic and non-cirrhotic patients, mean age 46±9.2, 64.4% men.	Liver Disease Quality of Life 1.0 (LDQOL1.0) second part (12 scales)	Symptom of liver disease, effect of liver disease, concentration, memory, quality of social interaction, health distress, sleep problem, loneliness, hopelessness, stigma of liver disease, sexual functioning and sexual problems.	Patients with decompensated cirrhosis had higher severity of concentration and memory problems and higher problems in sexual function, sleep, and liver disease effect, quality of social interaction, loneliness, hopelessness, health distress and liver disease stigma than patients with compensated cirrhosis.
Dwight et al. 2000 USA	Cross-section, convenience	50 patients with chronic HCV (18.2% had compensated cirrhosis), mean age 44.7±8.32, 58% men.	MAF Fatigue Questionnaire, back depression inventory (BDI).	Depression, fatigue	44% had history of major depression. 16% had depression or anxiety disorders. Depression score was higher among patients with history of depression than without (p=0.009). Depressed were more likely to report many of somatic (physical) symptoms than non-depressed (p=0.004). No significant difference in fatigue score between depressed and none depressed. Depressed reported significant impairment of their daily

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					activities due to fatigue. With controlling demographic characteristics and severity of disease, depression severity was associated with fatigue (beta=0.90, $p<0.0001$, $R^2=0.31$).
Elshahawi et al. 2011 Egypt	Cross-section, case control study, convenient	200 patients with HCV (Child-A),	Mini-International Neuropsychiatric Interview (MINI), Beck Depression Inventory (BDI)	Depression	Patients had higher depression than healthy control groups (n=200). Both groups of patients were receiving (n=100) and were not receiving (n=100) interferon therapy) had depression and no significant difference (MINI) between them. Depression symptom using BDI was higher among patients were receiving interferon than patients were not receiving (p=0.006).
Erim et al. 2010 Germany	Cross-section survey, NA	81 patients with HCV and not receive interferon therapy, mean age 47.1±11.9, 63% males	Beck Depression Inventory Hospital Anxiety and Depression Scale (HADS). Symptom Check List 90-R Sense of Coherence Scale	Depression, anxiety and emotional or psychological strain	Depression and anxiety symptoms were higher among patients than healthy people ($p<0.001$). 11.1% had mild to moderate depression and 22.2% had severe depression. Recently diagnosed, women and singles had higher depression than who had longer known of disease, men and married ($p\leq0.05$). These subscales of the general symptoms distress were higher among patients: somatization, compulsiveness, insecurity in social contact, aggression, phobic anxiety. Sense of coherence and gender was associated with severity and symptoms of depression.
Fritz and Hammer	Cross-section,	75 patients with	Bowel Disease	Depression and	No significant difference in depression

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
2009 Australia	consecutive	cirrhosis. Mean age 57±1.4 (range 24-82), 56% males.	Questionnaire, HAD	anxiety, gastrointestinal (GIT) symptoms	and anxiety among patients with Child-A and Child-B cirrhosis. According to the logistic regression: anxiety and depression were significantly associated with GIT symptoms. Depression and anxiety was higher among patients with dysphagia, while depression was higher among patients with bloating, dysphagia and diarrhea.
Girgrah et al. 2003 Canada	Cross-section, NA	30 patients with cirrhosis, Mean age 54.4±3.1, 93.3% males.	Fatigue assessment inventory (FAI) Centre for epidemiology depression scale (CES-D) Cardiac assessment	Fatigue and depression	Patients with liver cirrhosis had higher levels of fatigue compared to healthy people. Fatigue was higher among non-alcoholic related cirrhosis (i.e. HCV) than alcoholic related cirrhosis. Depression was higher among cirrhotic patients than healthy population. They had mild level of depression. **Factors:** there was no significant association between fatigue or depression and disease severity measuring by Child-Pugh score. Depressive symptoms associated with increase fatigue and poor mental health.
Haag et al. 2008 Germany	Prospective, cross-sectional study, consecutive	204 patients with CLD (49.01% with cirrhosis), 181 patients with FD	HADS	Anxiety and depression	Patients had higher anxiety and depression score compared to healthy blood donors and patients with functional dyspepsia.
Hauser et al. 2004 Germany	Cross-section, consecutive	88 patients (70.4% non-cirrhosis), mean age 48.6%±14.6, 50% females, 70.4% had	CLDQ HADS	Anxiety and depression	39.8% had depression; liver disease patients had higher depression than healthy people.

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
		non-cirrhosis			
Hilsabeck et al. 2005 USA	Correlation study, consecutive	94 patients (40.42% with cirrhosis, mean age 46.2±7.6, 57 males, 40.4% had cirrhosis	The revised version of Piper Fatigue scale, The back Depression Inventory-II	Depression, anxiety	Patients had mild depression symptoms. **Factors**: gender, psychiatric problem, depression, PF, SF and pain were associated significantly with fatigue. While age, marital status, drug abuse and disease stage were not associated with fatigue. **Regression test:** SF (variance=52%), PF (variance=10%), depression (variance=4%) and gender (variance=2%) were associated with fatigue
Kalaitzakis et al. 2006 Sweden	Cross-section, prospective	128 patients with cirrhosis, mean age 57.2±11.5, 61% males	Gastrointestinal symptom rating scale (GSRS)	Different gastrointestinal symptoms.	Comorbidities did not associate with symptom severity. Increased age associated with poor abdominal pain. Gastrointestinal symptom severity associated with hospitalization, severity of cirrhosis, encephalopathy and ascites but not associated with cause of cirrhosis. **Regression test:** gastrointestinal symptoms associated with liver cirrhosis severity, daily lactulose intake, gastrointestinal comorbidities and HRQOL.
Karaivazoglou et al. 2010 Greece	Cross-section, consecutive	84 patients with chronic viral hepatitis Mean age 46±16.7, 65.5% men	Beck depression inventory II, Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F)	Depression, fatigue.	14.3% of the patients had mild depression. Patients with HCV and patients with HBV had the same fatigue level. Depression was not significantly higher among patients with HCV than patients with HBV.

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
Kim et al. 2006a Korea	Cross-section, convenience	129 cirrhotic patients, mean age 53.6±9.28, 80% men	Experience scale to investigate the three dimensions of symptom (frequency, intensity and degree of distress	Disease specific symptoms (many symptoms)	Overall symptoms experience was relatively low. Individual symptoms showed significant association with gender. Females had more severe muscle cramps, bleeding of the gum/bruising more than males. Cause of cirrhosis did not associate with overall symptoms experience. Some (n=18) individual symptoms had significant differences according to cause of cirrhosis such as: bleeding of the gum/bruising that was more among patients with HCV more than others. The number of hospitalizations correlated significantly with overall symptoms experience. Number of hospitalizations correlated significantly with some of individual symptoms such as: nausea/vomiting, muscle cramps, drowsiness, and decrease of concentration.
Kim et al. 2006 Korea	Cross-section, convenience	129 cirrhotic patients, mean age 53.6±9.28, 80% men	Profile of mood states (POMS), Experience scale to investigate the three dimensions of symptom (frequency, intensity and degree of distress).	Different physical symptom (frequency, intensity and degree of distress). Psychological distress (Shin 1996). Depression, anxiety and anger.	Patients with liver cirrhosis had mild to moderate psychological distress (anxiety and depression). Patients with advanced stage of cirrhosis (Child-C) had higher depression and anxiety than compensated cirrhosis (Child- A/B). Fatigue symptom had the highest score followed by muscle cramp, dry mouth, and change in appearance, decrease in memory, anorexia, itching, dyspepsia,

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					drowsiness, abdominal pain, nausea/vomiting, bodily pain and urinary difficulty. **Factors:** only disease severity was associated with score of symptoms experience and psychological distress. Other factors were not associated significantly with symptoms experience or psychological distress, such as: age, gender, educational level, employment status, income, cause of cirrhosis and presence of hepatic carcinoma.
Kraus et al. 2000 Germany	Cross-section, NA	113 patients with chronic HCV (15.9% had cirrhosis-none Child-B/C),	HADS, State Trait Anxiety Inventory (STAI), Feiburg Questionnaire on Coping with Illness (FKV-FQCI)	Emotional state: depression and anxiety, State and trait aspects of anxiety.	22.3% had depression compared to healthy people, 3.2%.15.2% had high anxiety levels compared to healthy people, 6.8%.depression and anxiety were not significantly different between patients on drug use and patients did not. HCV genotype was not related to depression or anxiety scores. Patients above 50 years had higher depression than younger (p=0.02). Patients with early diagnosis (<6 months) had lower score of depression and anxiety than patients knowing their diagnosis more than 5 years (p≤0.003). Patients knowing their diagnosis more than 5 years had lower score of problem solving behaviour than early diagnosed patients. Search for meaning and religiousness was higher in older patients than younger patients (p<0.01).

Author	Methodology			Studied symptoms	Results
	Design/sampling method	**Size and characteristic of sample**	**Tools**		
Marchesini et al. 2001 Italy	Cross-section, consecutive	544 cirrhotic patients, mean age 60±11 (17-91), 63.9% males,	Nottingham Health Profile (NHP): second part, No standardized tool to assess symptoms of pruritus or muscle cramp	pruritus or muscle cramp in the last month.	In men 40% had affected sexual life. In women 52.6% had affected home life and 39.2% had affected social life. The most affected aspect of daily life in men with cirrhosis was sexual life and paid work. Women perceived their social and home life were the most affected aspects of daily life. **Factors:** symptoms of muscle cramps and pruritus associated significantly with sleep, energy, emotional reaction, social isolation, and physical mobility (NHP) and with BP, GH, SF, VT, RE, RP and PF (SF-36).
Moyer et al. 2003 Michigan/USA	Survey, consecutive	214 patients with HCV (27.6% had compensated cirrhosis), Mean age 46.9±7.9 (20-69), 59.3% males	Brief Symptom Index (BSI) Questions to assess Optimism/Pessimism	Emotional functioning (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism.	98 of the patients were realists, 17 were optimists, and 8 were pessimists. African Americans were more optimistic than Caucasians. Pessimists had higher level of emotional distress (BSI) than optimists and realists (p<0.05).Presence of cirrhosis and medical comorbidities were not related to optimism or pessimism. Psychiatric comorbidities was positively associated with pessimism (p=0.01).
Singh et al. 1997 USA	Prospective 100 days for all participants, 18 months for patients after transplantation,	81 cirrhotic patients, median age 47 (22-68), 80 males	Beck Depression Inventory Ways of Coping Scale Recent Events	Depression	64.2% had depression; the majority of depressed patients had a viral infection. There was no significant demographic different between the patients with different causes. Depressed patients

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
	consecutive		Inventory A self-assessed rating of Perceived Quality of Life Karnofsky Performance Score for rating physical functioning		had poorer adaptive coping, quality of life and functional status than no depressed patients. Uncertainty about the future, loss of independency, fearful of being a burden on their care providers, having suicidal thoughts, having no future, being ill frequently and frequent pain were significantly more frequent among depressed patients. Quality of life was poor and depressive symptoms were higher among patients who died during the study than alive. Survival in patients was not transplantation was lower in depressed patients (there was no significant different between the depressed and non-depressed patients in medical or demographic characteristics). Serum bilirubin was significantly higher among non-depressed patients. 21 patients who had not received transplantation during follow up period, the depression and Child-Pugh score were significantly higher and QOL was lower among who died than the survival patients. Depression increased mortality among cirrhotic patients.
Teuber et al. 2008 Germany	Cross-section, NA	215 untreated patients with chronic hepatitis C (16.7% had cirrhosis, Child-A/B),	Fatigue impact scale (FIS)	Fatigue	No significant difference in fatigue between patients with and without cirrhosis. disease stage and gender predicted fatigue level ($p \leq 0.04$)

Author	Methodology			Studied symptoms	Results
	Design/sampling method	**Size and characteristic of sample**	**Tools**		
		mean age 46.7±13.4 (19-79), 57% males			
Toda et al. 2005 Japan	NA, NA	117 patients with chronic viral hepatitis (45.3% with cirrhosis), Age: 19% < 50 years, 28% between 50-59 years, 53% > 60 years.	International index of erectile function (IILEF-5)	Erectile dysfunction	85% of patients with chronic liver disease had erectile dysfunction. The incidence of erectile dysfunction among patients with liver cirrhosis was higher (92%) than patients with chronic liver disease (78%). Patients with chronic liver disease had higher incidence of erectile dysfunction than normal people with the same age (50-59 years). The incidence of erectile dysfunction among age group 50-59 years was not higher than the health group. **Factors:** age and disease stage (Child-Pugh score) associated positively with erectile. PF and SF (SF-36) associated with erectile dysfunction. **Regression test:** age and serum albumin level predicted erectile dysfunction.
van der Plas et al. 2003 Netherlands	Survey, cohort sample	1175 patients with mixed disease stages, mean age 48±12, 43.8% males	Liver Disease Symptom Index (LDS1 2.0), Multidimensional Fatigue Index-20 (MFI-20)	Different symptoms and fatigue symptom	In comparison to healthy people, patients of the patients with chronic liver disease had worse pain. Fatigue was similar among different disease stages and liver transplant groups. Itch, pain in abdomen, sleepiness, and worry about the family situation, decrease appetite, depression, fear and jaundice were highest among patients with decompensated cirrhosis than non-cirrhotic patients. Joint pain was similar

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					for all disease stages. Compensated and decompensated cirrhotic patients had higher memory problems and change in personality than non-cirrhotic patients. Only patients with decompensated cirrhosis had higher financial limitation due to liver disease than other groups of patients. Change in time use as a result of liver disease increased significantly with increasing disease stage. Decreased sexual interest was higher only among patients with decompensated cirrhosis but not significantly different between patients with compensated cirrhosis, non-cirrhosis and transplantation. Patients with decompensated cirrhosis or transplantation had higher severity of decreased sexual activity than other groups. **Symptom limitation:** Patients with decompensated cirrhosis had higher perception of symptom limitations than non-cirrhotic patients.
van der Plas et al. 2004 Netherlands	Survey, Consecutive	1175 patients with mixed disease stages, mean age 48±12, 57.7% males.	Liver Disease Symptom Index (LDS1 2.0), MFI-20	Fatigue and all other symptoms	**Symptom severity:** 71.2% sleepiness during day, 69.6% change of personality, 69.3% change in use of time, 57.5% joint pain, 56.3% memory problems, 51.4% decreased sexual activity, 50.5% worry about family situation, 47.5% depression, 46% decreased sexual interest, 44.8%

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					financial affairs problems, 44.1% fear of liver disease complications, 39.6% itch, 39.3% right abdominal pain, 32.3% decreased appetite and 9.9% jaundice. **Hindrance of daily life due to symptoms:** 85.1% sleepiness during day, 83.8% joint pain, 77.6% depression, 71.4% decreased appetite, 66.6% worry about the family, 63.1% pain in right upper abdomen, 50.5% itch and 41.1% jaundice.
van der Plas et al. 2007 Netherlands	Cross-section, Observational study, cohort sample.	918 patients with mixed stages of disease, mean age 49±13, 58.5% women,	Liver Disease Symptom Index (LDS1 2.0), MFI-20	A list of symptoms and fatigue symptom	All groups had worse scores for fatigue than healthy people. Patients with viral hepatitis had higher fatigue than other groups with other causes of disease. Patients with autoimmune hepatitis had lower scores in reduction of activity (subscale of fatigue scale), reduction in motivation than patients with viral hepatitis, but they had the same level of general, physical and mental fatigue. Using the Odd ratio patients with viral hepatitis had a significantly higher odds of reporting severe worry about the family situation than others patients with other causes, had severe depression and severe fear of complications. Severe fear was influenced by gender and comorbidities. Severity of joint pain was significantly higher among patients with hemochromatosis than other

Author	Methodology			Studied symptoms	Results
	Design/sampling method	Size and characteristic of sample	Tools		
					groups. There was significant difference in severity of sleepiness during the day or severity of jaundice between different causes of liver disease. **Hindrance of daily life due to symptoms:** patients with viral hepatitis had higher severity of symptoms hindrance compared to other causes.
Wilson et al. 2010 USA	Cross-section, consecutive	65 patients with HCV (39% had grade IV fibrosis), Average age 49 years	Beck Depression Inventory II (BDI-II)	Depression	**Regression test**: **Factors predicted depression (BDI-II):** religious faith, ability to work, salary, social functioning and reaction to diagnosis, suicide attempt and vitality.
Wu et al. 2012 Taiwan	Correlation study, NA	40 cirrhotic patients mean age 63.3±14.02 (29-80 years), 77.5% males,	Fatigue Symptom Inventory (FSI), Seven-day Physical Activity Recall (seven-day PAR)	Fatigue: intensity, duration of fatigue and interference of fatigue on daily life (QOL).	The total mean score of subscale of fatigue interference QOL was 29.80±10.80 (possible scale score 0-70). 50% of the patients suffered from afternoon fatigue more than morning time. **Factors**: no significant association between disease stage, cause and normality of laboratory tests and fatigue (level or interference with QOL). Men and married significantly had higher physical activity than women and unmarried. No significant difference in levels of physical activities between patients according to disease stage and cause of cirrhosis. Patients with normal haemoglobin, haematocrit and white blood cells level had higher levels of physical activity than patients with

Author	Methodology			Studied symptoms	Results
	Design/sampling method	**Size and characteristic of sample**	**Tools**		
					abnormal values. Fatigue was negatively associated with level of physical activity.
Zandi et al. 2005 Iran	Quasi-experimental study control, Longitudinal cases register method random assignment to divide the sample into 20 control and 20 study groups	40 cirrhotic patients, Experimental group: age 40.8±12.5 (18-65 years), males 50%,	Self-Report Questionnaire, Need Assessment Questionnaire.	List of symptoms and needs	**Before the program:** the most reported educational needs among cirrhotic patients were: 70% controlling of abdominal distension, curative ways in cirrhosis (treatable or not/uncertainty), 65% ways of controlling fatigue, 60% principle of care and proper medications, 55% worry, 50% controlling pruritus and fatigue, ways to decrease muscle cramps, dry mouth, and dyspnoea, patterns of activity, rest, and sleep, 45% routes of transmission as well as diagnostic tests, 40% diagnostic procedures. Over three months of follow up these educational needs were reported by the patients higher than the other needs: 95% nutrition, 60% fatigue, anxiety and depression.

NA: not available

3.7 INSTRUMENTS USED TO ASSESS SYMPTOMS EXPERIENCE

Table 3-8 shows instruments that were used to assess a specific symptom such as depression; two related symptoms such as depression and anxiety or the full range of symptoms. A few studies assessed the full range of symptoms (Zandi et al. 2005; Kim et al. 2006 and 2006a; van der Plas et al. 2003, 2004 and 2007), while three tools were used to measure the full range of symptoms experience among patients with cirrhosis. They were: (1) experience scale to investigate the three dimensions of symptoms (frequency, intensity and degree of distress) (Kim et al. 2006 and 2006a), (2) Needs Assessment Questionnaire (Zandi et al. 2005). and (3) Liver Disease Symptom Index (LDS1-2.0) (van der Plas et al. 2003, 2004 and 2007).

The instruments vary in symptom content and extent of psychometric validation. Although the experience scale, which was developed and used by Kim et al. (2006) is a multidimensional tool that can measure the full range of symptoms experience from three aspects: frequency, intensity and distress, its psychometric properties are questionable. Kim et al. (2006) mentioned that the experience scale was developed based on the theory of unpleasant symptoms, without giving details about its development and construct validity. The second tool is the Need Assessment Questionnaire that was used to determine cirrhotic patients' need to direct the development of a self-care educational program (Zandi et al. 2005). Although the Need Assessment Questionnaire was useful in finding many symptoms that cirrhotic patients experienced, question response was as "yes" or "no" only. This means that this tool could not determine the severity of the symptom. Also, its validity and reliability were not mentioned or how it was constructed. On the other hand, the Liver Disease Symptom Index-2.0 is a psychometrically tested tool that was developed to assess liver disease specific HRQOL from two aspects: severity of symptoms and hindrance of daily activities due to symptoms (van der Plas et al. 2004).

3.8 SYMPTOMS EXPERIENCE IN CIRRHOTIC PATIENTS

The majority of the reviewed studies assessed only one symptom, two or three related symptoms, such as depression, anxiety, sleep and/or fatigue (Singh et al. 1997; Cordoba et al. 1998; Marchesini et al. 2001; Girgrah et al. 2003; Bianchi et al. 2005; Wu et al. 2012). Two studies assessed the full range of gastrointestinal symptoms (Kalaitzakis et al. 2006; Fritz and Hammer 2009). One paper indirectly reported a list of symptoms but in terms of patients' needs to assess the impact of a self-care program on improving cirrhotic patients' QOL (Zandi et al. 2005). Interestingly, only one paper investigated the socio-economic and emotional burden due to cirrhosis and hepatic encephalopathy on elderly patients and their caregivers (Bajaj 2008). Only van der Plas et al. (2003, 2004, and 2007) and Kim et al. (2006 and 2006a) assessed the full range of physical and psychosocial factors.

According to the reviewed studies, depression, anxiety and fatigue were the most commonly investigated symptoms. However, little is known about the full range of symptoms that patients with liver disease, particularly cirrhotic patients experience. Only the study by Kim et al. (2006 and 2006a) focused on exploring the full range of symptoms of cirrhotic patients. Van der Plas et al. (2003, 2004, and 2007) investigated the full range of symptoms but in mixed disease stages (non-cirrhotic, compensated, decompensated cirrhosis and post transplantation). Only one study examined symptoms of depression in patients with HCV (Child-A) and were on antiviral therapy (Elshahawi et al. 2011). Therefore, there is a need to study the full symptoms experience in liver cirrhotic patients in Egypt and elsewhere.

3.8.1 Types of Symptoms Experienced

Research has demonstrated that patients with liver cirrhosis experience a variety of symptoms (Table 3-8). However, the majority of the reviewed studies focused on assessing the severity of the physical symptoms such as gastrointestinal symptoms (Kalaitzaki et al. 2006; Fritz and Hammer 2009), or psychosocial symptoms such as depression and anxiety or psychological distress (Singh et al. 1997; Cordoba et al. 1998; Kim et al. 2006, Kim et al. 2006a; Fritz and Hammer 2009). Few of these studies assessed the general symptoms experience of patients with chronic liver disease (van der Plas et al. 2003, 2004 and 2007) and cirrhosis (Kim et al. 2006 and 2006a) in terms of prevalence, severity and distress.

3.8.1.1 Symptom Prevalence in Cirrhotic Patients

There were discrepancies between the studies in terms of assessed symptoms, methods of reporting the findings (e.g. reporting the score of symptoms (Kim et al. 2006 and 2006a) or reporting prevalence (van der Plas et al. 2004, Zandi et al. 2005). Therefore, to identify symptom prevalence among patients with liver cirrhosis, studies that provided prevalence of one or more experienced symptom were given priority. The other studies will be used to support the discussion.

The most commonly investigated symptom in liver disease patients is depression. Patients with liver disease were observed to have a high level of depression. Cirrhotic patients had a higher level of depression than healthy people (Girgrah et al. 2003), while patients with decompensated cirrhosis had a higher depression and anxiety level than patients with compensated cirrhosis (Bianchi et al. 2003; Kim et al. 2006 and 2006a). Overall 56.7% of cirrhotic patients had depression, 40.7% had mild-moderate depression, 10% had moderate to severe depression and 6% had severe to extremely severe depression (Bianchi et al. 2005). Depressed patients were more likely to die than non-depressed patients in the longitudinal study on death rate among 81 American patients with advanced stage of liver cirrhosis who were waiting for liver transplantation (Singh et al. 1997). In relation to other symptoms, Bianchi et al. (2005) showed that somatic symptoms (i.e. sleep disorders, fatigue, loss of appetite and weight, body image, loss of libido and inability to work) were more debilitating than psychological depression in cirrhotic patients. Kim et al. in 2006 found that patients with cirrhosis had mild to moderate psychological distress (i.e. anxiety and depression), where decompensated cirrhotic patients were more likely to have psychological distress.

Sleepiness during the day was found to be the most frequently reported symptom by two thirds of the patients (71.2%), while depression was reported by less than half of the patients (47.5%) (van der Plas et al. 2004). Cordoba et al. (1998) assessed the prevalence of sleep disturbance and its related factors in 44 cirrhotic patients without encephalopathy, comparing them to a matched group of patients with chronic renal failure. They found that patients with cirrhosis and patients with chronic renal failure had a higher prevalence of sleep disturbance. About 47.7% of cirrhotic patients had sleep disturbance, while 38.6% of patients with chronic renal failure had sleep disturbance but only 4.5% of healthy people had sleep disturbance. The most common problems related to sleep disturbance were short sleeping time at night, difficulties falling asleep and more frequent nocturnal awakening.

It has been found that depression and anxiety (using Beck Depression Inventory and State Trait Anxiety Inventory) were higher among patients with unsatisfactory sleep than with satisfactory sleep, although there were no significant differences between the two groups' socio-demographic and medical characteristics or cognitive functioning (Cordoba et al. 1998). Similarly, Bianchi et al. (2003) found that depression was significantly associated with increased sleeping disorders in cirrhotic patients. This association between sleep disorders and depression needs further research to explain the relationship as well as the mechanism between depression and sleeping problems. However, the results from this study should be considered with caution as few details were given about the tools used to assess the symptoms of sleeping disorder so these findings may be unreliable and invalid. The cross-sectional design also limited assessment of causal associations.

On the other hand, in the cross-sectional study by Kim et al. (2006 and 2006a) to assess symptoms experience and its association with psychological distress and QOL in 129 Korean patients with cirrhosis, the results showed that fatigue had the highest mean score followed by muscle cramp, dry mouth, change in appearance,…etc. Fatigue was also reported as being higher among cirrhotic patients than in healthy people, particularly in patients with non-alcoholic cirrhosis (i.e. HCV) (Girgrah et al. 2003). Half of the patients (20/40) suffered from afternoon fatigue and the average number of affected days due to fatigue was 3.15 (Wu et al. 2012).

In particular, the findings from the few observational cross-sectional studies that have examined general symptoms experience in patients with liver cirrhosis (van der Plas et al. 2004; Zandi et al. 2005; Kim et al. 2006) offer a valuable insight into the importance of assessing symptom prevalence. However, there are inconsistencies relating to symptom prevalence in the studies by van der Plas et al. (2003); Zandi et al. (2005) and Kim et al. (2006a). These may be due to the different measurements used, which make it difficult to compare the results. Also, it is impossible to generalize these results across countries, particularly to Egypt, which is culturally different and has a different healthcare system. Therefore, investigating the symptom prevalence in Egyptian patients with liver cirrhosis is urgently needed.

3.8.1.2 Hindrance of daily life due to symptoms

Although assessing the prevalence of symptoms is important to determine those most experienced among a specific group of patients, assessing symptom distress is also essential; because it is the dimension of symptom experience that determines patient suffering. Studying symptom distress can provide important and complementary information to symptom frequency to gain more insight into symptom experience and its impact on the patient's daily life and social activities (Tishelman et al. 2007).

In 2001, Marchesini et al. investigated 544 Italian patients with cirrhosis using two generic HRQOL tools (SF-36 and NHP).They found that the most affected aspect of daily life in men was sexual life and paid work. Women perceived their social and home life as the most affected aspect. It was also found that with an increased level of symptom severity such as muscle cramp and pruritus the impairment of social and daily activities also increased resulting in social isolation, sleeping problems, low vitality, emotional distress and physical disability (using NHP) (Marchesini et al. 2001). Fatigue interference in the QOL was also reported in cirrhotic patients. The total mean score of the subscale of fatigue interference QOL was 29.80±10.80 (possible scale score 0-70). This means that the general fatigue interference in the QOL was low, although the two domains of interference of fatigue on activity level and on normal work activity were the highest scores (5.20 and 4.98 out of 0-10) (Wu et al. 2012). Cirrhotic patients also had limitations in their daytime activities as a result of higher episodes of undesired sleepiness and prolonged napping times (Cordoba et al. 1998).

The study by van der Plas et al. (2004) was the only identified study that investigated prevalence of both severity and hindrance of symptoms in liver disease patients. They found that 71.2% of patients reported sleepiness during the day while 83.8% complained of joint pain hindering their daily activities. In the same study, the symptom of worry about the family situation was the third in symptom severity; and in hindrance of daily activities. While the symptom of itch was the fifth according to severity, however it became the seventh reported symptom that affected daily activities. Therefore, the prevalence of symptoms distress may be different to the prevalence of symptoms severity. In other words, symptoms may be severe but not affect the patients' daily life, while other symptoms may be mild but have a strong impact on the patients' daily activities. This suggests that although assessing prevalence of symptom severity is important, assessing prevalence of symptom distress is most important, as it reflects the most affected areas in patients’ social and daily activities. These findings on cirrhotic patients cannot be generalised because the studies had heterogeneous patients at different disease stages such as non-cirrhosis, compensated cirrhosis, decompensated cirrhosis and post transplantation. Also, the patients were recruited from the community where they were on databases for the liver disease association. Therefore, the prevalence of symptoms experience in cirrhotic patients in a clinical setting needs further research.

3.9 SELF-CARE AND SELF-MANAGEMENT

3.9.1 What is Self-Care and Self-Management?

Assessing and caring for symptoms is the responsibility of patients and healthcare providers. Two terms that are widely reported in the literature: self-care (SC) and self-management (SM) as essential for caring for patients with chronic diseases. *SC and SM appear as increasingly key concepts in clinical, research and policy literatures* (Jones et al. 2011, p. 175). However, there is no general census about their definition (Glasgow et al. 2003; Godfrey et al. 2011), although they are not similar (Jones et al. 2011).

In brief, *self-care* is a broad concept that includes '*the care of oneself' it may be performed in response to illness, injury, longstanding chronic conditions, or disability, and for a myriad of different reasons such as recovery; maintenance of health, prevention; or in the case of personal care – the preservation of self. Self-care can be self-instigated or follow a prescribed regime, and the process of care may be performed by individuals themselves or by a caregiver (professional, formal or informal)" (*Godfrey et al. 2011, p. 3).However, *self-management* is ''simple patient education or skills training, in that they are designed to allow people with chronic conditions to take an active part in the management of their own condition'' (Foster et al. 2007). Self-management refers to activities that are undertaken by individuals with chronic conditions with support from the health care providers (Health Department (HD), UK 2006). These activities are treating symptoms, coping with bio-psychosocial impacts of the disease to avoid deterioration in health condition and changing one’s lifestyle to adapt to the chronic disease and to keep the illness under control (Barlow et al. 2002; Glasgow et al. 2003).

Therefore, self-care is a very broad term, and self-management is a sub-set of the term self-care (Tomkins and Collins 2009). Tomkins and Collins (2009, p.5) suggest that “Outside hospitals or care homes, everyone self-cares all of the time but not everyone self-cares optimally”. Therefore, self-management strategies can support patients with chronic disease to improve their knowledge and skills that they need to maintain or promote their health condition and avoid deterioration under the supervision of healthcare professional.

3.10 SELF-CARE AND SELF-MANAGEMENT IN CIRRHOTIC PATIENTS

Depressed cirrhotic patients have poorer adaptive coping, QOL and functional status than non-depressed patients. They also face uncertainty about the future, loss of independence, fear of being a burden to their care providers; have suicidal thoughts, have no future, are ill frequently and frequently in pain (Singh et al. 1997). Therefore, because liver cirrhosis is a chronic and incurable disease it is important to look after these patients’ QOL by studying their health needs and symptoms experience in order to support them and provide the required care. The first step towards starting the caring process is to aim to improve these patients’ HRQOL and daily activities by assessing their symptoms experience and caring for it by improving their self-care strategies.

There is a wide interest in studying and practising self-care or self-management among people with various chronic illnesses to improve their quality of life (DeWalt et al. 2006; Foster et al. 2007; Davies and Batehup 2010). However, exploring symptoms experience and caring for patients with liver cirrhosis is still in its infancy and needs more attention from healthcare providers. The literature search yielded only one intervention study (Zandi et al. 2005) although there was no limit on design during the database search.

Zandi’s study is the only research that has developed a self-care program for cirrhotic patients based on their preferences. Zandi et al. (2005) developed a tool to assess these patients’ needs in which they asked the patients about the information they wanted and the time at which it was offered to them. This educational self-care program took three months of demonstration and follow up. The results showed that there was no significant difference between the two groups before the program in socio-demographic and clinical characteristics and in the domains of HRQOL (CLDQ). However, the studied group had a significant improvement in abdominal symptoms, fatigue, systemic symptoms, activity, worry and emotional domains, without significant changes in disease severity after the program. Furthermore, the HRQOL of the control group had significantly declined three months later in these domains: activity, worry and emotional status. These findings suggest that the control group had significantly more emotional problems, anxiety and activity impairment than the studied group who received the self-care program (Zandi et al. 2005). Therefore, studying symptoms experience and the patients' educational needs are essential for developing an intervention program to improve their HRQOL.

SECTION III: SOCIAL SUPPORT

Only three studies of social support among patients with liver disease were found (Blasiole et al. 2006; Erim et al. 2010; Wilson et al. 2010). These studies were descriptive, cross-sectional designs, and conducted among patients with HCV in the USA and Germany. Table 3-9 summaries these studies.

3.11 PERCEIVED SUPPORT IN LIVER DISEASE PATIENTS

Although the studies had inconsistencies in terms of methodology, conceptualization of social support and wide differences in participants' characteristics, patients with HCV (73%) reported that they had a supportive environment (Blasiole et al. 2006). Similarly, Wilson et al. (2010) investigated patients (66% males) with chronic HCV using one question to assess their social support "*do you have one or more people in your life who provide support for you when you are having a bad day*?". They found that the majority of patients (64/65) had people available during hard times. Cohen and Syme (1985) classified social support into two categories: (1) structured support that refers to the existence of relationships (i.e. marital status and number of networks), and (2) functional support that refers to interpersonal relationships that focus on providing particular functions such as care, material support and/or emotional support. Wilson et al (2010) only assessed structural support, but not functional support. Therefore, only the quantity of people available during hard times was assessed, but not the type, source and quality of this social support. Whether the patients were satisfied with the available support was not measured.

Erim et al. (2010) used a social support questionnaire (F-SOZU: 54 items, 4 scales and overall score) to examine the types of social support "emotional support, instrumental support, social integration and social strain" among patients with HCV (non-cirrhotic patients). Using overall score of perceived social support, the results showed that patients with HCV had higher levels of support than healthy people.

These results need further investigation in cirrhotic patients, since the majority of the patients were males (63%) in middle age (mean age 47.1±11.9) and were in the early stages of the disease and still able to do their work and daily activities. Unfortunately, the author did not give detailed results about how these patients perceived the different types of social support and which type of support was more beneficial for liver disease patients. Therefore, the representativeness of the results for the general population with liver disease, particularly with liver cirrhosis is uncertain. Besides, because culture and environment maybe important factors in perceived social support and their effects, it is essential to be cautious in generalizing these results to other cultures such as the Middle East. However, Erim et al's (2010) study contributed evidence about the relationship between anxiety and depression and perceived social support among patients with HCV. Low perceived support associated significantly with increasing severity and symptomatology of depression and anxiety; however, it did not associate any of them in multivariate analysis.

3.12 FACTORS ASSOCIATED WITH PERCEIVED SOCIAL SUPPORT

A few of the identified studies investigated factors associated with perceived social support among patients with liver disease (Blasiole et al. 2006; Erim et al. 2010). Many factors were associated with perceived social support including marital status, employment status, psychiatric comorbidities, time of interview (pre, during or post HCV-antiviral therapy) and method of getting infection (i.e. drug injection) (Blasiole et al. 2006). Age, gender (Blasiole et al. 2006; Erim et al. 2010), ethnicity, education, area of residence (rural vs. urban), cirrhosis and Child-Pugh score did not associate with social support (Blasiole et al. 2006). Therefore, it seems that marital status, employment status, hope in medical treatment and presence of psychiatric comorbidities may be important factors in perceived social support. Therefore, these factors should be considered in future studies, to develop the evidence for associations between socio-demographic and medical characteristics and perceived social support in liver disease patients, particularly cirrhotic patients.

3.13 SOURCES OF SUPPORT AMONG LIVER DISEASE PATIENTS

No study had investigated the perceived social support from a partner, family and others. Social support, particularly from a partner, family and friends may be essential when living with a life threatening disease that also affects the patient’s social life and daily activities. Cohen and Syme (1985) stated that social support can work as a buffer against the effects of stressors such as chronic disease. Therefore, it is essential to measure the perceived social support in patients with liver cirrhosis in Egypt to increase the knowledge of healthcare providers of the main sources of support that can affect these patients' HRQOL.

Table 3-9: Studies examining social support in liver disease patients

Authors/country	Design/Aim	Sample/Participants characteristic	Tools	Key results
Erim et al. 2010 Germany	**Design:** cross-section survey **Aim**: to examine depression and other psychopathological symptoms in HCV patients and to analyse how sense of coherence and social support influence them. Hypothesis: 1) patients with HCV differ in depression and psychological symptoms from normal population. 2) Higher level of sense of coherence and social support would be related to lower levels of anxiety and depression.	81 patients who met the inclusion criteria All had HCV, 63% males, mean age 47.1±11.9 chronically infected with HCV mean of years= 7.38±6.04. 25.9% had previous psychiatric therapy, 49.4% had co-morbidities, 49.4% had experience of receiving interferon therapy, and 30% had terminated interferon therapy due to side effects of anti-viral therapy.	• Social support questionnaire (F-SOZU) • Beck Depression Inventory • Hospital Anxiety and Depression Scale (HADS). • Symptom Check List 90-R • Sense of Coherence Scale	Patients with HCV had higher social support than healthy people. No association between age, gender and social support. Depressive and anxiety symptoms were higher among patients with chronic hepatitis C than norm. No significant association between socio-demographic characteristics, age, gender, marital and employment status and present of anxiety or depression. Sense of coherence was similar to norm. No association between sense of coherence and age and gender. These subscales of the general symptoms distress were higher among patients with CHV: somatization, compulsiveness, insecurity in social contact, aggression/hostility, phobic anxiety and psychoticism. Social support was significantly associated with depression and anxiety, but was not associated with them in the regression analysis. Sense of coherence (low) and gender (women) was associated with increasing depression severity and symptomatology. Employment status was not associated with depression severity or symptomatology in the regression analysis.
Wilson et al. 2010 USA	**Design:** Cross-section **Aim:** to assess the prevalence of HCV related depression in outpatients setting; assess the importance of biological, psychological and social factors in predicting	65 of consecutive sample All had HCV, 66% males, 55% married, 17% see a mental health provider, 18% currently receiving	• SF-36 (VT, SF and MH scales), • Beck Depression Inventory II (BDI-II) • Social functioning was assessed by using (one item)	98.5% of the patients said that they had social support. Social functioning, ability to work, income, and vitality could significantly associate with mental health. Religious faith, social functioning, reaction to diagnosis and vitality predicted depression. Age, gender, education and marital status did not associate with mental health domains (SF-36).

Authors/country	Design/Aim	Sample/Participants characteristic	Tools	Key results
	depression among patients with HCV.	interferon therapy. 39% had grade IV fibrosis.	and Scale of social functioning in SF-36.	
Blasiole et al. 2006 USA	**Design:** cross-sectional mixed method (quantitative and qualitative) **Aim:** To assess the social support and cause of social difficulties using this hypothesis: Poor social support among patients with HCV is related to emotional and physical problems	342 who met the inclusion criteria All had HCV, 62.6% males, Mean age 45.2±9.2, 62.0% live with partner, 35% currently unemployed, 64.3% rural residence, 26.4% had psychiatric co-morbidity, 23.8% had cirrhosis and 62.3% had HCV due to drug injection.	- HADS. - Sickness Impact Profile - Carlson Comorbidity Index - Child-Pugh score	73% had supportive environment. 45% had loss of relationship due to HCV, 56% had problems with family interaction due to HCV, 12% lost at least one friend because of HCV, 8% had social isolation feeling negativity from others, 7% have decided to withdraw from social activities with family or friends. Financial burden due to loss of work, high cost of anti-viral therapy, without insurance. **Causes of impaired social support:** Afraid to infect others, feeling discrimination, disease stress (concern about family condition), and fatigue. **Factors associated with perceived supportive environment** (who perceived high support): marital status (married), current employment status (employed), interview to treatment status (after therapy), number of psychiatric comorbidity (low), route of infection with HCV (non-drugs injection), depression (low), anxiety (low), physical symptoms (low) and psychosocial disturbances (low).

3.14 CONCLUSION

There is a growing interest in investigating the perceived HRQOL and QOL in patients with liver disease (various stages). Studies that have been carried out reached the same conclusion that patients with liver cirrhosis have a poorer generic and disease specific HRQOL than the normal population. However, the literature is not clear about which dimension of HRQOL are most affected, which may be related to differences in the cultural background and healthcare systems. Common factors that influence HRQOL have been identified, including demographic factors, socio-economic status, and clinical factors such as comorbidities. However, the heterogeneity of the participants in most of the previous studies is problematic regarding the generalisability of these studies' findings on patients with liver cirrhosis in Egypt particularly relating to perceived poor HRQOL. There is a concern regarding the composition of the samples in many of the studies, as most of the subjects were males, with a high standard of living and a high level of education. Ultimately, this makes generalisability of these findings to other groups of patients with liver cirrhosis and those from other cultural and educational backgrounds, for example patients in Egypt, questionable.

Thus, based on the literature review this study aims to: (1) describe HRQOL of Egyptian liver cirrhotic patients and to identify and evaluate the factors associated with (HRQOL) physical and mental health domains, (2) explore and describe experienced symptoms (prevalence, severity and hindrance) in Egyptian cirrhotic patients and to identify and evaluate factors associated with symptoms severity and symptoms hindrance (distress) and (3) explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to identify and evaluate factors associated with general perceived social support.

This will help healthcare professionals and health policy makers in Egypt to recognize the psychosocial problems of these patients, in the hope that healthcare services in Egypt will shift from physician-centred to patient-centred care and will integrate both the biomedical and the psychosocial models together during care for these patients.

4 CHAPTER 4- METHODOLOGY

This chapter presents justification for the philosophical paradigm, the methodological approach and the theoretical framework that were adopted in this study. Then, the research design, the population and sampling, and clinical settings are described as well as the procedures for data collection including an explanation of the measurements used and the recruitment strategy. Finally, ethical approval and ethical considerations are discussed.

4.1 THE PHILOSOPHICAL PARADIGM AND RESEARCH APPROACH

Although observing and explaining the world around us is part of human nature, daily observations are usually unsystematic and part of an aimless process that is carried out involuntarily. Observations carried out by researchers should be specific, objective, well focused and systematic to produce valid and replicable data (Black 1999). This study used a systematic research method to collect valid data in a systematic way in order to confirm existing knowledge and to create new knowledge (Langford 2001).

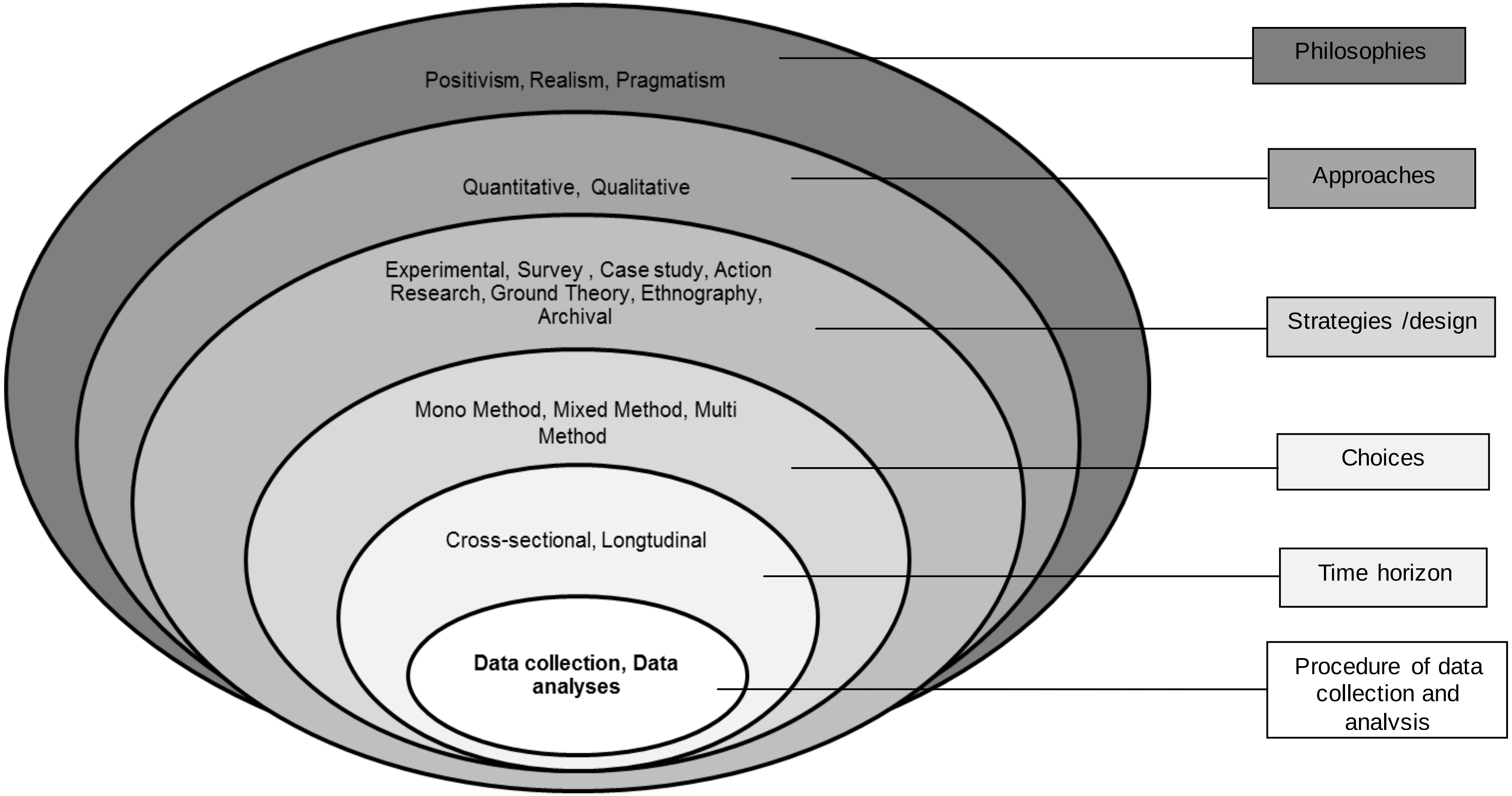
The research Onion (Diagram 4-1) was adapted from Saunders et al. (2009). It consists of many layers that reflect the steps of the research process, which were followed in this study, (1) finding the philosophical paradigm, (2) selecting the research method, (3) selecting the research design, (4) determining the choices, (5) determining the time horizon according to the time allocated to the research, and (6) planning the data collection procedure and data analysis process.

4.1.1 Philosophical Paradigm

The term *paradigm* refers to the general philosophical assumptions or view of an individual about the nature of the world and how its phenomena (i.e. experience or events) can be understood (Maxwell 1998; Broom and Willis 2007). Buetow (2007) claimed that research is a journey towards knowledge and understanding and a roadmap is essential to direct and guide this journey. Therefore, a paradigm is considered the roadmap that directs the research journey.

There are different philosophical positions (paradigms) that represent very different ideas about reality and how knowledge can be gained, for example positivism and interpretivism (Saunders et al. 2009). Each of these paradigms includes a specific methodological strategy linked to the stated assumptions (Broom and Willis 2007). Therefore, the relationship between the research philosophy and the research method is essential; because it allows the researcher to decide the research approach and the research method. It is also useful for recognizing any limitations which may disrupt the research (Easterby-Smith et al. 2002). A positivist paradigm, also called logical positivism (deductive approach) was adopted in this study. Positivism is based on the logical objectivity of studying the phenomena of interest and withholding personal beliefs and biases to avoid contamination of the phenomena under investigation (Remenyi et al. 1998; Polit and Beck 2008). Remenyi et al., (1998, p.33) maintain that *“the researcher is independent and neither affects nor is affected by the subject of the research”*. The fundamental assumption of the positivist paradigm is that nature is basically ordered and phenomena are not random events, but rather have antecedent causes, e.g. more than one factor can potentially be the cause of a perceived poor health status.

Diagram 4-1: The “Research Onion” adapted from Saunders et al. 2009, p.108



4.1.2 Research Approach

Quantitative research has been defined as *'a formal, objective, systematic process for generating numerical information about the world',* which '*is conducted to describe new situations, events, or concepts; examine relationships among variables; and determine the effectiveness of treatments in the world*' (Burns and Grove 2011, p. 34). Quantitative research assumes that phenomena are stable and can be predicted, and therefore they can be measured (Topping 2010). The main outcomes in this study can be measured through measurements, like the Health-Related Quality of Life (HRQOL) and symptoms; therefore, a quantitative approach was felt to be appropriate, primarily to find the frequency and association between factors, but also to develop a predictive model of factors that are related to these outcomes.

Furthermore, with the quantitative approach it is easier to minimize bias and to maintain an objective view while studying the phenomena (Reichardt and Rallis 1994) to develop valid and reliable results (Topping 2010). Grey (2009, p. 201) maintains that *"quantitative research emanates from an objectivist position which holds that reality exists independently of the researcher the truth is "out there*". Therefore, it is a highly structured method that can allow future replication of a study for comparison and confirmation, and development of inferences for future research (Gill and Johnson, 2002; Topping 2010).

The quantitative approach is the most common research method and is an essential part of health services research (Meadows 2003). In Egypt, this approach is the dominant and best-known research approach among health researchers (nurses and doctors). Therefore adopting this approach to conduct this study was most appropriate to communicate the results to healthcare providers as well as to health policy makers.

4.2 THEORETICAL FRAMEWORK

4.2.1 Importance of Using a Theoretical Framework

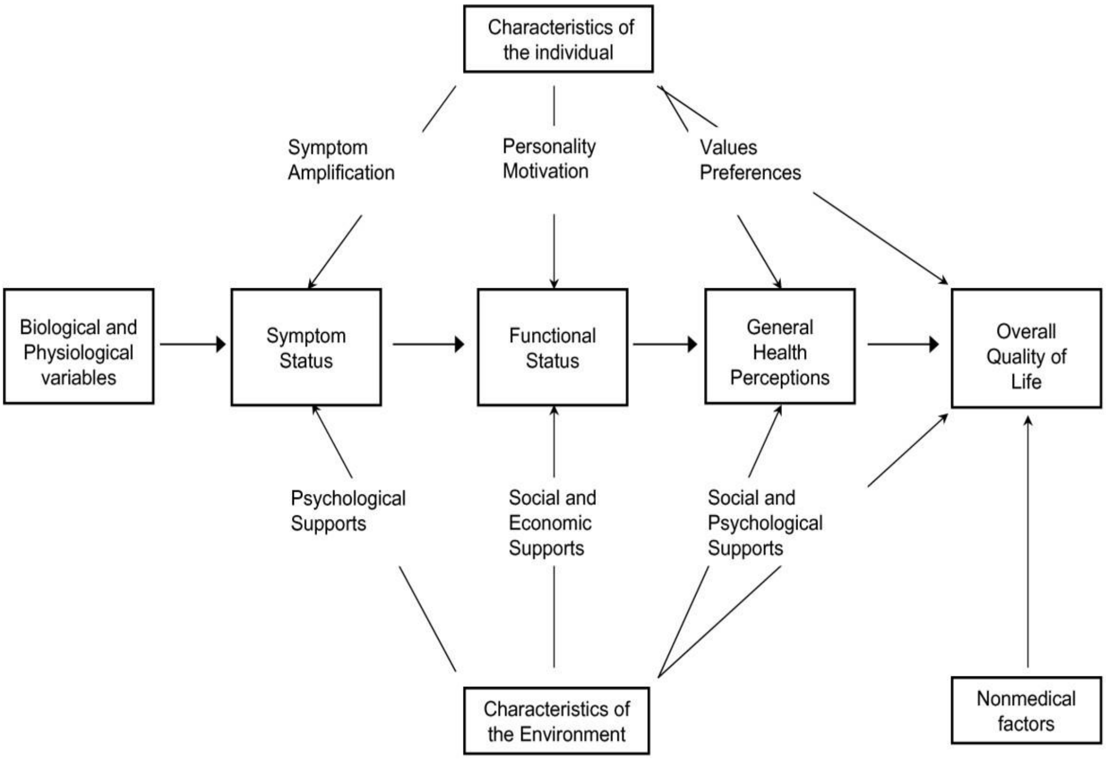
Many researchers acknowledge the importance of using a theoretical model as a framework to develop a research study because it can assist in investigating a specific phenomenon in an organized context (Fawcett and Downs 1992*;* Vallerand and Payne 2003; Burns and Grove 2003; Sousa and Kwok 2006). Moreover, using a tested theoretical framework can help the researcher to specify research concepts, the definitions of these concepts and the appropriate measurements for investigating these concepts (Vallerand and Payne 2003), as well as to specify and direct the relationship between these concepts (Wilson and Cleary 1995). To my knowledge, the previous studies used the theoretical framework of HRQOL outcomes to clarify the predictors of HRQOL among patients with chronic disease (Sousa and Kwok 2006).

In fact, the theoretical framework is a logical structure model of related concepts that can explain a specific phenomenon of interest by expressing assumptions and developing a philosophical view around this phenomenon (Burns and Grove 2003). Fawcett and Downs (1992) maintain that the theoretical model *'seeks to identify a phenomenon, discover its dimensions or characteristics, or specify the relationship between the dimensions'* (p. 4). Vallerand et al. (1998) also state that using a tested theoretical model can enhance the applicability of the HRQOL concept as a reliable and valid outcome measure. As a result, it can improve the utilization of study findings in a particular area of health practice (Burns and Grove 2003).

4.2.2 The Conceptual Framework of HRQOL Outcomes

The conceptual framework of HRQOL outcomes (Wilson and Cleary 1995) (Diagram 4-2) was used as a theoretical guide to: (1) write the research questions, (2) identify and define the variables, (3) identify the mediator variables, (4) direct the process of statistical analysis and (5) interpret the study findings. This framework integrates the two common models used for assessing health status: the biomedical model and the psychosocial model. The biomedical model focuses on assessing the aetiology of disease as well as physiological and clinical outcomes. It is useful to determine a medical diagnosis and medical treatment. The psychosocial model focuses on assessing different aspects of health status and overall quality of life (QOL/well-being). The framework addresses the difference between the clinical reported outcomes (CRO) and the patient reported outcomes (PRO), stressing the importance of investigating health status and QOL by using PRO. Therefore, patient preferences are the core of this framework and play an important role in understanding the HRQOL of patients.

Diagram 4-2**:** The original HRQOL outcomes model adopted from Wilson and Cleary (1995, p.60)



4.2.3 Components of the HRQOL Outcomes Model

The HRQOL outcomes model itself is quite complex. It acknowledges that health exists on a continuum from simple to complex outcomes with five determinants, each having multiple variables (Peterson and Bredow 2009). The five levels of health outcomes (Diagram 4-2) are:

<u>The first level</u> focuses on the biophysiological variables such as biological factors, medical history, disease severity as well as medical diagnosis. The first level is known as the CRO (or traditional clinical variables) that are commonly used in clinical practice.

The second level focuses on symptom status such as physical and psychological symptoms. The physical symptoms relate to feelings about the physical status (body); while psychological symptoms relate to feelings of fear, worry and frustration (mind).

There are many definitions of symptom. According to the model, a symptom is defined as *"a patient's perception of an abnormal physical, emotional or cognitive status*" (Wilson and Cleary 1995: 61). It is also defined as *'a subjective experience reflecting changes in the biopsychosocial functioning, sensations or cognition"* (Dodd et al. 2001, p. 669)*.* Lenz et al. (1997) define symptom as a '*perceived indicator of change in normal functioning as experienced by patients'*. The common theme between these definitions is that a symptom is a subjective feeling which reflects a change in normal functioning that may be physical, psychological and social. Also, a symptom is characterized by subjectivity and multidimensionality (Armstrong 2003).

Assessing symptom status is the first level of PRO; when healthcare providers assess a patient's symptom, the focus of caring shifts from caring for a specific part (organ) to caring for the person as a whole (holistic approach) (Wilson and Cleary 1995). PRO is an umbrella term which covers single dimensional or multidimensional measures of symptom, HRQOL and overall satisfaction (Asadi-Lari et al. 2004; Committee for Medicinal Products for Human Use (CHMP) 2005). Fallowfield (1990, pp. 22-23) confirmed that *'Healthy psychological functioning is a freedom from anxiety or depression and the ability to adapt and adjust to different* *illness states, which is crucial for the maintenance of a good QOL'.* Thus, evaluating symptoms is the essence of evaluating patients' perceptions of their health status. Investigating symptom status by simply asking the patient what s/he feels can be a simple and convenient method of measuring the patient's perceptions about his/her functional health status (Fairclough 2002).

The third level focuses on functional health status. Functional health status is defined as the patient's ability to perform particular defined tasks. The main domains include physical functioning, social functioning, role functioning, mental health, general health perception, vitality (energy/fatigue), cognitive functioning and pain. Many factors may be related directly or indirectly to functional health status, such as physiological factors, symptom status, individuals' characteristics and environmental factors (i.e. social support).

The fourth level is the perception of general health as defined by patients' evaluations of their past and current overall health status. According to the model, symptom can be key predictor of general health perception. Therefore assessing the association between symptom status and general health perception is important.

The fifth level looks at the overall QOL that is defined as the patients' subjective well-being or satisfaction with their life as a whole.

Wilson and Cleary in this framework declared that the concepts of HRQOL and QOL are used interchangeably. In this thesis only the term HRQOL was used to avoid overlapping between the two concepts that are conceptually different

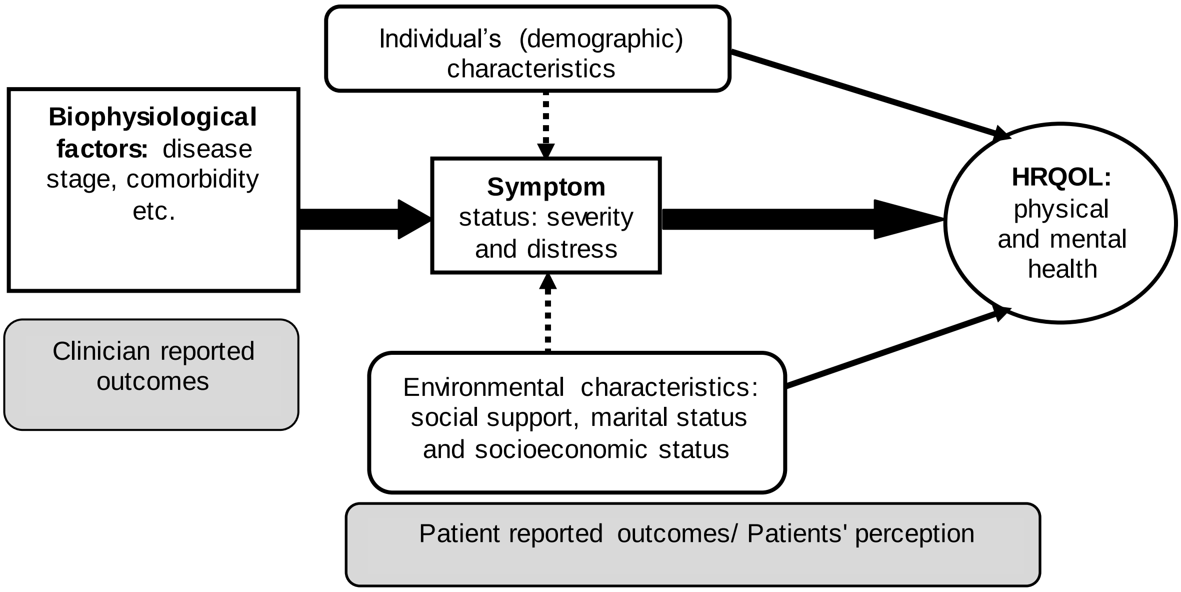
(Section 2.2). Also, the two terms HRQOL and health status are used interchangeably.

4.2.4 Justification of Using HRQOL Outcomes Model

The theoretical framework of HRQOL outcomes has been chosen for many reasons. First, because the developers of the model were medical practitioners, they explained and defined the concepts and relationships between these concepts in such a way that this model can be understood and used in healthcare practice (Peterson and Bredow 2009). Second, HRQOL is a multidisciplinary concept and many factors that extend beyond nursing and doctor interventions can affect it. Therefore, this model is helpful in providing clear boundaries for research or clinical practice that can improve different dimensions of health outcomes. Furthermore, the scope of this model can have an individualized focus as well as a group focus (Peterson and Bredow 2009). Third, although the model is beneficial to predict the causal pathway associations between the biophysiological variables, symptom, and HRQOL, the arrows in the model do not prevent reciprocal relationships between the concepts (Wilson and Cleary 1995). Thus, this model is appropriate for guiding this study as it is a cross-sectional survey that investigates the associations between HRQOL and other factors without specifying the cause and effect.Finally, this model is a widely used theoretical framework to explore HRQOL among patients with different chronic conditions; such as cardiac conditions, cancer and end-stage renal diseases (Mathisen et al. 2007; Krethong et al. 2008, Kring 2008; Ulvik et al. 2008). It has also been used for people with comorbidities, HIV and chronic liver disease (Henderson 2007) but never used before for patients with liver cirrhosis. Therefore, this model is the theoretical framework that has been used to test HRQOL of cirrhotic patients.

The concept of HRQOL is not a commonly used term in Egyptian healthcare systems or in the community. Therefore, it was assumed that the patients might not be familiar with the types of questions that measure HRQOL. For that reason, face-to-face interview was thought to be the most feasible method to complete the questionnaires so that unclear items could be probed, with caution to avoid affecting the patients' response. However, face-to-face interviews with participants was expected to be longer than the consultation time, which might increase the chance of missing eligible participants during the recruitment process. Having numerous studied concepts is was also critical in that this would also be time consuming. For this reason, the model of HRQOL outcomes was adapted for the current study (see Diagram 4-3) to examine selected factors only: demographic and biophysiological factors, social support, symptom experience and HRQOL.

Diagram 4-3: The revised HRQOL outcomes model adapted from Wilson and Cleary (1995)



4.3 RESEARCH METHODS

4.3.1 Study Design

The aim of this study is to describe HRQOL (health status) and symptoms experience of people with liver cirrhosis in Egypt as well as to identify a possible relationship between variables. Using a survey is a common research method in quantitative research, because it is a quick and inexpensive method that allows the collection of a significant amount of data from a sizeable population (Grey 2009; Jones and Rattray 2010). An epidemiological cross-sectional design obtains information from a single group of people at a single point in time: a 'snapshot' without any attempt to follow up over time (Ruane 2005; Mckenna et al. 2010).

This epidemiological cross-sectional design was used to conduct this study to: (1) determine the characteristics of people with liver cirrhosis in Egypt; (2) describe HRQOL and patients' symptoms, and explore the relationships between them and other independent factors such as socio-demographic characteristics, and to (3) find the prevalence of outcomes, such as these patients' symptoms (Seers and Critelton 2001; Meadows 2003; Levin 2006; Nieswiadomy 2008). Mckenna et al. (2010) suggested that a descriptive cross-sectional design can be used to describe the characteristics of a particular population, their health status and measure the prevalence of health outcomes.

A longitudinal study allows investigation of a causal link between independent and outcome factors (Mckenna et al. 2010). However, due to cost and time, it was decided to use a cross-sectional design for this study to also generate inferences and hypotheses (Levin 2006; Mckenna et al. 2010) and recommendations for future research in the area of HRQOL and symptoms experience among patients with liver cirrhosis in Egypt. Levin (2006, p.25) suggests that *"it is advisable to think carefully about what might be relevant because this is a good opportunity to gain a broad base of knowledge about subjects who have/do not have the outcome of interest".* Therefore, the HRQOL outcome model (Diagram 4-2) was used as the basic theoretical framework for this cross-sectional study to set the boundaries for this study and to provide the structure for data analysis and presentation of results.

4.3.2 Population

4.3.2.1 Sampling Method

A target population is a complete set of individuals who have the characteristics that the researcher is interested in studying, and to whom the study findings will be generalised or applied (Bruce et al. 2008; Nieswiadomy 2008). The target population in this study is all adults with liver cirrhosis in Egypt. Since it was impossible to recruit all people with liver cirrhosis from across Egypt or even one region, a study population was used (Procter et al. 2010). The study population is a subset of the target population from whom an accessible sample was taken over the three months' period of data collection based on specific inclusion criteria. Because a sampling framework for these patients was not available, a convenience sampling method was used to identify the study participants. Convenience sampling is a non-probability sampling method that is widely used in exploratory studies (Procter et al. 2010). The following inclusion and exclusion criteria were specified

Inclusion criteria

1. Aged 18 years or older,
2. Diagnosed with liver cirrhosis and so stated in the patient's medical records, and

3. Consented to take part in the study.

Exclusion criteria

1. Advanced stage of hepatic encephalopathy (≥ grade 2),
2. Primary Biliary Cirrhosis (PBC),
3. Post liver transplantation,
4. Hepatic carcinoma or malignancy,
5. Treatment with antiviral therapy, and
6. Neurological or communication problems.

The purpose of the criteria for this sampling strategy was to recruit a potential representative sample of people with liver cirrhosis. The age of 18 or above was decided, because the majority of patients with cirrhosis are above this age and capable to give consent. Patients in the advanced stage of hepatic encephalopathy (≥ grade 2) were excluded, because confused patients may have psychological as well as memory problems. Patients with PBC were excluded because they experience specific common types of disease related symptoms, such as jaundice and itching, more often than patients with liver cirrhosis resulting from other causes. PBC is also a more common cause of cirrhosis among women than men and among older people than younger ones (Younossi et al. 2001). Patients were also excluded if they had a liver transplantation, because they sometimes experience different symptoms and HRQOL (van der Plas et al. 2004). Patients who were diagnosed with hepatic carcinoma or any other malignancy were excluded because they sometimes undergo chemotherapy or radiotherapy that may lead to different symptoms experience. Similarly, patients who were on an antiviral therapy, such as hepatitis C anti-virus therapy were excluded because they usually experience severe fatigue and depression (Fried 2002). Finally, patients with any neurological or communication problems were excluded because they were unlikely to be able to give informed consent.

4.3.2.2 Sample Size

How many subjects should the researcher include? It is a question that is frequently asked at the beginning of a study (Nieswiadomy 2008, Field 2009). Indeed, determining sample size and dealing with non-response bias is necessary during the development of a quantitative cross-sectional survey study (Bartlett et al. 2001). Therefore, many factors should be considered for the calculation of the required sample size, including number of independent variables, alpha level (alpha/α = 0.05), expected effect sizes (how strong of the relationship between independent variable and dependent factor that is going to measure), and the power (size of power to detect this effect, beta/β=0.20) (Tabachnick and Fidell 2001).

Filed (2009) suggests that the ratio of cases to the independent variables is a rule of thumb to calculate the required sample size, 10 to 15 cases for each independent variable in the model. However, this rule of thumb may not be helpful in finding the sample size that can identify the required effect size and the size of power to detect this effect. Thus, recruiting a larger sample size is better. Therefore, Field (2009) recommends these two rules of thumb to calculate the required minimum sample size based on the effect size. The first method is used to test the overall fit of the model (R^2): N = 50 + 8 k (k is the number of independent variables). The second method is used to test the contribution of each individual independent variable to explain dependent factors: N = 104 + k.

As there are 14 independent variables in this study (HRQOL is the outcome) the minimum required sample size is 162 to test the overall fit of the model, and 118 to test the individual independent variable. This method assumes a medium effect size relationship between the independent variable and the dependent variable (outcome), alpha=0.05 and β=0.20 (Tabachnick and Fidell 2001) when data is normally distributed. Also, a priori sample size calculator for multiple regression showed that with anticipated effect size (f^2) = 0.15, statistical power of 80%, probability level of 0.05 and with 14 independent variables, 135 was the required sample size (Soper 2012). Therefore, a sample size of 401 was enough for developing the regression models of HRQOL, symptom experience and perceived social support.

4.4 ETHICAL APPROVAL AND ETHICAL CONSIDERATIONS

4.4.1 Ethics Committee Approval

The study was conducted in accordance with ethical approval granted by the internal Ethics Committee at the University of Stirling, the Department of Nursing and Midwifery Research Ethics Committee (DREC) (Appendix 4-1) and the Research Ethics Committee Board of the National Hepatology and Tropical Medicine Research Institute (NHTMRI) in Egypt (Appendix 4-2).

4.4.2 Egyptian Educational Bureau Approval

To get approval to conduct this study in Egypt, the research proposal, the questionnaires, a brief description of the study, ethical approval from DREC and the names and addresses of the data collection settings were sent to the office of the Egyptian Educational Bureau in London (the sponsor for Egyptian PhD students in the UK). Approval was granted to start the scientific mission for data collection (field work) after the submitted documents were considered and reviewed by all concerned institutions in Egypt. Following that, the research proposal and relevant documents were submitted to the Internal Research Ethics Committee Board of the NHTMRI in Egypt to obtain ethical approval as described earlier. Data collection began once the necessary approvals had been obtained.

4.4.3 Ethical Considerations

The key principles of research ethics that the researcher must uphold are protection from harm, autonomy, privacy and confidentiality (Burns and Grove 2003). A summary of the ethical considerations that were addressed in this study, relating to the patient population, are presented in the following discussion.

4.4.3.1 Potential Risks

There was no intervention in patient care in this study. The patients were simply interviewed to complete the study questionnaires. Therefore, there was no risk of physical or psychological harm in this study. Furthermore, there was no risk of social or economic harm because the patients who took part in this study were not attending specifically to take part in this study. They were recruited during their follow up visit or admission to an inpatients clinic.

The researcher, who is a nurse, was alert to any suggestions of embarrassment from participants and checked at each stage that they were happy to continue with the interview. It was made clear, especially to less well educated patients, that their participation was voluntary, and that they could withdraw from the study at any time without giving a reason. As the interview started, patients were told that they could take breaks whenever necessary to avoid fatigue or exhaustion, and again, the researcher looked out for tiredness and checked with the participant that they were happy to continue. The patients were approached in a sensitive manner and were given a full description of what the study required.

Due to the religious and cultural background of the Egyptian population, there were two questions that the researcher assumed would be embarrassing, especially for unmarried patients, particularly women. These questions are the last two items in the LDSI-2.0 and they relate to sexual problems (desire and activity). Therefore, the researcher did not ask unmarried females these questions, and these questions were given zero score. Furthermore, for unmarried males these questions were asked after clarifying to them that these questions were optional and that they did not need to answer if they did not wish to. Therefore, the likelihood that the participants would experience any anxiety, stress, or embarrassment during their participation in this study was minimised.

4.4.3.2 Autonomy, Confidentiality and Data Handling

The researcher ensured that the patients had complete autonomy to decide whether to participate without any pressure. To ensure the participants' autonomy, they were informed that their participation was entirely voluntary and that they could withdraw from the study at any time, without negatively affecting the treatment or care they received.

The confidentiality of the participants was preserved throughout the study and participants were reassured that anything they said during the interview would be kept confidential and would be used for the study purpose only without mentioning the patients' identity in any documents (i.e. thesis and publishing paper). Identifiable information like telephone numbers, email and home addresses, and any other information that might identify them, were not collected during the interview as they were not required for this study. Because this was a cross-sectional (snapshot) study, the researcher did not need to contact the participants again.

Respect for the participants' privacy was secured by conducting the interview in a private area in the outpatient clinic. This was to ensure the patients' privacy and confidentiality, and to avoid disturbance as well. For the participants who were recruited from the inpatient clinics interviews were conducted in the patient's admission room. If there was a relative with the patient, permission from the patient was obtained before conducting the interview as to whether her/his relative could be in the room during the interview.

With respect to data handling, each participant was assigned a unique code (number) on the questionnaires during the study and all data were kept on a password-protected personal computer at the University of Stirling, and a personal Laptop used for fieldwork. The password was known only to the researcher. The questionnaires and research data on the computer did not contain any patient identifiable information.

4.4.3.3 Informed Consent

The principle of informed consent means that participants are provided with sufficient and understandable information about the aims of the study. It also means that participants are informed of the nature of the information that is being collected and how much time they will be required to contribute before giving consent. In fact, the usual way to provide information to participants is through a patient information sheet which provides a written record of what the study is about.

The participants were informed verbally and in writing using an information sheet (Appendix 4-3 and Appendix 4-4), which was developed with consideration for uneducated participants. Written information and consent sheets were provided, but the sheets were made more accessible through the use of pictures and illustrations. Furthermore, the study was explained verbally to patients who could not read. Written consent (Appendix 4-5 and Appendix 4-6) was obtained from the participants who could write and was obtained from an available witness if the participant could not write. A witness could be a family member (husband, wife, sister, brother, close relative like cousin); a nurse caring for the patient or the head nurse of the department. Some patients (21.6%) gave verbal consent and refused to write their name on the consent sheet (more details see section 5.4.2).

4.5 DATA COLLECTION PROCESS

According to Meadows (2003), the data collection process should be objective, systematic and replicable. Therefore, the key questions for designing the data collection procedure were as suggested by Nieswiadomy (2008): What? How? When? The revised theoretical framework of HRQOL outcomes (Diagram 4-3) was used to answer these questions systematically.

4.5.1 Measurements

Taillefer et al. (2003, p. 310) stated that *'a failure to provide an a priori definition of the main concept is as serious and unacceptable as not providing hypotheses or research questions in an empirical study, and can lead readers to make inaccurate interpretations about a model, the results of a study, or the use and misuse of a model'.* Therefore, it is essential to define the research concepts theoretically and operationally. The following sections outline the theoretical definitions of the investigated variables and clarify how these concepts were measured.

4.5.1.1 Theoretical Definition of Variables (What?)

The theoretical definition is a conceptual definition which aims to clarify the theoretical meaning of a variable that may be derived from the theoretical framework or developed through concept analysis (Fawcett 1999). For this study the investigated concepts are defined theoretically as follows.

Biophysical status

This describes the patient's biophysical status because of liver cirrhosis in terms of disease stage, cause of liver cirrhosis, number of liver cirrhosis complications and number of comorbidities.

Liver cirrhosis

A patient with liver cirrhosis was defined as an individual who had been diagnosed by a physician as having cirrhosis, was not responding to antiviral therapy (i.e. Interferon), and had stopped it at least four months before data collection. In addition, patients who were not eligible for interferon therapy and requiring just conservative medical management were eligible for this study.

Symptoms experience

Symptoms experience is the patient's perception of the presence of physical or/and emotional problems that reflect the severity of their symptoms (Wilson and Cleary 1995).

Hindrance of symptoms

This means to what extent the symptom that the patient experiences limits or restricts his/her daily and social activities (van der Plas et al. 2004).

General health perception

General health perception describes a patient's perception of his/her current and past overall health status (Wilson and Cleary 1995).

HRQOL

HRQOL is the patient's subjective perception of the impact of their disease and/or its treatment on the various aspects of their daily life, including physical functioning, psychological status and social functioning (Anderson and Burckhardt 1999; Taylor 2000).

Environmental characteristics (Perceived social support)

Environmental characteristics were defined as the perceived social support from a patient's perspective. Social support is '*the extent to which an individual believes that his/her needs for support, information, and feedback are fulfilled'* (Procidano and Heller 1983, p. 2).

4.5.1.2 Operational Definition of Variables (How?)

The operational definition clarifies how the variable is measured. For measuring concepts that were defined theoretically, it was essential to define them operationally. An operational definition means the availability of valid and reliable tools that can be used to measure these concepts (Burns and Grove 2003). A valid measurement should have these characteristics: it measures what it is intended to measure, is clear, comprehensible, uses unambiguous wording, and is relevant and consistent (Fairclough 2002; Ruane 2005). In this study the instruments that were already available in Arabic were given priority as translating questionnaires is costly and time-consuming.

For data collection, a face to face structured interview technique was used. Although self-completion questionnaires are often sent by post, enabling large samples to be reached, response rates tend to be low and, this method is inappropriate for illiterate people. Hence, face-to face interview using short questions and simple language was used to avoid respondent misunderstandings (Meadows 2003). In this study one questionnaire and three scales were used to collect the study data in a structured and systematic manner.

Background data sheet

The background data sheet was used to collect the individual's characteristics and medical history (Appendix 4-7 and Appendix 4-8). This sheet was developed by reviewing previous studies that were conducted among people with liver disease. The sheet was divided into two parts, individual characteristics and medical history.

Individual characteristics: Socio-demographic data (i.e. age, gender, marital status, educational level, area of residence, current employment status, cause of unemployment) were collected from the patients themselves, as this data is not usually recorded in the medical documents.

All socio-demographic data were classified according to the Egyptian norm using the Egyptian census (Central Agency for Public Mobilization and Statistics 2011). For example, the categories for marital status were single (never married), married, and widowed / divorced / separated. The level of education was categorised into illiterate, primary, preparatory, secondary (public/technical) and higher education (students enrolled or graduated from university). Employment status was classified into employed (working now), unemployed (not working now) and housewife (woman does not work at all). Causes of unemployment (not working) were classified into liver disease and other causes (i.e. retirement, age and no job available). These socio-demographic variables have all been shown to be important factors associated with HRQOL in patients with liver cirrhosis in previous studies (Kim et al. 2006; Sobhonslidsuk et al. 2006; Bjornsson et al. 2009; Hsu et al. 2009). It was also important to determine the cause of unemployment to investigate the impact of this disease on patients' ability to work which might cause a financial burden (Sobhonslidsuk et al. 2006). Financial burden was an item in LDSI-2.0 that was used to assess its severity as a result of liver disease.

Medical history: This referred to the cause of cirrhosis, complications of cirrhosis, number of hospital admissions related to liver disease, causes of hospital admissions, comorbidity number and types, and disease stage. This part of the questionnaire was completed by accessing and reviewing the patient's medical records. However, the medical files of many patients were neither organized nor complete, particularly among patients attending the outpatient clinics. Because these medical files did not contain a history of previous hospitalizations related to liver disease, and co-morbidities, these two questions were addressed to the patients themselves.

The stage of liver cirrhosis was classified into compensated and decompensated cirrhosis. Compensated cirrhosis means that the liver is coping with the damage and maintains its important functions. Thus, patients with compensatory liver cirrhosis do usually not have any complications of liver disease. In contrast, in decompensated cirrhosis, the liver is not able to perform all its functions adequately, and patients often have serious complications such as splenomegaly, bleeding varices, ascites and/or encephalopathy (Smeltzer and Bare 2004; Porth and Matfin 2009).

Therefore, participants who had cirrhosis but had not yet developed clinical de-compensated complications (splenomegaly, ascites, oesophageal variceal bleeding or encephalopathy) in the year of data collection were classified as compensated cirrhosis. Participants who had developed any of the liver disease complications in the year of data collection were classified as decompensated cirrhosis (Cordoba et al. 2003; van der Plas 2003; Gutteling et al. 2006; Ong et al. 2008; Gutteling et al. 2008).

Comorbidity was assessed by asking the patients if they had been diagnosed with any disease other than liver disease. Comorbidities have been shown to be associated with perceived functional health status among patients with liver cirrhosis in prior studies (Marchesini et al. 2001; Cordoba et al. 2003; Kalaitzakis et al. 2006; Bjornsson et al. 2009; Hsu et al. 2009). Also, these variables are required to develop an individualized care plan to improve the perception of functional health among people with cirrhosis.

HRQOL (perceived health status)

The Medical Outcome Short-Form 36 version 2 (SF-36v_2) is a generic HRQOL instrument that has been used widely to assess health status (Ware et al. 1993). The US version 2.0 of the SF-36 (SF-36v_2) (Appendix 4-9) was developed in 1996 to correct deficiencies identified in the original version (version 1.0) (Ware et al. 2000). The SF-36 has been culturally adapted to different languages as part of the International Quality of Life Assessment (IQOLA) Project (Ware et al. 2008).

The SF-36 is a generic HRQOL tool used worldwide to assess health status among general and specific populations with different health conditions. Furthermore, evidence shows that the SF-36 is a more sensitive tool to assess changes in patients' health conditions over time than other generic health status measures like the Nottingham Health Profile, and the Sickness Impact Profile (Beaton et al. 1997). SF-36 is a tool that can be self-administered or completed with assistance in less than 10 minutes (El-Serafy et al. 2009). The psychometric properties (validity and reliability) of the Arabic version have been tested (Appendix 4-10) (Coons et al. 1998; Sabbah et al. 2003; Mrabet et al. 2004) and it has been widely used among Egyptians patients with chronic conditions, such as liver transplantations and chronic hepatitis C infections (Tanamly et al. 2004; Kamal et al. 2006; El-Serafy et al. 2009). It was therefore judged that the SF-36v_2 was the most appropriate measurement for this study. Permission to use the SF-36v_2 in this study was granted by QualityMetric Incorporated (Appendix 4-11), and a license was obtained (license number: QM009535), (components of SF-36 see section 3.3.1)

Kosinski (2009) argues that maintaining the data quality through accuracy of entering, coding and scoring is essential to ensure the study quality and giving valid results. QualityMetric Incorporated have developed software that can be used to enter patients' responses to the 36 items of the SF-36, to simplify the scoring process and to provide reliable results. This software has many advantages: it tracks the quality of the data entry process by giving an alert message to complete a missing item before starting the scoring operation; it provides a standardized scoring method, thereby avoiding errors (Kosinski 2009) and wasted time and effort; it yields less biased data and estimates the missing responses (Kosinski et al. 2000). For these reasons, the scoring software was purchased from Quality Metric Inc for data entering and scoring SF-36.

Ware et al. (2000) introduced a norm-based score (NBS), which uses a cut-off point of mean = 50 and standard deviation (SD) = 10. It is therefore possible to meaningfully compare scores for the eight-scale profile and the physical and mental summary measures with this cut-off score (Kosinski et al. 2000). It is also possible to interpret the SF-36 results without the need of a previous study to be used as a norm. A mean score below 50 indicates a poorer health status and a mean score above 50 indicates a better health status than the population average (Maruish and DeRosa 2009). For interpreting the SF-36 domains and the two component summary scores, the guideline suggested by Ware and Gandek (1998); Ware et al. (2000) was used (Appendix 4-12).

General health perception

The general health perception was assessed using item one in SF-36. Patients were asked to rate their general health on a 5-point ordinal scale ranging from one "excellent" to five "poor". This approach has been used in liver disease research (Sobhonslidsuk et al. 2006).

Perceived symptom severity and hindrance of symptom

Comprehensive and valid disease specific measurements of symptoms can be an excellent predictor of HRQOL (Wilson and Cleary 1995). Several questionnaires have been developed and used to measure disease specific HRQOL in patients with liver disease; these include the Hepatitis Quality of Life Questionnaire (Bayliss et al. 1998), the Chronic Liver Disease Questionnaire (Younossi et al 1999), the Liver Disease Quality of Life Instrument (Gralnek et al. 2000), the Hepatitis B

Quality of Life Instrument (Spiegel et al. 2007) and the Chronic Liver Disease Quality of Life Questionnaire (Lee et al. 2008). However, some are too narrowly focused (Bayliss et al. 1998; Younossi et al 1999; Gralnek et al. 2000; Spiegel et al. 2007), and others are too long (Gralnek et al. 2000) and do not address the extent to which symptoms affect patients' HRQOL (Younossi et al 1999; Lee et al. 2008).

In contrast, the Liver Disease Symptom Index 2.0 (LDSI-2.0) (Appendix 4-13) is a psychometrically tested questionnaire that has been widely used among patients at different stages of chronic liver disease, mainly in the Netherlands (Unal et al. 2001; van der Plas et al. 2003; van der Plas et al. 2004; Gutteling et al. 2008; Gutteling et al. 2008a; Kuiper et al. 2010). The index was designed by experts in liver disease (hepatologists) to help healthcare providers understand the experience of patients with liver disease and how their symptoms influence their daily life. Thus, not only does it assess symptom severity, it also addresses how symptoms influence patients' daily living. Gutteling et al. (2007) maintains that the LDSI-2.0 is the best specific disease tool, because it is short, measures possible liver disease specific symptoms, and covers the impact of these symptoms on patients' daily activities.

In accordance with the scoring instructions provided by Gutteling et al. (2008), scores for all of the items on each subscale were added to obtain a value for the individual subscales. Possible scores for each subscale ranged from 0-60 for the severity of symptoms and 0-36 for hindrance of symptoms. A higher score on the symptoms severity subscale represents a higher perception of symptoms severity, and a higher score on the hindrance of symptoms subscale represents a higher perception of the limitations of daily activities as a result of these symptoms. Table 4-1 summarises the method used to report the result of LDSI-2.0.

The LDSI-2.0 is available in English and is in public use. However, an Arabic version that could provide essential new information about patients with liver disease in Egypt did not exist before conducting the pilot study. The translation process and the testing of the validity and reliability of the LDSI-2.0 are discussed in detail in Chapter 5.

Table 4-1: LDSI-2.0 scoring system

Scale	Total Items	Subscales	Subscales Items	Response scale	Score range (minimum and maximum sum of responses)	Sum of score for each category
LDSI-2.0	24	Symptoms severity	15	0-4	Minimum=0 (no symptom) Maximum =60 (very severe symptom)	0-60
		Hindrance of symptoms	9	0-4	Minimum=0 (no debility in daily life as a result of symptoms) Maximum =36 (very severe debilities in daily life as a result of symptoms)	0-36

<u>Perceived adequacy of social support</u>

Given the importance of choosing a measurement that can assess the perceived adequacy of social support that was specific to the research context, it was vital to identify an instrument which had been specifically designed to measure the perceived adequacy of social support from different sources of support. Searching the literature found that the multidimensional scale of perceived social support (MSPSS) (Appendix 4-14) is a commonly used instrument for measuring the adequacy of social support. The MSPSS was developed in the USA by Zimet et al.

(1988 and 1990). The three subscales assess the perception of the adequacy of social support from three specific sources: family, friends and significant others (Zimet et al. 1988; Zimet et al. 1990). Each subscale has four items that are rated on a seven point scale in the English version or are rated on a three point scale in the Arabic version. An increasing score represents increasing perceived adequacy of social support.

The original MSPSS has an internal consistency reliability with Cronbach alpha’s for total MSPSS = 0.85 and for the sub-scales 0.85 or greater, as well as adequate construct validity. Although the MSPSS was originally developed to assess social support among university undergraduates, it has been translated and psychometrically tested in a number of studies worldwide among people with different illnesses (Nakigudde et al. 2009; Ramaswamy et al. 2009; Wongpakaran et al. 2011) including in Arabic (Aroian et al. 2010).

The Arabic MSPSS (Appendix 4-15) was translated and back translated by a team of bilingual speakers following the protocol for translation to give a high quality translated version (Aroian et al. 2010). It is the most appropriate tool for measuring perceived social support among patients with liver cirrhosis in this study for many reasons. (1) It can assess the individuals’ subjective perceptions of the adequacy of social support from the main source of support (spouse, family spouse friends). (2) It is the shortest and simplest tool available (12 items); Zimet et al. (1988; 1990) stated that it can be used when time is limited and a number of questionnaires need to be used at the same time. (3) An Arabic version of MSPSS is available (Aroian et al. 2010) and has been widely used among Arabic people (Ramaswamy et al. 2009; Aroian et al. 2010). It showed good construct validity and internal consistency reliability with Cronbach alpha’s for total MSPSS = 0.74 (Aroian et al. 2010). Written permission to use the Arabic version of MSPSS was sought and granted by Professor Aroian as the translator for the tool and from Professor Zimet as the original author (Appendix 4-16).

The MSPSS can be computed to give the total and subscale scores for each of the three sources of support (spouse, family and friends). The total score and subscale scores were calculated by adding up the participant's responses to give a total score. In accordance with the scoring instructions provided by Aroian et al. (2010), scores for all of the items on each subscale were added to obtain a value for the individual subscales. Possible scores for each subscale ranged from 12-36 (adjusted score 1-3). Table 4-2 summarises the method of the MSPSS scoring that was used to report the result of MSPSS.

Table 4-2 : Scoring system of MSPSS

Scale	Items	Subscales	Items	Response scale	Score range (Sum of responses)	Steps of scoring	Categories	Adjusted Scores
MSPSS	12	Spouse support	4	1-3	12-36 (Married) 8-24 (Unmarried)	Sum of responses Subtraction of sum of responses on the number of scale items Number of items: 12 for married 8 for unmarried	Disagree Neutral Agree	1 2 3
		Family support	4	1-3				
		Friends' support	4	1-3				

4.5.2 Overview of Clinical Settings

The study was conducted in three hospitals in Cairo, Egypt. The National Hepatology and Tropical Medicine Research Institute (NHTMRI), the Section of Tropical Medicine in Kaser El-Ani Teaching Hospital, and the Centre Doctor Yassin Abdel Ghaffar Charity for Diseases of the Liver and Research (CDYCDLR). These hospitals were primarily considered because they offer both local and regional, inpatient and outpatient hepatic health services.

4.5.2.1 Hospital 1: NHTMRI

The NHTMRI is the largest specialist liver disease and tropical medicine institute not only in Egypt but also in the Middle East. The Institute is considered to be an international research centre, and was selected by the University of Maryland in the USA and the World Health Organisation to conduct clinical research in tropical and liver diseases. It was established in the era of King Fuad, first King of Egypt, in 1931. The institute provides free services for all Egyptians with liver disease, including consultations, medical and surgical interventions, and antiviral therapy for hepatitis. Therefore, many patients from varies governorates in Egypt attend the outpatient clinic daily, both for consultation and admittance to the departments.

4.5.2.2 Hospital 2: Section of Tropical Medicine

Kaser El-Ani is a national teaching hospital that provides free healthcare services for Egyptians from varies governorates. The Section of Tropical Medicine is one of many sections in this hospital. It provides healthcare for patients with different medical health problems, especially gastroenterology and tropical illness. According to the annual statistics of Cairo University Teaching Hospital, 2285 patients were admitted with liver cirrhosis in the year 2004 to 2005 to Kaser El-Ani Teaching Hospital alone (Department of Statistics and Medical Documentation 2005).

4.5.2.3 Hospital 3: CDYCDLR

The CDYCDLR was constructed and opened in 1999. It was created by Doctor Yassin Abdel Ghaffar, a Professor of liver disease, with contributions from other people who shared in funding this project. The centre is right in the middle of Nasr City, Cairo. It is a private hospital that provides healthcare for people with liver disease (adult and children) from different economic backgrounds. Many patients attend the centre daily for medical consultations in the outpatient clinics, while others are admitted to inpatient departments. According to the annual report the number of visitors to the centre and the beneficiaries of its services are around 20,000 patients every year.

4.5.2.4 Justification for Clinical Settings

These hospitals were selected because many people with liver disease (men and women) come daily from different regions in Egypt (both rural and urban) to these hospitals to get inpatient and/or outpatient management. These patients have varied socio-economic, cultural and educational backgrounds. As a result, they provide a representative cross-section of the population, thus allowing generalization of the study results.

4.5.3 Recruitment Process

A sampling frame is a method of selecting people of interest in order to stratify the sample and contact them. A construct sampling frame that includes the whole population of interest with their various characteristics such as age and gender is an ideal method to select the sample systematically, which can then be representative of the entire population (Bruce et al. 2008). However, this method (sampling frame) is impossible when the population's contact details (addresses and telephone numbers) and time of consultation in the clinic are not available. Therefore the following recruitment strategy was designed to facilitate systematic data collection from a large representative sample from three hospitals during the three months of field work (from June to August 2011).

The feasibility of the recruitment method was tested by conducting a pilot study for a month in one of the selected hospitals. The three hospitals have little differences in the routine of work that might influence the recruitment process. Therefore, the following part clarifies the places of data collection and the methods of recruitment that were used in this study.

4.5.3.1 Recruitment from Hospital 1: NHTMRI

The work routine in the outpatient clinic and inpatient department in the NHTMRI is as follows. The outpatient clinic is open from 9am till 1pm daily except Friday. Therefore the recruitment process started in outpatients at 9am till 1pm to ensure that all the eligible patients who attended on that day had a chance to participate in this study. In the inpatient clinic the family’s visiting time is from 2pm till 5pm. Therefore, the admitted patients were recruited in the inpatient clinic after finishing the recruiting process in the outpatient clinic at 1 pm. Recruitment at the outpatient clinic was quite different to recruitment in the inpatient departments.

<u>Outpatient recruitment</u>

The outpatient clinic has two liver consulting rooms worked at the same time by two physicians. After discussions with the staff, it was decided that the researcher would wait in one of the two rooms and the consultant would introduce her to eligible patients after finishing the consultation. Once the consultation was finished the interview started.

It is important to highlight that in the pilot study interviews were conducted before the consultation. It was difficult to follow the same strategy in this setting because it was impossible to know which patients would be eligible before their consultation with the physician. Because the consultation time was less than 20 minutes, sometimes the consultation of the next patient was over before the interview with the last patient was finished. Therefore, to avoid missing any eligible patients, the physician helped the researcher by sending patients first to the pharmacy inside the institute to collect their prescribed medication. As this process takes time, patients who were willing to take part in the study could return to the researcher. The researcher wrote the patients name in a list before they left the consultation room to go to the pharmacy in order to record who was missed or did not return to participate in the study.

Inpatient recruitment

In the inpatient clinic there are two sides, one for females and one for males. The physician and the head nurse of each side helped the researcher to identify eligible patients who had been admitted.

4.5.3.2 Recruitment from Hospital 2: Section of Tropical Medicine

The Section of Tropical Medicine is an inpatient clinic, which has two sides, one for females and one for males. Each side can take at least 20 patients. Therefore, the physician helped the researcher to find eligible patients and to write their names on a list.

Kaser El-Ani Teaching Hospital is near the NHTMRI, around 15 minutes on foot. Therefore, it was easy for the researcher to go to Kaser El-Ani after finishing recruitment at the NHTMRI. Indeed, recruitment from the Section of Tropical Medicine in Kaser El-Ani Teaching Hospital was most appropriate in the afternoon to avoid interfering with routine work. Physicians make their ward rounds before 1 pm and the family visits from 1 to 5 pm. Therefore recruitment after 4 pm was the most appropriate time. Eligible patients, who could not be interviewed that day because of a family visit or a critical condition, were recruited the next day, since their names were on the researcher's list.

4.5.3.3 Recruitment from Hospital 3: CDYCDLR

The routine of work in the outpatient clinic differs from the inpatient clinic at CDYCDLR. At the inpatient clinic, family visiting time is between 12am and 9pm. The outpatient consultation is from 9am till 4pm. Therefore, there were only two hours to recruit from the inpatients between 10am and 12pm, i.e. before visiting time. Recruitment from the outpatient clinic took place between 12pm and 4pm. Recruitment from the outpatient clinic was quite different to recruitment from the inpatient clinic.

Inpatient recruitment

In the inpatient clinic the names of all admitted patients were displayed on a board, together with the room numbers. The physician helped in identifying eligible patients and put their names on a list. This strategy ensured that as few patients as possible were missed. The researcher could recruit all the eligible admitted patients on that day except those in a critical stage (bleeding or after an endoscopy) who could be recruited once their condition had stabilized. Some of these patients could not be recruited because they were either discharged before the next day or transferred to another hospital. If eligible patients could not be interviewed before visiting time, they could still be recruited the next day.

Outpatient recruitment

The outpatient clinic has two consultation rooms attended by two physicians. The waiting area was crowded with patients waiting for a consultation, some of whom might have been eligible for the study.

Initially, the researcher decided to compile a list of patients' names one day before the consultation in order to recruit all eligible patients systematically. However, this turned out to be an inappropriate strategy because sometimes new cases were seen without registration while others cancelled their consultation. After discussion about the appropriate recruitment strategy with the staff, it was decided that the researcher wait in the outpatient clinic and the outpatient nurse administrator introduce her to eligible patients. This strategy ensured that both the researcher knew of the eligible patients attending the clinic that particular day, and that as few patients as possible were missed. The number of eligible patients per day during the recruiting month (pilot study) ranged from two to five patients and the time of consultation ranged from 15 - 30 minutes.

The patients were interviewed before and/or after the consultation. For example, a patient might start the interview but was then called in to the consultant. When the patient returned he/she would complete the interview. In the pilot study, the majority (n = 23, 88.5%) of participants who were recruited from the outpatient clinic completed their interview before the consultation. Others completed the SF-36 before the consultation and afterwards the other instruments. The researcher was very keen to complete the interviews before patients were seen by the consultant as any news about the progress of the disease or a worsening status might have affected the patients' perceptions and bias their responses. Table 4-3 illustrates the timetable of sample recruitment from the three hospitals.

Table 4-3: Timetable of sample recruitment from the three settings

Setting	**Day of visit**	**Time of recruitment**	
		Outpatient	**Inpatient**
NHTMRI	Sunday-Wednesday	9 am-1 pm	1.30 -3 pm
Kaser-Elani	Sunday-Wednesday	N/A	4 -6 pm
CDYCDLR	Saturday and Thursday	12 am - 4 pm	10 - 12 am

N/A: not applicable

4.5.3.4 Interview Steps in the Inpatient Clinics

A list of names of patients that might be eligible for the study was made available.

1. The researcher went to the patient's room, introduced herself, explained the information sheet and asked the patient if s/he wanted to join the study.

2. Written or verbal consent was taken before conducting the interview.

3. The interview was conducted in the patient's room. If other patients shared the same room, and the patient was unable to go to a separate place for the interview, the curtain was pulled around the patient's bed to preserve his/her privacy. In my experience, there was enough space between the patients' beds to avoid being overheard. If a relative was with the patient, the researcher asked the patient if her/his relative could remain in the room during the interview. Some of the participants agreed while others refused.

4.5.3.5 Data Collection Assistant

Recruiting the sample from the three settings on the same day, especially from NHTMRI and CDYCDLR was impossible because the CDYCDLR is about an hour's travel time or more from NHTMRI. Therefore, a data collection assistant became essential. A nurse educator in the Faculty of Nursing, Cairo University with experience in data collection was found. In addition to her work at the faculty she was also studying for a Masters' degree and was able to assist in the data collection process on her days off, i.e. Thursday and Saturday. She recruited eligible patients from the NHTMRI on these two days and the researcher recruited from CDYCDLR on the same days. It was therefore essential to design a systematic recruitment strategy based on the hospital day work. A training protocol for the data collection assistant was used to avoid data collection bias (Appendix 4-17).

4.6 DATA ANALYSIS

4.6.1 Checking Data Set Accuracy

Before starting scale scores and data analysis it was vital to check the data accuracy. Therefore, initial analysis outputs were conducted to check for missing and extreme values that were out of the range of normal possible values (Pallant 2007).

The nominal and categorical data was inspected by running frequency tables, while continuous data were inspected by running descriptive statistics. The initial analysis outputs of frequency and descriptive tests were checked to correct any errors before starting data analysis. Some minor errors were noted and amended before any analysis was conducted. Following this, the data were again checked using frequencies for non-numerical data and descriptive analysis for numerical data to confirm the accuracy of the data set.

4.6.2 Computing Scales Scores

Following the data accuracy check, scale scores were calculated. Three instruments were needed to compute the total and subscales scores; LDSI-2.0, MSPSS and SF-36. The computations were carried out for LDSI-2.0 and MSPSS by creating new variables using the transform option in SPSS following the scoring system that was explained. The SF-36 subscales and both component scores were computed using the QMI Software Program.

4.6.3 Checking Data Normality and Outliers

Continuous data were investigated for normality by observing the Q-Q Plot and the histogram. It was noted that the Q-Q Plot was straight and the histogram was normally distributed, suggesting normality of the data. The Skewness value for each continuous variable was checked. Variables were considered normally distributed if the Skewness value was between -1 and +1 (Pallant 2007). The Skewness value of all the continuous variables fell between -0.9 and + 0.4, suggesting that they were normally distributed. Additionally, the continuous variables were tested for linearity by checking the scatter-plots between each of the independent variables with the dependent variable (i.e. MCS and PCS).The data did not show any outliers.

4.6.4 Statistical Analysis Procedure

The IBM SPSS (Statistical Package for the Social Sciences) software (Edition Standard v18, United States) was used for data analysis. Descriptive statistics including frequency for nominal and categorical variables; and mean ± standard division and median for continuous variables were computed. The Pearson product moment correlation coefficient (r) was used to assess the relationship between two parametric variables, and the Spearman's rank order correlation (rho) was used to assess the relationship between non-parametric variables.

Parametric statistical techniques such as the independent sample t-test and the one way analysis of variance (ANOVA) test were used to assess the difference between group mean scores. Independent t-tests were used to compare and to find the differences between the mean scores of two groups. Otherwise, ANOVA was used for multiple group comparisons. If the ANOVA output was statistically significant, the post-hoc technique was used to find which of the three groups were statistically different. When there are multiple statistical comparisons to be made, this increases the risk of type 1 error. However, corrections were made for this by reporting the Bonferroni correction value for the ANOVA tests.

A non-parametric statistical technique, chi-square for independence (cross table), was used to compare the frequencies of nominal variables for two groups, for example to find the difference between two groups, such as males and females symptoms experience. All statistical tests were two tailed with $p < 0.05$ as the significance level.

To examine factors associated with physical and mental health domains, multiple linear regression analysis was used. This is a complex statistical technique based on numerous data assumptions such as adequacy of sample size, no-multicollinearity, no-singularity, no-outliers, normality and no-homoroscedasticity (Pallant 2007; Field 2009). Therefore, these assumptions were investigated before presenting the regression results and developing the regression model. There were no violations to these assumptions. Multiple regression analysis was conducted using the stepwise method, because it enabled finding variables that are most important in explaining the physical and mental health domains of people with liver cirrhosis. As a result, the stepwise method was useful in avoiding bias because there was no prior decision regarding the order of entering the variables in the model, especially as this was an exploratory study (Field 2009).

4.7 CONCLUSION

This chapter has presented the aims of the study and the research questions, and has discussed the philosophical paradigm underlying the research. Also, it has described in detail the method chosen to carry out this study, including an explanation of the study design, sample, measurements and recruitment strategy. A cross-sectional survey design and the convenience sampling method were selected to conduct this study.

5 CHAPTER 5- PILOT STUDY

This chapter describes and justifies the pilot study that was conducted before the main study. Then, the process of translation and cross-cultural adaptation of the translated tool are clarified. Finally, results and discussion of the findings are presented at the end of the chapter.

5.1 BACKGROUND

A pilot or feasibility study is usually conducted to guide the researcher to evaluate the (1) appropriateness of the recruitment strategy; (2) appropriateness of the instruments; (3) estimating the needed sample size; (4) identifying confounding variables that need to be controlled; and (5) adequacy of the researcher's skills and required training before the main study is carried out (Polit and Beck 2010). A pilot study is also a trial run to provide information regarding a measurement's validity, reliability and the cross cultural adaptation of a translated instrument in order to reveal problems relating to the measurement's content, administration and scoring (Guillemin et al. 1993; Fowler 1995; Litwin 1995; Waltz et al. 2010).

Furthermore, conducting a pilot study of survey instruments is an essential step to assess the practical issues that may affect the study's validity (Fowler 1995) such as (1) problems with the wording of the instructions or items of the questionnaire and (2) the length of the interviews (Fowler 1995; Waltz et al. 2010). The pilot study will also give the researcher a chance to find any unexpected errors, to avoid bias when collecting the main study data and to allow correction or redesigning of the study in advance before expending too much time or other resources (Litwin 1995).

There are two factors which may contaminate the main study as a result of the pilot study (1) including the pilot study data in the parent study; and (2) recruiting the same participants into the main study (van Teijlingen and Hundley 2001). It was therefore crucial to separate the pilot and parent studies' data reports and the participants.

5.2 JUSTIFICATION

Using an existing valid and reliable measurement, which is psychometrically well tested, is better than using an instrument for which there is no psychometric evidence (Polit and Beck 2008). The Liver Disease Symptom Index-2.0 (LDSI-2.0) did not exist in Arabic before conducting this study; therefore it was essential to translate it into Arabic. However, tool translation alone cannot guarantee that the tool is valid and reliable.

Parahoo (2006) claimed that the best method to assess an instrument's quality is by carrying out a pilot study. Testing the psychometric properties of a tool before using it in a large study has many advantages such as (1) the participants' responses to an instrument's items will give an idea of whether they understood the items; (2) it is possible to evaluate the appropriateness of the tool's format for the population that will be studied; (3) it is possible to assess the relevancy of the tool's items to the population that will be studied; and (4) it is possible to find out whether the length of the tool and its structure are likely to affect the participants' way of response (Parahoo 2006). Thus, considering the respondents' views about the instrument was an important step that the researcher took to check the quality of the translated LDSI-2.0.

5.3 AIMS

The aim of this pilot study was to make the first translation of the LDSI-2.0 English version into Arabic and to examine its psychometric properties among a sample of people with liver cirrhosis in Egypt.

The specific objectives were to (1) assess the feasibility of using the translated LDSI-2.0 (Arabic version); (2) assess its construct convergent validity; and (3) examine its retest reliability.

5.4 METHODS

Permission to translate the LDSI-2.0 into Arabic and use it in the current study was granted by the original author (van der Plas et al. 2004) (Appendix 5-1).

5.4.1 Permission from the Clinical Setting to Conduct the Study

According to the policy of the Egyptian educational bureau, a PhD student must submit all the study documents (proposal, ethical approval and other relevant documents) to obtain formal approval for the research before travelling and collecting the study data. Accessing and recruiting patients is a critical and sensitive issue. It was therefore essential to personally contact the administrators of the chosen hospitals to obtain permission to carry out the pilot study in the clinical setting for one month.

The CDYCDLR was the most suitable hospital (Section 4.5.3.3) for this pilot study because it is a specialized hospital caring for people with liver disease from all the different regions in Egypt as well as from different socio-economic and educational backgrounds. The variation in the characteristics of the participants was important when testing the translated LDSI-2.0 feasibility and its psychometric properties.

An email to explain the background of the study (the study's aims, design, tools of data collection, recruitment strategy and consent) was sent to the Administrations Committee of CDYCDLR to obtain their permission to collect data for the pilot study. The Administrations Committee granted the required permission.

5.4.2 Written Consent

It is still a big challenge for Egyptian health researchers (Rashad et al. 2004; Ahmed and Dewedar 2011) to obtain written consent. The problem is that some ethical principles for conducting the research may be misunderstood by some Egyptians (Rashad et al. 2004), believing that they lose their right to change their mind and withdraw from the study if signing a consent form (Ahmed and Dewedar 2011; Wazaify et al. 2009). As a result, they may be reluctant or refuse to give written consent although they are happy to support the research (Khalil et al. 2007).

Therefore, providing the research participants with clear and understandable information about the importance and legality of their written consent was essential to enhance the trust between the participants and the researcher for an informed consent process (Khalil et al. 2007). Prior to enrolment, patients were given a verbal explanation of the written information sheet, which was developed with consideration for uneducated participants. The information (Appendix 5-2 and Appendix 5-3) and consent sheets (Appendix 5-4 and Appendix 5-5) were made more accessible by using pictures and illustrations.

Unfortunately, due to the time constraints for data collection (one-month) patients who were happy to participate in this pilot study but refused to give written consent could not be excluded. Although the researcher clarified the process of participants' anonymity and confidentiality, many insisted that they would only give verbal consent. Therefore, for patients who wanted to participate in this pilot study but did not want to give written consent, verbal consent was acceptable.

5.4.3 Process of Translation and Cultural Adaptation of LDSI-2.0

The international standardized guidelines for the cross-cultural adaptation of instruments (Guillemin et al. 1993), consisting of five steps (1) translation; (2) back translation; (3) committee review; (4) pre-testing; and (5) weighting of scores were followed (Diagram 5-1).

5.4.3.1 Forward Translation

The LDSI-2.0 was translated by two independent bilingual translators who were native Arabic speakers and proficient in English. One of these translators (Translator 1: T1) was aware of the underpinning concepts and objectives of the questionnaire while the other translator (Translator 2: T2) was not. This was useful to elicit unexpected meanings from the original version and helped to detect errors and divergent interpretations of ambiguous items in the original tool.

5.4.3.2 Back Translation

Two qualified translators who were native English speakers (T3 and T4) and proficient in Arabic carried out the back translation. The back translators were not aware of the underpinning concepts and objectives of the questionnaire. This was to ensure they were free from bias.

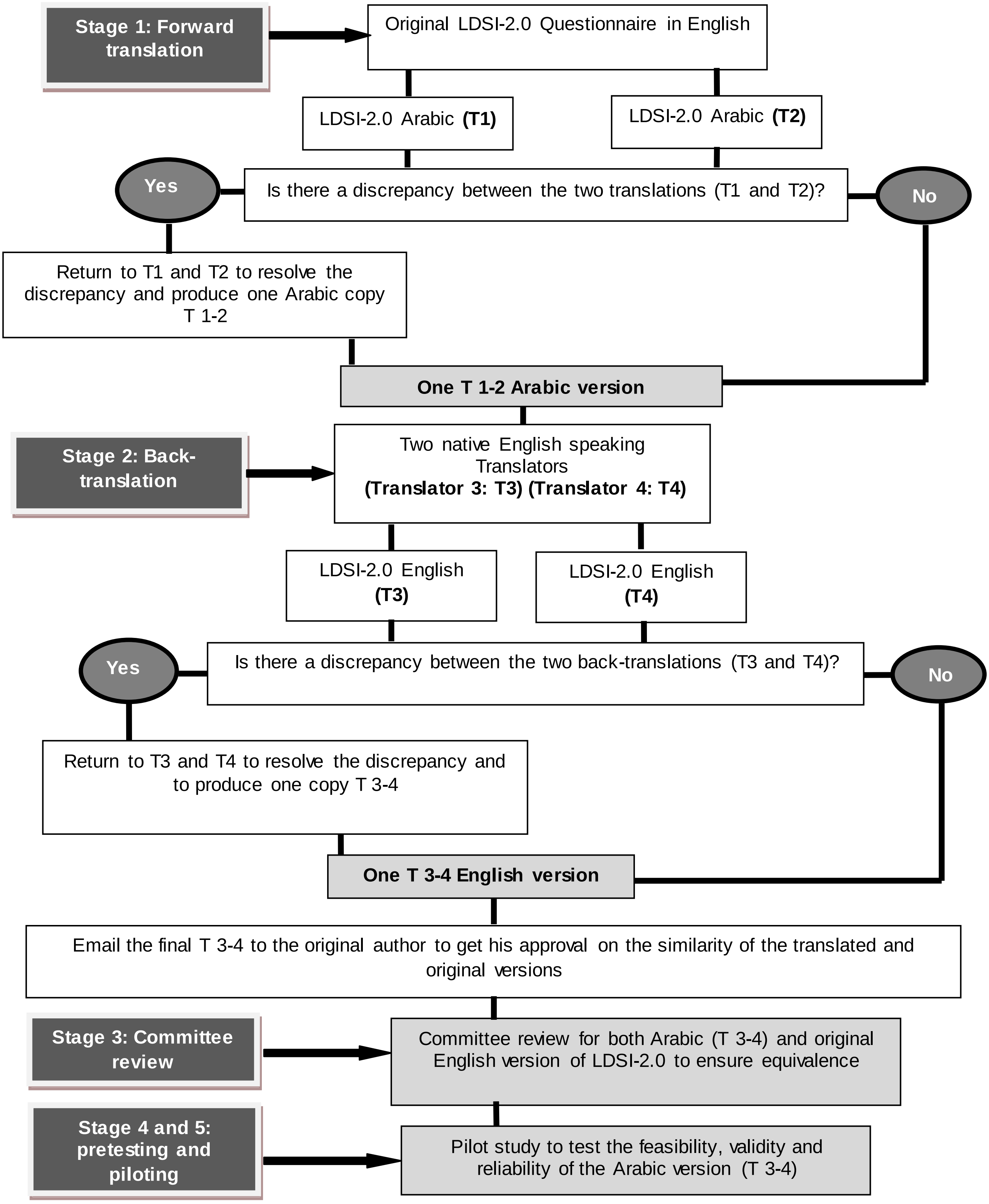
5.4.3.3 Face and Content Validity

To assess the face and content validity of the translated LDSI-2.0, a review committee of five experts (Appendix 5-6), was asked to review the content of the Arabic version by comparing it with the original version, considering appropriateness, adequacy and validity. All committee members were native Arabic speakers highly qualified in English. The committee members received the original LDSI-2.0 as well as the Arabic version and a guidance sheet (Appendix 5-7) designed by the researcher. The researcher incorporated the feedback from the committee in the development of the penultimate version of the Arabic LDSI-2.0.

5.4.3.4 Field Pre-Testing

To complete the steps of cross-cultural adaptation and to check the quality of the translated LDSI-2.0 it was necessary to pre-test the questionnaire in a pilot study (Guillemin et al. 1993; Fowler 1995).

Diagram 5-1: Translation process



5.4.4 Data Collection

5.4.4.1 Recruitment Process

Data were collected between December 2010 and January 2011 over a one month period. During the pilot study, the researcher elected to be present at the hospital for four days per week to ensure the appropriate identification of eligible participants and to explain the study's purpose and pilot stage. Physicians working in the hospital identified the patients who met the inclusion criteria and gave permission to ask them to participate in the study.

An interview with the participants at time 1 (T1) was carried out to complete the tools and to ascertain whether: (1) the words in the questionnaire were clear; (2) patients could understand the questions and answer them; and (3) no difficulties were encountered in completing these instruments. Patients were interviewed for approximately 45 minutes in a private place in the hospital. A series of instruments (SF-36v$_2$, LDSI-2.0 and background sheet) were administered to the participants once, while the LDSI-2.0 was administered twice with a maximum of three days in between.

5.4.4.2 Instruments

Three instruments were used for data collection: the background data sheet, the translated LDSI-2.0 and SF-36. Additionally, an observation sheet was utilized to evaluate the feasibility of Arabic LDSI 2.0 (Appendix 5-8). The observation sheet was completed by the researcher while patients completed the translated LDSI 2.0. It consisted of open ended questions to clarify what patients meant when they answered each question. The observation sheet was designed to assess the content validity and translation quality of the Arabic LDSI-2.0.

5.4.4.3 Interview Procedure

The researcher interviewed all the participants according to the sequential steps formulated in section 4.5.3.4 and additionally received consent from the participants who agreed to be interviewed for a second time (T2) (for test-retest reliability).

5.5 DATA ANALYSIS

The IBM Statistical Package for Social Sciences (SPSS), Edition Standard v18 was used for data analysis and tabulation.

5.5.1 Psychometric Properties of the Translated LDSI-2.0

5.5.1.1 Testing the Feasibility of the Translated LDSI-2.0

Testing the translated LDSI-2.0 for readability and comprehension was an important factor before conducting the main study. Therefore, the administration time (time taken to complete the questionnaire) and the questions deemed difficult to answer were recorded during the interview.

An item was defined as difficult if the patient (1) did not provide a specific answer; (2) gave an open ended answer; or (3) gave a misunderstood answer. Additionally, after each question answered on the translated LDSI-2.0 the patient was asked to clarify what was meant by each answer. This '*probe technique'* was used to encourage the participants to explain their understanding of the questions to determine whether they had understood the questionnaire items correctly (Guillemin et al. 1993; Kitapcioglu et al. 2004).

The feasibility of the translated LDSI-2.0 was tested in terms of administration time and the percentage of questions considered difficult to answer. Descriptive statistics were used to describe the range of completion times. If less than 5% of all the items in the translated LDSI-2.0 were misunderstood, it was judged feasible to administer (Unal et al. 2001; van der Plas et al. 2004).

5.5.1.2 Testing the Initial Validity of the Translated LDSI-2.0

Construct validity investigates to what extent the measurement assesses what it is intended to measure (Litwin 1995), which is the most important characteristic of an instrument. Convergent validity is a subtype of the construct validity that examines the general agreement between measurements that theoretically are assumed to be similar or interrelated. Polit and Beck (2010) argue that *'Construct validity is essentially a hypothesis testing endeavour, which is typically linked to a theoretical perspective about the construct'* (p. 379).

The SF-36 is a generic HRQOL that does not contain any disease specific items such as sleep adequacy, cognitive functioning, sexual functioning, health distress, family functioning, self-esteem, eating, recreation/hobbies, communication, and symptoms/problems (Ware et al. 1993) as compared to the LDSI-2.0 that is a disease specific HRQOL questionnaire. However, there are similar items addressed in both the generic and the disease specific HRQOL questionnaires (SF-36 and LDSI-2.0). Therefore, to assess the construct validity of the Arabic LDSI-2.0, the top 10 correlations with the highest magnitude between items of the LDSI-2.0 and domains of SF-36 were identified in van der Plas's study (van der Plas et al. 2004) (see Table 5-1). For example, it was hypothesised that the mental health domains in SF-36 could moderately correlate with items of depression and hindrance of depression in the LDSI-2.0, suggesting that the item of depression and the domain of mental health measure similar construct. These associations were tested in the pilot study.

Table 5-1: Association between SF-36 and LDSI-2.0 items that produced correlations of the highest magnitudes in study by van der Plas's et al. (2004)

SF-36 domains	LDSI-2.0 items (r value)
BP	Joint pain 1 (-0.67) * Hindrance joint pain 2 (-0.67) *
MH	Depression 3 (-0.61) * Hindrance depression 4 (-0.59)*
SF	Hindrance depression 5 (-0.59)* Depression 8 (-0.55)*
VT	Hindrance depression 6 (-0.55)* Depression 7 (-0.55)* Hindrance sleep 9 (-0.54)*
RE	Hindrance depression 10 (-0.54)*

Note: it was hypothesized that there would be a relationship between the listed items of LDSI-2.0 and the domains of SF-36.
*P < 0.0002,

To examine the convergent validity of the LDSI-2.0, Spearman's rho rank correlation coefficient (r_s) test was utilized. The Spearman's correlation matrix examined the convergent relationship between the LDSI-2.0 items and the eight subscales of SF-36. It was also used to test the convergent relationship between specific symptom severity items and their accompanying symptom hindrance items, based on data obtained at T1. The Spearman's correlation coefficient scale from (-1 to +1) was used to assess the level of correlation, with particular attention paid to those judged most likely to be correlated. A Spearman's correlation value < 0.40 was considered as low, 0.40-0.70 as moderate and > 0.70 as high (Fayers and Machin 2000).

5.5.1.3 Testing the Reliability of the Translated LDSI-2.0

The test-retest reliability was examined using data obtained from the participants (n = 27) who completed the translated LDSI-2.0 at both T1 and T2 (van der Plas et al.

2004; Waltz et al. 2010). A short interval of maximum three days was selected to decrease the potential variation in symptom severity that might lead to disagreement between the test and retest results (van der Plas et al. 2004).

To evaluate the retest reliability the statistical test weighed Kappa (K) was utilized. The Kappa (K) test assesses the proportion of chance of agreement between first time and second time measures (Viera and Garrett 2005; McDowell 2006; Waltz et al. 2010). Interpretation of the K result was as follows: Kappa < 0.20 poor, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good and 0.81-1.00 very good reliability (Fayers and Machin 2000; van der Plas et al. 2004; Viera and Garrett 2005).

To test the internal consistency of the translated LDSI-2.0's multi-item scales, Chronbach's alpha coefficients were used; alpha ≥ 0.70 was considered an acceptable level of internal consistency (Nunnally and Bernstein 1994).

5.6 RESULTS

5.6.1 Translation Result

5.6.1.1 Forward Translation

In Arabic, many synonyms have the same meaning. Therefore, the main difference between the two forward translations was the actual Arabic words used, although their meanings were similar. A member of the research team (an Arabic native speaker qualified in English) and the two translators discussed the two versions of the forward translation, to give one Arabic version (T 1 - 2).

5.6.1.2 Back Translation

The main discrepancies between the two back translations were small words, although the translations were similar. The two back translators carried out a reconciliation of these minor differences to give the final back translation LDSI-2.0 (T 3 - 4) which was emailed to the original author for his feedback and approval.

5.6.1.3 Face and Content Validity

Modifications to the wording of some items were made to ensure clarity for an Arabic speaking person (Egyptians). For example, in item 12 the phrase “with respect to mortgaging or insurance” was removed, as this is not relevant to Arabic people. A clear instruction is one of the most important characteristics of instrument (Parahoo 2006). Thus, a brief introduction was added to the Arabic LDSI-2.0 to show participants how they could respond to questions (Appendix 5-9).

5.6.2 Pilot Study Result

Forty-three patients met the inclusion criteria and were invited to participate in the pilot study. Three patients refused to participate and two did not complete the interviews (Diagram 5-2).

Diagram 5-2: Pilot study sample flow diagram and consent

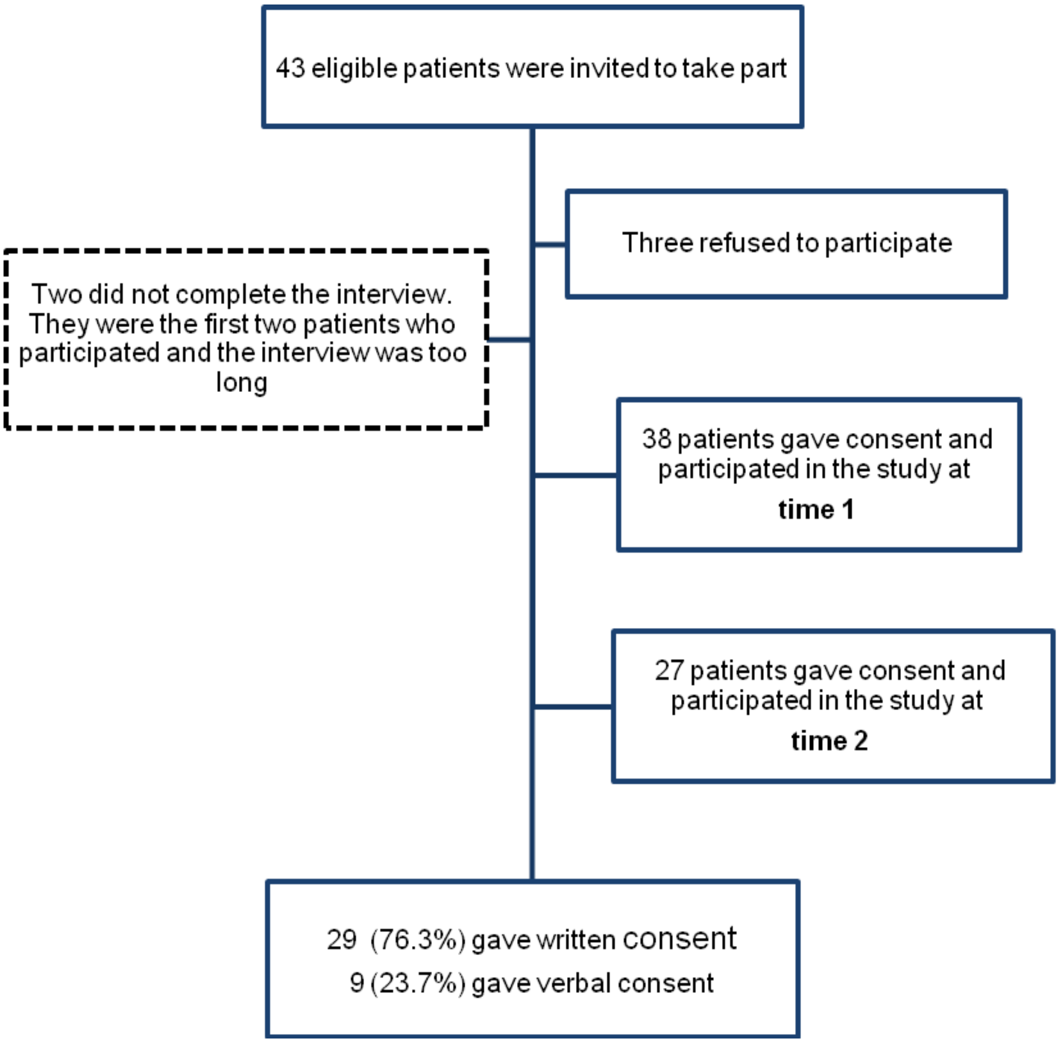


Table 5-2 shows the characteristics of the participants: 38 patients with liver cirrhosis enrolled in the study; 26 (68.4%) in-patients and 12 (31.6%) outpatients. There was a reasonable balance between men and women and those living in urban and rural areas. For the majority of the sample (78.9%), hepatitis C caused their cirrhosis, and 82% had decompensated cirrhosis.

Table 5-2: Characteristics of the participants (demographic and medical data)

Characteristics		**n = 38**	**100 (%)**
Gender	Men Women	26 12	68.4 31.6
Age	Mean (±SD) 50.21 (8.40) age ranged from 21 - 66 years		
Education level	Illiterate Can read and write Basic education Higher education	9 11 11 7	23.7 28.6 28.9 18.4
Current employment status	Employed Unemployed	17 21	44.7 55.3
Reason for unemployment	Liver disease Retirement No specific reason	7 2 29	18.4 5.3 76.3
Place of Residence	Rural Urban	20 18	52.6 47.4
Medical fees	Patient or Relatives Insurance Zaka (charity)	23 10 5	60.5 26.3 13.2
Marital status	Single (never married or Widowed) Married	3 35	7.9 92.1
Setting of data collection	Outpatient Inpatient	26 12	68.4 31.6
Cause of cirrhosis	Hepatitis C Hepatitis B Bilharzias Hepatitis C & Bilharzias	30 1 4 3	78.9 2.6 10.5 7.9
Cirrhosis stage	Compensated Decompensated	7 31	18.4 81.6
Previous hospital admission	Yes No	19 19	50 50
Number of comorbidities	Without comorbidities With one comorbidities With >1 comorbidities	17 15 6	44.7 39.5 15.8

5.6.2.1 Translated LDSI-2.0 Feasibility

The LDSI-2.0 was completed in a face-to-face interview lasting 5-15 minutes, with a median completion time of 10 minutes and a mean of 9.6± (standard deviation (SD) 1.88) minutes. 89.4% of participants completed the questionnaire in less than or equal to 10 minutes. The interview time to complete all the instruments did not exceed 45 minutes. The items were clear and understandable for all participants and there were no unanswered questions.

During the interviews of the first five patients, direct responses were hard to elicit for three items and more clarification was required. For example, for item 1 “severity of itch”, three of the participants gave irrelevant responses such as eye itch or gum itch. The item was therefore modified to “severity of skin itch”. Although item 8, “Fear of complications” was clear to the majority of participants, it elicited unspecific responses such as “I do not know” or “only Allah (God) knows that”. This kind of response is culturally and religiously appropriate, as developing complications are seen as in “God’s hand”. It was therefore decided that such a response did not necessarily mean that the respondent had misunderstood the item. For item 10 “remembering things”, some participants, especially those who were illiterate, gave a response which suggested that they did not understand the question. This item was therefore changed to “to what extent did you have difficulty in remembering things since liver disease”. To ensure that participants understood the question, they were then asked to give an example.

The LDSI-2.0 response scale

The original LDSI-2.0 is an index scored on a 5-point scale ranging from zero ‘not at all’ to 4 ‘to a high extent’. This scale was unclear for a minority of the participants, especially the uneducated ones. With input from the patients, the scale was not changed but clarified by adding the terms *"0. Not at all, 1. Mild, 2. Moderate, 3. Severe, 4. Very severe"*. These terms (mild, moderate, severe and very severe) were only used with patients who found it difficult to understand the original scale. They were not added to the questionnaire to avoid confusion in future use.

Finally, an open-ended question was added at the end of the LDSI-2.0 (Are there any other symptoms you experienced during the last week?) to ensure that all symptoms that participants could have suffered from were recorded. Twenty-six (68.42%) participants indicated that the tool covered all symptoms which hindered their daily activities but nine added muscle cramp, two added insomnia, five added dark skin colour or brown colour and one added constipation. All these participants indicated that these symptoms affected their daily activities and their social interaction to a high extent.

5.6.2.2 Translated LDSI-2.0 Validity

Table 5-3 and Table 5-4 present the Spearman's rho correlation coefficient (r_S) that was used to examine the convergent relationships between items of the LDSI-2.0 and eight domains of the SF-36. The result showed that there were no high correlations between LDSI-2.0 and SF-36, but there was moderate correlation between some of LDSI-2.0 items and SF-36 (r_S ranged from 0.40 to 0.61). As was hypothesised, hindrance of depression in the LDSI-2.0 was convergent with many domains of SF-36 such as role limitation due to emotional problems (r_S = -0.54) and vitality (r_S = -0.41). Hindrance of depression item was expected to correlate moderately with the domains of MH and SF in SF-36 (Table 5-1). However, the level of correlation was lower than the previous study (van der Plas et al. 2004).

The LDSI-2.0 depression item was expected to correlate moderately with the domains of VT, MH and SF in the SF-36 (Table 5-1). The results showed that depression item was convergent with the domain of MH in the SF-36 (r_S = - 0.40), as expected. However, the association between the depression item and the domain of vitality showed low correlation (r_S = - 0.36). On the other hand, the items of joint pain, hindrance of joint pain and hindrance of sleepiness during the day were not correlated with any of the SF-36 domains, despite the previous study identifying associations.

Interestingly, only the item of abdominal pain (LDSI-2.0) had a moderate convergent correlation with the domain of bodily pain (SF-36) (r_s = - 0.45), in contrast to the previous study (van der Plas et al. 2004) that found a moderate convergent correlation between the LDSI-2.0 items of joint pain and abdominal pain, and the SF-36 domain of bodily pain (Table 5-1).

Unexpectedly, the hindrance of a decreased appetite showed a moderate convergent association with four domains of SF-36 (PF, RE and GH). The items of decreased sexual interest and sexual activity were moderately correlated with two domains in the SF-36: PF and VT. These items seem to be important disease-related symptoms that might interfere with the HRQOL of patients with liver cirrhosis.

The result also showed that symptoms and hindrance of itch on activity and sleeping, joint pain, sleepiness during the day and jaundice had a low correlation with all of the SF-36 domains, suggesting that these items had divergent relationships with SF-36.

Table 5-3: Convergent validity of the translated LDSI-2.0 by means of Spearman’s rho correlation (r_s) between its items and the SF-36 domains (n = 38)

SF-36	Itch	HITC	IHS	JP	HJP	ABP	HAP	SLD	HSLD	WOR	HWOR	DAP	HDAP	DEP	HDEP	FDC	J	HJ
PF	-0.07	-0.33*	-0.20	-0.15	-0.22	**-0.46****	**-0.47****	0.06	-0.09	-0.33*	**-0.50****	-0.45**	-0.50**	**-0.56****	**-0.61****	-0.24	-0.11	-0.12
RP	-0.07	-0.14	-0.01	-0.04	0.06	-0.32*	-0.31	-0.06	-0.06	0.14	-0.01	-0.25	-0.35*	-0.22	-0.29	-0.22	-0.10	-0.07
RE	0.08	-0.02	0.12	0.06	-0.13	-0.25	-.031	0.15	0.03	-0.10	-0.26	-0.26	-0.55**	-0.33*	-0.54**	-0.36*	-0.16	-0.19
BP	-0.00	-0.14	-0.15	-0.08	-0.06	-0.45**	-0.38*	-0.09	-0.28	-0.22	-0.39*	-0.41**	-0.42**	-0.17	-0.25	-0.02	-0.02	-0.04
VT	-0.07	-0.04	-0.03	0.05	0.02	-0.23	-0.28	-0.06	-0.13	-0.29	-0.36*	-0.28	-0.42**	-0.36*	-0.41**	-0.39*	0.18	-0.01
MH	-0.07	-0.14	-0.12	-0.18	-0.21	-0.30	-0.30	-0.14	-0.21	-0.29	-0.37*	-0.37*	-0.43**	-0.40*	-0.33*	-0.15	-0.10	0.001
SF	-0.04	-0.01	0.02	0.17	0.08	-0.16	-0.19	0.01	-0.07	-0.21	-0.30	-0.19	-0.31	-0.10	-0.23	-0.28	0.04	-0.05
GH	-0.15	-0.30	-0.26	-0.16	-0.15	-0.25	-0.25	-0.17	-0.27	-0.13	-0.25	-0.59**	-0.59**	-0.38*	-0.47**	-0.40*	0.03	-0.11

*Correlation is significant at the p value < 0.05, ** Correlation is significant at the p value ≤ 0.001 (2- tailed)

Spearman’s (r_S) value < 0.40 low correlation (slight information overlapping between LDSI item and SF-36 domains), r_s value ≥ 0.40 and < 0.70 moderate correlation (moderate information overlapping), $r_s \geq 0.70$ (strong information overlapping)

The bold values in the table are items with $r_s \geq 0.40$ (moderate correlation or overlapping)

The underlined values are the results according to the 10 hypotheses in Table 5.1

LDSI 2.0’S items:

Itch: severity of itch, **HITC:** hindrance of itch in daily activities, **HIS:** hindrance of itch in sleeping, **JP:** severity of joint pain, **HJP:** hindrance of joint pain in daily activity, **ABP:** severity of right abdominal pain, **HAP:** hindrance of abdominal pain in daily activities, **SLD:** severity of sleepiness during the day, **HSLD:** hindrance of sleepiness during the day in daily activities, **WOR:** severity of worry about the family situation, **HWOR:** hindrance of worry about the family situation in daily activities , **DAP:** severity of decreased appetite, **HDAP:** hindrance of decreased appetite in daily activities , **DEP:** severity of depression, **HDEP:** hindrance of depression in daily activities or social contact, **FDC:** severity of fear disease complications, **J:** severity of jaundice, **HJ:** hindrance of jaundice in daily activities or social contact

Table 5-4: Convergent validity of the translated LDSI-2.0 (extra six items) by means of Spearman's rho correlation (r_s) between these items and the SF-36 domains (n = 38)

SF-36	**Memo**	**PersoCh**	**Time**	**Financial**	**Sex.Int**	**Sex.Act**
PF	-0.39*	**-0.47****	-0.39*	-0.27	**-0.47****	**-0.52****
RP	-0.05	-0.35*	**-0.49****	-0.17	-0.27	-0.31
RE	-0.06	-0.21	-0.34*	-0.14	-0.36*	**-0.44****
BP	-0.25	-0.19	-0.24	-0.10	-0.28	-0.16
VT	-0.10	**-0.45****	**-0.51****	-0.28	**-0.55****	**-0.54****
MH	-0.37*	-0.23	-0.24	-0.12	-0.36*	-0.32
SF	-0.02	-0.37*	-0.36*	-0.18	**0.54****	0.38*
GH	-0.32*	**-0.40***	**-0.43****	-0.25	0.33*	0.30

*Correlation is significant at the p value < 0.05, ** Correlation is significant at the p value ≤ 0.001 (2- tailed)

The bold values in the table are items with r_s ≥ 0.40 (moderate correlation or overlapping)

LDSI-2.0's extra items:

Memo: severity of remembering, **PersoCh:** severity of changing personality, **Time:** severity of using and managing time, **Financial:** hindrance in financial affairs, **Sex.Int:** severity of decreasing sexual interest and **Sex.Act:** severity of degreasing sexual activity.

Table 5-5 displays the Spearman's rho correlation between paired items (items of symptom severity and accompanying symptom hindrance) of the LDSI-2.0. The results showed that correlation coefficients ranged from medium to high (r_s ranging from 0.44 to 0.93). In general, symptom severity items correlated strongly with their accompanying hindrance symptom item rather than with other items. However, only three items, joint pain, abdominal pain and sleep day, had a high correlation with their accompanying items (0.89, 0.93 and 0.84 respectively).

Table 5-5: Construct convergent validity of the translated LDSI-2.0 by means of spearman's rho correlation between symptom items and their accompanying symptom hindrance items (n = 38)

Severity and hindrance item pairs	**Inter item Spearman's correlation (r_s value)**
Itch (3)	Itch hampered activity 0.44** Itch hampered sleep 0.65**
Joint pain (2)	0.89**
Abdominal pain (2)	0.93**
Sleepiness during the day (2)	0.84**
Worry (2)	0.56**
Decreased appetite (2)	0.74**
Depression (2)	0.73**
Jaundice (2)	0.74**

**Correlation is significant at the 0.001 level (2 tailed); p value ranged from (0.001-0.0005). The bold r_s values are the values of items that have low to moderate correlation with their paired items.

5.6.2.3 Translated LDSI-2.0 Test-Retest Reliability

The test-retest reliability of the translated LDSI-2.0 was examined using the Kappa test with the 27 patients who gave consent to take part in a second interview. Seventeen items of LDSI-2.0 showed a moderate to very good retest reliability (Kappa value 0.62 - 0.94). Seven items did not produce Kappa values because of an inequality of response. To solve this problem, a non-parametric marginal homogeneity test was used to examine the retest reliability of these seven items, with p value ranging from 0.13 to 0.76 ($p > 0.05$) indicating that there was no significant change in the participants' second responses (Table 5-6).

Table 5-6: Test-retest reliability of the translated LDSI-2.0 by kappa test and nonparametric, marginal homogeneity test (n = 27)

LDSI items	**Kappa value**	**Non Par, Marginal homogeneity test P-value**
Itch	0.84	
Itch hampered activity	-	0.31
Itch hampered sleep	-	0.16
Joint pain	0.84	
Joint hampered	0.94	
Abdominal pain	0.74	
Abdominal pain hampered	0.74	
sleepiness during the day	0.73	
Sleepiness during the day Hampered	0.79	
worry	-	0.12
Worrying hampered	0.62	
Decrease appetite	0.89	
Decrease appetite hampered	-	0.76
Depression	0.67	
Depression hampered	-	0.13
Afraid complication	-	0.18
Jaundice	0.80	0.14
Jaundice hampered	-	0.43
Memory	0.76	
Personality change	0.80	
Financial	0.81	
Use time differently	0.94	
Sexual interest	0.94	
Sexual activity	0.67	

5.6.2.4 Translated LDSI-2.0 Internal Consistency

Chronbach's alpha coefficient for multi-items scales ranged from 0.73 to 0.96. Alpha ≥ 0.70 is considered the acceptable level of internal consistency (Nunnally and Bernstein 1994) (Table 5-7).

Table 5-7: Internal consistency reliability of the translated LDSI-2.0 by means of alpha coefficient between symptom items and their accompanying symptom hindrance items (n=38)

Severity and hindrance item pairs concerning Items (N)	Alpha coefficient (α value)
Itch (3)	0.84
Joint pain (2)	0.95
Abdominal pain (2)	0.96
Sleepiness during the day (2)	0.90
Worry (2)	0.73
Decreased appetite (2)	0.87
Depression (2)	0.86
Jaundice (2)	0.81

5.6.2.5 Sample Size

With a sample size of 38, this study had 90% power to identify a Pearson's correlation of 0.5 (and lower with Spearman's correlation co-efficient), with statistical significant at $p \le 0.05$.

5.7 DISCUSSION

Before this research was undertaken, valid and reliable short Arabic disease-specific tools to assess symptoms related to liver disease and hindrance of these symptoms on patients' daily activities (disease specific HRQOL tool) did not exist. Therefore, in this pilot study, an Arabic version of the LDSI-2.0 was developed, its psychometric properties were tested and its administration showed that it has acceptable validity and retest reliability.

5.7.1 Translation Process

The translation process is the most common method of preparing instruments for cross-cultural research (Sperber 2004; Cha et al. 2007). The process of translating a tool into a different language can be difficult and requires a considerable investment of time and money (Sperber 2004; Acquadro et al. 2008). For this reason, the translation process was funded by the School of Nursing, Midwifery and Health, University of Stirling, and it took around three months to complete before the pilot study could commence.

Sperber 2004, (p. S124) claimed that questionnaire translation is *'often an afterthought, treated as an unimportant part of the study protocol and implemented without attention to the critical issues involved'*. However, appropriate translation of the instrument can enhance research quality and validity (Sperber 2004). Selecting the proper translation technique and procedure was a vital step to maintain the equivalence between the two versions of the tool (Cha et al. 2007). The guideline for standards of questionnaire translation (Guillemin et al. 1993) was used to carry out the translation process to maintain the conceptual and semantic equivalence of the translation with the original LDSI-2.0. The translation process was carried out by highly qualified translators (Sperber 2004) to prevent difficulties that might result from tool translation that might threaten the study's validity. Although the back-translation was time consuming and expensive, it is important to keep the equivalence of semantic words (meaning), idiomatic expressions and grammatical form between the translated questionnaire and its original source (Guillemin et al. 1993; Sperber 2004).

Finally, the original author of the LDSI-2.0 and the review committee approved the quality of the translation. The review committee also approved the face and content validity of the Arabic LDSI-2.0. Field testing (piloting) was recommended in the international guidelines. Therefore, the translated LDSI-2.0 was used with a sample of people with liver cirrhosis in Egypt to complete the cross-cultural adaptation of the Arabic LDSI-2.0.

5.7.2 Pilot Study Key Results

5.7.2.1 Arabic LDSI-2.0 Feasibility

The LDSI-2.0 is a multidimensional short questionnaire that consists of 24 items. The findings indicate that the Arabic version of the tool can be completed quickly in clinical settings through interviews, even with illiterate patients or those with more advanced disease. In this study, the median completion time of the translated LDSI-2.0 was 10 minutes, which is a little higher than in a previous study which recorded a median completion time of 6 minutes (Unal et al. 2001). This discrepancy may have arisen because different completion methods were used, as participants in the earlier study completed the questionnaire themselves, whilst in this study the participants were interviewed. It could also be that to read the questions in Arabic takes longer than in English.

Although the majority (68.42%) of the participants indicated that the tool covered all symptoms that hindered their daily activities, a number of other symptoms like muscle cramp, difficulty with sleeping at night, dark skin colour (brown) and constipation, were added by a few of the participants as they affected their daily activities and social interaction to a high extent. It is therefore recommended that the open ended question be kept in the Arabic version to collect all relevant symptoms experienced by these patients.

5.7.2.2 Arabic LDSI-2.0 Construct Validity

Validity means the degree to which an instrument measures what it is intended to measure (Fowler 1995; Litwin 1995; Liobiondo-Wood and Haber 1994; McDowell 2006). The foundation of all rigorous research designs is the use of measurement tools that are psychometrically sound (DeVon et al. 2007). Validity is one of the most essential characteristics of an instrument and is a prerequisite for quantitative tools and for assuring the integrity of study findings (Polit and Beck 2008). Knowing what type of psychometric properties to look for can be a very important step in proving the tool's validity, such as convergent construct validity (DeVon et al. 2007).

Convergent construct validity is used to determine the extent to which two or more instruments measure the same construct (item) after administration to the same individuals at the same time and under the same conditions (Liobiondo-Wood and Haber 1994; Litwin 1995; McDowell 2006). Convergent construct validity is measured by using correlation tests. Correlations indicate whether there is an overlapping between the measurements' items, establish whether the tested scale's items measure the same concept, and give either redundant or complementary information depending on the magnitude of the association (van der Plas et al. 2004). As the SF-36 questionnaire is validated in Arabic it was used as the gold standard instrument to test the convergent validity of the LDSI 2.0, which is a disease specific HRQOL questionnaire. Thus, both measurements (LDSI-2.0 and SF-36) were completed during patient interview.

The result showed that there was a moderate correlation between a minority of LDSI-2.0 items and SF-36. According to the stated hypotheses (see Table 5-1), the results have shown that there were specific items of LDSI-2.0 that moderately correlated with specific domains of SF-36 as was expected (in total three correlations). For example, hindrance of depression in the LDSI-2.0 was convergent with role limitation due to emotional problems in the SF-36. Additionally, the item of depression was convergent with the domain of mental health in the SF-

36, and hindrance of depression was convergent with the domain of vitality. This result means there is moderate overlapping between the provided information by the two tools regarding these items and domains. Also, as was expected, the item of depression correlated with the domain of vitality and the item of hampered depression correlated with domain of mental health, although r's value of both correlations was less than 0.40, suggesting only slight overlapping.

However, r's values of the remaining five correlations that were expected for Table 5-1 were ≤ 0.23, suggesting that these items in LDSI-2.0 had divergent relationships with the SF-36. For example, there was a divergent association between the item of joint pain in the LDSI-2.0 and the domain of bodily pain in the SF-36, suggesting that joint pain as a specific type of pain is complementary to the bodily pain.

For instance, in this study, the item of abdominal pain (LDSI-2.0) showed a convergent correlation with the SF-36 domain of bodily pain, while the prior study of van der Plas et al. in 2004 found a convergent relationship between joint pain and abdominal pain as well as the domain of bodily pain (SF-36). This result suggests that the domain of bodily pain in the SF-36 assesses a general pain, while the items of pain in the LDIS-2.0 (joint pain and abdominal pain) examine specific types of pain. Therefore, the items of the LDSI-2.0 as a specific disease index can give complementary information to the generic SF-36.

Furthermore, the results show that disease specific items such as itch, hindrance of itch on daily activity, hindrance of itch on sleeping, jaundice, hindrance of jaundice and hindrance in financial affairs showed a divergent association with all domains of SF-36. These results are consistent with the previous study of van der Plas et al.

in 2004. This result supports the hypothesis that the SF-36 does not examine disease specific items. Thus, there was a slight to moderate overlapping information between the two measurements, suggesting that the disease specific HRQOL questionnaire (LDSI-2.0) can be used to complement the generic HRQOL measurement (SF-36), and it is, therefore, important to use both tools when investigating HRQOL.

Interestingly, the items of hindrance of decreased sexual interest and sexual interest unexpectedly had a convergent moderate association with multiple domains of vitality and PF (SF-36); that suggested moderate overlapping. Indeed, the association is logical, and it means that patients with low vitality or low PF are more likely to have low sexual interest or sexual activity. Furthermore, sexual activity had a moderate correlation with role limitation due to emotional problems, and sexual interest had moderate correlation with social functioning. These findings supported the construct validity of the Arabic LDSI-2.0 because sexuality theoretically can reflect the individual’s vitality, physical functioning and relationship with their partner. For instance, in 2005, Toda et al. found that significant predictors of erectile dysfunction among patients with cirrhosis were PF, SF and RP. However, it is worth noting that this study investigated sexual health in terms of erectile function among males, but not desire or activates therefore the study’s findings cannot be generalised to females’ sexual health. Therefore, based on these findings, there is a need for future research to investigate the association between sexuality and HRQOL among patients (males and females) with cirrhosis.

It is important to highlight that difference in the results between the current study and prior study (van der Plas et al. 2004) may be due to differences between the

Egyptian and Dutch populations and differences in symptoms of concern that may be relevant to their HRQOL.

All the items of symptoms, such as joint pain and hampered of joint pain had a moderate to high correlation with their accompanying items of hindrance of these symptoms. This finding is similar to the previous study by van der Plas in 2004 which found that the correlation value ranged from 0.52 to 0.80. These results suggest information overlapping between these items and their accompanying items. However, van der Plas et al. (2004) found that hindrance of symptoms had a higher negative influence on HRQOL than increasing symptoms severity. Therefore, the items of symptoms severity and items of symptoms hindrance measure different aspects of HRQOL (van der Plas et al. 2004).

Additionally, the convergent relationships between all symptom severity items and their accompanying symptom hindrance items showed a strong relationship, rather than with other symptom hindrance items. This result is very similar to the study of van der Plas et al. in 2004, suggesting construct validity and internal items consistency of the LDSI-2.0.

5.7.2.3 Arabic LDSI-2.0 Reliability

High reliability of a measurement is not evidence of its validity, but unreliability is evidence of its invalidity (Polit and Beck 2008). However, reliability and validity are interrelated criteria for the tool (Polit and Beck 2008). A measuring tool cannot assess what it is intended to measure if it is inconsistent (unreliable) (Polit and Beck 2008). Reliability means to what extent the instrument gives consistent results over time (Liobiondo-Wood and Haber 1994), and whether it is free from measurement error with repeated measures (Waltz et al. 1991; Litwin 1995).

Test-retest reliability

The test-retest reliability is the most common type of reliability procedure that is used to assess an instruments' reliability (stability over time) (Litwin 1995). The test-retest reliability procedure is conducted by administering the same instrument to the same individuals under the same conditions on two or more separate times to evaluate whether the measurement gives the same results (Liobiondo-Wood and Haber 1994; Litwin 1995; McDowell 2006; Waltz et al. 2010). The time interval between the repeated measures depends on the phenomena being measured (Waltz et al. 1991; Liobiondo-Wood and Haber 1994; Waltz et al. 2010). Therefore, test-retest reliability was carried out using data obtained from the participants (n = 27) who completed the translated LDSI-2.0 at both times 1 and 2.

Internal consistency reliability

The results of the current study show that the alpha coefficients for the subscales exceeded the acceptable value > 0.70 (Nunnally and Bernstein 1994) indicating that the Arabic LDSI-2.0 subscales are internally consistent. This confirms the result of an earlier study, which found all alpha values > 0.78 (range 0.79 - 0.86) (Unal et al. 2001).

5.8 LIMITATIONS AND RECOMMENDATIONS

Although this is the first study to use an Arabic version of LDSI-2.0, which is available for future use, its limitations must be acknowledged.

The study design was cross-sectional in nature; which involves the collection of data at one time. The participants were predominately patients with liver cirrhosis. The disease stage was categorised as patients with compensated or decompensated cirrhosis according to liver disease complications during the year of data collection. However, the strength of the current study is the heterogeneity of the study participants, which included patients from both outpatient and inpatient clinics, as well as males and females from both rural and urban areas in Egypt. Therefore, the translated LDSI-2.0 can be used with a wide range of patients with liver cirrhosis in Egypt.

The small sample size, from only one hospital, limited the validation that could be carried out, although the initial validity was good. It is therefore recommended that further research will continue the psychometric validity testing of the translated LDSI-2.0 among Arabic patients at different chronic liver disease stages; to evaluate the construct known group validity and to carry out factor analysis that was not done in the original LDSI-2.0.

5.9 CONCLUSION

The pilot study was a particularly useful stage for translating and testing the feasibility, validity and reliability of the LDSI-2.0. The translated LDSI-2.0 was found to be feasible, valid and reliable with patients at different stages of cirrhosis, suggesting that the Arabic LDSI-2.0 is a satisfactory tool for future research of symptoms or QOL related liver disease in the Egyptian population.

The pilot study was also useful to confirm the feasibility of daily recruitment rates (minimum and maximum), and the expected sample size for the main study. Additionally, it was helpful in identifying issues of concern for the main study such as time of interviews, recruitment strategy and whether three months of field work would be enough to recruit a large enough sample for the main study. This study reinforced the importance of the researcher attending the clinic settings daily and being systematic in the recruitment of a large sample size during the three months.

In particular, the pilot study helped to confirm that the daily rate of recruitment would range from 2 to 7 eligible participants from one setting. It is also important to acknowledge that the pilot phase findings were strengthened by the diverse range of patients that were recruited. For example, the participants were from a wide age range, males and females from rural and urban regions and with different social backgrounds, allowing a range of perceptions to be obtained.

6 CHAPTER 6- RESULTS

6.1 INTRODUCTION

This chapter presents the findings from the cross-sectional survey (main study) analysis. The study had three aims as stated in section 1.3. This chapter addresses the first aim of the study:

First aim: To describe Health-Related Quality of Life (HRQOL) of Egyptian liver cirrhotic patients and to identify and evaluate factors associated with (HRQOL) physical and mental health domains. The chapter is structured in three sections. Section I describes: (a) participant characteristics and (b) HRQOL of people with liver cirrhosis in Egypt. Section II presents factors associated with HRQOL using bivariate data analysis: (a) socio-demographic characteristics; (b) medical data; (c) symptoms experience and (d) perceived adequacy of social support. Section III presents factors associated with HRQOL using multivariate (stepwise multiple linear regression) analysis, followed by a summary of the chapter.

6.2 PARTICIPANT CHARACTERISTICS

Participants were recruited from three clinical settings in the biggest city in Egypt (Cairo), from both inpatient and outpatient clinics if they had been diagnosed with compensated or decompensated liver cirrhosis.

Recruitment rates were monitored and recorded on a daily basis and were accurately maintained through the study. The reasons why patients refused to take part in the study, or indeed withdrew from the interview were recorded. The recruitment phase in the study lasted three months and was conducted from June to August 2011. During this time, 415 patients were identified as being eligible to participate in the study; two of them were not approached because their consultant advised that these patients were too anxious to participate. The total number of participants who gave consent and participated in the study was 401 (Diagram 6-1).

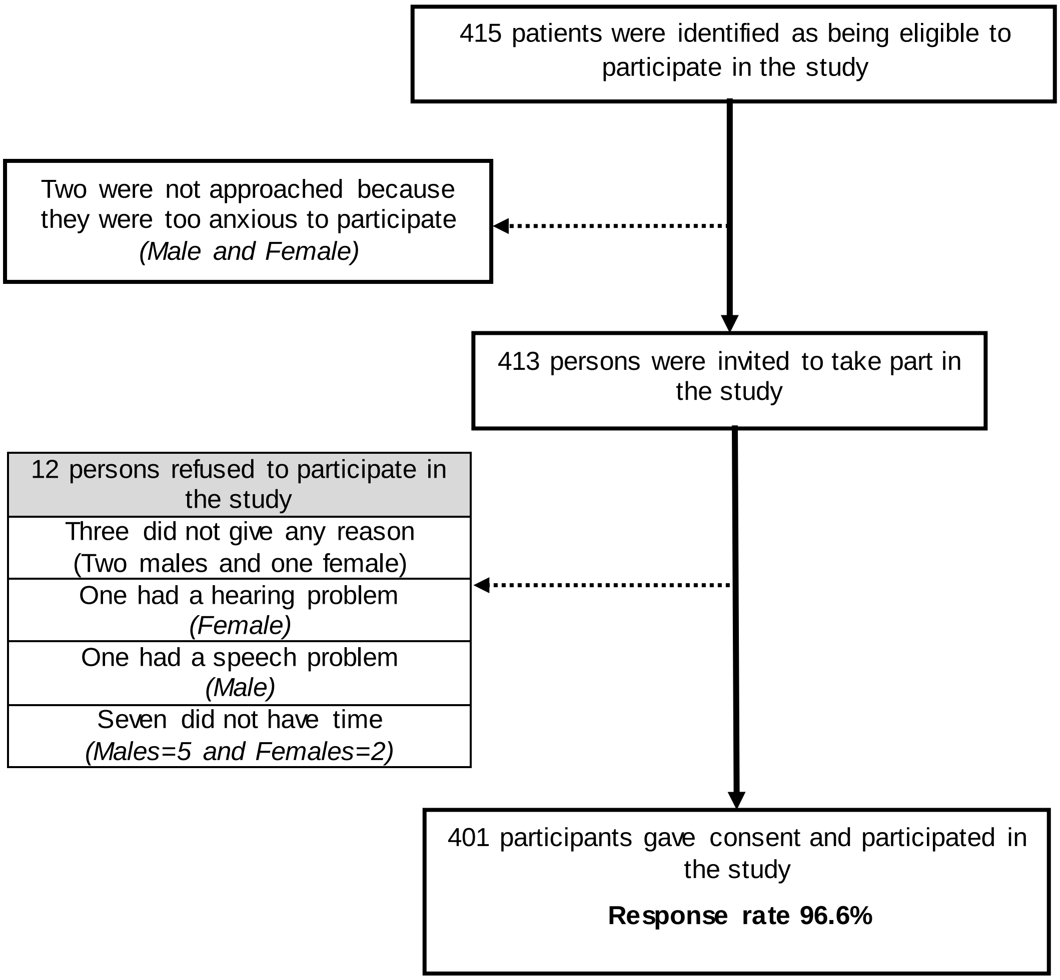
The researcher obtained permission from the patient before conducting the interview as to whether her/his relative could be in the room during the interview. The majority of the patients who participated in the study preferred to be interviewed alone. Data collection time lasted between 20-40 minutes per participant and was dependent on the patients' health status and as well as their ability to provide further details about their experience with the disease.

Whilst interviewing the participants to complete the questionnaires some of them felt the need to "explain" their answer. Therefore this information not used as data, but used as quotes for illustration. Illustrative quotes from qualitative quotes are seen as a way of illuminating the quantitative results and thus are treated as part of discussion. Therefore, these quotes are not really being treated as data in this study. The participants were Arabic speakers so as a result their quotes were translated into English.

The following quote illustrates the interest of the participants to talk about their health status.

‘I need to talk and express my feelings because I cannot say this to anyone … I am feeling comfortable to talk...there is no one who can understand me’. Female (303)

Diagram 6-1: Sample flow diagram



6.2.1 Socio-Demographics Characteristics and Medical Data

Just over half of the participants were female (56.6%), 77.3% were married with mean age 53.25 ± (standard deviation-SD) 9.0 that ranged from 22 to 76 years (Table 6-1). The mean age of males was 52.44±8.804 and mean age of females was 53.87±9.185 and age did not differ significantly between males and females, t (1, 399) = 0.1579. Only 17% of participants in this study were currently employed, although the majority (90%) were less than 65 years old. 53.4 % of the participants were housewives, while 39.0% were unemployed (stopped working) due to their inability to work as a result of liver disease.

The majority of the participants (80.3%) were recruited from outpatient departments and were equally distributed between compensated and decompensated stages of liver cirrhosis (50.1% and 49.0%) respectively. There was no significant different between males (compensated = 81, decompensated = 93) and females (compensated = 120, decompensated = 107) disease stage X^2 (1, n = 401) = 1.570, p = 0.210. 62% of the patients reported suffering from at least one additional chronic disease (comorbidities) such as diabetes (27.7%) and hypertension (20.2%). Liver cirrhosis complications such as splenomegaly (64.6%) were prevalent. 153 (38.2%) of the patients had experienced hospital admission at least once as a result of liver disease. Ascities (23%) and bleeding (13.2%) were the most common causes of hospital admission (Table 6-2).

Table 6-1: Participants' socio-demographic characteristics, n=401

Demographic data		**N (%)**
Age	Mean ± SD	53.25 ± 9.0
Age categories	22-44 45-64 65+	55 (13.7) 306 (76.3) 40 (10.0)
Gender	Males Females	174 (43.4) 227 (56.6)
Marital status	Married Single (never married, widowed, divorced)	310 (77.3) 91 (22.7)
Education	Cannot read and write Basic education (Primary, preparatory, secondary) Higher education (university)	219 (54.6) 163 (40.0) 19 (4.7)
Residence	Urban Rural	255 (63.6) 146 (36.4)
Medication fees	The patient Relatives or family Complete insurance Insurance and the patient Charity/Zakat Combined (Treatment at state expense and the patient)	39 (9.7) 29 (7.2) 7 (1.7) 6 (1.5) 2 (0.5) 318 (79.3)
House occupation	Own Rent	260 (64.8) 141 (35.2)
Type of work	Employee (officers with stable salary) Worker (manual work without stable salary) Housewife (women do not work) farmer	56 (14.0) 136 (33.9) 178 (44.4) 31 (7.7)
Current employment status	Employed Unemployed	68 (17.0) 333 (83.0)
Cause of unemployment (n=333 unemployed)	Housewives Liver disease Other reasons (Retirement, no job available)	178 (53.4) 130 (39.0) 25 (7.5)

Table 6-2: Participants' medical data, n = 401

Medical data	**Variables**	**N (%)**
Setting of data collection	Outpatient Inpatient	322 (80.3) 79 (19.7)
Disease Stage	Compensated cirrhosis Decompensated cirrhosis	201 (50.1) 200 (49.9)
Cause of cirrhosis	Hepatitis C virus (HCV) HCV and Bilharzias Bilharzias Cryptogenic (unknown cause) Hepatitis B virus (HBV) HCV and HBV Autoimmune Portal vein thrombosis	217 (54.1) 151 (37.7) 14 (3.5) 7 (1.7) 5 (1.2) 4 (1.0) 2 (0.5) 1 (0.2)
Complications of cirrhosis	Splenomegaly Ascities Oesophageal Varices (OV) with bleeding OV without bleeding Portal hypertension Hepatic encephalopathy (Grade 1)	259 (64.6) 179 (44.6) 57 (14.2) 82 (20.4) 47 (11.7) 19 (4.7)
Number of hospital admissions related to liver disease	Never admitted Admitted 1-5 times Admitted >5 times	248 (61.8) 69 (17.2) 84 (20.9)
Cause of hospital admission	Ascities and/or edema Gastrointestinal Bleeding Hepatic coma Abdominal pain Jaundice Fever Spontaneous bacterial peritonitis Anemia	91(23) 53 (13.2) 31 (7.7) 29 (7.2) 8 (2) 7 (1.7) 6 (1.5) 4 (1)
Comorbidities	Without comorbidities ≥1 comorbidities	151 (38) 249 (62)
Types of comorbidities	Diabetes Mellitus Hypertension Gastrointestinal disease Musculoskeletal disease Renal disease Heart disease Asthma	111 (27.7) 81 (20.2) 53 (13.2) 52 (12.96) 30 (7.5) 24 (6) 18 (4.5)

6.3 HRQOL OF CIRRHOTIC PATIENTS AND ASSOCIATED FACTORS

6.3.1 HRQOL of Egyptian Cirrhotic Patients

The Means (± SD) of the eight subscales of SF-36 and the two component summary scores are provided for the entire sample (n = 401) then broken down by demographic characteristics, medical data and symptoms experience, in order to identify the factors associated with HRQOL.

No Egyptian study so far has used the SF-36 to establish a norm-based standard of comparison between people with cirrhosis and the normal population in Egypt. Ware et al. (2008) suggest using a norm-based or cut-off score of a mean of 50 and a standard deviation of 10 to interpret the results of SF-36. A mean score below 50 indicates a poor HRQOL and a mean score above 50 indicates a better HRQOL (Maruish and DeRosa 2009).

Table 6-3 shows that the mean scores of the eight domains of the SF-36 for the total sample ranged from 28.93 to 36.29, suggesting that these patients had poor perceived health. Role limitations due to physical health problems (RP) and mental health (MH) were the lowest rated domains (Mean = 28.37 and 28.93 respectively), while vitality (VT) and physical functioning (PF) were the highest rated domains (Mean = 36.29 and 35.20 respectively). Additionally, the mental component summary score (MCS) was lower than the physical component summary score (PCS) (Mean = 31.55 and 35.56 respectively).

Table 6-3: Means of SF-36 domains of patients with liver cirrhosis in Egypt

SF-36 Domains		**n = 401**	
		Egyptian people with liver cirrhosis (out of cut-off score 50)	**Egyptian people with liver cirrhosis (Out of score 0-100)**
		Mean ± SD	**Mean ± SD**
Physical health	PF	35.20±11.78	48.13±27.98
	RP	28.37±11.28	27.31±28.81
	BP	34.94±13.50	35.68±31.96
	GH	34.80±11.02	38.95±23.12
Mental health	VT	36.29±11.98	30.86±23.99
	SF	33.01±14.76	45.36±33.82
	RE	31.11±16.41	46.90±35.18
	MH	28.93±15.73	37.58±27.94
PCS		35.56±10.43	
MCS		31.55±14.42	

6.3.2 General Health Perception among Egyptian Cirrhotic Patients

The perception of patients' general health was assessed using a single question (item 1 in SF-36) that asked the patients to rate their health in general. This question was rated on the 5-point ordinal scale ranging from one "Excellent" to five "Poor". For statistical analysis, the 5-point scale order was reversed during the analysis process using the transform option in SPSS to be from one "Poor" to five "Excellent" without affecting the actual meaning of the scale.

Table 6-4 summarises the description of patients' general health perception. The results show that 183 (45.6 %) of the patients rated their general health (GH) as fair followed by 168 (41.6) who rated their general health as poor. Very few patients rated their general health as good or excellent.

Table 6-4: Perceived general health as rated by liver cirrhotic patients

n = 4 01	
Rating scale of perceived general health	**n (%)**
Poor	168 (41.9)
Fair	183 (45.6)
Good	41(10.2)
V. good	6 (1.5)
Excellent	3 (0.7)

Compared to one year ago, patients were asked to rate how they perceive their health in general now. Results show that 67.8% of the patients in general perceived their health was worse than one year ago (Table 6-5).

Table 6-5: Perceived general health compared to one year ago as rated by liver cirrhotic patients

n = 401	
Rating scale of health transition	**n (%)**
Much better now than one year ago	12 (3.0)
Somewhat better now than one year ago	70 (17.5)
About the same as one year ago	47 (11.7)
Somewhat worse now than one year ago	169 (42.1)
Much worse now than one year ago	103 (25.7)

6.3.3 Factors Associated with HRQOL among Cirrhotic Patients

Various factors associated with HRQOL (physical health and mental health domains) were examined. These factors were socio-demographic characteristics, medical data, disease stage, symptoms experience and perceived adequacy of social support.

6.3.3.1 Socio-Demographic Characteristics

To explore the association between socio-demographic factors and HRQOL, as measured by the SF-36, the study sample was divided into two groups according to gender, marital status and employment status; and into three groups according to age and education.

Table 6-6 shows the difference in HRQOL according to age, gender and marital status. In relation to the difference between the age groups, RP [f (2, 398) = 3.03, p = 0.04] was the only domain that was statistically significant, with much higher RP for the 22-44 year age group (38.47) than for the 65+years (25.75) group. Using Post-hoc statistical analysis Tukey Bonferroni identified a statistically significant difference between the two age groups [mean difference = - 5.58, Std Error = 2.33, p = 0.04].

When investigating gender, women had lower mean scores than men in all eight domains, as well as in the two component summary scores of SF-36. All results were statistically significant**.** PF, bodily pain (BP), VT and MH were the poorest rated domains among women [t (399) = 5.18, 4.09, 4.42 and 4.95 respectively] (Table 6-6).

Table 6-6: HRQOL stratified by age, gender and marital status

SF-36	**Age**				**Gender**			**Marital status**		
Domains	**22-44 years N=55**	**45-64 years N=306**	**65+ years N=40**	**f (p)**	**Men N=174**	**Women N= 227**	**t (p)**	**Single N= 91**	**Married N=310**	**t (p)**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	
PF	38.47±11.45	34.47±11.63	33.25±12.79	2.82(0.06)	38.58±12.00	32.61±10.89	5.18(0.0005)	32.68±12.11	35.94±11.59	2.33 (0.02)
RF	31.34±11.67	28.18±11.23	25.75±10.58	3.05(0.04)	30.70±12.52	26.58±9.89	3.68(0.0005)	27.44±11.16	28.64±11.32	0.90(0.37)
BP	35.54±13.89	34.71±13.47	35.83±13.50	0.18(0.83)	38.03±14.0	32.56±12.64	4.09(0.0005)	32.47±12.17	35.66±13.81	1.99 (0.04)
GH	34.98±11.73	34.35±10.95	37.97±10.19	1.92(0.14)	36.54±10.69	33.46±11.10	2.79(0.0005)	35.00±11.15	34.74±11.00	0.20 (0.83)
VT	39.03±12.15	35.62±11.91	37.57±11.96	2.15(0.11)	39.24±12.67	34.02±10.92	4.42(0.0005)	34.32±11.32	36.86±12.12	1.85(0.07)
SF	34.54±15.40	32.68±14.64	33.40±14.98	.38(0.68)	34.66±14.70	31.74±14.71	1.96(0.050)	32.64±14.31	33.12±14.90	0.27(0.78)
RE	32.13±16.69	31.23±16.25	28.77±17.39	.52(0.59)	33.29±16.73	29.44±15.99	2.34(0.02)	29.57±16.09	31.59±16.50	1.03(0.30)
MH	28.15±14.88	29.00±16.07	29.52±14.57	0.09(0.90)	33.26±16.27	25.62±14.49	4.95(0.0005)	25.72±13.84	29.88±16.14	2.42(0.02)
Component summary scores										
PCS	38.27±11.48	35.11±10.22	35.25±10.21	2.17(0.11)	37.93±10.96	33.75±9.64	4.05(0.0005)	34.39±9.80	35.91±10.60	1.27(0.22)
MCS	31.48±13.69	31.52±14.58	31.86±14.45	0.01(0.99)	34.34±15.20	29.40±13.43	3.44(0.001)	29.68±12.38	32.09±14.93	1.55(0.16)

In relation to the association between marital status and HRQOL, singles had a poorer HRQOL than married people, particularly in the domains of PF, BP and MH [t (399) = 2.33, 1.99 and 2.42, p < 0.05], but not in the summary scores.

Table 6-7 demonstrates the association between the level of education and HRQOL domains. There was a statistically significant difference between the educational groups in PF, RP, BP, VT and MH [f (398) = 4.05, 6.58, 6.99, 9.14 and 6.31 respectively, p < 0.02], and in the two component summary scores. Post hoc Tukey Bonferroni tests showed that illiterate people had significantly lower scores than educated people in PF, RP , BP, VT and MH, and in the two component summary scores (p < 0.04) (Table 6-8).

Table 6-7: HRQOL studied by education level

SF-36	**Education level**			
Domains	**Illiterate N=219**	**Basic education N=163**	**Higher education N=19**	**f (p)**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	
PF	33.72±11.06	36.80±11.96	38.53±15.80	4.05 (0.01)
RP	26.62±9.92	30.17±12.28	33.14±13.78	6.58 (0.002)
BP	32.70±12.62	37.44±13.92	39.27±15.50	6.99 (0.001)
GH	34.44±10.99	34.82±10.81	38.73±12.84	1.32 (0.26)
VT	34.64±10.37	37.38±12.97	45.85±15.25	9.14 (0.0005)
SF	32.15±14.55	33.90±15.08	35.32±14.36	0.90 (0.40)
RE	30.16±16.58	31.82±15.89	36.03±18.41	1.37 (0.25)
MH	27.27±14.89	29.88±15.96	39.93±18.78	6.31 (0.002)
Component summary scores				
PCS	34.02±9.95	37.35±10.46	37.90±13.07	5.36 (0.0005)
MCS	30.49±14.08	31.98±14.21	40.06±17.49	4.03 (0.01)

Table 6-8: Statistically significant differences between groups according to education level using Post Hoc test

SF-36	Education level		Mean difference	p value
PF	Illiterate	Lower educated	-3.08	0.03
RP	Illiterate	Lower educated	-3.55	0.006
		Higher educated	-6.52	0.03
BP	Illiterate	Lower educated	-4.74	0.002
VT	Illiterate	Higher educated	-11.20	0.0005
MH	Illiterate	Higher educated	-12.65	0.002
	Lower educated	Higher educated	-10.04	0.02
PCS	Illiterate	Lower educated	-3.32	0.006
MCS	Illiterate	Higher educated	-9.56	0.01

Only the significant result that were reported

Table 6-9 shows the association between employment status and HRQOL. The eight domains and the two component summary scores were poorer among unemployed than employed people (p = 0.0005). There were no statistically significant differences between people living in rural and urban regions in Egypt.

Table 6-9: HRQOL stratified by residential area and current employment status

SF-36	**Residence area**			**Current employment status**		
Domains	**Rural N=146**	**Urban N=255**	**t (p)**	**Employed N=68**	**Unemployed N=333**	**t (p)**
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
PF	35.05±11.95	35.29±11.70	0.19(0.84)	43.35±11.61	33.54±11.11	6.58(0.0005)
RP	28.34±11.47	28.39±11.20	0.04(0.96)	36.61±12.18	26.69±10.33	6.99(0.0005)
BP	35.10±14.18	34.84±13.13	0.17(0.85)	41.04±14.12	33.69±13.05	4.17(0.0005)
GH	35.73±10.73	34.26±11.16	1.30(0.19)	40.08±9.89	33.72±10.94	4.43(0.0005)
VT	36.05±11.08	36.42±12.49	0.30(0.76)	44.19±12.09	34.67±11.31	6.24(0.0005)
SF	34.70±14.73	32.04±14.71	1.73(0.08)	39.93±13.43	31.59±14.63	4.33(0.0005)
RE	31.44±16.25	30.92±16.53	0.30(0.76)	40.96±15.76	29.10±15.82	5.63(0.0005)
MH	28.48±16.04	29.19±15.58	0.43(0.66)	37.67±15.82	27.15±15.13	5.18(0.0005)
Component summary scores						
PCS	35.79±10.79	35.43±10.24	0.32(0.74)	41.53±11.99	34.34±9.66	5.34(0.0005)
MCS	31.88±14.30	31.36±14.51	0.34(0.72)	46.22±14.96	29.78±13.66	5.64(0.0005)

6.3.3.2 Disease Stage and Medical Data

To explore the association between disease stage and medical data and HRQOL as measured by the SF-36, the study sample was divided into two groups according to disease stage and hospital setting, and was divided into three groups according to cause of liver disease, number of complications, comorbidities and hospitalization.

Table 6-10 shows that the domain of physical health (i.e. PF and RP) and the PCS [t (399) = 3.10, 2.68 and 3.52 respectively, $p < 0.009$] were lower among patients with decompensated cirrhosis than among patients with compensated cirrhosis. Causes of liver cirrhosis, on the other hand, were not significantly related to HRQOL domains.

Table 6-10: HRQOL stratified by disease stage and cause of cirrhosis

SF-36	**Disease stage**			**Cause of liver cirrhosis**			
Domains	**Compensated N= 201**	**Decompensated N= 200**	**t (p)**	**Viruses (B or C) N= 226**	**Mix (Viruses and Bilharzias) N=151**	**Others causes N=24**	**f (p)**
	Mean ± SD	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
PF	37.00±11.74	33.39±11.56	3.10(0.002)	34.58±11.384	36.56±12.054	32.48±13.204	1.96(0.141)
RP	29.87±11.98	26.87±10.35	2.68(0.008)	28.60±11.261	28.52±11.495	25.22±10.134	0.99(0.370)
BP	36.08±13.08	33.79±13.86	1.70(0.08)	34.77±13.501	35.56±13.744	32.55±12.251	0.54(0.578)
GH	35.76±11.18	33.82±10.79	1.76(0.07)	34.52±11.043	35.48±11.049	33.07±10.798	0.64(0.523)
VT	37.33±11.66	35.23±12.23	1.76(0.07)	36.16±12.434	36.54±11.527	35.83±10.854	0.06(0.938)
SF	31.55±15.61	30.67±17.20	1.50(0.13)	32.79±14.808	33.95±14.607	29.13±15.165	1.16(0.313)
RE	34.11±14.73	31.90±14.73	0.53(0.59)	30.10±16.527	32.81±16.313	29.96±15.704	1.30(0.272)
MH	29.05±15.79	28.82±15.71	0.14(0.88)	28.30±15.658	29.87±16.035	29.01±14.878	0.44(0.640)
Component summary scores							
PCS	37.37±10.09	31.48±14.72	3.52(0.0005)	35.59±10.341	36.02±10.715	32.34±9.293	1.29(0.274)
MCS	31.61±14.14	31.48±14.72	0.08(0.92)	30.85±14.567	32.65±14.022	31.21±15.654	0.71(0.489)

Table 6-11 summarises the association between the number of liver cirrhosis complications and HRQOL. Four domains of physical health (PF, RP, BP and GH), one domain of mental health (i.e. VT) and the PCS were significantly related to the number of liver cirrhosis complications. Post-hoc statistical analysis using Tukey Bonferroni identified that patients without any or with only 1-2 liver disease complications had a higher score of HRQOL than people with 3-4 complications (Table 6-12).

Additionally, Table 6-11 shows the difference in HRQOL between patients who were in inpatient departments and patients who were in outpatients. Three domains of physical health (PF, RP and BP) [t (399) = 4.22, 2.63 and 3.72 respectively, $p \leq 0.009$], two domains of mental health (i.e. VT and Social functioning (SF)) [t (399) = 3.00 and 3.12 respectively, $p < 0.004$] and the PCS [t (399) = 4.48, $p = 0.0005$] were lower among patients in inpatient clinics than patients in outpatient clinics.

Table 6-11: HRQOL stratified by hospital setting and number of liver cirrhosis complications

SF-36	**Hospital setting**			**Complications of liver cirrhosis**			
Domains	**Outpatients N= 322**	**Inpatients N= 79**	**t (p)**	**Without complications N=74**	**With 1-2 complications N=244**	**With 3-4 complications N=83**	**f (p)**
	Mean ± SD	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
PF	36.41±1158	30.29±11.37	4.22(0.0005)	37.38±10.54	35.37±12.00	32.77±11.85	3.09(0.04)
RP	29.10±11.53	25.39±9.74	2.63(0.009)	29.49±12.03	28.98±11.56	25.58±9.28	3.29(0.03)
BP	36.16±13.77	29.95±11.11	3.72(0.0005)	33.37±10.40	36.48±14.33	31.79±12.87	4.42(0.01)
GH	34.99±11.14	34.00±10.53	0.74(0.47)	36.03±11.20	35.37±10.91	32.01±10.83	3.48(0.03)
VT	37.17±12.13	32.69±10.70	3.00(0.003)	36.10±10.98	37.43±12.22	33.09±11.66	4.12(0.01)
SF	34.14±14.6	28.41±14.50	3.12(0.002)	33.63±14.47	33.36±14.90	31.42±14.66	0.61(0.54)
RE	31.11±16.20	31.13±17.33	0.01(0.99)	32.56±15.37	31.28±16.95	29.32±15.69	0.79(0.45)
MH	29.35±16.09	27.23±14.16	1.16(0.28)	30.68±16.32	29.26±15.69	26.43±15.20	1.56(0.21)
Component summary scores							
PCS	36.69±10.38	30.95±9.37	4.48(0.0005)	36.02±8.90	36.41±11.05	32.67±9.36	4.12(0.01)
MCS	31.77±14.36	30.64±14.71	0.62 (0.53)	32.64±14.20	31.87±14.67	29.63±13.84	1.00(0.36)

Table 6-12: Statistically significant differences between groups according to liver disease complications using Post Hoc test

SF-36	**Liver disease complications**		**Mean difference**	**p value**
PF	Without complications	With 3-4 complications	4.61	0.03
RP	With 1-2 complications	With 3-4 complications	3.40	0.04
BP	With 1-2 complications	With 3-4 complications	4.69	0.01
GH	With 1-2 complications	With 3-4 complications	3.35	0.04
VT	With 1-2 complications	With 3-4 complications	4.33	0.01
PCS	With 1-2 complications	With 3-4 complications	3.73	0.01

Only the significant result that were reported

Table 6-13 shows the association between the number of comorbidities and HRQOL. All domains of physical health, two domains of mental health (VT and SF) and the PCS were significantly associated with the number of co-morbidities. Post-hoc statistical analysis using the Tukey Bonferroni identified that patients without comorbidities had a higher HRQOL score than patients with comorbidities ($p < 0.05$) (Table 6-14).

Table 6-13: HRQOL stratified by the number of comorbidities and the number of hospital admission

SF-36	**Number of Comorbidities**				**Number of Hospitalization related to liver disease**			
Domains	**Without comorbidities N=152**	**With 1-3 comorbidities N=235**	**With 4-6 comorbidities N=14**	**f (p)**	**Never admitted N=248**	**Admitted 1-5 N=125**	**Admitted >5 N=28**	**f (p)**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
PF	38.24±12.13	33.51±11.35	30.58±7.27	8.92(0.0005)	37.18±11.37	32.32±12.02	30.50±10.55	9.91(0.0005)
RP	31.49±12.88	26.65±9.80	23.27±8.00	10.43(0.0005)	29.99±12.02	25.62±9.20	26.24±10.59	6.96(0.001)
BP	37.52±14.77	33.65±12.43	28.40±11.91	5.60(0.004)	36.81±13.86	32.62±12.83	28.70±9.52	7.42(0.001)
GH	36.46±11.24	33.99±10.76	30.26±10.69	3.60(0.02)	35.63±11.01	34.23±10.82	30.00±10.97	3.56(0.02)
VT	38.90±13.25	34.91±10.73	30.90±12.67	6.77(0.001)	37.97±11.77	33.86±12.14	32.24±10.55	6.78(0.001)
SF	36.07±15.76	31.34±13.84	27.63±13.29	5.84(0.003)	34.18±14.38	32.76±15.09	23.74±13.59	6.49(0.002)
RE	33.25±17.52	29.83±15.48	29.50±17.85	2.08(0.12)	32.62±16.10	28.79±16.66	28.11±16.98	2.78(0.06)
MH	31.33±16.34	27.48±15.25	27.28±14.71	2.87(0.058)	30.65±16.29	26.26±14.47	25.67±14.40	3.93(0.02)
Component summary scores								
PCS	38.30±11.39	34.17±9.46	29.16±8.01	10.41(0.0005)	37.15±10.53	33.46±9.93	30.89±8.788	8.49(0.0005)
MCS	33.72±15.25	30.25±13.86	29.73±12.18	2.80(0.06)	32.89±14.25	29.84±14.48	27.24±14.40	3.23(0.04)

Table 6-14: Statistically significant differences between groups according to comorbidities using Post Hoc

SF-36	Comorbidities		Mean difference	p value
PF	Without comorbidities	With 1-3 comorbidities	4.73	0.0005
		With 4-6 comorbidities	7.66	0.04
RP	Without comorbidities	With 1-3 comorbidities	4.84	0.0005
		With 4-6 comorbidities	8.22	0.02
BP	Without comorbidities	With 1-3 comorbidities	3.86	0.01
		With 4-6 comorbidities	9.12	0.03
VT	Without comorbidities	With 1-3 comorbidities	3.99	0.004
		With 4-6 comorbidities	7.99	0.04
SF	Without comorbidities	With 1-3 comorbidities	4.73	0.006
MH	Without comorbidities	With 1-3 comorbidities	3.85	0.04
PCS	Without comorbidities	With 1-3 comorbidities	4.12	0.0005
		With 4-6 comorbidities	9.13	0.004

Only significant results were reported

Table 6-13 presents the association between the number of admissions to the hospital (hospitalization) and HRQOL. There was a statistically significant difference between the three groups of hospital admissions in all domains of SF-36, except for the domain of role limitations due to emotional problems (RE). Post-hoc statistical analysis using the Tukey Bonferroni identified seven domains of HRQOL (PF, RP, BP, GH, VT, SF and MH) and two component summary scores which were higher among patients who were never admitted to hospital than among patients who had experienced hospitalization ($p < 0.05$) (Table 6-15).

Table 6-15: The statistically significant difference between groups according to the number of hospital admissions using Post Hoc test

SF-36	Number of hospital admissions		Mean difference	p value
PF	Never admitted	Admitted 1-5 times Admitted above 5 times	4.86 6.68	0.0005 0.01
RP	Never admitted	Admitted 1-5 times	4.36	0.001
BP	Never admitted	Admitted 1-5 times Admitted above 5 times	4.18 8.10	0.01 0.007
GH	Never admitted	Admitted above 5 times	5.62	0.02
VT	Never admitted	Admitted 1-5 times Admitted above 5 times	4.10 5.72	0.0005 0.04
SF	Never admitted Admitted 1-5 times	Admitted above 5 times	10.44 9.02	0.001 0.009
MH	Never admitted	Admitted 1-5 times	4.38	0.03
PCS	Never admitted	Admitted 1-5 times Admitted above 5 times	3.68 6.25	0.003 0.007

Only the significant results were reported

6.3.3.3 Symptoms Experience

Because the data from the LDSI-2.0 subscales included in the analysis was continuous, the parametric test of correlation (Pearson product moment correlation coefficient, r) was used to test for statistically significant associations between patients' perceptions of severity of symptoms and the extent to which they were hampered by these symptoms, and HRQOL (Table 6-16).

Table 6-16 shows the correlation between symptoms experience and HRQOL. It was noted that both LDSI-2.0 subscales of symptom severity and hindrance of daily life due to symptoms had a statistically significant negative association with all domains of SF-36 ($r \leq -0.519$, $p < 0.001$). Symptoms severity had a highly significant association with the domains of VT and MH and the MCS ($r = -0.494$, -0.492 and -0.519 respectively, $p < 0.001$), but the magnitude of the association was low with the domain of PF ($r = -0.382$, $p < 0.001$).

Similarly, hindrance of daily life due to symptoms **(**the extent to which the patients were hampered by these symptoms) had a highly significant correlation with the domains of VT and MH and the MCS (r = -0.435, -0.424 and -0.462 respectively, p < 0.001), but it had a lower association with the domain of SF (r = -0.350, p < 0.001).

6.3.3.4 Social Support

As explained before, the MSPSS contains the total score for the perceived adequacy of social support but also contains three subscales that represent three sources of social support: spouse, family and friends. As in previous analysis of symptoms experience, the Pearson product moment correlation coefficient (r) test of correlation was used to assess the association between perceived social support and HRQOL.

Table 6-16 shows that perceived social support (total score) had a statistically significant positive association with all domains and the MCS of SF-36 (r = 0.270, p < 0.001), but not with PCS (r = 0.061). Perceived social support from a spouse had a statistically significant positive association with all domains and the two component summary scores of SF-36. It has a high correlation with GH, VT and MH and the MH (r = 0.270, 0.261, 0.338 and 0.292 respectively, p ≤ 0.001). Perceived social support from the family had a statistically significant positive association with only four domains of mental health (VT, SF, RE and MH) (r = 0.128, 0.125, 0.132 and 0.190, p ≤ 0.01) and the MCS (r = 0.200, p < 0.001). Perceived social support from friends had a statistically significant positive association only with the domain of MH and the MCS (r = 0.122 and 0.105 respectively, p <0.01). The results showed that the highest correlation was between perceived spousal support and the domain of MH and the MCS (r = 0.338 and 0.292 respectively, p < 0.001).

Table 6-16: Association between HRQOL and symptoms experience and perceived social support by Pearson's correlation

	n = 401					
SF-36 Domains	**Symptoms severity**	**Hindrance of Symptoms**	**Perceived social support**	**Perceived spouse support N=311**	**Perceived family support**	**Perceived friends support**
	r value	**r value**	**r value**	**r value**	**r value**	**r value**
PF	-0.382**	-0.386**	0.139**	0.150**	0.071	0.048
RP	-0.442**	-0.388**	0.120*	0.132*	0.054	0.061
BP	-0.431**	-0.421**	0.125*	0.219**	0.062	0.009
GH	-0.455**	-0.385**	0.144**	0.270**	0.089	0.012
VT	-0.494**	-0.435**	0.221**	0.261**	0.128*	0.076
SF	-0.392**	-0.350**	0.152**	0.176**	0.125*	0.034
RE	-0.431**	-0.422**	0.160**	0.165**	0.132**	0.061
MH	-0.492**	-0.424**	0.295**	0.338**	0.190**	0.122*
Component summary scores						
PCS	-0.366**	-0.349**	0.061	0.123*	0.003	0.011
MCS	-0.519**	-0.462**	0.270**	0.292**	0.200**	0.105*

Correlation is significant at 2 tailed
*P<0.01 **P<0.001

Table 6-17 and Diagram 6-2 summarise the factors that are significantly associated with the physical and mental health domains (HRQOL) of people with liver cirrhosis using bivariate analysis. Many factors were significantly associated with the two component summary scores of SF-36. Factors that were significantly associated with physical health were gender, education, employment status, disease stage, complications of liver disease, comorbidities, symptoms severity and hindrance of daily life due to symptoms. Physical health domains (PCS) was most highly correlated with comorbidities, the number of hospitalizations, educational level and employment status [f (398) = 10.41 and 8.58, t (399) = 5.36 and 5.34 respectively, p ≤ 0.0005].

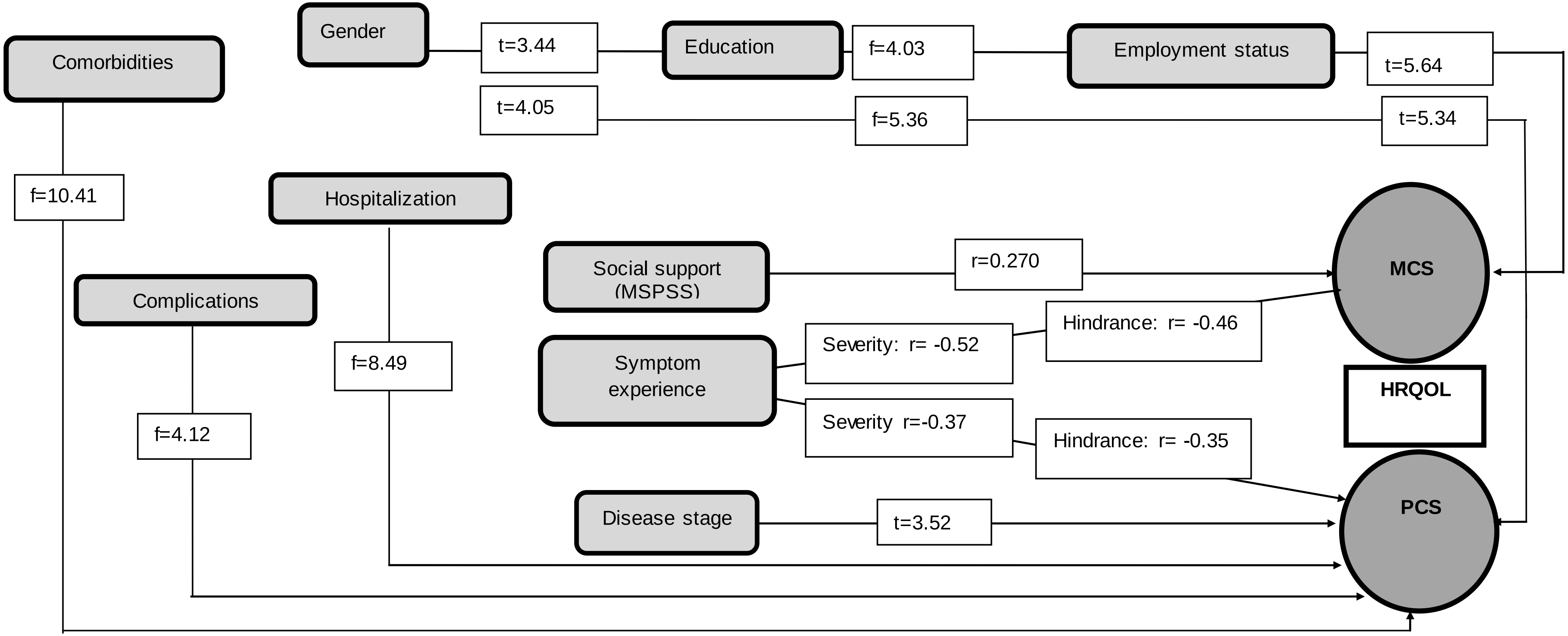
Factors that were significantly associated with mental health domains (MCS) were gender, educational level, employment status, number of hospitalisations, social support and symptoms severity. MCS was most highly correlated with employment status and educational level [t (399) = 5.64 and 4.03 respectively, $p \le 0.01$].

Table 6-17: Summary of factors associated with HRQOL (PCS and MCS) among Egyptian cirrhotic patients

Variables	**Classifications**	**N**	**HRQOL**			
			PCS		**MCS**	
			Mean ± SD	**t or f (p)**	**Mean ± SD**	**t or f (p) d**
Gender	Male	174	37.93±10.96	**4.05(0.0005)**	34.34±15.20	**3.44(0.001)**
	Female	227	33.75±99.64		29.40±13.43	
Marital status	Single	91	34.39±9.80	1.27(0.22)	29.68±12.38	1.55(0.16)
	Married	310	35.91±10.60		32.09±14.93	
Residential area	Rural	146	35.79±10.7	0.32(0.74)	31.88±14.30	0.34(0.72)
	Urban	255	35.43±10.249		31.36±14.51	
Educational level	Illiterate	219	34.02±9.95	**5.36(0.0005)**	30.49±14.08	**4.03(0.01)**
	Basic education	163	37.35±10.46		31.98±14.21	
	High education	19	37.90±13.07		40.06±17.49	
Employment status	Employed	68	41.53±11.99	**5.34(0.0005)**	46.22±14.96	**5.64(0.0005)**
	Unemployed	333	34.34±9.66		29.78±13.66	
Disease stage	Compensated	201	37.37±10.09	**3.52(0.0005)**	31.61±14.14	0.08(0.92)
	Decompensated	200	31.48±14.72		31.48±14.72	
Cause of cirrhosis	Viruses	226	35.59±10.341	1.29(0.274)	30.85±14.567	0.71(0.489)
	Bilharzias and viruses	151	36.02±10.715		32.65±14.022	
	Others	24	32.34±9.293		31.21±15.654	
Hospital setting	Outpatient	322	36.69±10.38	**4.48(0.0005)**	31.77±14.36	0.62(0.53)
	Inpatient	79	30.95±9.37		30.64±14.71	
Complications	Without complications	74	36.02±8.90	**4.12(0.01)**	32.64±14.20	1.00(0.36)
	1-2 complications	244	36.41±11.05		31.87±14.67	
	3-4 complications	83	32.67±9.36		29.63±13.84	
Comorbidities	Without comorbidities	152	38.30±11.39	**10.41(0.0005)**	33.72±15.25	2.80(0.06)
	1-3 comorbidities	235	34.17±9.46		30.25±13.86	
	4-6 comorbidities	14	29.16±8.01		29.73±12.18	
Hospitalization	Never admitted	248	37.15±10.53	**8.49(0.0005)**	32.89±14.25	**3.23(0.04)**
	Admitted 1-5 times	125	33.46±9.93		29.84±14.48	
	Admitted >5 times	28	30.89±8.78		27.24±14.40	

Association is significant at the p level < 0.05 (2 tailed)

Diagram 6-2: Summary of factors associated with HRQOL (PCS and MCS) among Egyptian cirrhotic patients



Only the significant results are presented, all associations were significant at p level < 0.05 (2 tailed)

6.3.4 Multivariate analysis: Factors associated with HRQOL (PCS and MCS)

As we have seen, HRQOL was measured using the SF-36 that gave two component summary scores, physical health (PCS) and mental health (MCS) domains. Stepwise regression method was used to find factors associated with HRQOL (PCS and MCS). The PCS and MCS were considered two dependent variables. Therefore, it was essential to develop a regression model for each of these dependent variables independently.

The socio-demographic characteristics, medical data, symptoms experience and social support (independent variables) that correlated significantly with the PCS and MCS (dependent variables) were combined and tested by multivariate analysis (multiple linear regression).

The following variables were entered all together into the regression analysis to develop Model 1 for physical health and Model 2 for mental health. (1) symptoms severity, (2) hindrance of symptoms, (3) perceived spouse support, (4) perceived family support, (5) perceived friends support, (6) disease stage (dummy code), (7) number of comorbidities, (8) number of liver cirrhosis complications and (9) socio-demographic characteristics (age, gender, marital status, employment status, education and area of residence (dummy code)). The significance limit to enter and leave the multiple regression steps was set at $p = 0.05$ (Field 2009).

6.3.4.1 Factors Associated with Physical Health domains (PCS)

Table 6-18 presents the multiple regression analysis (Model 1) that was constructed using the stepwise method to answer the sub-research question 2.1.

An initial investigation was conducted to ensure the non-violation of the regression assumptions of multicollinearity, normality, linearity, and homoscedasticity.

The first model (Model 1) included symptoms experience (severity and hindrance), the three subscales of perceived social support (spouse, family and friends), socio-demographic factors and medical data. Physical health (PCS) was the dependent variable.

The results show that the Model 1 could significantly explain 19% of the variation in PCS (R^2 = 0.190, R^2_{adj} = 0.180, p = 0.0005) (Table 6-18). Four variables were significantly associated PCS [symptoms severity (b = -0.287, p = 0.0005), employment status (b = -0.152, p = 0.005), number of comorbidities –b = -0.134, p = 0.01) and disease stage (b = 0.122, p = 0.02)]. This means that patients with high severity of symptoms, unemployed, with increasing number of comorbidities and with advanced disease stage are more likely to report low perceived PCS. Symptoms severity has the strongest contribution (28.7%) to explain PCS, while disease stage has the lowest contribution (12.2%).

Although Model 1 could significantly explain the PCS (p = 0.0005), around 81% of the variation in PCS could not be explained by the model, suggesting that there are other associated factors that have an influence on physical health domains, which need further research to be explored

Table 6-18: Summary of factors associated with physical health (PCS) using multivariate analysis

<table>
<tr><th rowspan="2">Model 1</th><th colspan="2">df</th><th colspan="2">F</th><th>R</th><th>R^2</th><th>R^2_{adj}.</th><th>Sig.</th><th rowspan="3" colspan="2">Collinearity Statistics</th></tr>
<tr><th colspan="2">4/306</th><th colspan="2">17.987</th><th>0.436</th><th>0.190</th><th>0.180</th><th>0.0005</th></tr>
<tr><th rowspan="2">Factors</th><th rowspan="2">Unstandardized coefficient B</th><th rowspan="2">Standardized coefficient Beta</th><th rowspan="2">t</th><th rowspan="2">Sig.</th><th colspan="4">95% CI of beta</th></tr>
<tr><th colspan="2">Lower</th><th colspan="2">Upper</th><th>Tolerance</th><th>VIF</th></tr>
<tr><td>Constant</td><td>46.554</td><td></td><td>24.775</td><td>0.0005</td><td colspan="2">42.857</td><td colspan="2">50.252</td><td></td><td></td></tr>
<tr><td>Symptoms severity</td><td>-0.228</td><td>-0.287</td><td>-5.285</td><td>0.0005</td><td colspan="2">-0.313</td><td colspan="2">-0.143</td><td>0.897</td><td>1.115</td></tr>
<tr><td>Employment status</td><td>-4.215</td><td>-0.152</td><td>-2.816</td><td>0.005</td><td colspan="2">-7.160</td><td colspan="2">-1.269</td><td>0.911</td><td>1.098</td></tr>
<tr><td>Number of comorbidities</td><td>-1.241</td><td>-0.134</td><td>-2.554</td><td>0.011</td><td colspan="2">-2.197</td><td colspan="2">-0.285</td><td>0.961</td><td>1.041</td></tr>
<tr><td>Disease stage</td><td>2.548</td><td>0.122</td><td>2.324</td><td>0.021</td><td colspan="2">0.391</td><td colspan="2">4.705</td><td>0.956</td><td>1.046</td></tr>
</table>

VIF: Variance inflation factor

Dummy codes: gender: 0 males, 1 females, **disease stage:** 0 decompensated, 1 compensated, **employment status:** 0 employed, 1 unemployed, **marital status:** 0 single, 1 married, **educational level:** 0 educated, 1 uneducated, **area of residence:** 0 rural, 1 urban

6.3.4.2 Factors Associated with Mental Health domains (MCS)

Table 6-19 presents the multiple regression analysis (Model 2) that was constructed using the stepwise method to answer the sub-research question 2.2. The second model (Model 2) included the two subscales of symptoms experience (severity and hindrance) and the three subscales of perceived social support (spouse, family and friends), socio-demographic factors and medical data as the independent variables (variables used in model 1); and mental health (MCS) as the dependent variable.

It was discovered that Model 2 significantly predicted 31.7% of the variation in MCS (R^2 = 0.317, R^2_{adj} = 0.308, p = 0.0005). Four variables significantly predicted MCS [symptoms severity (b = -0.436, p = 0.0005), perceived spouse support (b = 0.135, p = 0.007), employment status (b = -0.116, p = 0.02) and perceived family support (b = 0.097, p = 0.046)]. This means that patients with high severity of symptoms, unemployed, with low perceived support from spouse and family are more likely to report low perceived MCS. Symptoms severity made the strongest contribution (43.6%) to explain MCS, while perceived family support made the lowest contribution (9.7%).

Although Model 2 could significantly predict the MCS (p = 0.0005), around 68.3% of the variation in MCS could not be explained by the model, suggesting that there are other factors that have an associate with mental health domains and need further research to be explored.

In conclusion, symptoms severity made the strongest contribution in explaining both aspect of HRQOL, PCS (28.7%) and MCS (43.6%). However, hindrance of symptoms did not associate with any of them. Many of somatic variables associated with PCS while psychosocial variables associated with MCS. For example, disease stage and number of comorbidities were associated with only PCS, while perceived social support, from spouse and family, was significantly associated with MCS but not PCS.

Table 6-19: Summary of factors associated with mental health (MCS) using multivariate analysis

<table>
<tr><th rowspan="2">Model 2</th><th colspan="2">df</th><th colspan="2">F</th><th>R</th><th>R^2</th><th>$R^2_{adj.}$</th><th>Sig.</th><th colspan="2" rowspan="3">Collinearity Statistics</th></tr>
<tr><td colspan="2">4/306</td><td colspan="2">35.427</td><td>0.563</td><td>0.317</td><td>0.308</td><td>0.0005</td></tr>
<tr><th rowspan="2">Factors</th><th rowspan="2">Unstandardized Coefficients B</th><th rowspan="2">Standardized coefficient Beta</th><th rowspan="2">t</th><th rowspan="2">Sig.</th><th colspan="4">95% CI of beta</th></tr>
<tr><th colspan="2">Lower</th><th colspan="2">Upper</th><th>Tolerance</th><th>VIF</th></tr>
<tr><td>Constant</td><td>40.911</td><td></td><td>9.944</td><td>0.0005</td><td colspan="2">32.815</td><td colspan="2">49.007</td><td></td><td></td></tr>
<tr><td>Symptoms severity</td><td>-0.478</td><td>-0.436</td><td>-8.585</td><td>0.0005</td><td colspan="2">-0.587</td><td colspan="2">-0.368</td><td>0.868</td><td>1.152</td></tr>
<tr><td>Perceived spouse support</td><td>2.573</td><td>0.135</td><td>2.705</td><td>0.007</td><td colspan="2">0.702</td><td colspan="2">4.445</td><td>0.896</td><td>1.116</td></tr>
<tr><td>Employment status</td><td>-4.447</td><td>-0.116</td><td>-2.330</td><td>0.020</td><td colspan="2">-8.202</td><td colspan="2">-0.692</td><td>0.903</td><td>1.107</td></tr>
<tr><td>Perceived family support</td><td>1.873</td><td>0.097</td><td>2.008</td><td>0.046</td><td colspan="2">0.038</td><td colspan="2">3.709</td><td>0.961</td><td>1.041</td></tr>
</table>

6.4 CONCLUSION

The study shows that Egyptians with liver cirrhosis have poor HRQOL. Using bivariate analysis, many factors had a significant correlation with HRQOL, including socio-demographic characteristics, medical data, symptoms experience and perceived social support. Females, illiterate people and the unemployed had the worst PCS and MCS. Patients with decompensated cirrhosis, comorbidities and complications of liver cirrhosis had the worst PCS. Additionally, the results suggest that PCS and MCS decrease with increasing severity of symptoms and hindrance of daily life due to symptoms. Also, perceived social support had a statistically significant positive relationship with MCS, with patients with perceived low levels of social support, particularly from spouse and family, having the worst MCS.

Finally, multiple regression analysis showed that symptoms severity was the main factor that was associated with both PCS and MCS. Disease stage and the number of comorbidities were associated with PCS, while perceived social support from spouse and family was associated with MCS.

7 CHAPTER 7- RESULTS

7.1 INTRODUCTION

This chapter presents further results from the cross-sectional study (main study) analysis. The study has three aims as stated in section 1.3. Chapter 6 covered the first aim of this study. This chapter will cover the second and the third aims of this study:

Second aim: To explore and describe experienced symptoms (prevalence, severity and hindrance) in Egyptian cirrhotic patients and to identify and evaluate factors associated with symptoms severity and symptoms hindrance (distress).

Third aim: To explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to identify and evaluate factors associated with general perceived social support.

Therefore, the chapter is divided into two sections. Section I describes the symptoms experience of people with liver cirrhosis and how these symptoms affect their daily activities. It also presents factors that are associated with and predicted symptoms experience. Section II describes the perceived social support and factors associated with perceived availability of social support. Finally, a summary of this chapter is presented.

7.2 SYMPTOMS EXPERIENCE

Experienced symptoms were investigated by using the LDSI-2.0 that contains 24 items, which describe the disease specific HRQOL. The LDSI-2.0 is divided into two subscales. One subscale assesses the severity of various physical and psychological symptoms as well as the social dysfunctional experience over the previous week, which consists of 15 items. The other subscale examines how much people’s daily or social activities are affected by some of these symptoms and it contains 9 items.

7.2.1 Symptoms Experience among Egyptian Cirrhotic People

The Means (± SD) of the total score (disease specific HRQOL) and the two subscales (symptoms severity and hindrance of daily activities due to symptoms) of the LDSI-2.0 are provided for the entire sample (n = 401). Additionally, the prevalence of symptoms severity and the prevalence of the impact of symptoms on daily or social activities in patients with cirrhosis are presented.

Results in table 7-1 show that the mean score of the overall LDSI-2.0 was 46.16 ± SD (20.75); the high score indicates a poor disease-specific HRQOL as a result of liver disease. The mean score of the symptoms severity subscale was higher than the mean score of the symptoms hindrance subscale, suggesting that symptoms severity was higher than hindrance of daily life due to these symptoms among these patients.

Table 7-1: Symptoms experience by total and subscales scores of LDSI-2.0

Variables	**n=401**				**Instrument possible range**
LDSI-2.0	**Mean ± (SD)**	**Median**	**Percentiles**		
Disease specific HRQOL	46.16 ± (20.75)	49.00	25 50 75	30.00 49.00 61.00	0-96
Symptoms severity	32.61 ± (13.15)	35.00	25 50 75	24.00 35.00 43.00	0-60
Symptoms hindrance	13.54 ± (8.54)	13.00	25 50 75	7.00 13.00 20.00	0-36

7.2.2 Prevalence of Experienced Symptoms

In order to assess the prevalence of reported symptoms among patients with liver cirrhosis, it was essential to transform the scale responses to "Yes" for those who answered 1 to 4 (have symptoms) and "No" for those who answered not at all (no symptoms). Table 7-2 shows the prevalence of the 15 symptoms that were reported by the patients who answered yes. The majority of the patients had one or more of a wide range of physical and psychosocial symptoms (Table 7-2). Joint pain was reported by 78.3% of the whole sample, decreased appetite by 75.6%, memory problems by 77.3%, difficulty of using time effectively as a result of liver disease by 90% and financial affairs resulting from liver disease by 80%. On the other hand, jaundice was the only symptom that few of these people experienced (27.2%).

Table 7-3 shows the additional symptoms that were not measured in the LDSI-2.0 but were reported by the patients. Indeed, to explore all the symptoms that these patients experienced, an additional question was added to the LDSI-2.0, which asked if other symptoms had been experienced over the last week. Muscle cramp was the most frequent additionally reported symptom (37.15%) followed by difficulty in sleeping at night (26.68%).

Table 7-2: Percentage of patients reporting symptom severity and hindrance of symptom by answering yes

LDSI-2.0 items	**n = 401 (100%)**	
	Prevalence of people reported Symptom severity n (%)	**Prevalence of people reported hindrance of daily activities due to symptom (Among symptomatic) n (%)**
Itch	210 (52.4)	Activity: 103 (25.7) Sleep: 125 (31.2)
Joint pain	314 (78.3)	282 (70.3)
Right abdominal pain	259 (64.6)	208 (51.9)
Sleepiness during the day	290 (72.3)	213 (53.1)
Worry about the family situation	300 (74.8)	231(57.6)
Decreased appetite	303 (75.6)	237 (59.1)
Depression	291 (72.6)	246 (61.3)
Fear disease complications	281 (70.1)	N/A
Jaundice	109 (27.2)	65 (16.2)
Memory problems	310 (77.3)	N/A
Changing personality	283 (70.6)	N/A
Hindrance in financial affairs	321 (80)	N/A
Difficulty managing time	361 (90)	N/A
Decreasing sexual interest	256 (63.8)	N/A
Decreasing sexual activity	255 (63.6)	N/A

N/A: Not applicable

Table 7-3: Prevalence of additional symptom severity and hindrance of symptom

Additional symptoms	**n = 401 (100%)**	
	People reported Symptom severity n (%)	**Prevalence of people reported hindrance of daily activities due to symptom (Among symptomatic) n (%)**
Difficulty in sleeping at night	107 (26.68)	95 (23.69)
Muscle cramp	149 (37.15)	122 (30.42)
Heart burn	62 (15.46)	40 (9.97)
Constipation	11 (2.74)	11 (2.74)

These additional reported symptoms were not combined with the LDSI-2.0 score

7.2.3 How Symptoms Affect Daily Activities of People with Liver Cirrhosis

The mean score of the impact of symptoms on daily and social activities (hindrance of symptoms) was 13.54 ± SD (8.54) with a median of 13 (Table 7-1). The increased score means impaired daily and social activities as a result of symptoms. Some of the patients had one or more of a wide range of physical and psychosocial symptoms that impacted on their daily and social activities (Tables 7-2 and 7-3), such as hindrance of daily life due to joint pain (70.3%), and depression (61.3%). In other words, joint pain and depression were the symptoms that influenced these people's activities in their daily life most. Itching was the symptom that interfered least with their daily life (27.2%).

7.2.4 Factors Associated with Experienced Symptoms

To assess the factors associated with the severity of symptoms and the impact of these symptoms on daily life, the sample (n = 401) was broken down into groups according to socio-demographic characteristics and disease stage, as discussed in Chapter 6.

7.2.4.1 Socio-Demographic Characteristics

As can be seen from Table 7-4, the means of symptoms severity was significantly higher among females, illiterate people and the unemployed ($p \leq 0.002$). This suggests that gender, educational level and employment status have a significant impact on the perceived severity of symptoms. Moreover, the limitation in their daily activities because of symptoms was higher in those same groups (i.e. females, illiterates, unemployed) and married ($p \leq 0.04$). Therefore, further statistical analyses (chi-square test) were done to compare these groups.

Table 7-5 shows the prevalence of symptoms severity and hindrance of daily life due to symptoms among males and females. There was a significant difference in the types of symptoms experienced between men and women. Women were more likely than men to report symptoms of joint pain, right abdominal pain, decreased appetite, depression, jaundice, memory problems, changing personality and difficulty in managing time ($p \leq 0.02$). On the other hand, men were more likely than women to report symptoms of sexuality problems (decreased sexual interest and activity) ($p = 0.0005$). However, males and females have the same symptoms of worry about the family situation, itching, fear of disease complications and problems in financial affairs.

Table 7-4: Association between socio-demographic characteristics and symptoms experience

Variables	**Classifications**	**N**	**Symptoms experience, n = 401**			
			Symptoms severity		**Symptoms hindrance**	
			Mean ± SD	**t or f (p)**	**Mean ± SD**	**t or f (p)**
Gender	Male	174	29.11±13.48	**4.79(0.0005)**	10.65±8.15	**6.20(0.0005)**
	Female	227	35.29±12.25		15.76±8.19	
Age	22-44	55	33.40±15.33	0.015(0.54)	14.11±9.32	0.31(0.73)
	45-64	306	32.74±12.65		13.35±8.20	
	65+	40	32.61±13.15		14.20±10.07	
Marital status	Single	91	30.70±11.58	1.57(0.11)	15.15±8.73	**2.05(0.04)**
	Married	310	33.17±13.54		13.07±8.45	
Residential area	Rural	146	31.68±13.40	1.06(0.28)	13.26±8.87	0.49(0.61)
	Urban	255	33.14±12.99		13.70±8.37	
Educational level	Illiterate	219	34.48±11.83	**5.39(0.0005)**	14.84±8.16	**6.11(0.002)**
	Basic education	163	30.64±14.15		12.15±8.76	
	Higher education	19	27.89±15.56		10.42±8.81	
Employment status	Employed	68	24.84±14.44	**5.54(0.0005)**	9.16±7.50	**4.75(0.0005)**
	Unemployed	333	34.20±12.30		14.44±8.48	

Table 7-5: The proportion of symptom severity and hindrance of symptom among males and females

Symptom severity	**Gender (n)**		**Chi-square (X^2)**	**p value**	**phi coefficient**
	Males N= 174 n (%)	**Females N=227 n (%)**			
Itch	85(48.85)	125(55.06)	1.27	0.25	0.06
Joint pain	106(60.91)	208(91.62)	52.88	**0.0005**	0.37
Right abdominal pain	89(51.14)	170(74.88)	23.24	**0.0005**	0.25
Sleepiness during the day	122(70.11)	168(74.08)	0.56	0.45	0.04
Worry about the family situation	122(70.11)	178(78.41)	3.17	0.07	0.09
Decreased appetite	117(67.24)	186(81.93)	10.73	**0.001**	0.17
Depression	111(63.79)	180(79.29)	11.12	**0.001**	0.17
Fear disease complications	120(67.95)	161(70.92)	0.09	0.75	0.02
Jaundice	34(19.54)	75(33.03)	8.39	**0.004**	0.15
Memory problems	122(70.11)	188(82.81)	8.35	**0.004**	0.15
Changing personality	112(64.36)	171(75.33)	5.18	**0.02**	0.11
Hindrance in financial affairs	141(81.03)	180(79.29)	0.09	0.76	0.02
Difficulty managing time	147(84.48)	214(94.27)	9.45	**0.002**	0.16
Decreased sexual interest	131(75.28)	125(55.06)	16.58	**0.0005**	0.20
Decreased sexual activity	136(78.16)	119(52.42)	27.08	**0.0005**	0.26
Hindrance of symptom	**Males N= 174 n (%)**	**Females N=227 n (%)**	**Chi-square (X^2)**	**p value**	**phi coefficient**
Itch hindrance activity	39(22.41)	64(28.19)	1.43	0.23	0.06
Itch hindrance sleep	51(29.31)	74(32.59)	0.35	0.55	0.035
Hindrance of joint pain	91(52.29)	191(84.14)	46.34	**0.0005**	0.34
Hindrance of right abdominal pain	70(40.22)	138(60.79)	15.87	**0.0005**	0.20
Sleep hindrance	81(46.55)	132(58.14)	4.86	**0.02**	0.11
Hindrance of worry	92(52.87)	139(61.23)	2.48	0.11	0.08
Hindrance of decreased appetite	92(52.87)	145(63.87)	4.48	**0.03**	0.11
Hindrance of depression	91(52.29)	155(68.28)	9.94	**0.002**	0.16
Hindrance of jaundice	20(11.49)	45(19.82)	4.43	**0.03**	0.11

In terms of the hindrance of symptom, women were more likely than men to experience limitations in their daily and social activities due to symptoms of joint pain, right abdominal pain, decreased appetite, depression, sleepiness during the day and jaundice ($p \leq 0.03$) (Table 7-5).

Although there was no significant difference between men and women in reporting sleepiness during the day, there was a significant difference between them in terms of the impact of sleepiness on their daily lives. Women were more likely than men to have limitations in their daily life due to this symptom. Therefore, the assessment of symptoms experience showed to include not only the severity of the symptom but also the effect of this symptom on daily life.

Table 7-6 presents the prevalence of symptom severity and hindrance of daily activities due to symptom among single and married people. There was a significant difference in the types of symptoms experienced between married and single people. Singles were more likely than married people to report symptoms of joint pain and worry about the family situation ($p \leq 0.04$). In contrast, married people were significantly more likely to report a decrease in sexual interest and activity ($p = 0.0005$). In terms of the impact of symptoms on daily life, single and married people were likely to experience a similar level of impact of symptoms on their daily activities.

Table 7-6: The proportion of symptom severity and hindrance of symptom among unmarried and married

Symptom severity	**Marital status (n)**		**Chi-square (X^2)**	**p value**	**phi coefficient**
	Single N=91 n (%)	**Married N=310 n (%)**			
Itch	47(51.64)	163 (52.58)	0.001	0.97	0.008
Joint pain	81(89.01)	233(75.16)	7.14	**0.008**	-0.14
Right abdominal pain	66(72.52)	193(62.25)	2.81	0.09	-0.09
Sleepiness during the day	60(65.93)	230(74.19)	2.00	0.15	-0.07
Worry about the family situation	76(83.51)	224(72.25)	4.15	**0.04**	-0.109
Decreased appetite	74(81.31)	229(73.87)	1.72	0.18	-0.073
Depression	71(78.02)	220(70.96)	1.42	0.23	-0.066
Fear disease complications	61(67.03)	220(70.96)	0.34	0.55	0.036
Jaundice	31(34.06)	78(25.16)	2.38	0.12	-0.08
Memory problems	70(76.92)	240(77.41)	0.00	1.00	0.0005
Changing personality	67(83.51)	216(69.67)	0.35	0.55	-0.036
Hindrance in financial affairs	70(76.92)	251(80.96)	0.49	0.48	0.042
Difficulty managing time	83(91.20)	278(89.67)	0.05	0.81	-0.021
Decreased sexual interest	10(10.98)	246(79.35)	139.48	**0.0005**	0.596
Decreased sexual activity	10(10.98)	245(79.03)	137.75	**0.0005**	0.592
Hindrance of symptom	**Single N=91 n (%)**	**Married N=310 n (%)**	**Chi-square (X^2)**	**p value**	**phi coefficient**
Itch hindrance activity	27(29.67)	76(24.51)	0.72	0.39	-0.049
Itch hindrance sleep	32(35.16)	93(30.00)	0.65	0.42	-0.047
Hindrance of joint pain	69(75.82)	213(68.70)	1.38	0.24	-0.065
Hindrance of right abdominal pain	54(59.34)	154(49.67)	2.25	0.13	-0.081
Sleep hindrance	48(52.74)	165(53.22)	0.00	1.00	0.004
Hindrance of worry	56(61.53)	175(56.45)	0.55	0.45	-0.043
Hindrance of decreased appetite	55(60.43)	182(58.70)	0.03	0.86	-0.015
Hindrance of depression	63(69.23)	183(59.03)	2.67	0.10	-0.088
Hindrance of jaundice	16(17.58)	49(15.80)	0.059	0.80	-0.020

Table 7-7 shows the prevalence of symptom severity and hindrance of symptom among the employed and unemployed. The proportion of symptoms of right abdominal pain, depression, changing personality, difficulty managing time and jaundice was significantly higher among the unemployed than the employed ($p \leq 0.01$). In terms of the impact of symptom on daily life, the prevalence of the impact of joint pain, right abdominal pain, decreased appetite and depression on daily and social activities was higher among the unemployed than the employed ($p \leq 0.01$).

Table 7-7: The proportion of symptom severity and hindrance of symptom among employed and unemployed

Symptom severity	**Employment status**		**Chi-square (X^2)**	**p value**	**phi coefficient**
	Employed N=68 n (%)	**Unemployed N=333 n (%)**			
Itch	30(44.11)	180(54.05)	1.85	0.17	0.075
Joint pain	47(69.11)	267(80.18)	3.44	0.06	0.10
Right abdominal pain	33(48.52)	226(67.86)	8.40	**0.004**	0.152
Sleepiness during the day	49(72.05)	241(72.37)	0.0005	1.00	0.003
Worry about the family situation	52(76.47)	248(74.47)	0.03	0.84	-0.017
Decreased appetite	46(67.64)	257(77.17)	2.28	0.13	0.083
Depression	38(55.88)	253(75.97)	10.46	**0.001**	0.169
Fear disease complications	47(69.11)	234(70.27)	0.002	0.96	0.009
Jaundice	10(14.70)	99(29.72)	5.70	**0.01**	0.127
Memory problems	47(69.11)	263(78.97)	2.59	0.10	0.088
Changing personality	38(55.88)	245(73.57)	7.68	**0.006**	0.146
Hindrance in financial affairs	50(73.52)	271(81.38)	1.71	0.19	0.074
Difficulty managing time	53(77.94)	308(92.49)	11.74	**0.001**	0.182
Decreased sexual interest	40(58.82)	216(64.86)	0.65	0.42	0.047
Decreased sexual activity	40(58.82)	215(64.56)	0.57	0.44	0.045
Hindrance of symptom	**Employed N= 68 n (%)**	**Unemployed N= 333 n (%)**	**Chi-square (X^2)**	**p value**	**phi coefficient**
Itch hindrance activity	12(17.64)	91(27.32)	2.28	0.13	0.08
Itch hindrance sleep	14(20.58)	111(33.33)	3.70	0.054	0.103
Hindrance of joint pain	37(54.41)	245(73.57)	9.03	**0.003**	0.157

Hindrance of right abdominal pain	24(35.29)	184(55.25)	8.23	**0.004**	0.150
Sleep hindrance	39(57.35)	174(52.25)	0.40	0.52	-0.038
Hindrance of worry	38(55.88)	193(57.95)	0.03	0.85	0.016
Hindrance of decreased appetite	31(45.58)	206(61.86)	5.53	**0.01**	0.124
Hindrance of depression	30(44.11)	216(64.86)	9.39	**0.002**	0.160
Hindrance of jaundice	6(8.82)	59(17.71)	2.66	0.10	0.091

7.2.4.2 Disease Stage and Medical History

As can be seen, the mean score of symptoms severity was significantly higher among patients with decompensated cirrhosis than patients with compensated cirrhosis ($p = 0.009$) (Table 7-8). In other words, it seems that the perceived severity of symptoms increases with the progressive stage of cirrhosis. Besides that, the mean score of perceived symptoms severity extensively increased with the increasing number of complications and comorbidity ($p \leq 0.008$). This means that there was a significant positive correlation between the number of both comorbidities as well as liver disease complications and severity of symptoms.

Table 7-8 shows that severity of symptoms also had a significant positive association with the number of admissions to hospital because of liver disease. For example, whereas the mean score of symptoms severity for those never admitted to hospital was 30.59, the mean score for those admitted <5 times was much lower (35.22) than the mean score for those admitted >5 times (38.82) ($p = 0.0005$). On the other hand, the severity of symptoms did not have a significant association with the causes of cirrhosis. Furthermore, the mean score of the impact of the symptoms on daily activities significantly increased with the advanced stage of cirrhosis, comorbidities, complications and hospitalizations ($p < 0.05$).

The data in Table 7-8 identifies that a significant difference was found in the mean score of the LDSI-2.0 related subscales between the groups in terms of disease stage. The disease stage has a relationship with the type of symptoms experienced similar to those found in prior studies. For example, Bjornsson et al. (2009) found that the proportion of depression and pain symptoms were higher among patients with decompensated cirrhosis than in patients with compensated cirrhosis. Therefore, it was important to run further statistical analyses (chi-square test) to compare the two groups of disease stages (compensated and decompensated cirrhosis).

Table 7-8: Association between disease stage and medical history and symptoms experience

Variables	Classifications	N	Symptoms experience, n = 401			
			Symptoms severity		Hindrance of symptoms	
			Mean ± SD	t or f (p)	Mean ± SD	t or f (p)
Disease stage	Compensated	201	30.91±14.06	**2.61(0.009)**	12.44±8.70	**2.59(0.01)**
	Decompensated	200	34.32±11.95		14.65±8.27	
Cause of cirrhosis	Viruses	226	32.40±13.70	0.29(0.74)	13.81±8.56	1.55(0.21)
	Viruses & Bilharzias	151	32.60±12.45		12.77±8.59	
	Others	24	34.58±12.39		15.79±7.90	
Hospital setting	Outpatient	322	32.10±13.37	1.67(0.11)	13.42±8.61	0.56(0.57)
	Inpatient	79	34.68±12.04		14.03±8.30	
Complications	Without complications	74	29.86±13.27	**4.94(0.008)**	12.36±8.47	**3.81(0.02)**
	With 1-2 complications	244	32.21±13.25		13.14±8.48	
	With 3-4 complications	83	36.22±12.07		15.76±8.52	
Comorbidities	Without comorbidities	152	29.17±13.79	**8.99(0.0005)**	12.22±8.84	**3.07(0.048)**
	With 1-3 comorbidities	235	34.55±12.28		14.29±8.32	
	With 4-6 comorbidities	14	37.29±12.86		15.36±7.72	
Hospitalization	Never admitted	248	30.59±13.40	**8.85(0.0005)**	12.56±8.50	**4.72(0.009)**
	Admitted 1-5 times	125	35.22±11.74		14.83±7.85	
	Admitted >5 times	28	38.82±13.21		16.43±10.61	

There was a significant difference in the types of symptoms experienced between patients with decompensated cirrhosis and patients with compensated cirrhosis. For instance, patients with decompensated cirrhosis were more likely than patients with compensated cirrhosis to have sexual problems (decrease in desire and activity) and difficulty in managing time (P ≤ 0.002). Moreover, in terms of the symptom hindrance, the impact of right abdominal pain, sleepiness during the day and decreased appetite on daily and social activities was higher among patients with decompensated cirrhosis than in patients with compensated cirrhosis (p ≤ 0.03) (Table 7-9).

Table 7-9: The proportion of symptom severity and hindrance of symptom among compensated and decompensated patients

Symptom severity	**Disease stage (n)**		**Chi-square (X^2)**	**p value**	**phi coefficient**
	Compensated N=201 n (%)	**Decompensated N=200 n (%)**			
Itch	101(50.24)	109(54.5)	0.56	0.45	0.043
Joint pain	165(82.08)	149(74.5)	2.96	0.08	-0.092
Right abdominal pain	123(61.19)	136(68)	1.74	0.18	0.071
Sleepiness during the day	138(68.65)	152(76)	2.34	0.12	0.082
Worry about the family situation	146(72.63)	154(77)	0.79	0.37	0.050
Decreased appetite	146(72.63)	157(78.5)	1.56	0.21	0.068
Depression	142(70.64)	149(74.5)	0.56	0.45	0.043
Fear disease complications	135(67.16)	146(73)	1.36	0.24	0.064
Jaundice	53(26.36)	56(28)	0.06	0.79	0.018
Memory problems	156(77.61)	154(77)	0.001	0.97	-0.007
Changing personality	137(68.15)	146(73)	0.91	0.34	0.053
Hindrance in financial affairs	164(81.59)	157(78.5)	0.422	0.51	-0.039
Difficulty managing time	171(85.07)	190(95)	9.92	**0.002**	0.166
Decreased sexual interest	113(56.21)	143(71.5)	9.49	**0.002**	0.159
Decreased sexual activity	109(54.22)	146(73)	14.45	**0.0005**	0.195
Hindrance of symptom	**Compensated N=201 n (%)**	**Decompensated N=200 n (%)**	**Chi-square (X^2)**	**P value**	**phi coefficient**
Itch hindrance activity	45(22.38)	58(29)	1.96	0.16	0.076
Itch hindrance sleep	57(28.35)	68(34)	1.23	0.26	0.061

Hindrance of joint pain	147(73.13)	135(67.5)	1.26	0.26	-0.062
Hindrance of right abdominal pain	93(46.26)	115(57.5)	4.62	**0.03**	0.112
Sleep hindrance	93(46.26)	120(60)	7.04	**0.008**	0.138
Hindrance of worry	109(54.22)	122(61)	1.61	0.20	0.069
Hindrance of decreased appetite	99(49.25)	138(69)	15.36	**0.0005**	0.201
Hindrance of depression	115(57.21)	131(65.5)	2.56	0.10	0.085
Hindrance of jaundice	29(14.42)	36(18)	69	0.40	0.048

7.2.4.3 Social Support and General Health Perception

Table 7-10 presents the association between perceived social support and symptoms experience. The correlation between the total score of the LDSI-2.0 related subscales and the total score of the MSPSS identifies that there was a significant inverse relationship between symptoms experience and perceived adequacy of social support ($p \leq 0.006$). This result suggests that with a perceived high social support there is a low perception of symptoms severity or vice versa. These results agree with the theory of unpleasant symptoms, which indicates that with insufficient social support there is a potential increase in the severity of symptoms (Lenz et al. 1997).

Table 7-10 shows the correlation between the LDSI-2.0 related subscales and the MSPSS related subscales. It was found that the severity of symptoms was negatively associated with the perceived availability of social support, particularly support from spouse and family ($r = 0.27$, $p = 0.0005$ and $r = 0.16$, $p = 0.001$, respectively). On the other hand, the severity of symptoms does not have a significant relationship with the perceived availability of friends' support among these patients.

Moreover, Table 7-10 presents the association between symptoms experience and perceived general health. There was a significant negative association between perceived symptoms severity and general health perception. This suggests that the increase of symptoms severity and hindrance of daily activities due to symptoms worsens the perceived general health and vice versa (r=-0.288, p = 0.0005 and r=-0.304 p = 0.0005, respectively).

Table 7-10: Association between perceived social support and general health perception and symptoms experience

MSPSS	LDSI-2.0	
	Symptoms severity r (p value)	Hindrance of symptoms r (p value)
Social support total score	-0.206 (0.0005)	-0.205 (0.0005)
Spouse Support N=311 (married patients)	-0.272 (0.0005)	-0.237 (0.0005)
Family support	-0.166 (0.001)	-0.137 (0.006)
Friends support	-0.048 (0.335)	-0.055 (0.275)
General health perception	-0.288 (0.0005)	-0.304 (0.0005)

Correlation is significant at the p level < 0.05 (2 tailed)

7.2.5 Multivariate analysis: Factors associated with Symptoms Experience

Tables 7-11 (Model 1) and 7-12 (Model 2) show the multiple regression models that were constructed using the stepwise method to explore factors associated with symptoms severity and hindrance of symptoms. To develop the regression model for each of the dependent factors (i.e. symptoms severity and hindrance of symptoms), all the socio-demographic and medical variables (used in deveoping model 1 and 2 in HRQOL, section 6.3.4) and social support from three sources (spouse, family and friends) were entered into the regression analysis together.

Related to the factors associated with symptoms severity (Table 7-11 - Model 1) the results show that the model significantly explained 19.6% of the variation in symptoms severity ($R^2 = 0.196$, $R^2_{adj} = 0.180$, $p = 0.0005$). Six variables significantly associated with symptoms severity [spouse support (b = -0.207), marital status (b = 0.181), gender (b = 0.175), number of liver cirrhosis complications (b = 0.154), employment status (b = 0.148) and family support (b = 0.124), $p \leq 0.01$). Low perceived spouse support, being married, females, increasing number of liver cirrhosis complications, being unemployed, and low perceived family support were significantly associated with increasing symptoms severity among this group of patients with liver cirrhosis. Perceived spouse support, marital status and gender made the strongest contribution in explaining severity of symptoms (20.7%, 18.1% and 17.5% respectively). This suggests that these psychosocial variables are most important in explaining severity of symptoms among these patients. On the other hand, somatic factors such as number of liver disease complications made less contribution although this explained about 15.4% of the variation in severity of symptoms.

Perceived social support particularly from a spouse (b = -0.207, p =0.0005) was the highest associated source of support, followed by perceived family support (b = -0.124, p = 0.01), while friends' support was not significantly associated with symptoms severity. People with a high perception of social support from spouse and family were more likely to have a low perception of severity of symptoms.

Although model 1 (Table 7-11) could significantly explain the overall severity of symptoms (p = 0.0005), around 80.4% of the variation in severity of symptoms could not be explained by the model, suggesting that there are other factors that have an influence on perceived severity of symptoms, which need to be explored further.

Table 7-11: Summary of factors associated with symptoms severity using multivariate analysis

<table>
<tr><th rowspan="2">Model 1</th><th colspan="2">df</th><th colspan="2">F</th><th>R</th><th>R^2</th><th>$R^2_{adj.}$</th><th>Sig.</th><th colspan="2" rowspan="2"></th></tr>
<tr><td colspan="2">6/304</td><td colspan="2">12.333</td><td>0.442</td><td>0.196</td><td>0.180</td><td>0.0005</td></tr>
<tr><th rowspan="2">Independent factors</th><th rowspan="2">Unstandardized Coefficients β</th><th rowspan="2">Standardized coefficient Beta (b)</th><th rowspan="2">t</th><th rowspan="2">Sig.</th><th colspan="4">95% Confidence interval for B</th><th colspan="2">Collinearity Statistics</th></tr>
<tr><th colspan="2">Lower</th><th colspan="2">Upper</th><th>Tolerance</th><th>VIF</th></tr>
<tr><td>Constant</td><td>31.276</td><td></td><td>8.095</td><td>0.0005</td><td colspan="2">23.673</td><td colspan="2">38.878</td><td></td><td></td></tr>
<tr><td>Gender</td><td>4.638</td><td>0.175</td><td>2.930</td><td>0.004</td><td colspan="2">1.523</td><td colspan="2">7.753</td><td>0.741</td><td>1.349</td></tr>
<tr><td>Marital status</td><td>5.684</td><td>0.181</td><td>3.327</td><td>0.001</td><td colspan="2">2.322</td><td colspan="2">9.047</td><td>0.891</td><td>1.123</td></tr>
<tr><td>Perceived spouse support</td><td>-3.590</td><td>-0.207</td><td>-3.777</td><td>0.0005</td><td colspan="2">-5.461</td><td colspan="2">-1.720</td><td>0.884</td><td>1.131</td></tr>
<tr><td>Employment status</td><td>5.175</td><td>0.148</td><td>2.593</td><td>0.010</td><td colspan="2">1.248</td><td colspan="2">9.101</td><td>0.814</td><td>1.229</td></tr>
<tr><td>Perceived family support</td><td>-2.188</td><td>-0.124</td><td>-2.379</td><td>0.018</td><td colspan="2">-3.999</td><td colspan="2">-0.378</td><td>0.973</td><td>1.028</td></tr>
<tr><td>Number of liver cirrhosis complications</td><td>1.888</td><td>0.154</td><td>2.931</td><td>0.004</td><td colspan="2">0.621</td><td colspan="2">3.156</td><td>0.962</td><td>1.040</td></tr>
</table>

VIF: Variance inflation factor

Dummy codes: gender: 0 males, 1 females, **disease stage:** 0 decompensated, 1 compensated, **employment status:** 0 employed, 1 unemployed, **marital status:** 0 single, 1 married, **educational level:** 0 educated, 1 uneducated, **area of residence:** 0 rural, 1 urban

In terms of the impact of symptoms on daily activities (symptom hindrance) (Table 7-12 - Model 2) the results show that the model significantly predicted 14% of the variation in hindrance of symptoms (R^2 = 0.140, R^2_{adj} = 0.132, p = 0.0005). Three variables were significantly associated with the hindrance of daily activities due to symptoms: gender (b = 0.259, p = 0.0005), perceived social support from spouse (b = -0.169, p = 0.002) and number of liver cirrhosis complications (b = 0.167, p = 0.002). Being female, low perceived support from spouse and increasing number of liver cirrhosis complications were associated with more limitations in daily life due to symptoms. Gender made the strongest contribution (25.9%) in explaining hindrance of daily life due to symptoms, while number of liver cirrhosis complications and perceived spouse support made a similar level of contribution in explaining hindrance of symptoms (16.7% and 16.9% respectively).

Interestingly, only gender, perceived spouse support and number of liver cirrhosis complications were significantly associated with both dimensions of symptoms experience, severity and hindrance. Therefore, healthcare providers should consider these factors during the development of intervention programs to treat symptoms among cirrhotic patients. However, many variables associated with severity of symptoms but did not associate with hindrance of symptoms such as marital status, perceived family support and employment status (Tables 7-11 and 7-12).

Although model 2 (Table 7-12) predicted the overall hindrance of symptoms significantly (p = 0.0005), around 86% of the variation in hindrance of symptoms could not be explained by the model, suggesting that there are other factors that have an influence on perceived hindrance of daily life due to symptoms, which need further research to be explored.

Table 7-12: Summary of factors associated with hindrance of daily activities due to symptoms using multivariate analysis

<table>
<tr><th rowspan="2">Model 2</th><th colspan="2">df</th><th colspan="2">F</th><th>R</th><th>R^2</th><th>R^2_{adj}.</th><th>Sig.</th><th colspan="2" rowspan="2"></th></tr>
<tr><td colspan="2">3/307</td><td colspan="2">16.672</td><td>0.374</td><td>0.140</td><td>0.132</td><td>0.0005</td></tr>
<tr><th rowspan="2">Independent factors</th><th rowspan="2">Unstandardized coefficient
β</th><th rowspan="2">Standardized coefficient
Beta (b)</th><th rowspan="2">t</th><th rowspan="2">Sig.</th><th colspan="4">95% Confidence interval for B</th><th colspan="2">Collinearity Statistics</th></tr>
<tr><th colspan="2">Lower</th><th colspan="2">Upper</th><th>Tolerance</th><th>VIF</th></tr>
<tr><td>Constant</td><td>13.560</td><td></td><td>6.995</td><td>0.0005</td><td colspan="2">9.745</td><td colspan="2">17.374</td><td></td><td></td></tr>
<tr><td>Gender</td><td>4.458</td><td>0.259</td><td>4.665</td><td>0.0005</td><td colspan="2">2.578</td><td colspan="2">6.339</td><td>0.910</td><td>1.099</td></tr>
<tr><td>Number of liver cirrhosis complications</td><td>1.334</td><td>0.167</td><td>3.147</td><td>0.002</td><td colspan="2">0.500</td><td colspan="2">2.168</td><td>0.994</td><td>1.006</td></tr>
<tr><td>Perceived spouse support</td><td>-1.910</td><td>-0.169</td><td>-3.052</td><td>0.002</td><td colspan="2">-3.142</td><td colspan="2">-0.679</td><td>0.913</td><td>1.096</td></tr>
</table>

7.3 PERCEIVED SOCIAL SUPPORT

The third aim of this study was to explore and describe how cirrhotic patients in Egypt perceived social support from spouse, family and friends and to identify the predictive factors of general perceived social support. Social support was investigated by using the Multidimensional Scale of Perceived Social Support (MSPSS) that contains 12 questions, which assess the availability of social support generally. The MSPSS is divided into three subscales, which assess the availability of social support from a spouse, family and friends. An increasing score shows there is increasing perceived availability of social support.

7.3.1 Social Support among Egyptian Cirrhotic People

Table 7-13 presents the means ± SD for the total MSPSS and the three subscales. The means were as follows: total MSPSS (2.02), spouse (2.45), family (1.93), and friends (1.83). As can be seen, the mean score of perceived spouse support was the highest; while the mean score of perceived friends' support was the lowest. This result suggests that Egyptians patients with liver cirrhosis perceive the spouse as the main source of social support followed by family and friends respectively.

Table 7-13: Perceptions of social support among people with liver cirrhosis

Variables	**n = 401 (100%)**		**Instrument range**
MPSS	**Mean ± SD**	**Median**	
Total score	2.02±0.537	2	1-3
Spouse subscale (n=311 married)	2.45±0.757	3	1-3
Family subscale	1.93±0.745	2	1-3
Friends subscale	1.83±0.732	1.75	1-3

7.3.2 Perceptions of Social Support from Spouse, Family and Friends

Table 7-14 shows the perceptions of patients with liver cirrhosis about the social support from spouse, family and friends. Married people agreed that their spouse (husband or wife) provided them with different kinds of support. For instance, 67.5% of them feel their spouse is around when they need him/her and 71.7% of them share their joys and sorrows with their spouse. Likewise, 64.9% of married people feel their spouse cares about their feelings.

In relation to the perception of adequacy of family support, it was observed that 52.6% felt that their families do not really try to help them. At the same time, 52.1% reported that they get the emotional help and support that they need from their families. Compared with patients' perceptions about the adequacy of friends' support, 65.6 % of patients reported that they cannot count on their friends during hard times, and 57.9% claimed that their friends do not really try to help them. However, 51.1% of the patients said that they could share their joys and sorrows with their friends (Table 7-14). These results suggest that the majority of the patients see a partner to be more helpful than family and friends, and the main source of instrumental and emotional support. Furthermore, the family was found to be more supportive than friends. However, most of the patients perceive their friends as a source of sharing their joys and sorrows but not as a source for tangible support (like providing services or money).

Table 7-14: Perceptions of patients with liver cirrhosis about social support from a spouse, family and friends

Items	**n (%)**	**Frequency, n (%)**		
		1. Disagree	**2. Natural**	**3. Agree**
Spouse subscale My spouse is around when I am in need	311 (100%)	79(25.4)	22(7.0)	**210(67.5)**
My spouse with whom I can share my joys and sorrows		64(20.5)	24(7.7)	**223(71.7)**
My spouse is a real source of comfort to me		68(21.8)	31(9.9)	**212(68.1)**
My spouse in my life who cares about my feelings		82(26.3)	27(8.6)	**202(64.9)**
Friends subscales My friends really try to help me	401 (100%)	**232(57.9)**	31(7.7)	138(34.4)
I can count on my friends when things go wrong		**263(65.6)**	20(5.0)	118(29.4)
I have friends with whom I can share my joys and sorrows		161(40.1)	35(8.7)	**205(51.1)**
I can talk about my problems with my friends		**226(56.4)**	32(8.0)	143(35.7)
Family subscale My family really tries to help me	401 (100%)	**211(52.6)**	29(7.2)	161(40.1)
I get the emotional help and support I need from my family		153(38.3)	39(9.7)	**209(52.1)**
I can talk about my problems with my family		**199(49.6)**	39(9.7)	163(40.6)
My family is willing to help me make decisions		**228(56.9)**	31(7.7)	142(45.4)

7.3.3 Factors Contributing to Perceptions of Adequacy of Social Support

To determine the factors which are associated with a perceived low or high social support among people with liver cirrhosis in Egypt; the sample (n=401) was broken down into groups according to socio-demographic characteristics and disease stage, as discussed in Chapter 6.

7.3.3.1 Socio-Demographic Characteristics

Table 7-15 presents the comparison of perceived social support of the entire study group according to gender. An independent sample t-test was conducted to compare the mean score of perceived social support among males and females. There was a statistically significant gender difference in the total MSPSS score (t = 4.822, p = 0.0005) and spouse subscale score (t = 5.412, p = 0.0005). Females were more likely than males to perceive a low availability of support in general and from the husband in particular.

Table 7-16 shows the comparison of the perception of social support between the study entire groups according to age. There was a statistically significant association between age and perceived social support (total score) ((f = 5.13, p = 0.006). In addition, the mean score of the subscale of perceived family support was significantly higher among younger than elderly patients ≥ 45 (f = 3.19, p = 0.04).

Table 7-15: Perception of social support according to gender

Variables	n = 401				
	Gender	**n**	**Mean ± SD**	**t**	**P value**
MPSS					
Total score	Males	174	2.17±0.50	4.822	**0.0005**
	Females	227	1.91±0.53		
Spouse subscale	Males	161	2.66±0.63	5.412	**0.0005**
	Females	150	2.22±0.80		
Family subscale	Males	174	1.99±0.74	1.569	0.117
	Females	227	1.88±0.74		
Friends subscale	Males	174	1.91±0.73	1.954	0.051
	Females	227	1.76±0.72		

Table 7-16: Perception of social support according to age

Variables	n = 401				
	Age group	**n**	**Mean ± SD**	**f**	**p value**
MPSS					
Total score	22-44	55	2.21±0.48	5.13	**0.006**
	45-64	306	2.01±0.53		
	65+	40	1.87±0.56		
Spouse subscale	22-44	49	2.53±0.73	0.48	0.61
	45-64	242	2.44±0.76		
	65+	20	2.34±0.76		
Family subscale	22-44	55	2.16±0.73	3.19	**0.04**
	45-64	306	1.90±0.74		
	65+	40	1.84±0.76		
Friends subscale	22-44	55	1.97±0.738	2.29	0.10
	45-64	306	1.83±0.74		
	65+	40	1.64±0.63		

Table 7-17 presents the difference in perception of social support according to educational level. The results show that there was a significant association between perceived social support and level of education. The mean score of MSPSS was statistically significant lower among illiterates than other groups (f = 5.83, p = 0.003). The mean score of perceived family support was also lower among illiterates than other groups (f = 7.28, p = 0.001).

Table 7-17: Perception of social support according to educational level

Variables	n = 401				
MPSS	Education level	n	Mean ± SD	f	p value
Total score	Illiterate	219	1.96±0.54	5.83	**0.003**
	Basic education	163	2.08±0.52		
	Higher education	19	2.33±0.50		
Spouse subscale	Illiterate	155	2.39±0.77	1.52	0.22
	Basic education	138	2.48±0.74		
	Higher education	18	2.68±0.64		
Family subscale	Illiterate	219	1.82±0.72	7.28	**0.001**
	Basic education	163	2.02±0.76		
	Higher education	19	2.39±0.56		
Friends subscale	Illiterate	219	1.81±0.73	0.61	0.54
	Basic education	163	1.83±0.74		
	Higher education	19	2.00±0.61		

Tables 7-18 and 7-19 present the perception of social support according to marital status and area of residence. There was a statistically significant relationship between the total MSPSS score and both marital status and area of residence. In terms of general perceived social support (total score), married people and those living in rural areas had higher general perceived social support than unmarried people (t = 4.51, p= 0.0005) and those living in urban areas (t = 2.41, p= 0.01). However, there was no statistically significant difference according to the source of support between married and single people and rural and urban areas.

Table 7-18: Perception of social support according to marital status

Variables	n = 401				
MPSS	Marital status	N (%)	Mean ± SD	t	p value
Total score	Single	91	1.81±0.63	4.51	**0.0005**
	Married	310	2.09±0.49		
Family subscale	Single	91	1.84±0.76	1.20	0.22
	Married	310	1.95±0.73		
Friends subscale	Single	91	1.73±0.73	1.46	0.14
	Married	310	1.86±0.73		

Table 7-19: Perception of social support according to area of residence

Variables	n = 401				
MPSS	Residence area	n	Mean ± SD	t	p value
Total score	Rural	146	2.11±0.53	2.41	**0.01**
	Urban	255	1.98±0.53		
Spouse subscale	Rural	117	2.54±0.73	1.67	0.10
	Urban	194	2.39±0.76		
Family subscale	Rural	146	2.00±0.72	1.41	0.16
	Urban	255	1.89±0.75		
Friends subscale	Rural	146	1.90±0.71	1.61	0.10
	Urban	255	1.78±0.73		

Table 7-20 shows the perception of social support according to employment status. There was a statistically significant difference between employed and unemployed peoples' perception about available social support. Employed patients had a higher mean score of general perceived social support than the unemployed (t= 4.348, p = 0.0005). Also, perceived social support from three sources, spouse, family and friends, was higher among employed than unemployed (t ≤ 2.137, p ≤ 0.03).

Table 7-20: Perception of social support according to employment status

Variables	n = 401				
MPSS	Employment status	n	Mean ± SD	t	p value
Total score	Employed	68	2.28±0.509	4.348	**0.0005**
	Unemployed	333	1.97±0.529		
Spouse subscale	Employed	61	2.78±0.579	3.925	**0.0005**
	Unemployed	250	2.36±0.774		
Family subscale	Employed	68	2.10±0.713	2.137	**0.03**
	Unemployed	333	1.89±0.748		
Friends subscale	Employed	68	2.05±0.731	2.755	**0.006**
	Unemployed	333	1.78±0.725		

7.3.3.2 Disease Stage

Table 7-21 presents the perception of social support according to disease stage by comparing compensated and decompensated cirrhotic patients. Results show that there was a statistically significant difference only in the subscale of perceived family support between the two disease stages (t = 2.11, p = 0.03). Patients with decompensated cirrhosis had a higher mean score of perceived social support than patients with compensated cirrhosis. This result suggests that with advanced disease stage, social support particularly from the family increases

Table 7-21: Perception of social support according to disease stage

Variables	**n = 401**				
MPSS	**Disease stage**	**n**	**Mean ± SD**	**t**	**p value**
Total score	Compensated	201	1.98±0.50	1.51	0.13
	Decompensated	200	2.06±0.56		
Spouse subscale	Compensated	158	2.43±0.74	0.245	0.80
	Decompensated	153	2.46±0.77		
Family subscale	Compensated	201	1.85±0.70	2.11	**0.03**
	Decompensated	200	2.01±0.77		
Friends subscale	Compensated	201	1.81±0.68	0.56	0.57
	Decompensated	200	1.85±0.77		

7.3.3.3 General Health Perception

Table 7-22 presents the association between the perception of social support and general health perception. There was a significant positive association between the perception of social support and general health perception, suggesting that when social support decreases the general health perception also decreases or vice versa (r= 0.208, p = 0.0005). The mean score of the spouse support subscale reporting the highest correlation with the general health perception (r= 0.209, p = 0.0005). This means that the social support from a spouse influences the general health perception more than the support of family and friends. However, because this study is a cross-sectional design it is not possible to infer a causal relationship.

Table 7-22: Association between perception of social support and general health perception

MSPSS	General health perception rho value	P value
Social support total score	0.208	**0.0005**
Spouse Support (n=311/married patients)	0.209	**0.0005**
Family support	0.137	**0.006**
Friends support	0.093	0.64

7.3.4 Multivariate analysis: Factors Associated with Perceived Social Support

Table 7-23 shows the multiple regression model that was developed using the stepwise method to explore factors associated with perceived social support [i.e. MSPSS total score (depended factor)]. To develop the regression model, all the socio-demographic characteristics [age, gender, marital status, educational level and employment status, area of residence (dummy code)], and medical variables [disease stage (dummy code), number of comorbidities and number of liver cirrhosis complications] were entered into the regression analysis together as independent factors.

The results in Table 7-23 show that the model significantly explained 10.9% of the variation in perceived social support (R^2 = 0.109, R^2_{adj} = 0.100, p = 0.0005). Four variables were significantly associated with overall perceived social support [Gender (b = -0.135, age (b = -0.117), Marital status (b = 0.136) and employment status (b = -0.124), p ≤ 0.01]. The findings suggest that females, unmarried, unemployed and elderly patients had low perceived social support. Marital status made the strongest contribution (13.6%) followed by gender (13.5%) to explain perceived social support in patients with liver cirrhosis.

Although model 1 (Table 7-23) significantly (p = 0.0005) predicted the overall perceived social support, around 89 % of the variation in perceived social support could not be explained by the model, suggesting that there are other Independent factors that have an influence on perceived social support, which need further research to be explored.

Table 7-23: Summary of factors associated with perceived social support (MSPSS total score) using multivariate analysis

<table>
<tr><th rowspan="2">Model 1</th><th colspan="2">df</th><th colspan="2">F</th><th>R</th><th>R^2</th><th>$R^2_{adj.}$</th><th>Sig.</th><th colspan="2" rowspan="3">Collinearity Statistics</th></tr>
<tr><td colspan="2">4/396</td><td colspan="2">12.083</td><td>0.330</td><td>0.109</td><td>0.100</td><td>0.0005</td></tr>
<tr><th rowspan="2">Independent factors</th><th rowspan="2">Unstandardized Coefficients B</th><th rowspan="2">Standardized coefficient Beta</th><th rowspan="2">t</th><th rowspan="2">Sig.</th><th colspan="4">95% Confidence interval for B</th></tr>
<tr><th colspan="2">Lower</th><th colspan="2">Upper</th><th>Tolerance</th><th>VIF</th></tr>
<tr><td>Constant</td><td>2.490</td><td></td><td>13.842</td><td>0.0005</td><td colspan="2">2.137</td><td colspan="2">2.844</td><td></td><td></td></tr>
<tr><td>Gender</td><td>-0.146</td><td>-0.135</td><td>-2.510</td><td>0.012</td><td colspan="2">-0.260</td><td colspan="2">-0.032</td><td>0.780</td><td>1.282</td></tr>
<tr><td>Age</td><td>-0.007</td><td>-0.117</td><td>-2.394</td><td>0.017</td><td colspan="2">-0.013</td><td colspan="2">-0.001</td><td>0.935</td><td>1.070</td></tr>
<tr><td>Marital status</td><td>0.174</td><td>0.136</td><td>2.667</td><td>0.008</td><td colspan="2">0.046</td><td colspan="2">0.303</td><td>0.863</td><td>1.158</td></tr>
<tr><td>Employment status</td><td>-0.177</td><td>-0.124</td><td>-2.383</td><td>0.018</td><td colspan="2">-0.323</td><td colspan="2">-0.031</td><td>0.836</td><td>1.197</td></tr>
</table>

VIF: Variance inflation factor

Dummy codes: gender: 0 males, 1 females, **disease stage:** 0 decompensated, 1 compensated, **employment status:** 0 employed, 1 unemployed, **marital status:** 0 single, 1 married, **educational level:** 0 educated, 1 uneducated, **area of residence:** 0 rural, 1 urban

7.4 CONCLUSION

This chapter aimed to explore symptoms experience and its predictive factors by using the LDSI-2.0. The analysis of the LDSI-2.0 identified that the patients in this study experienced severity of various symptoms and hindrance in their daily activities because of these symptoms. The most commonly reported symptoms among these patients were the difficulty of managing time as a result of liver disease, financial problems because of liver disease and memory problems. It was also noted that some symptoms could influence daily activities of these patients more than others could for example; joint pain and depression. Therefore, these symptoms need more attention from healthcare providers when caring for these patients.

Bivariate analysis showed that there was a significant association between symptoms experience related subscales and gender, education, employment status, disease stage, complications of liver cirrhosis, and comorbidities. Women, uneducated and unemployed people, and patients with decompensated cirrhosis, multiple complications and comorbidities were more likely to perceive a high severity of symptoms and hindrance in their daily activities due to these symptoms. Singles were more likely to report more hindrance on their daily activities than married patients as a result of symptoms.

Moreover, numerous factors significantly influenced the type of symptoms experienced, suggesting that different patients experience different of symptoms. For example, there was a significant difference in the type of symptoms experienced by women and men. Women were more likely than men to suffer from joint pain, right abdominal pain, decreased appetite, depression, jaundice, memory problems and personality change, while men were more likely than women to suffer from sexual problems. In relation to the association between social support and symptoms experience, there was a significant inverse relationship between them. Perceptions of symptoms severity and hindrance of daily activities due to symptoms were significantly associated with social support, particularly from spouse and family. Furthermore, symptoms experience (i.e. severity and hindrance of daily activities due to symptom subscales) was negatively associated with general health perception.

Finally, the stepwise multiple regression analysis was used to evaluate factors associated with symptoms experience for two subscales of LDSI-2.0, severity and hindrance of symptoms, among this population. Gender, perceived spouse support and number of liver cirrhosis complications were associated with symptoms severity and hindrance of daily activities due to symptoms.

The third aim of this study was explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to identify and evaluate factors associated with general perceived social support using the MSPSS. The analysis of the MSPSS identified that patients with liver cirrhosis in Egypt perceived their spouse as the greatest source of social support followed by family and friends. A comparison of social support according to the socio-demographic characteristics found that females were more likely than males to perceive low social support from their partner as well as from friends. In addition, elderly, illiterate and unemployed were more likely to report low perceived social support. Using multiple regression analysis found that age, gender, marital status and employment status were significantly associated with overall perceived social support.

8 CHAPTER 8- PROPERTIES OF INSTRUMENTS

8.1 INTRODUCTION

As acknowledged in Chapter 4, this is the first time that the Arabic Liver Disease Symptom Index-2.0 (LDSI-2.0) and Multidimensional Scale of Perceived Social Support (MSPSS) have been used among Egyptian patients in general and among patients with liver cirrhosis specifically. In addition, the MSPSS has not been used in Arabic men; it has been only used in Arabic immigrant women in the USA. Therefore, this chapter aims to evaluate the psychometric properties of the three measures: LDSI-2.0, MSPSS and Short Form-36v$_2$ (SF-36v$_2$) in patients with liver cirrhosis using the dataset. Table 8-8 summarises the concepts studied, the measures used, and the psychometric properties.

Griffiths and Rafferty (2010) argued that researchers should evaluate the psychometric properties of instruments and not simply believe the claims of others that the tool is valid. Reliability and validity are the key indicators of the quality of an instrument (Kimberlin and Winterstein 2008). Reliability (internal consistency) means that the items within a scale are theoretically homogeneous and are measuring the same construct (DeVellis 2003). A commonly used statistical method for estimating the internal consistency is Cronbach's alpha coefficient (α). Therefore, the alpha coefficient was investigated for the three instruments used in this study. Alpha coefficients range from 0.00 to 1.00 (Kimberlin and Winterstein 2008), with a value of 0.70 or higher indicating an acceptable level of reliability (Nunnally and Bernstein 1994; DeVellis 2003). Validity reflects the extent to which the instrument measures what it is intended to measure. Therefore, the validity of the three instruments used in this study (LDSI-2.0, MSPSS and SF-36) was also investigated.

8.1.1 Background about Factor Analysis

Factor analysis (FA) is a statistical technique that is commonly used to develop or evaluate an instrument structure. As suggested by de Vet et al. (2005) factor analysis is an essential step in the validation of multi-item questionnaires. It aims to evaluate the factor structure (dimensions of the questionnaires). Factor analysis is a sophisticated statistical technique that can reveal whether or not the pattern of responses on a number of items can be explained by a smaller number of underlying factors.

There are two different methods of factor analysis (exploratory or confirmatory). The two methods make different assumptions about the data and how they should be handled and it is crucial to select the most suitable method to provide answers to different research questions (de Vet et al. 2005). Floyd and Widaman (1995) suggest that exploratory factor analysis (EFA) should be used when there is no previous hypothesis about the instrument's factor structure (number of dimensions and associations between items). Confirmatory factor analysis (CFA) is appropriate if the instrument has a prior hypothesis that is based on a theory or previous analysis, and it can be used to test the fitness of the hypothesized model (the measurement’s factor structure).

8.2 VALIDITY AND RELIABILITY OF ARABIC LDSI-2.0

In 2004, van der Plas et al. investigated the psychometric properties of LDSI-2.0 in terms of feasibility, validity (construct and known group / discriminant validity) and reliability (internal consistency and test-retest reliability). Its construct validity was evaluated in terms of convergent and divergent validity with SF-36 among Dutch people with chronic liver disease and cirrhosis (van der Plas et al. 2004). Similarly, construct validity of the Arabic LDSI-2.0 was investigated among a sample of 38 patients with liver cirrhosis in Egypt (Youssef et al. 2012) (in the pilot study-Chapter 5). The pilot study could not be used for additional validity tests such as factor analysis or known group validity as they usually require a large sample size (Tabachnick and Fidell 2007). Therefore, to complete the validation process the main study sample (n = 401) was used to investigate the construct validity and the internal consistency reliability of the Arabic LDSI-2.0.

8.2.1 LDSI-2.0 Construct Validity

8.2.1.1 LDSI-2.0 Discriminant Validity

Known group validity aims to assess the ability of the LDSI-2.0 to discriminant between subgroups that differ for example by gender or disease stage. Based on the reviewed literature, it was hypothesized that the mean scores of the symptoms severity and hindrance of symptoms subscales of, for example, women and patients with decompensated cirrhosis would be higher than those of men and patients with compensated cirrhosis (Armstrong 2003; van der Plas et al. 2004). Results in Chapter 7 confirmed these hypotheses, suggesting the discriminant validity of the Arabic LDSI-2.0 to find significant differences between patients according to gender and disease stage.

8.2.1.2 LDSI-2.0 Exploratory Factor Analysis

Exploratory factor analysis is the appropriate test if the tool does not have a prior structure hypothesis and has not been used before in a specific group of patients or language (de Vet et al. 2005). Factor analysis (FA) for LDSI-2.0 has not previously been investigated; thus exploratory factor analysis was most suitable according to Field's suggestion (2009). There is no previous study with which to compare the results. However, van der Plas et al. (2004) hypothesized that the LDSI-2.0 has two subscales that are related (symptom severity and hindrance of symptom), and an additional six items as discussed in section 4.5.1.2. Based on van der Plas et al. (2004) suggestions, it was hypothesized that the two related items (e.g., depression severity and depression hampered daily life) should be loaded together because these items measure a related concept (depression).

The following steps were followed according to Pallant (2007):

1. Suitability of data for factor analysis was checked by determining the adequacy of the sample size and the strength of items intercorrelation. De Vet et al. (2005) suggest that before conducting any type of factor analysis a sufficient sample size is required to give reliable results. There is no general agreement about the minimum required sample. However, the ratio of the number of cases to the number of variables is helpful to decide whether the sample is sufficient. Four to ten cases per item is the rule of thumb to decide the required sample size (de Vet et al. 2005). Therefore, for LDSI-2.0 (24 items), 10 cases x 24 items = 240 subjects would be enough to give reliable factor structure. Therefore, a sample size of 401 (without missed data) is sufficient to give a reliable factor structure. For instance, strength of items

intercorrelation was tested using the Kaiser-Meyer-Olkin (KMO) measure. KMO ranges from 0.0 to 1.0, with 0.6 the minimum required value to give reliable factor analysis and indicating adequacy of sample to give strong intercorrelation among items (Tabachnick and Fidell 2007).

2. The next step was to select the factor extraction technique, in other words determine the smallest number of factors that could be used to measure the interrelations among the variables. Principal component analysis, the most commonly used technique, was used.

3. The Orthogonal rotation (varimax) method was also selected as a factor rotation method because its solution is usually easier to interpret and report and is the most commonly used (de Vet et al. 2005).

A principal component analysis (PCA) was used to compute the 24 items factor loading with orthogonal rotation (varimax). The KMO measure verified the sampling adequacy for the analysis. Overall KMO value was 0.77 and all KMO values for individual items were greater than 0.62; that is above the acceptable limit of 0.60 (Tabachnick and Fidell 2007). Chi-Square = 5374.930, df = 276, $p < 0.0001$, indicates that correlations between items were sufficiently large for PCA. An initial analysis was run to obtain eigenvalues for each component in the data. Only factors with an eigenvalue > 0.7 explaining the maximum cumulative variance were interpreted as suggested by Field (2009). Eleven components had eigenvalues over Jolliffe's criterion of 0.7 and in combination, explained 84.46% of the variance. To assess the most significant loadings in interpreting the factor solution, items that had value ≥ 0.50 was considered significant (Hair et al. 2010). Most items showed the highest factor loadings on the original factors (Tables 8-1 and 8-2).

Table 8-2 shows the factor loading after rotation. Items that cluster on the same components suggest that they are measuring related concepts. Table 8-3 summarises the 11 factors related to a relevant symptom component. For example, Factor 1 included three items related to itching (i.e. itch severity, itch hampered sleep, itch hampered daily life). Factor 2 included three items (depression severity, depression hindrance and afraid of complications), which may indicate mental health. Factor 3 included two items: sexual interest and sexual activity that related to sexual health. These results support the hypothesis that LDSI-2.0 is a multidimensional tool, and items that were assumed to be structurally related were loaded together.

Table 8-1: Exploratory factor analysis for 24 items of Arabic LDSI-2.0 (n = 401)

Rotated Component Matrix^a											
Items	**Component/Factors**										
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Itch hampered sleep	0.856				0.116	0.170					
Itch	0.851		0.104								0.168
Itch hampered	0.843	0.145		0.145							
Depression	0.104	0.825		0.138		0.206	0.144	0.110		0.208	
Depression hampered		0.817		0.158	0.166	0.148	0.162	0.120	0.118	0.137	
Afraid of complications	0.125	0.621	0.156					0.344			0.183
Sexual interest		0.107	0.945								
Sexual activity		0.127	0.939							0.104	
Joint pain	0.146			0.919							0.117
Joint hampered	0.101	0.152		0.905	0.140	0.126					0.106
Abdominal pain hampered	0.104	0.180	0.108	0.100	0.907			0.131			
Abdominal Pain	0.120			0.144	0.900	0.134				0.132	0.114
Decreased appetite		0.150				0.871	0.116	0.151			
Decreased appetite hampered		0.142	0.143	0.102	0.131	0.863		0.102			
Sleepiness during the day		0.105	0.107				0.924				
Sleepy hampered	0.122	0.109		0.125	0.122		0.895				
Worry		0.165				0.115		0.890		0.165	
Worry hampered		0.220		0.105	0.126	0.145		0.840			
Yellow skin hampered									0.911		
Yellow skin						0.139			0.900		
Financial problems	0.104	0.158			0.110		0.106	0.114		0.879	0.136
Use time differently		0.296	0.197	0.121		0.305		0.239	0.121	0.622	0.101
Difficult memory	0.135			0.123	0.113						0.871
Personality change		0.422	0.169	0.160	0.108		0.102			0.157	0.609
Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.											
Rotation converged in 6 iterations.											

Table 8-2: Summary of the exploratory factor analysis for the loaded factors for the Arabic LDSI-2.0 (n = 401)

Rotated Component Matrix											
Items	**Component/Factors**										
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Itch hampered sleep	0.856										
Itch	0.851										
Itch hampered	0.843										
Depression		0.825 [a]									
Depression hampered		0.817 [a]									
Afraid of complications		0.621 [a]									
Sexual interest			0.945								
Sexual activity			0.939								
Joint pain				0.919							
Joint hampered				0.905							
Abdominal pain hampered					0.907						
Abdominal Pain					0.900						
Decreased appetite						0.871					
Decreased appetite hampered						0.863					
Sleepiness during the day							0.924				
Sleepy hampered							0.895				
Worry								0.890			
Worry hampered								0.840			
Yellow skin hampered									0.911		
Yellow skin									0.900		
Financial problems										0.879	
Use time differently										0.622	
Difficult memory											0.871
Personality change		0.422									0.609
Eigenvalues	6.88	2.02	1.81	1.65	1.47	1.38	1.22	1.19	0.96	0.90	0.81
% of variance	28.65	8.41	7.53	6.89	6.14	5.73	5.08	4.94	3.98	3.75	3.36
Internal consistency / α	0.84	[a] 3 items 0.90	0.94	0.91	0.91	0.84	0.90	0.84	0.83	0.70	0.61
a: Reliability of the three items											

Table 8-3: Factorial structure of the Arabic LDSI-2.0 (24 items)

Factor number	Number of items	Name of items	Suggested factor name
1	3	Itch severity, itch hampered sleep and itch hampered daily life	Itching
2	3	Depression severity, depression hindrance and afraid of complications	Mental health
3	2	**Sexual interest*** and **sexual activity***	Sexual health
4	2	Joint pain and Joint hampered	Joint pain
5	2	Abdominal pain and abdominal pain hampered	Abdominal pain
6	2	Decreased appetite and decreased appetite hampered	Appetite change
7	2	Sleepiness during the day and Sleepy day hampered	Sleepiness
8	2	Worry and Worry hampered	Worry
9	2	Jaundice and jaundice hampered	Jaundice
10	2	**Financial problems as a result of liver disease* and use time differently as a result of liver disease***	Extra items
11	2	**Difficult memory*** and **personality change***	Extra items

***Bolded items**: are the items that are considered extra according to van der Plas et al. 2004

8.2.2 LDSI-2.0 Reliability

The internal consistency reliability was investigated for each subscale of the LDSI-2.0. The results in Table 8-2 revealed Cronbach's alpha value ranged from 0.70 to 9.4, suggesting internal consistency reliability of the Arabic LDSI-2.0 in liver cirrhotic patients.

8.3 VALIDITY AND RELIABILITY OF ARABIC MSPSS

8.3.1 MSPSS Construct Validity

The studies that developed and reported validity of the MSPSS (Zimet et al. 1988; Aroian et al. 2010) were used to develop the following two hypotheses that helped to test the factorial and construct validity of MSPSS in liver cirrhotic patients: (1) the factor structure was assumed to give three independent factors for support from family, spouse and friends and (2) the discriminant validity was investigated by testing the following theoretical hypotheses:

I. Social support would be negatively associated with perceived symptom severity (Lenz et al. 1997), and with increasing social support there would be fewer symptoms of depression and anxiety (Zimet et al. 1988).

II. According to the model of HRQOL outcomes, perceived social support would be positively associated with general health perceptions (Wilson and Cleary 1995).

Therefore, the construct validity of the MSPSS was tested using confirmatory factor analysis to test the first hypothesis, and discriminant validity to test the second hypothesis.

8.3.1.1 MSPSS Confirmatory Factor Analysis

De Vet et al. (2005) stated that if the aim of the analysis is to confirm the existing factor structure; then confirmatory factor analysis is more appropriate. The MSPSS has a hypothesized factor structure that was supported by previous studies (Zimet et al. 1988; Aroian et al. 2010). Therefore, to test the construct validity of the MSPSS, confirmatory factor analysis was used.

The more appropriate technique for CFA is Structural Equation Modelling (SEM) (Tabachnick and Fidell 2007). SEM is a specific statistical technique that is used to test hypotheses about the relationships between observed variables (measured items) and unobserved factors (latent variables). SEM needs a formal model to be estimated (Field 2009). Consistent with the original MSPSS (Zimet et al. 1988 and 1990) and the MSPSS-AW (Aroian et al. 2010) we anticipated obtaining a three-factor structure for the MSPSS. Thus, the SEM was developed where the three factors in circles and the items in boxes, see Figure 8-1. To assess this proposed factor structure, CFA was performed.

As discussed in section 8.2.1.2, a large sample size is a crucial requirement for conducting factor analysis. Using the rules of thumb method of ratio of cases to items, 120 cases are sufficient to give reliable results (de Vet et al. 2005). Therefore, a sample size of 401 was sufficient to give a reliable factor structure.

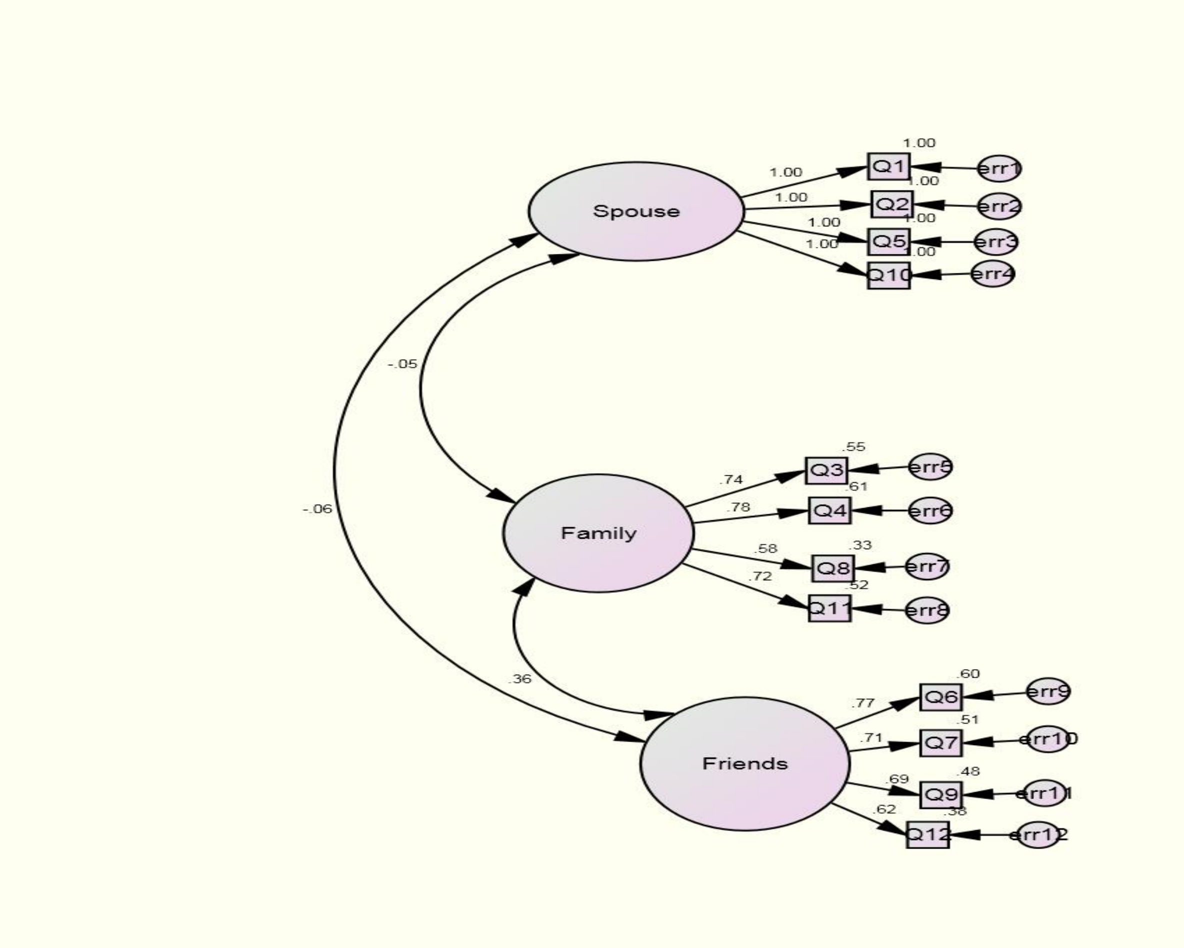
A proposed model that represented the 12 items and the three factors of MSPSS was developed (Figure 8-1) using Analysis of Moment Structures (AMOS) Version 19. Fitting of the model was based on criteria that were suggested by Tabachnick and Fidell (2007), where these criteria indicate a significant fitting model:

Comparative Fit Index (CFI) > 0.95 and Root Mean Square Error of Approximation (RMSEA) ≤ 0.06.

Figure 8-1 shows the standardized factor loadings using the Maximum Likelihood Estimates obtained with the total sample for the three subscales of the MSPSS. The standardized factor loadings for the 12 items ranged from 0.62 to 1.0, and all were statistically significant ($p < 0.0001$). The result exceeds the stated criteria, suggesting that the overall fit of the CFA model was good: a Chi-square (χ^2) = 109.47, df = 51, $p < 0.0001$, CFI = 0.995 and RMSEA = 0.054. This finding is consistent with previous studies that investigated MSPSS using factor analysis and confirmed that MSPSS has three independent factors or sources of support (Zimet et al. 1988; Nakigudde et al. 2009; Aroian et al. 2010; Wongpakaran et al. 2011).

The results of correlations between the subscales reveal that there is a weak association ($r = 0.06$) between the subscales of spouse and friends (Figure 8-1). However, Zimet et al. (1988) found that there was a moderate association ($r = 0.63$) between the two subscales of friends and significant other, which was modified in the Arabic MSPSS to be spouse (i.e. Husband) (Aroian et al. 2010). Participants in Zimet et al.'s (1988) study were undergraduate healthy students (mean age = 18.6±0.88) who were studying away from their families. Thus, Zimet and colleagues considered it to be logical that these students could not separate between their friends and significant others, e.g. girl/boyfriend, spouse, physician…etc. In contrast, participants in this study were adult patients (mean age 53.25 ± 9.0) from a different cultural background; also the subscale of significant other was clearly defined (i.e. spouse) in the Arabic MSPSS. As a result, the patients could differentiate between support from friends and spouse.

Figure 8-1: A proposed model and standardized estimation of the MSPSS



Arrows in the model indicate the hypothesized relationships, and coefficients above each arrow are estimated standardized regression weights. Squares represent observed variables (MSPSS items), and circles represent latent variables.

8.3.1.2 MSPSS Discriminant Validity

To test the stated hypotheses, Pearson's test was used to obtain the correlation between MSPSS and related subscales, and general health perception, symptoms severity and symptoms hampered. Also, perception of social support according to area of residence (rural vs. urban) was tested using the non-parametric independent t-test (see Chapter 7). As was noted, there was a statistically significant relationship between age and perceived social support. The mean score of the subscale of perceived family support was statistically significantly higher among younger than elderly patients (f = 5.13, p = 0.006) (Table 7-16). It was also found that the severity of symptoms was negatively associated with the perceived availability of social support, particularly support from spouse and family (r = 0.27, p = 0.0005 and r = 0.16, p = 0.001, respectively) (Table 7-10). There was a significant positive association between perceptions of social support and general health (r= 0.208, p = 0.0005), particularly from the spouse and family (r= 0.209, p = 0.0005; r = 0.136, p = 0.006) (Table 7-22). In terms of the relationship between perceived social support and area of residence, people in rural areas perceived higher social support than people in urban areas (t = 2.41, p = 0.01). These findings confirmed the stated hypotheses and suggested known group validity of the MSPSS in the liver cirrhotic population in Egypt.

8.3.2 MSPSS Reliability

MSPSS demonstrated high internal consistency with an alpha of 0.80 (Table 8-4). Also, the Cronbach's alpha for the three subscales of MSPSS was > 0.78 with the spouse subscale having the highest alpha value (alpha = 0.97). This indicates acceptable internal consistency of this measurement as a whole and for its related subscales (Nunnally and Bernstein 1994).

The point rating scale of 1-3 that was suggested by Aroian et al. (2010) was used to present this study's results. According to Aroian et al. (2010) suggestion, the three point rating scale (1-3) was transformed into a seven point rating scale 1-7 (disagree = 1, neutral = 4 and agree = 7) to maintain the comparability with previous studies that used the MSPSS. Table 8-4 shows the means, standard deviations and alpha coefficients of the MSPSS among patients with liver cirrhosis in Egypt compared with the original study (Zimet et al. 1990) and the study that translated it (Aroian et al. 2010). As was noted, the spouse subscale had the highest mean score (mean = 6.27 ± SD = 1.898), followed by the family and friends subscales.

Table 8-4: Means, standard deviations and alpha coefficient of the MSPSS for current study and prior studies

MSPSS	**Current study**		**Aroian et al. 2010**		**Zimet et al. 1990***	
	Mean ± SD	**Reliability Alpha coefficient**	**Mean ± SD**	**Reliability Alpha coefficient**	**Mean ± SD**	**Reliability Alpha coefficient**
Total scale	6.47±1.50	0.80	5.51±1.10	0.74	6.01±0.90	0.90
Spouse	6.27±1.89	0.97	6.43±1.36	0.89	6.39±0.88	0.90
Family	5.22±2.55	0.79	5.75±1.63	0.73	6.02±1.16	0.90
Friends	4.70±3.13	0.79	4.34±2.04	0.80	5.64±1.27	0.94

Note: Total scale and subscale scores are averaged over items ranged from 1 to 7

***** The reported result for pre-partum (pregnant women)

8.4 VALIDITY AND RELIABILITY OF ARABIC SF-36V_2

SF-36 has been used among patients with different health conditions in Egypt over a long period. However, its validity and reliability have not yet been investigated in Egypt. In psychosocial and medical sciences, a construct such as HRQOL is usually measured by means of a multi-item health status tool. Therefore, it is important to investigate these questionnaires extensively before using them (de Vet et al. 2005).

Testing the validity of the SF-36 focuses on assessing the related hypothesis (Ware et al. 2008). As explained in Chapter 4, the SF-36 has a standardized software program that was used to compute the scales score. Furthermore, this software gives an analytical report that is called "Data Quality Evaluation Report". This report is useful in explaining the reliability and validity of SF-36 among the studied group. Therefore, this report is used to present the validity and reliability of SF-36 among patients with liver cirrhosis in Egypt.

8.4.1 SF-36 Construct Validity

The following steps that were suggested by McHorney and colleagues (1994) were followed to investigate the construct validity and internal consistency of the SF-36 among patients with liver cirrhosis in Egypt.

1. Item validity (convergent and discriminant validity)
2. Scale validity
3. Internal consistency

8.4.1.1 SF-36 Item Level Validation

For testing the SF-36 items validity, the hypotheses that were developed by Ware et al. (2008) were followed.

Hypothesis-1: Correlations between items and their hypothesized scale scores should equal 0.40 or greater (Item convergent validity). Table 8-5 shows that 97.1% of items had a correlation coefficient of 0.40 or greater with their hypothesized scale, showing that SF-36 has satisfactory convergent validity.

Hypothesis-2: The correlation between each item and its hypothesized scale should be significantly higher than the correlation between that item and other scales (Items discriminant validity). Table 8-6 shows that after correcting overlapping between items, 98.4% of items correlated significantly higher with their hypothesized scale than with other competing scales score, suggesting scaling success of SF-36. However, the items of PF01, GH01 and SF02 seemed to fail in discriminate validity because they were not more highly correlated with their hypothesised scale items than with alternative scales. However, these correlations were not significant (Table 8-6), suggesting that their discriminant validity is acceptable.

Table 8-5: Multi-trait / multi-item correlation matrix (convergent validity/success rate)

Items	**Scales**							
	PF	**RP**	**BP**	**GH**	**VT**	**SF**	**RE**	**MH**
Scale = PF - Physical Functioning								
PF01	0.50*	0.52	0.29	0.25	0.38	0.32	0.26	0.22
PF02	0.66*	0.60	0.35	0.31	0.48	0.37	0.40	0.24
PF03	0.65*	0.48	0.31	0.22	0.38	0.36	0.27	0.22
PF04	0.65*	0.53	0.45	0.33	0.51	0.32	0.39	0.28
PF05	0.65*	0.40	0.31	0.21	0.38	0.28	0.29	0.27
PF06	0.64*	0.49	0.42	0.35	0.48	0.37	0.31	0.32
PF07	0.72*	0.57	0.43	0.34	0.49	0.42	0.28	0.35
PF08	0.79*	0.56	0.42	0.30	0.49	0.39	0.23	0.33
PF09	0.68*	0.44	0.31	0.26	0.37	0.34	0.18	0.25
PF10	0.52*	0.36	0.28	0.19	0.25	0.29	0.23	0.20
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = RP - Role Physical								
RP01	0.62	0.80*	0.39	0.35	0.55	0.41	0.46	0.37
RP02	0.61	0.83*	0.42	0.36	0.54	0.42	0.46	0.37
RP03	0.62	0.81*	0.41	0.33	0.58	0.41	0.42	0.37
RP04	0.56	0.71*	0.40	0.37	0.51	0.40	0.44	0.37
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = BP - Bodily Pain								
BP01	0.46	0.39	0.82*	0.38	0.50	0.46	0.24	0.40
BP02	0.48	0.48	0.82*	0.42	0.55	0.48	0.32	0.46
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = GH - General Health								
GH01	0.41	0.41	0.38	0.45*	0.49	0.39	0.34	0.38
GH02	0.18	0.24	0.23	0.43*	0.26	0.28	0.25	0.30
GH03	0.32	0.32	0.33	0.57*	0.41	0.32	0.23	0.38
GH04	0.13	0.15	0.22	0.38*	0.30	0.22	0.27	0.31
GH05	0.35	0.32	0.34	0.59*	0.44	0.34	0.30	0.33
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = VT - Vitality								
VT01	0.42	0.44	0.38	0.38	0.53*	0.35	0.34	0.35
VT02	0.40	0.44	0.38	0.37	0.59*	0.36	0.34	0.48
VT03	0.56	0.57	0.47	0.47	0.59*	0.44	0.44	0.46
VT04	0.41	0.45	0.45	0.41	0.56*	0.34	0.38	0.54
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = SF - Social Functioning								

SF01	0.31	0.33	0.38	0.35	0.32	0.49*	0.32	0.33
SF02	0.52	0.47	0.47	0.40	0.52	0.49*	0.33	0.41
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = RE - Role Emotional								
RE01	0.35	0.44	0.27	0.34	0.43	0.33	0.83*	0.48
RE02	0.36	0.47	0.29	0.35	0.46	0.34	0.87*	0.49
RE03	0.37	0.49	0.25	0.38	0.46	0.38	0.76*	0.42
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = MH - Mental Health								
MH01	0.17	0.23	0.26	0.27	0.25	0.25	0.28	0.44*
MH02	0.29	0.36	0.34	0.37	0.49	0.35	0.45	0.72*
MH03	0.24	0.26	0.35	0.37	0.49	0.34	0.33	0.66*
MH04	0.38	0.38	0.40	0.42	0.55	0.38	0.49	0.71*
MH05	0.37	0.42	0.42	0.46	0.55	0.38	0.42	0.72*

Note: * Item-scale correlation corrected for overlap (relevant item removed from its scale for the correlation). Starred correlations are hypothesized to be highest in the row of correlations.

Table 8-6: SF-36 item-level discriminant validity tests (scaling success)

Items	**Scales**							
	PF	**RP**	**BP**	**GH**	**VT**	**SF**	**RE**	**MH**
Scale = PF - Physical Functioning								
PF01	**	-1	2	2	2	2	2	2
PF02	**	1	2	2	2	2	2	2
PF03	**	2	2	2	2	2	2	2
PF04	**	2	2	2	2	2	2	2
PF05	**	2	2	2	2	2	2	2
PF06	**	2	2	2	2	2	2	2
PF07	**	2	2	2	2	2	2	2
PF08	**	2	2	2	2	2	2	2
PF09	**	2	2	2	2	2	2	2
PF10	**	2	2	2	2	2	2	2
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = RP - Role Physical								
RP01	2	**	2	2	2	2	2	2
RP02	2	**	2	2	2	2	2	2
RP03	2	**	2	2	2	2	2	2
RP04	2	**	2	2	2	2	2	2
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = BP - Bodily Pain								
BP01	2	2	**	2	2	2	2	2
BP02	2	2	**	2	2	2	2	2
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = GH - General Health								
GH01	1	1	1	**	-1	1	2	1
GH02	2	2	2	**	2	2	2	2
GH03	2	2	2	**	2	2	2	2
GH04	2	2	2	**	1	2	2	1
GH05	2	2	2	**	2	2	2	2

Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = VT - Vitality								
VT01	2	1	2	2	**	2	2	2
VT02	2	2	2	2	**	2	2	2
VT03	1	1	2	2	**	2	2	2
VT04	2	2	2	2	**	2	2	1
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = SF - Social Functioning								
SF01	2	2	2	2	2	**	2	2
SF02	-1	1	1	1	-1	**	2	1
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = RE - Role Emotional								
RE01	2	2	2	2	2	2	**	2
RE02	2	2	2	2	2	2	**	2
RE03	2	2	2	2	2	2	**	2
Items	Scales							
	PF	RP	BP	GH	VT	SF	RE	MH
Scale = MH - Mental Health								
MH01	2	2	2	2	2	2	2	**
MH02	2	2	2	2	2	2	2	**
MH03	2	2	2	2	2	2	2	**
MH04	2	2	2	2	2	2	2	**
MH05	2	2	2	2	2	2	2	**

Levels of Scaling Success Presented in the Table mean the following
2 = Item-scale correlation is significantly higher (2 standard errors or more) for the hypothesized scale than for the competing scale.
1 = Item-scale correlation is higher for the hypothesized scale than for the competing scale, but not significantly.
-1 = Item-scale correlation is lower for the hypothesized scale than for the competing scale, but not significantly.
-2 = Item-scale correlation is significantly lower (2 standard errors or more) for the hypothesized scale than for the competing scale.

8.4.1.2 SF-36 Scale Level Validity

Two hypotheses were examined to assess the scale level validity of SF-36:

Hypothesis-1: Scales measuring physical health (PF, RP, and BP) should have higher correlations with each other than with the other scales that measure mental health domains (MCS).

Hypothesis-2: Scales measuring MCS (MH, RE, and SF) should have higher correlations with each other than with the other scales that measure physical health domains (PCS).

Furthermore, SF-36 scales measuring PF, RP, and BP were expected to be more highly correlated with an empirically derived PCS than with MCS. Also, SF-36 scales measuring SF, RE, and MH were expected to be more highly correlated with an empirically derived MCS than with PCS; while the two scales measuring GH and VT were expected to overlap between MCS and PCS (Ware et al. 1994). The results that are presented in (Table 8-7) supported these hypotheses, and suggest validity of the SF-36 dimensionality into the two summary components.

Table 8-7: Construct validity and internal reliability of SF-36

Domains	**Number of Items**	**Correlation (rs)**		**Internal Reliability**	**Item-total correlation**
		MCS	**PCS**		
PF	10	0.334**	**0.815****	0.89	0.49-0.78
RP	4	0.448**	**0.726****	0.90	0.71-0.82
BP	2	0.393**	**0.708****	0.87	0.78-0.78
GH	5	0.511**	**0.505****	0.71	0.38-0.58
VT	4	**0.661****	0.563**	0.76	0.53-0.58
SF	2	**0.602****	0.471**	0.65	0.49-0.49
RE	3	**0.806****	0.145**	0.90	0.76-0.86
MH	5	**0.858****	0.180**	0.84	0.43-0.72

* $P < 0.0005$, p value significant at 2-tailed

8.4.1.3 SF-36 Reliability

The QualityMetric report using the data of the current study identified that 87.5% of scales had Cronbach's alpha coefficients ≥ 0.70, suggesting good reliability. SF scale (2 items) was the only scale that had alpha coefficients less than 0.7 ($\alpha = 0.65$) (Table 8-7). The alpha coefficient is quite sensitive to the number of items on the scale, with scales consisting of less than 10 items commonly having low values of alpha (i.e. 0.5) (Pallant 2007). Therefore, alpha coefficients of 0.50 or 0.60 suggest satisfactory reliability (Nunnally, 1978).

Table 8-8: Summary of the studied concepts and used measures and their psychometric properties

Studied concepts	Measures			Psychometric properties of English and Arabic versions	
	Name	**Structure**	**Scoring**	**English: Validity/ Reliability**	**Arabic: validity and reliability**
HRQOL: physical and mental health domains	SF-36v$_2$	Eight domains and two components summary score The past 4 weeks	Old a logarithm score from 0-100 Cut-off score: mean= 50 ± standard division 10)	Reliability ranged from 0.68 (social functioning)-0.93 (physical functioning) (Ware et al. 1994) content, concurrent, criterion, construct and predictive validity establised (Ware 2000)	Internal consistency: alpha coefficient ranged from 0.57-0.88 retest reliability ranged from 0.29-0.80 (Coons et al. 1998) Internal reliability: alpha coefficient ranged from 0.65-0.90 (in the current study)
Symptoms experience: Frequency, severity and hindrance (distress)	LDSI-2.0	Total score: Disease specific HRQOL Two subscales: Symptom severity and symptom distress The past week	Index scored on a 5-point scale ranging from zero 'not at all' to 4 'to a high extent'	Construct validity: low to moderately correlated with the SF-36 Retest reliability (Kappa value 0.32–0.91) (van der Plas et al. 2004)	Construct validity: moderate to high correlated with the SF-36 Retest reliability (Kappa value 0.62–0.94). Chronbach's alpha coefficient for the multi-item scales ranged from 0.73 to 0.96 (Youssef et al. 2012)
Social support from different sources	MSPSS	Total score: general perceived social support Three subscales: Spouse support Family support Friends support	English version scored on a 7-point Likert scale Arabic version scored on a 3-point Likert scale	Alpha coefficient of MSPSS= 0.90 and for subscales=0.90-0.94 (Zimet et al. 1990)	Alpha coefficient of MSPSS= 0.74, for subscales=0.73-0.89 (Aroian et al. 2010) Alpha coefficient of MSPSS= 0.80, for subscales=0.79-0.97 (in the current study)

8.5 CONCLUSION

This chapter aimed to test the psychometric properties of measures used in this study using the main study data. Exploratory factor analysis confirmed that the Arabic LDSI-2.0 is a valid multidimensional tool that can discriminate between known groups. It also has satisfactory internal consistency reliability.

The confirmatory factor analysis result showed that the Arabic MSPSS has three subscales (spouse, family and friends), which were replicated within this sample of patients with cirrhosis, providing support for the construct validity of the MSPSS. Furthermore, the overall MSPSS and its subscales have high internal consistency reliability.

The data Quality Evaluation report of the SF-36 software was summarised and confirmed that the Arabic SF-36 has construct validity and it has high internal consistency reliability in patients with cirrhosis in Egypt. However, future research is suggested to test its validity in healthy people to develop the norm-based standard.

In conclusion, in this study the results revealed that the three Arabic measures: LDSI-2.0, MSPSS and SF-36v2 are valid and have high internal consistency reliability. Thus, these tools can be used in future research in patients with liver cirrhosis in Egypt.

9 CHAPTER-9: DISCUSSION AND CONCLUSION

This chapter discusses the key findings in order to answer the research questions in three separate sections: Section I: Health-Related Quality of Life (HRQOL) and its associated factors. Section II: symptom experience and its associated factors and section III: perceived social support and its associated factors. It also presents the theoretical, practical and research implications of this thesis. Recommendations for improving healthcare practice in Egypt and future research are explained, followed by discussing the internal and external strengths and limitations of the study. Finally, a conclusion is provided.

SECTION I: HRQOL AND ITS ASSOCIATED FACTORS

The first aim of this study was to describe HRQOL of Egyptian liver cirrhotic patients and to identify and evaluate the factors associated with (HRQOL) physical and mental health domains. Table 9.1 presents the major research questions and the key findings. To the best of my knowledge, this is the first study investigating HRQOL and its psychosocial associated factors among liver cirrhotic patients in Egypt. It is also the first study that has used both generic and disease specific questionnaires to investigate HRQOL (Power of sample, section 4.3.2.2).

Table 9-1: Research questions and key findings

Discussed points	Research questions	Findings
HRQOL of Egyptian cirrhotic patients	1.1 How do patients with liver cirrhosis in Egypt perceive their (HRQOL) physical and mental health?	All the domains and the physical and mental health summary scores of generic SF-36, are poor, suggesting that patients with liver cirrhosis in Egypt have a significantly worse perceived HRQOL.
General health perception	1.2 How do patients with liver cirrhosis perceive their general health?	45.6% of the patients rated their general health as fair; 41.6% rated their general health as poor. Very few patients rated their general health as good or excellent. 67.8% of the patients perceived their health as worse than one year ago
Factors associated with (HRQOL) physical health/PCS and mental health/MCS in cirrhotic patients	1.7 Do disease stage, symptoms experience (severity and hindrance), perceived social support, socio-demographic factors and medical data explain the perception of the physical health of patients with liver cirrhosis?	Model 1 could significantly explain 19% of the variation in PCS. Four factors were significantly associated with PCS: symptoms severity, disease stage, comorbidities and employment status.
	1.8 Do disease stage, symptoms experience (severity and hindrance), perceived social support, socio-demographic factors and medical data explain the perception of the mental health of patients with liver cirrhosis?	Model 2 could significantly explain 31.7% of the variation in MCS. Four variables significantly predicted the variations in MCS: symptoms severity, employment status, spousal support and family support. Symptoms severity made the strongest contribution to explain PCS and MCS. Social support from spouse and family was significantly associated with MCS only.

9.1 HRQOL OF EGYPTIAN CIRRHOTIC PATIENTS

The study findings show that all the domains, and the physical and mental health summary scores of generic Form-36v$_2$ (SF-36v$_2$) in liver cirrhotic patients in Egypt are under the norm (cut-off score 50) (Table 6-3). This suggests that patients with liver cirrhosis in Egypt have poor physical, mental and social health status. These findings are consistent with those from several international observational studies in cirrhotic patients in comparison with healthy people (Marchesini et al. 2001; Arguedas et al. 2003; Hauser et al. 2004; Bao et al. 2007) and with non-cirrhotic patients (Younossi et al. 2001; Svirtlih et al. 2008). The results, also, are similar to the Egyptian study among patients with chronic HCV (Child-Pugh A/B) (Basal et al. 2011). Similarly, using SF-12 HCV patients with mixed disease stages (non-cirrhosis and compensated and decompensated cirrhosis) had lower HRQOL in all domains than the standardised cut-off score (Hsu et al. 2009).

Summary scores for physical (PCS) and mental health (MCS) showed that although both aspects of health were poor, the MCS was lower than the PCS. This suggests that Egyptian cirrhotic patients may experience more deterioration in their mental health domains than in their physical health domains. In contrast, reviewing liver and chronic disease studies across countries showed that PCS was usually lower than MCS (Table 9-2). Hopman et al (2009) reviewed data of 10 studies including 2418 patients (rate of participation > 77%) with different chronic conditions, including renal failure, osteoarthritis, multiple sclerosis, heart failure, and chronic leg ulcers to determine the association between disease, age, and HRQOL (using SF-36 or SF-12). They concluded that all chronic diseases had a significant negative impact on the physical aspects of health; although mental health domains remained relatively unaffected (Hopman et al. 2009). However, Egyptian cirrhotic patients had poorer MCS than Western people with liver and other chronic diseases. There is no clear reason for this. One possible explanation is that psychotherapy and support groups available to people in the West are not available in Egypt, which may be a factor that influences the perceived HRQOL.

For instance, in England guidelines give essential information for healthcare providers to implement the HCV Action Plan (Department of Health 2004). The Scottish Intercollegiate Guidelines Network (SIGN) also recommend that healthcare professionals treating patients with liver disease, particularly with HCV are directed to observe and assess signs of depression using the hospital anxiety and depression scale (HADS).for all patients receiving anti-HCV therapy before, during and after the process of treatment. Communication and psychological support for patients without therapeutic treatment like cirrhotic patients should be provided. Patients with depression are referred to specialists for treatment (SIGN 2006).

Table 9-2: HRQOL of Egyptian cirrhotic patients compared to Western liver disease patients and other chronic conditions

HRQOL	**Current study**	**Arguedas et al. 2003**	**Younossi et al. 2001**	**Hauser et al. 2004**	**Teuber et al. 2008**	**Reviewed 5 studies by Hopman et al. 2009**				
	Liver cirrhosis	Advanced cirrhosis	HCV/HBV	HCV	Advanced cirrhosis	Renal Failure	Osteoarthritis	Heart Failure	Chronic wound	Multiple Sclerosis
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
PCS	35.56±10.43	28±11	41±13	40.94±12.06	42.3±11	33.2±11.8	25.3±7.3	30.9±8.6	33.8±0.2	33.5±10.6
MCS	31.55±14.42	43±13	46±12	43.21±11.98	44.5±13.7	50.1±11.2	50.2±12.5	48.4±0.9	48.7±11.5	46.0±12.2

9.1.1 General Health Perception Among Egyptian Cirrhotic Patients

General health perception (GHP) has been reported as an essential health indictor that can predict survival rate (Wilson and Cleary 1995). In this study, patients with liver cirrhosis were asked to self-rate how they perceive their general health using a single question (item 1) in the SF-36. The results showed that 87.2% of patients felt their general health was poor or fair, while only a very few felt it was good. This indicates that the majority of Egyptian cirrhotic patients have low perceived health in general. In comparison with the only identified study that assessed perceived general health in liver disease patients using a similar scale, Sobhonslidsuk et al. (2006) found that only 25.6% of 250 cirrhotic and non-cirrhotic patients in Thailand reported poor general health, which shows that Egyptian cirrhotic patients have a poorer perception of their general health than Thai patients (South East Asia). However, more than half of the patients in Sobhonslidsuk's study were non-cirrhotic, while all the patients in this study had cirrhosis, which might explain the inconsistency in the results. Sobhonslidsuk et al. (2006) also observed that health perception decreased with increasing disease severity.

Comparing health over the last 12 months about 68% of the patients perceived their health as worse than a year ago [using the second item in the SF-36 (item 2: health transition)]. Marchesini et al. (2001) showed that only 45.7% of cirrhotic Italian patients felt their health had deteriorated in the last year. This study findings suggest that may be due to the low healthcare resources, as well as the low quality of care that Egyptian patients receive, they have low perceived general health (recommendations, see section 9.8.1).

According to the model of HRQOL outcomes, evaluating the link between symptom status and GHP can explore an essential finding (Wilson and Cleary 1995). In this study, GHP was associated negatively with perceived symptom severity and hindrance of symptoms (see section 7.2.4.3), suggesting that patients with high perceived symptoms severity and hindrance of symptoms are more likely to have poor perceived general health. Due to the cross-sectional nature of the study, it was impossible to identify the direction of the association between symptoms and GHP. However, this finding supports the hypothesis that symptoms are important factors in perceived general health (Wilson and Cleary 1995). Treating symptoms and teaching patients how to care for these symptoms (self-management programs) may improve these patients GHP. There is a line of evidence that self-management can improve perceived health status, knowledge, self-efficacy, as well as decrease the number of hospital admission among patients with various chronic conditions (Lorig et al. 1999; Barlow et al. 2002).

9.2 FACTORS ASSOCIATED WITH HRQOL IN EGYPTIAN CIRRHOTIC PATIENTS

9.2.1 Demographic Characteristics

In current study, many demographic factors were shown to be significantly associated with perceived HRQOL (section 6.3.3.1), as hypothesised by Wilson and Cleary’s model (1995). Women, the illiterate and the unemployed significantly experienced lower physical and mental health. However, there was no significant difference regarding marital status and area of residence (rural vs. urban). This suggests that the disease itself affects people's HRQOL in rural or urban areas similarly, particularly if healthcare services for liver disease patients from the two regions are the same.

The reason for showing no significant difference in perceived HRQOL according to marital status is possibly that singles in Egypt usually live with their families, who are the main source of support. Although, marital status was not associated with physical or mental health, it was significantly associated with social support that is significantly associated with mental health. A longitudinal study (baseline and 12 months follow up) conducted in US for 1,817 chronically ill people found that marital status indirectly affected mental health through social support but did not affect physical or mental health directly (Sherbourne and Hays 1990).

Although, female and illiterate Egyptian cirrhotic patients had poorer physical and mental health, gender and level of education were not associated with HRQOL. This may be due to the sample size. Likewise, the current study results are in line with the findings of several Western and Eastern liver studies that investigated the association between socio-demographic variables and HRQOL using bivariate analysis. For example, it was found that women were more likely to have poor HRQOL, particularly in physical health (Sobhonslidsuk et al. 2006; Afendy et al. 2009; Karaivazoglou et al. 2010), RP, BP, GH, VT, MH (Afendy et al. 2009) and RE (Teuber et al. 2008). However, gender was not associated with physical or mental health domains in Spanish cirrhotic patients (Les et al. 2010), or among German patients at different stages of liver disease (Haag et al. 2008), or with chronic hepatitis C (Hauser et al. 2004).

In this study, there was no significant difference in perceived physical and mental health domains according to age, although there was a significant decrease in perceived RP among elderly people. Basal et al. (2011) and Haag et al. (2008) found that age was significantly associated with PCS but not with MCS. Similarly, Dan et al. (2008) found that older patients had poorer PF than younger ones. Based on these findings it seems that there is a discrepancy between this study and previous studies regarding the association between age and HRQOL. However, it is worth noting that the domains of RP and PF are two elements of the PCS. This means that age is associated with physical health, but it is not associated with mental health domains in liver disease and cirrhotic patients. Nevertheless, age was not independently associated with physical and mental health domains in this study when it was entered in the regression analysis. Likewise, Bondini et al. (2007) and Hauser et al. (2004) showed that age was not associated with physical and mental health domains in patients with chronic HBV and HCV. Theoretically, it is hypothesised that socio-demographic characteristics have a smaller influence on perceived health status and well-being than symptoms, and it could be confounders, which affect HRQOL indirectly but may not be important factors like symptom status (Wilson and Cleary 1995).

9.2.2 Socioeconomic Factors

In this study, employment status and level of education were examined as key indicators of socioeconomic status. Illiterate and unemployed people had significantly lower PCS and MCS than those educated and employed. However, using regression analysis, only the employment status was significantly associated with PCS and MCS. Cohen and Wills (1985) argue that poverty, work overload, unemployment and chronic diseases are examples of general stressors that can affect physical and mental health. Thus, the inability to work or the loss of a job, which is the main source of economic support for the majority of Egyptian people, is an important factor that might affect their PCS and MCS. This finding is consistent with previous studies of liver disease patients whatever the disease stage. The ability to work, salary and social functioning positively predicted the perceived mental health and depression symptoms in patients with chronic HCV in US, more than other biological and socio-demographic (i.e. laboratory results, age and gender) factors (Wilson et al. 2010).

Hannon (2012, p. 17) suggests that *"Work and employment play a central role in people's lives and are essential factors in social inclusion and well-being".* Employment is an important requirement to meet the basic needs of life, and work is not only to cover physical needs but is also essential for mental health (Linn et al. 1985). Therefore, the unemployed are more likely to experience psychological and physical symptoms such as anxiety and depression, particularly if they do not have other sources of economic support (Linn et al. 1985). In the current study, more than half of the participants were housewives and 39% were unemployed, which means they were more vulnerable to low socioeconomic status. Using the disease-specific HRQOL tool (LDSI-2.0), unemployed cirrhotic patients were also more likely to report right abdominal pain, depression and a perceived change in their personality (Table 7-7).

The following are examples of translated (from Arabic to English) quotes from patients who participated in this study, which reflect how an insecure social life and the loss of economic support affect their health status:

> *'I am living with my son, he is 24 years old and is mentally retarded; my husband left the house because he was afraid to get the infection. I cannot work and my second son is married and cannot support me. So, I do not know how I can live and I am continually thinking about my son, how he will live without me, I am worried, depressed and sad. I cannot work like before the disease to cover needs of my daily life; I do not have any power…I want to live with dignity… I do not have*

> *money to do the required lab investigation to follow up my health condition' Women 44 years.*

> *'I am ill with an incurable disease and my wife is young and we do not have children, my wife wishes to be a mum. Also, I am an employee in the private sector and there is no consideration for my health condition because I have to work like my healthy colleagues' Man 36 years.*

Therefore, unemployment is a common result of liver cirrhosis that reflects negatively on the patients' economic status. In the current study about 39% (130/333) reported that liver cirrhosis was the cause of their inability to work, and 80% (321/401) said that they had financial difficulties. Similarly, van der Plas et al. (2003) showed that patients with advanced stage of cirrhosis had a higher probability of financial limitations due to liver disease. Furthermore, HRQOL (SF-12) of chronic HCV patients at different stages of disease was predicted by depression, use of interferon, fatigue, joint pain and problems in financial affairs (Gutteling et al. 2006). In the current study one of the patients experienced job loss and difficulties in finding a job due to viral hepatitis.

> *'I was working in a cheese factory and now I do not work because I have HBV and as you know it can spread by food and to work in this job I need a certificate of free from infectious disease…I have energy to work but what I can do and who will give me work while I have this disease…I always sit in my home not doing anything else' Man 49 years.*

Chronic disease is a stressor that can interfere with an individual's social and work roles; therefore these types of stressors need continuous psychological adaptation (Cohen and Wills 1985; Tijhuis et al. 1995) and economic support in the form of providing medical treatment and healthcare services free or at low cost. In this study, 79.8% of patients reported that medication fees were shared between the patients and the state of insurance, while only 1.7% had full insurance that covered their medical care. This may be because the majority of the patients were workers, farmers, housewives or unemployed. According to the report of the Ministry of Health and Population and the National Committee for the Control of Viral Hepatitis in Egypt, The *‘Egyptian constitution enshrines free medical care as a basic right for all citizens, and though access to primary healthcare is fairly widespread, this ideal has yet to be fully realized’* (Dalglish 2008, p. 10). Therefore, there is an urgent need to reform healthcare policy in Egypt to provide these patients with full health insurance.

9.2.2.1 Biophysical Factors

Association between biophysical factors and perceived HRQOL was evaluated using these variables: disease stage, number of comorbidities, and number of complications, as a widely used indicator of health status in clinical setting (Wilson and Cleary 1995). Only disease stage and comorbidities were negatively associated with physical health domains (PCS) (section 6.3.4.1). However, none of the medical variables was associated with mental health domains (MCS) (section 6.3.4.2). This finding is consistent with previous liver disease studies (Arguedas et al. 2003; Fritz and Hammer 2009). In patients with mixed disease stages, disease severity was associated with PCS but not MCS (Sobhonslidsuk et al. 2006; Haag et al. 2008).

In this study, the commonly reported comorbidities were medical comorbidities (see table 6-2), number of comorbidities was associated with only PCS. This finding is consistent with previous studies (Hauser et al. 2004; Hsu et al. 2009). For example, using the stepwise multiple regression analysis, number of medical comorbidities was significantly associated with only PCS, while the presence of psychiatric comorbidities, assessed by the HADS, was associated with MCS (Hauser et al. 2004).

In this study the cause of disease was classified into three groups: viruses (B or C), mixed (viruses and bilharzias) or others causes. About 92% of participants had viral hepatitis with or without bilharzias. Inconsistencies in criteria used to categorise causes of disease make it difficult to compare findings between studies. However, the current study's results are similar to some previous studies. For example, Kalaitzakis et al. (2008) found that mental and physical health did not significantly differ by cause of cirrhosis (hepatocellular, cholestatic, alcoholic and hepatitis C cirrhosis). Kim et al. (2006) also found that there was no significant difference in QOL by cause of liver cirrhosis (HCV, HBV and alcohol).

On the other hand, using different classifications, Afendy et al. (2009) investigated whether the cause of cirrhosis (i.e. alcoholic liver disease, autoimmune hepatitis, viral hepatitis, non-alcoholic fatty liver disease and cholestatic liver disease) is associated with the HRQOL. The results showed that the non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease were significantly associated with poor physical health. However, NAFLD, autoimmune hepatitis and cholestatic liver disease were significantly associated with poor mental health domains (Afendy et al. 2009). The possible reason for this discrepancy may be due to the method of classifying the cause of liver disease. Also, in the current study there may be a lack of statistical power to differentiate between patients according to cause of cirrhosis due to small number of people with other causes compared to people viruses (B or C) and mixed (viruses and bilharzias). Therefore, it is recommended that future studies examine whether the cause of cirrhosis is related to HRQOL by measuring this association using an adequate sample size for each cause and a common valid classification strategy.

9.2.3 Social Support

Social environment has been hypothesised to be an important factor in the individual's perceived HRQOL. Supportive family and friends can improve the patient's physical, social and role functioning (Wilson and Cleary 1995). However, no previous study was found that examined the association between perceived social support and HRQOL in liver disease and cirrhotic patients. Therefore, the MSPSS was used for the first time in these participants to examine this association.

The regression analysis disclosed that perceived spouse and family support are positively associated with MCS, but not with PCS, suggesting that spouse and family support have more influence on mental health domains than physical health domains. Theoretically, it has been hypothesised that a supportive family can improve the patient's physical, social and role functioning (Wilson and Cleary 1995). However, in this study perceived social support was significantly associated with only mental health. These findings are consistent with research conducted among patients with other chronic disease. For example, using another social support questionnaire (Interview Schedule for Social Interaction, 50 items assess perceived availability and adequacy of social support), for people with cardiac disease, Arestedt et al. (2012) found that social support was associated specifically with mental but not with physical health domains (SF-12). In a study with a 12 months follow up investigating the impact of perceived social support on HRQOL in people with chronic heart failure, Bennett et al. (2001) found that an increase in social support significantly predicted improvement in perceived HRQOL. A decrease in emotional and informational support significantly predicted an increase in hospital admissions due to different causes; increasing positive social interaction decreased hospital admissions due to cardiac problems (Bennett et al. 2001). Perceived higher social support decreased symptoms of depression among cardiac patients (Frasure-Smith et al. 2000). Also, in patients with head and neck cancer, perceived higher social support was associated with better mental health domains (SF-36) and lower symptoms of depression (Beck Depression Inventory); however social support was not associated with physical health (Karnell et al. 2007).

According to the Buffer and Main effect theory (Cohen and Wills 1985), social support can prevent the occurrence of stressors; modify the patient's perceptions of their illness; and enhance coping skills that can reflect on the patient's health. Low social support may increase mortality or morbidity in different groups (Vandervoort 1999; Lyyra and Heikkinen 2006), suggesting that increased social support has a positive influence on health outcomes.

9.2.4 Symptoms Experience

This is the first study that has investigated a full range of physical and psychosocial symptoms (using LDSI-2.0) and their association with HRQOL among liver cirrhotic patients in Egypt. Symptom severity was significantly associated with physical and mental health, suggesting that patients with high symptom severity were more likely to report poor HRQOL. The results support the model of HRQOL, where symptom is an essential determinant of health status (Wilson and Cleary 1997). The results also are consistent with several studies that examined associations between severity of various symptoms and HRQOL. Somatic symptoms (i.e. muscle cramps, pruritus) (Marchesini et al. 2001), psychiatric symptoms (i.e. depression and anxiety) (Haag et al. 2008), gastrointestinal symptoms (Kalaitzakis et al. 2006), and symptoms of fatigue, joint pain, abdominal pain and decreased appetite (Gutteling et al. 2006) were associated with HRQOL in patients with chronic liver disease or cirrhosis. Patients with high severity of symptoms are more likely to have poor HRQOL.

In a large cross-sectional survey of 544 Italian cirrhotic patients, Marchesini et al. (2001) entered many of the independent variables in a logistic regression analysis such as marital status, disease severity, recent hospitalisation, liver disease complications and comorbidities, and symptom severity of muscles cramps and pruritus during the last month. They found that severity of muscle cramps significantly predicted mental and physical health. However, disease severity and recent hospitalisation predicted physical health only (Marchesini et al. 2001). Therefore, the current study findings are consistent with previous studies that suggest that severity of symptoms is an important factor in explaining perceived physical and mental health domains in cirrhotic patients. However, symptom severity explained 28.7% of the variation in physical health and 43.6% of the variation in MCS, suggesting that symptom severity contributed more in explaining MCS than PCS of cirrhotic patients in Egypt. There is no similar study to compare these results with.

In this study, hindrances in daily life due to symptoms were not significantly associated with any aspect of HRQOL. The total score of the LDSI-2.0 (items measuring hindrance of symptoms) was used to find the association between hindrance of symptoms and HRQOL. In other identified studies that used LDSI-2.0

(such as van der Plas et al. 2004), the researchers used the items separately to find their association with HRQOL. Therefore, there is no similar study to compare with. However, van der Plas et al. (2004) found that both severity and hindrance of symptoms was associated with HRQOL, with hindrance of symptoms having a higher influence on HRQOL than severity of symptoms. It is worth noting that van der Plas et al. (2004) conducted their study among a general liver disease population from the Dutch Liver Association (DLA), with most participants on-cirrhotic (42.5%), which means they were more likely to be engaged in social activities. For instance, van der Plas and colleagues (2004) compared the participants from clinical settings who had compensated and decompensated disease stage with participants from the DLA. They found that symptom severity and hindrance were significantly associated with HRQOL among clinical and DLA participants. However, the liver disease DLA population had a higher prevalence of symptom hindrance than the clinical population. Therefore, they suggest that DLA participants may not be representative of a clinical population of chronic liver patients. In this PhD study, all the participants had cirrhosis with most of them housewives or unemployed, and they were recruited from inpatients and outpatients clinics. This means that these participants were more likely to be experiencing severity of symptoms than hindrance of daily activities due to symptoms (see tables 7-1 and 7-2), as they may not have been fully engaged in daily and social activities. In van der Plas et al.'s (2004) study, the frequency of reporting hindrance of symptoms was higher than severity of symptoms (see table 9-4). Therefore, it is recommended that the two different dimensions of symptoms should be measured, that is severity and hindrance. van der Plas et al. (2004, p.

1477) state that '*this supports the value of including symptom severity items as well as symptom hindrance items in the disease-specific questionnaire'.*

SECTION II: SYMPTOMS EXPERIENCE AND ITS ASSOCIATED FACTORS

Theoretically, symptoms experience means: (1) including a person's perception of whether s/he observes any change in feeling or behaviour, (2) evaluating symptom severity, its effect on daily life, cause and method of treatment from a person's perception and (3) physiological, psychological, socio-cultural and behavioural response of the person to this symptom (Dodd et al. 2001). It was not possible to address overall symptoms experience in depth in this study. Thus, "symptoms experience" reflects symptom severity and distress from the patient's perception using LDSI-2.0.

The second aim of this study was to explore and describe experienced symptoms (prevalence, severity and hindrance) in Egyptian cirrhotic patients and to identify and evaluate factors associated with symptoms severity and symptoms hindrance (distress).

Table 9-3: Research questions and key findings

Discussed points	Research questions	Key findings
Overall symptoms experience of cirrhotic patients		The mean of the LDSI-2.0 total score was 46.16 ± SD (20.75) with a median of 49. The mean score of symptoms severity was 32.61 ± SD (13.15) and symptoms hindrance was 13.54 ± SD (8.54), the high score indicates the severity and hindrance of symptoms.
Prevalence of symptom severity and hindrance	2.1 What symptoms do patients with liver cirrhosis experience?	The majority of the patients had one or more of a wide range of physical and psychosocial symptoms. Joint pain, decreased appetite, memory problems, difficulty of using time effectively, financial difficulties and muscle cramp, difficulty in sleeping at night were the most frequently reported symptoms.

	2.2 Which of the reported symptoms limit the daily activities?	Joint pain, depression and decreased appetite were the main hindrances. Muscle cramp and difficulty in sleeping at night were additional hindrances symptoms.
Factors associated with symptoms experience: severity and distress using multivariate analysis	2.7 What are the factors associated with symptoms experience?	Model 1: the regression model significantly explained 19.6% of the variations in overall symptoms severity. Six variables significantly associated with symptoms severity: gender, marital status, perceived spouse support, employment status, perceived family support and number of liver disease complications. Females, unemployed and married with increased liver disease complications and patients with a low perceived social support were more likely to experience high severity of symptoms. Model 2: the regression model significantly explained 14% of the variation in hindrance of daily activities due to symptoms (distress). Three variables significantly associated with symptoms hindrance: gender, perceived spouse support and number of liver cirrhosis complications. Gender, number of liver cirrhosis complications and perceived social support from spouse significantly associated with symptoms severity as well as hindrance of symptoms. Gender (females) and perceived spouse support (low) made the strongest contribution in explaining increasing severity of symptoms and hindrance of daily activities due to symptoms.

9.3 SYMPTOMS EXPERIENCE OF EGYPTIAN CIRRHOTIC PATIENTS

Self-reporting of experienced symptoms and their characteristics is the gold standard for studying symptoms (Dodd et al. 2001). LDSI-2.0 assesses symptoms in general as disease specific HRQOL and provides two subscales to examine symptoms severity and hindrance. The sum score of all relevant items was used (Gutteling et al. 2008) to assess general severity but not general hindrance of symptoms.

In the current study, two general subscales were used independently to assess the two summary dimensions of symptoms experience: severity and hindrance. The use of this tool is a new contribution that confirms its simplicity and feasibility for assessing overall symptoms severity and distress. The mean score of symptoms severity was higher than the mean score of symptoms distress, suggesting that patients were more likely to report severity of experienced symptoms than hindrance of symptoms. One explanation may be that because most of the patients were housewives, unemployed and admitted in the hospitals, their hindrance of symptoms is lower than severity. Alternatively, this result may relate to the ability of patients to cope with symptoms, which does not bother their daily life. Further research is required to identify coping strategies among these patients and their associations with symptom experience.

9.3.1 Prevalence of Severity and Hindrance of Symptoms

Each person experiences symptoms (distressed or not) differently, with certain symptoms more stressful than others (Wilson and Cleary 1995). The developers of the LDSI-2.0 stated that *'single items have not been combined into multi-item scales, as we are of the opinion that in clinical practice results of separate symptom severity and symptom hindrance items are easier to interpret and more valuable for patient management'* (van der Plas et al. 2004, p. 1470). In view of that, it was important to run further analysis to explore the prevalence of separate symptoms in terms of severity and distress on daily activities.

More than two-thirds of patients reported joint pain, decreased appetite, worry, depression and sleepiness as well as muscle cramps and difficulty in sleeping at night, which were not measured by LDSI-2.0. However, joint pain, depression, decreased appetite and worry made the biggest impact on their daily and social activities. These findings increase our insight into the most important symptoms that negatively can affect these patients’ daily life and may be treatable, such as depression and decreased appetite. Moreover, they support that a symptom is a multidimensional concept that should be measured from different dimensions such as severity and distress (Lenz et al. 1997).

Teunissen et al. (2007) acknowledge that assessing symptom prevalence is important not only for clinical practice, as it enables healthcare providers to focus on the more prevalent symptoms, but also to anticipate problems that need more attention while developing care plans and directing healthcare policy. Also, studying symptom distress can provide important and complementary information to symptom severity to gain insight into symptoms experience and its impact on patients’ daily lives and social activities (Tishelman et al. 2007).

The study by van der Plas et al. (2004) is the only one that examined and presented the frequency of severity and hindrance (distress) of symptoms using LDSI-2.0. Table 9-4 presents the frequency of severity and hindrance of symptoms in this study compared to the study by van der Plas et al. (2004). However, it is important to acknowledge that cultural aspects, such as beliefs and values unique to the individual's ethnicity and religion, can reflect the person's perception of symptoms (Dodd et al. 2001).

Table 9-4: Symptoms experience in Egyptian and Dutch liver disease and cirrhotic patients

LDSI-2.0 items	This study		van der Plas et al.'s study (2004)	
	Prevalence of people reported Symptom severity n%	Prevalence of people reported hindrance of daily life due to symptom (Among symptomatic) %	Prevalence of people reported Symptom severity n%	Prevalence of people reported hindrance of daily life due to symptom (Among symptomatic) %
Itch	210 (52.4)	Activity: (25.7) Sleep: (31.2)	451 (39.6)	50.5
Joint pain	314 (78.3)	70.3	654 (57.5)	83.8
Right abdominal pain	259 (64.6)	51.9	451 (39.3)	63.1
Sleepiness during the day	290 (72.3)	53.1	817 (71.2)	85.1
Worry about the family situation	300 (74.8)	57.6	578 (50.5)	66.6
Decreased appetite	303 (75.6)	59.1	370 (32.3)	71.4
Depression	291 (72.6)	61.3	544 (47.5)	77.6
Jaundice	109 (27.2)	16.2	113 (9.9)	41.1

The current study found that the frequency of reported symptoms was higher in Egyptian than in Dutch patients at mixed stages of liver disease. However, it is the most frequently reported symptoms in both Egyptian and Dutch patients were joint pain and worry about the family situation. This suggests that regardless of cultural differences, liver disease affects patients' physiologically by affecting their musculoskeletal system resulting in joint pain and psychologically resulting in worry about their families' situation. However, both groups experienced other symptoms differently. This finding supports the model of HRQOL outcomes that hypothesises that reporting of symptoms is influenced by a number of cultural characteristics (Wilson and Cleary 1995).

Depression and joint pain were the most reported hindrance symptoms for daily activities among Egyptians and Dutch. However, Egyptian patients reported that decreased appetite was one of the most reported hindrance symptoms to their daily activities, while Dutch patients reported sleepiness during the day. This suggests that while there are common symptoms shared between liver disease patients across countries, other symptoms may differ from one country to other.

The literature review revealed that depression (Girgrah et al. 2003; Kim et al. 2006) was the most commonly studied and supported symptom among liver disease patients with more than half of cirrhotic patients suffering from depression (Bianchi et al. 2005). Thus, routine assessment and treatment of depression among cirrhotic patients in Egypt is urgently needed. Kraus et al. (2000) showed that recently diagnosed liver disease patients without advanced cirrhosis had significantly lower depression and anxiety symptoms and higher problem solving skills than longstanding ones (> 5 years). In a longitudinal study of American cirrhotic patients on a waiting list for liver transplantation, Singh et al. (1997) found that mortality was higher among depressed than non-depressed patients. Therefore, it is recommended that liver disease patients should be regularly assessed for depression, anxiety and inappropriate coping styles (Kraus et al. 2000).

The literature review has showed that pathophysiological bone changes due to liver disease is common among cirrhotic patients, which may be related to joint pain. Gallego-Rojo et al. (1998) studied 35 viral cirrhotic men to determine the prevalence of osteoporosis. Compared to a matched controlled healthy group, it was found that liver cirrhotic patients had a lower bone mass density and prevalence of osteoporosis was high (53%). Similarly, in a cohort study among cirrhotic patients due to viral or alcoholic disease, Cijevschi et al. (2005) studied 150 gender-balanced patients to determine the prevalence of osteoporosis using the Dual Energy X-ray Absorptiometry-DXA. It was found that 38% had osteoporosis or osteopenia and the low Body Mass Index was used as the high predictive risk factor.

In this study, decreased appetite was one of the most commonly reported symptoms. However, some of the patients unexpectedly mentioned that they decreased their food intake because they were afraid of liver disease complications. This suggests that some patients perceived that eating itself, not the type of food, was a risk factor for developing complications. This means that some of the Egyptian cirrhotic patients may not have sufficient information about an appropriate diet and how to self-manage. Therefore, opening the channel of communication about silent symptoms will help to provide supportive health information that can reflect positively on the patients' symptoms experience and to enhance their QOL. Constant et al. (2005) showed that patients who reported physicians as the source of their information were more likely to have a lower perceived disease severity than patients who reported other sources of information such as significant others and television.

In addition, some patients reported difficulty in sleeping at night and muscle cramps as additional experienced symptoms that were not measured by the LDSI-2.0. They also reported these symptoms hindered their daily activities.

‘The muscle cramp wakes me up from sleeping’ Man 39 years.

‘Muscle cramp affects my life to a high extent, one day I was driving, my leg cramped then I stopped till the cramp was relieved’ Man 55 years.

These results are consistent with the Marchesini et al. (2001) study, which found that 36% of cirrhotic patients reported muscle cramps, which was also a key factor associated with perceived poor physical and mental health. The literature review shows that cirrhotic patients have a higher prevalence of muscle cramps than a healthy control group, and pathophysiological changes such as the presence of ascites are predictive factors (Angeli et al. 2003). The literature has also shown that cirrhotic patients have more sleeping disorders such as daytime sleepiness, insomnia and frequent nocturnal awakening, although there was no significant relationship between sleeping problems and clinical and laboratory parameters (Mostacci et al. 2008). Therefore, further studies are required to develop a symptom management program to teach patients how to manage their symptoms effectively in order to improve their health status as well as their QOL.

9.4 FACTORS ASSOCIATED WITH SYMPTOMS EXPERIENCE

According to the theory of unpleasant symptoms (Lenz et al. 1997) and the conceptual model of HRQOL outcomes (Wilson and Cleary 1995) many biophysiological, psychosocial and situational factors can predict symptom experience. In this study, multiple linear regression analysis found that being female, increasing number of liver disease complications and low perceived social support from spouse were associated with increasing severity and hindrance of symptoms. While, being unemployed, married and with low perceived support from family were significantly associated with increased severity of symptoms only. The results are consistent with the hypothesis of the model of HRQOL that suggests that reporting of symptoms is influenced not only by biophysiological factors but also by the demographic as well as cultural background of the patient (Wilson and Cleary 1995).

To the best of my knowledge, this is the first study that has examined factors associated with symptoms experience using a multiple regression analysis and has investigated the relationship between social support and overall symptoms experience. Therefore, it was difficult to compare these findings with other studies. However, assessing symptom experience by using bivariate analysis and different questionnaires among cirrhotic patients in Korea, Kim et al. (2006 and 2006a) found that the overall score of symptoms experience was not associated with age, gender and cause of disease. However, disease stage was associated with the overall score of symptoms experience and there was a significant difference between men and women in reporting individual symptoms.

Erim et al. (2010) investigated depression symptoms (using Beck Depression Inventory) among HCV non-cirrhotic patients and found that women were more likely to have depression than men. In other chronic diseases, Teunissen et al. (2007) conducted a systematic literature review of 44 studies with 25,074 patients with incurable cancer; six of these studies assessed gender differences in symptom prevalence. There was a significant gender difference in all of these studies, with dysphagia and insomnia being more common among males and nausea and vomiting in females (Teunissen et al. 2007). In line with this, this study found that there was a significant gender difference in reporting particular symptoms; for example, women were more likely to report depression and joint pain and men to report decreased sexual activity. These findings not only support the validity and sensitivity of the Arabic LDSI-2.0, but also highlight the symptoms that are commonly experienced by Egyptian cirrhotic men and women. These results could be the foundation for developing a future symptoms management program.

This study's findings also show that perceived adequacy of social support is associated with symptoms experience. This finding is new and it contributes to understanding the relationship between perceived social support and symptom experience among these patients. Social support particularly from spouse was negatively associated with severity and hindrance of symptoms (disease specific HRQOL). However, perceived family support was associated only with severity of symptoms. This is a logical finding as the majority of the participants were married and the supporting role of the spouse can decrease the burden of daily life due to symptoms. However, this result in general supports the assumption of the model of HRQOL outcomes, in that when the patient has a surrounding supportive environment (spouse, family or friends) symptom burden will decrease and the patients' HRQOL will improve.

Interestingly, the study found that perceived social support from spouse and family was significantly associated with only the psychosocial domains of generic HRQOL; mental health domains (SF-36).It is well established that lack of social support can cause psychological symptoms such as anxiety or depression, which may have a negative influence on health status (Cohen and Wills 1985). Karnell et al. (2007) showed that with decreasing social support there was an increase in the severity of depressive symptoms among patients with head and neck cancer. Social support has also been found to be significantly related to patients' survival rate. For instance, several longitudinal studies have shown that high social support, especially perceived emotional support, is strongly related to improved psychological and physical health outcomes as well as to a decrease in mortality rate (Brummett et al. 2005; Lyyra and Heikkinen 2006). Staniute et al. (2011) have therefore suggested that healthcare providers should pay more attention to patients with low social support during the development of a rehabilitation program. Therefore, perceived social support may be essential in perceiving better mental health and symptom experience among these patients.

Interestingly, in this PhD study, the number of liver cirrhosis complications did explain some variance in symptoms severity (14.4%) and hindrance (16.9%), although disease stage could not. Several liver disease complications were dentified in the Egyptian cirrhotic patients, with most of these patients had more than two of liver disease complications (see tables 6-2 and 6-11).

Interestingly, when HRQOL was stratified by disease stage, it was found that only two domains of physical health significantly were poorer among decompensated than compensated (PF and RP). However, when HRQOL was stratified by number of liver cirrhosis complications, the four domains of physical health were poorer among patients with 3-4 complications than with 1-2 (see tables 6-11 and 6-12). Therefore, disease stage was significantly associated with generic physical health (SF-36), although it was not associated with disease specific HRQOL (LDSI-2.0). However, the number of liver disease complications was significantly associated with symptom experience (disease specific HRQOL) but not with generic HRQOL. This finding is logical as having more than one complication such as ascities and oesophageal bleeding at once can cause several mixed symptoms. In fact, the relationship between biophysiological variables and symptom experience is likely to be very complex (Wilson and Cleary 1995).Therefore, further future research aiming to evaluate the association between type of liver cirrhosis complications and generic and disease specific HRQOL will be helpful to understand this relationship.

SECTION III: SOCIAL SUPPORT AND ITS ASSOCIATED FACTORS

Social support has been found to be essential for enhancing coping skills for people with chronic disease. Social support has three dimensions: emotional, informational, and instrumental (Williams et al. 2004). Coping also has three dimensions: emotion focused (thoughts/actions intended to control negative feelings), problem focused (direct actions intended to alter threatening circumstances), and perception focused (thoughts intended to control the meaning of threatening circumstances) (Vilhjalmsson 1993). Therefore, it was essential to study how patients with cirrhosis perceive their social support in general and from different sources. Social support has been found to be related to an individual's demographic characteristics (Zimet et al. 1990). Finding antecedent factors for perceived social support provides insight into people who are more likely to report low support. Thus, vulnerable groups should be considered during the development of self-management and intervention programs.

Therefore, the third aim of this study was to explore and describe how cirrhotic patients in Egypt perceive social support from spouse, family and friends and to evaluate factors associated with general perceived social support. Table 9-5 presents the major research questions and the key findings.

Table 9-5: Research questions and key findings

Discussed points	Research questions		Findings
Perceived social support among liver cirrhotic patients	3.1.	How do patients with liver cirrhosis in Egypt perceive the available social support?	The perceived social support score was relatively high, with the support from a spouse rating the highest.
Perceptions of Social Support from Spouse, Family and Friends	3.2.	Do patients with liver cirrhosis perceive adequacy of social support from spouse, family and friends?	More than half of the married patients perceived that their spouses (husband or wife) provided them with different kinds of support. More than half of the sample perceived that

		their families did not really try to help them although they gave emotional help and support. Support from friends was perceived as the lowest source of support. More than half of the patients reported that they could not count on their friends during hard times, although they could share their joys and sorrows with their friends.
Factors associated with perceived social support using multivariate test	**3.5** What are the factors associated with perceived adequacy of social support among liver cirrhotic patients in Egypt?	The regression model significantly explained 10.9% of the variation in perceived social support. Four variables associated significantly with overall perceived social support: gender, age, marital status and employment status. Being females, unmarried, unemployed and elderly patients were more likely to perceive low social support. Gender (13.5%) and marital status (13.6%) made the strongest contribution to explain social support.

9.5 PERECIVED SOCIAL SUPPORT AMONG EGYPTIAN CIRRHOTIC PATIENTS

Perceived social support score was relatively high, with the support from a spouse rating the highest. This suggests that patients perceive the spouse as the master source of social support followed by family and friends respectively.

In Egyptian society, the family is the central source of support for singles; while for married people, the spouse is the central support. The majority of the participants were married (77.3%) therefore, it was logical to find that spousal support was the main source of support. This finding is consistent with a study that examined perceived social support among Arab immigrant married women in the US (Aroian et al. 2010). Furthermore, in a study of Arab American adolescents, Ramaswamy et al. (2009) found that family was the main source of support, followed by friends.

This finding reflects the importance of spouse and family as key sources of support for Arabic people in or out of home. Similarly, in a cross-sectional study of 240 postpartum women in Uganda, Nakigudde et al. (2009) showed that perceived support from a significant other (spouse) followed by family were the highest sources of support, while support from friends was low. In a study by Zimet et al. (1990), three groups: pregnant women, adolescents and paediatric residents in a training course were compared using MSPSS. It was found that married women perceived support from a significant other (i.e. husband, partner or friend) to be higher than single women, while there was no significant difference in terms of support from family and friends between the two groups. This supports the association that a spouse may be the central source of support for married people.

9.5.1 Perceptions of Social Support from Spouse, Family and Friends

This study found that more than half of the married patients perceived that their spouses (husband or wife) provided them with different kinds of support; they were there when needed and cared about their feelings. However, more than half of the sample perceived that their families did not really try to help them and were not willing to help them make decisions although they gave them emotional help and support. Therefore, it seems that type of support may be a significant factor requiring further research, as this study aimed to study the general perceived support from the surrounding people.

On the other hand, support from friends was perceived as the lowest source of support. More than half of the patients reported that they could not count on their friends during hard times, and that they would not help them, although they could share their joys and sorrows with them. This suggested that *'the availability of* *someone with whom to have a good time may be less beneficial to the health of a chronic disease patient than the availability of someone to help with daily chores'* (Sherbourne and Hays 1990, p. 329). For instance, Lindsey et al. assessed structural and functional social support in Egyptian cancer patients in 1985. They found that the reported social support network was n = 591, 57.5% were families and 15.8% were friends. This suggests that few friends but many families are included in the Egyptian cancer patients' network. Also, spouses were perceived to provide more support than families, while friends provided less (Lindsey et al. 1985). Thus, family and spouse support is the main source of support among chronically ill patients in Egyptian

9.6 FACTORS ASSOCIATED WITH PERCEIVED SOCIAL SUPPORT

Identifying actors that could be associated with perceived social support was important, as it has not been done in in Egypt. However, using the model of Wilson and Cleary (1995) could not help to understand the relationship between demographic and medial variables and perceived social support. This is a limitation in the model of HRQOL. However, this is an area where it could be improved.

Furthermore, no study could be found to compare these findings to. The results show that marital status, gender, age and employment status are significantly associated with perceived social support. Unmarried people, females, the unemployed and elderly cirrhotic patients are vulnerable groups with perceived low social support. However, in a study of elderly patients with chronic heart failure (mean age 79 years) in Sweden, Arestedt et al. (2012) showed that men, living alone, had financial problems and in advanced disease stage had low availability or adequacy of social support. Consistently, the results of this study support findings of studies that used MSPSS and investigated the association between marital status and perceived support, particularly from a significant other. For example, Zimet et al. (1990) compared perceived support from three sources between married and single people, and found that married people reported significantly higher support from a significant other than singles, and there was no significant difference according to the support from family or friends. Similarly, in 445 Dutch and Danish cardiac patients, Pedersen et al. (2009) showed that having a partner was associated with perceived high support.

In this study, cirrhotic women in Egypt were more likely to perceive low social support. There is conflicting evidence in the literature about the nature of the relationship between gender and perceived social support (Norris et al. 2008). For example elderly women with chronic heart failure reported significantly better social support especially availability of attachment compared to man (Arestedt et al. 2012). Also, women with cancer in Sweden reported significantly higher social support than men (Bertero 2000).

On the other hand, several studies showed a significant association between gender and perceived social support. For instance, Staniute et al. (2011) investigated the association between social support and HRQOL among 560 patients in Palanga (Lithuania) with coronary artery disease. They found that perceived social support had a significant effect on the HRQOL in patients with coronary artery disease, especially in females. Also, in a recent longitudinal cohort study (baseline and 12 month follow up) Norris et al. (2008) investigated 2394 people in Canada undergoing catheterization for coronary artery disease. After adjustment for all the variables, the results showed that women reported significantly more depressive symptoms, physical limitations, and treatment dissatisfaction, as well as lower social support and QOL than men at baseline and at 12 months (Norris et al. 2008).

It is difficult to interpret the discrepancy in findings related to gender and social support. However, there are two suggested explanations: first, the type of participant characteristics (e.g. age and cause of disease) and the social support questionnaires were different in their structure and conceptualization. Second, the cultural background may affect patients' perception and experience with illness. For example, Egyptian women with rheumatoid arthritis, compared to Dutch women, experienced significantly higher loneliness, depression and anxiety. They also reported a higher need for help with their daily and household activities (El-Mansoury et al. 2008). In line with that, Bosworth et al. (2000) showed that women received less assistance with household duties from informal caregivers, while men got more support from their spouses than women. Men were more likely to involve their spouses in their recovery, resuming work and keeping physically fit were important to them. Women reported that they had less social support up to one year after a myocardial infarction than men (Bosworth et al. 2000).

Therefore, our findings confirm previous studies in terms of lower perceived social support among women with chronic disease, when comparing men and women’s HRQOL. Egyptian cirrhotic women were more likely to report depression, joint pain, decreased memory, decreased appetite, abdominal pain and difficulty to manage time (using LDSI-2.0). All these symptoms hinder their daily activities and social contacts. The majority of women in this study were housewives, suggesting little chance of developing friendships, which may cause them to require more support from husband and families; however the level of the provided support may not be sufficient to meet their needs.

Liver disease is most commonly due to HCV, which may have a negative impact on the relationship between spouses, particularly their intimacy (Blasiole et al. 2006) and their social activities. The following quotes are from female patients those participated in this study:

During completing the LDSI-2.0 a woman responded to that item *'My sexual interest has decreased since I know I have a liver disease'* (item 10), and said that *'the disease has not decreased it but increased it, because I feel I need my husband now more than before but he is always away and neglects me and even refuses to touch me when I ask him to help me to stand up from the floor' Women* 50 years and has ascities.

> *'I am not concerned about the disease and I am not worried about it, but the problem is my husband who does not look after me or support me. All the time he says bad words to me; like you are ill, and you are useless, it is better to burn yourself to die' Women 50 years.*

> *'My husband eats out of the home and does not eat any food I prepare, also he says bad words that hurt me, every time he says look, other ladies are healthy and you are not, look at yourself' Women 50 years has ascities.*

> *'Me and my husband sleep in separate rooms since we have known I have the virus C and there is no sexual relation for 4 years till now, also he does not touch me, he is afraid of infection' Women 40 years.*

> *'My husband married another woman when he knew I am infected with HBV and lives with his new wife in other flat. I asked him to remain married (not divorce me) for my children's sake because there is not anyone who can care for them' Women 34 years.*

> *'I become weak and my children go away from me because I am frequently admitted to hospital and this makes me so sad and depressed. I do not know how they eat or are cared for while I am in the hospital. My husband goes to work every day and leaves them alone in the flat even when I am back at home I cannot do anything; I feel fatigue all the time, my husband is young and strong and I cannot give him his rights and this makes him to quarrel with me how can I solve this problem and what can I do' Women 37 years.*

Therefore, a qualitative study is required to examine the impact of liver disease on the partner relationship and on the patients', partners' and children's HRQOL in order to find a supportive management method.

The study found that the level of perceived support decreased with increasing age. This finding is inconsistent with a study of HCV non-cirrhotic German patients, using the Social Support Questionnaire (F-SOZU) where age and gender were not associated with social support (Erim et al. 2010). The difference in cultural background and disease stage may be the cause for the inconsistency in findings.

9.6.1 Disease Stage and Perceived Social Support

This study's findings show that there is a statistically significant difference in perceived social support from families of patients with decompensated and compensated cirrhosis. Patients at an advanced stage of cirrhosis are more likely to gain higher social support from their family than patients in an early stage of cirrhosis. This suggests that with increasing disease severity there is increasing family support. These findings support previous studies of patients with chronic HCV which found that patients with a chronic physical illness are more likely to receive equal or higher levels of support than healthy people (Erim et al. 2010).

On the other hand, this PhD study showed that there was no significant difference in perceived social support from spouse or friends according to disease stage. The reason for these findings is unclear. However, a possible explanation may be that according to the culture of Egyptian people the family and spouse are usually the main source of support particularly during illness; but friends may support emotionally. However, their effect may not be as strong as the family and spouse. For example, in this study more than half of the patients reported that their friends did not really try to help them (57.9%), they cannot count on their friends when things go wrong (65.6%) and they cannot talk about their problems with their friends (56.4%). However, in regression analysis, disease stage was not significantly associated with perceived social support.

9.7 FINDINGS' IMPLICATIONS

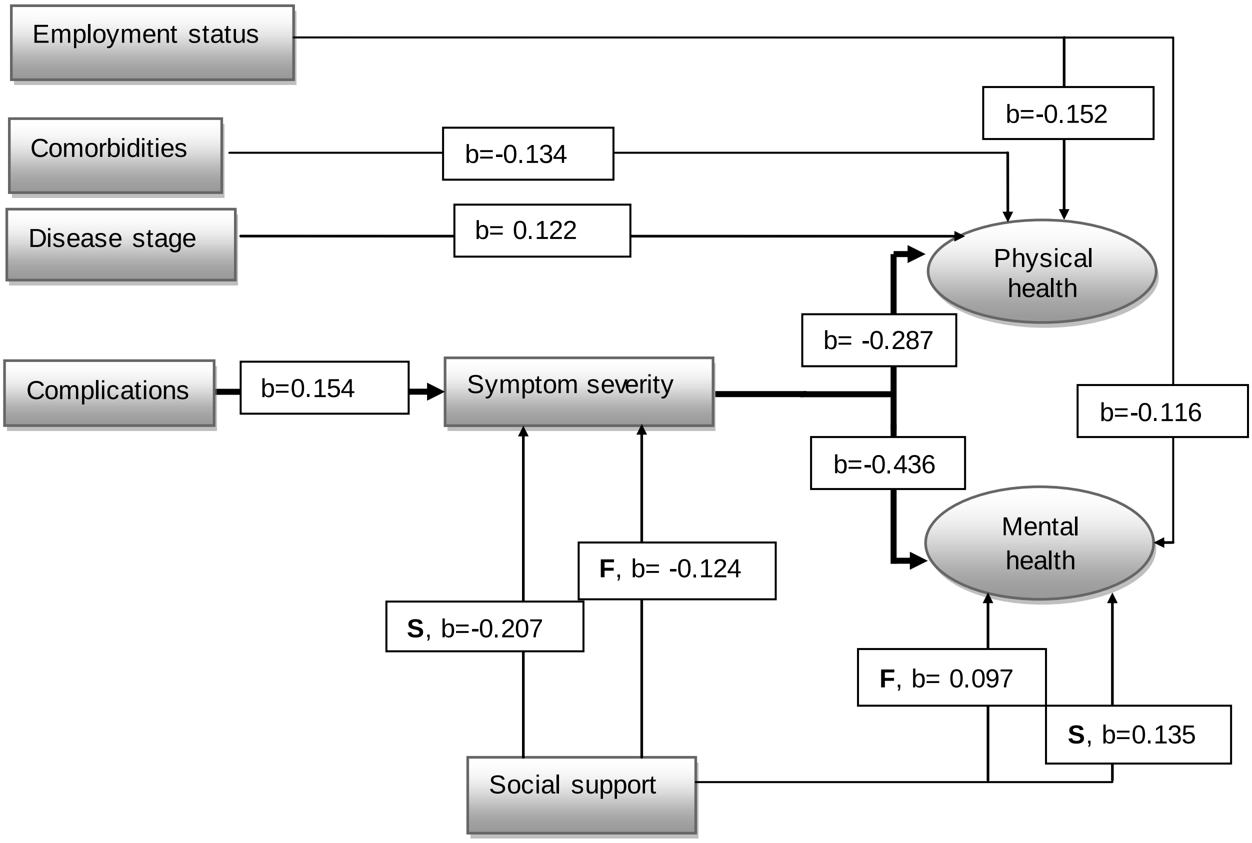
9.7.1 Implication for Theory

One of the strengths of this study is the use of the conceptual model of HRQOL outcomes by Wilson and Cleary (1995) for the first time for patients with liver cirrhosis. It helped to direct this study in terms of selecting the studied concepts, defining these concepts theoretically and operationally and directing data analysis. This study helped to confirm the practicality and feasibility of using this model to explore factors associated with HRQOL. Similarly, Sousa and Kwok (2006) found that *'this model places concepts in a context and will be useful to guide the development of new theories. This model, as described and tested, could be used as a tool to assess interventions and organizational performance within the new paradigm'* (p. 735).

Using regression analysis, two models were developed to find the factors associated with physical and mental HRQOL. The results showed that symptoms severity made the strongest contribution in explaining both aspect of HRQOL, PCS (28.7%) and MCS (43.6%). Social support from a spouse and family was significantly ($p \leq 0.04$) associated with MCS only; and they explained 13.5% and 9.7% of the variation in MCS respectively. These findings support the conclusion that symptoms are the greatest associated factor with HRQOL. Furthermore, social support was significantly associated with HRQOL and symptoms experience as hypothesised by the model. Diagram 9-1 summaries the study results, and the relationships between the studied concepts that confirm the hypotheses of the HRQOL conceptual model outcomes.

The HRQOL conceptual model outcomes by Wilson and Cleary (1995) was investigated before, using Structural Equation Modeling, and fitted well with clinical data. For example, the pathways hypotheses were tested by Henderson et al. (2012) and showed that social support significantly predicted symptom status, while symptom status and social support significantly predicted general health perceptions and overall QOL. Also, environmental factors such as income significantly predicted symptom status and general health perceptions.

Diagram 9-1: Summary of the relationship between the studied concepts



Note: F: Family support**, S:** Spouse support**,** dummy code of disease stage: 0 decompensated, 1 compensated

In a recent study of patients with HIV, Sousa and Kwok (2006) tested the HRQOL model outcomes. They found that with increasing symptom status there was poorly perceived functional health, where symptom status explained 49.0% of the variance in functional health. Also, patients who experienced more symptoms and less functional health had low perceived general health. Following the pathway of the model, they found that patients who experienced increased symptom status and had poor perceived general health were likely to report poor QOL. For instance, in patients with renal failure and on haemodialysis, Kring (2008) found that symptoms of anxiety and depression, general health perception, and level of albumin significantly predicted QOL, while gender, age, marital status and income level did not, suggesting a need to explore other contributing factors to explain QOL. Generally, this means that the pathways from symptom status to general health perception to overall QOL are reliable and can give valid results consistent with the original theoretical model of Wilson and Cleary (1995); and symptom status is the factor most associated with HRQOL.

In this study, although regression models could significantly explain PCS and MCS, 81% of the variation in PCS and 68.3% of the variation in MCS could not be explained. Therefore, these results suggest that there must be other factors that have an influence on HRQOL that need to be investigated in future research.

9.7.2 Implications for Practice

Sousa and Williamson stated that *'Nursing continues to struggle to identify outcomes that measure quality of care. Traditional outcomes, such as morbidity and mortality, do not provide sufficient information about quality of patient care'* (2003, p. 572). This study's findings are important as they increase our insight into HRQOL and experienced symptoms. These findings contribute to healthcare professionals' understanding of how patients perceive their health status and the psychosocial factors that influence their perception. Thus, improvement of patients' perception of their physical and mental health domains will be through managing symptoms and satisfying their psychosocial needs. Managing symptoms is the core of nursing practice. Therefore, healthcare professional, and nurses in particular, are responsible to develop symptom management programs to meet patients' psychosocial needs.

Smith et al. (1994) conducted a meta-analysis using randomized experimental and controlled studies to investigate the effectiveness of symptom management intervention in cancer patients. Results showed that symptom management interventions were effective in relieving symptoms such as pain, nausea, vomiting and anxiety. Thus, symptom management programs will be helpful to decrease peoples' suffering and improve their perception of their physical and mental health. Also, in a randomised control study, Lorig et al. (1999) investigated the effectiveness of a designed self-management program in changing health behaviours, health status, and health service utilization over a six-month period in 952 patients with chronic heart and lung diseases. Findings showed that groups who received the self-management programs, experienced improvements in weekly minutes of exercise, cognitive symptom management, communication with physicians, self-reported health, as well as decreases in reporting disability, and social/role activity limitations. Moreover, hospitalizations (admission and staying) decreased. The researchers summarised that the intervention program was designed to meet the patients' needs and it was feasible and beneficial for these patients, including those with comorbidity.

Understanding how patients perceive their HRQOL as well as determining its associated factors such as symptoms and social support is clinically valuable for several reasons. Firstly, healthcare professionals, particular nurses, will develop a prioritised symptom management program according to the main experienced symptoms. Secondly, social support has been found to influence patients' perceptions about severity of symptoms and mental health domains. Thus, nurses should encourage involvement of the patient's family in any nursing intervention, particularly in symptom management programs that can enhance these patients mental health domains and decrease being troubled by experienced symptoms. Family support can be enhanced by increasing their understanding about the patient's health condition and his/her psychosocial needs that need to be fulfilled by the family. Hence, in Egypt it is important to acknowledge the patient's family in the healthcare policy and healthcare delivery system by providing support services and resources that make them more responsive to patients' needs.

Involving these patients in peer support groups and getting support from others in their communities will enhance their health status; it was argued that as *"inadequate social support without effective intervention may result in negative outcomes"* (Bertero 2000, p. 94). Therefore, patient-management and family-management programs are urgently needed not only for patients but also for their families to satisfy their needs and enhance their capabilities to support and care for patients. This will happen if there is effective communication between patients, families and their healthcare providers, as well as by improving health literacy regarding their disease and enhancing their coping skills.

Interaction between patients and healthcare professionals was considered an essential aspect for therapeutic relationships. The literature showed that communication with patients about their experienced symptoms had a positive influence on their health outcomes. Jackson (2005) conducted a survey in 500 people attending a primary care clinic. They were interviewed pre and post clinicians' visit in order to find the association between patient-clinician communication and the influence on symptom relief and functional health. Results showed that when discussion about experienced symptoms took place, patients were more satisfied with the provided care, less likely to worry after a visit, and had greater symptom improvement two weeks post-visit. This suggests that discussions about symptoms can help to improve patients' health outcomes and symptoms experience as well as increase their satisfaction with healthcare.

Self-management or self-care interventions have been found to be beneficial in health outcomes of patients with chronic diseases such as heart failure, cancer and asthma. However, their impacts on patients with chronic liver disease or cirrhosis are uncertain and need research. For example, Grady (2008) reviewed seventeen randomised controlled trials (RCTs), and four longitudinal studies (pre/post or repeated measures design) that evaluated the effect of self-care on QOL in patients with heart failure. They found that nine RCTs showed significant improvement in the intervention group’s QOL compared with the control group or those that received usual care. All four longitudinal studies also showed significant improvements in QOL from baseline to follow-up. Jovicic et al. (2006) also systematically reviewed six RCTs to determine the effectiveness of self-management interventions on health outcomes (health-related quality of life and hospital readmission and mortality rates) in a total of 857 patients with heart failure. They demonstrated that self-management significantly improved adherence to prescribed medical advice and decreased rates of hospital readmissions although its effect on mortality rate and QOL was not significant.

The only identified quasi-experimental study that was conducted among Iranian cirrhotic patients demonstrated that a self-care educational intervention could significantly improve abdominal symptoms, fatigue, systemic symptoms, activity, worry and emotional domains, without significant changes in disease severity. However, HRQOL of the control group who did not receive the intervention significantly declined three months later in domains of activity, worry and emotional status (Zandi et al. 2005). Studying symptoms experience and involving patients in their care plans by asking them their educational needs are essential step before developing self-care intervention programs to improve these patients' HRQOL. Lorig and Holman (2003) argue that self-management education is a problem-based approach that must be developed on the basis of patients' needs and perceived problems. For example, assessing the patients' major concerned symptoms can help in developing effective self-management programs that are based on patients' needs. In this study, the majority of patients reported that depression, decreased appetite and joint pain limit their daily activities. Therefore, developing self-care or self-management interventions that aim to improve patients' ability to cope with these kinds of symptoms are needed.

Patients with chronic disease usually make daily decisions about how to self-manage their illness. Thus, collaboration between the patient and healthcare professional has become an essential paradigm of providing and enhancing self-management interventions. Self-management interventions complement traditional methods of care by supporting patients to be active members in managing their chronic condition. Traditional patient education offers only information and technical skills, while self-management education teaches problem-solving skills (Bodenheimer et a. 2002).

9.7.3 Implications for Research

There is a shortage of valid HRQOL measures in Arabic that can be used in research studies or in clinical settings. This study contributed to current knowledge by translating and validating the disease specific HRQOL questionnaire (LDSI-2.0) that is simple and easily understood by patients, even those who are illiterate. The psychometric properties of LDSI-2.0 were confirmed and published to be available for future use. Also, the psychometric properties of SF-36 and MSPSS were investigated. The results supported the validity of these tools and their reliability among patients with cirrhosis in Egypt, and they can also be used in future research or clinical practice.

In this study, symptoms severity have been identified as the key factor associated with perceived HRQOL in Egyptian cirrhotic patients, it explained about 41% of the variance in MCS and 29% of the variance in PCS. Therefore, this study is the foundation for developing future research in symptom management. Self-management is a patient concern and uses a problems-based approach. Future studies into intervention programs that aim to improve patients' symptom experience or perceived HRQOL using a self-management educational program are warranted.

9.8 RECOMMENDATIONS

9.8.1 Recommendations for Improving Healthcare Practice in Egypt

There is growing concern to solve the problem of spreading liver disease as a national health problem in Egypt. In 2008, the Egyptian Ministry of Health launched a National Control Strategy for treating and preventing viral hepatitis, including the opening of 20 national treatment reference centres providing antiviral hepatitis for free to those with national health insurance or who cannot pay (Guerra et al. 2012). There is a need to develop medical research that focuses on the treatment of viral hepatitis (Dalglish 2008), and to construct specific liver disease institutes.

The medical model as the main approach for providing healthcare services has contributed to some extent to improve health. By preventing HBV through obligatory anti-HBV vaccinations for children and optional vaccinations for adults, providing physical examination, continuous routine check-ups for hemodynamic parameters and tumour markers as well as trying to provide free or low cost medicine for patients with viral hepatitis and cirrhosis. However, according to this study's findings, cirrhotic patients in Egypt have poor HRQOL, which means that the available healthcare services may not be enough to enhance satisfaction regarding their health status. Bowling (2005) maintains that a medical model is no longer enough; particularly in cases of chronic or life threatening diseases. Therefore, it is recommended that *'The best measure of quality is not how well or how frequently a medical service is given, but how closely the result approaches the fundamental objectives of prolonged life, relieving distress, restoring function and preventing disability'* (Ware et al. 2008, p.3).

Increasing the quality of healthcare is a growing interest globally. Thus, sufficient and qualified healthcare providers, nurses in particular, are considered the backbone of the healthcare system worldwide (Ma et al. 2012). In Egypt, the nursing sector faces many challenges; a shortage of nurses in general and qualified nurses in particular (Farag 2008). The ratio of nurse to population is estimated to be 33.5 nurses per 10,000 people, which is too low to provide adequate care (WHO 2008). A brief background explanation will help to understand why the quality of nursing in Egypt is so low.

Three types/levels of nurses' education are currently available in Egypt: (1) Secondary school nursing education (low level), who account for 94% of the current nurses in Egypt, (2) Technical institutes of health (two years of nurses’ education after secondary school), resulting in a high nursing Diploma, which account for about 0.5% of nurses in Egypt, and (3) University nursing education (four years of nurses’ education after secondary school plus one year internship in clinical settings), resulting in a baccalaureate of nursing sciences; which account for about 1.0% of nurses in Egypt (Farag 2008; Ma et al. 2012)..

The majority of qualified nurses prefer to work in private hospitals, a teaching career or migrate to countries where nurses are paid more (Farag 2008). Therefore, the majority of current nurses in the public health sector, which is the major sector in Egypt, are without a basic standard of nursing qualification. That means they do not have the ability to make decisions regarding the patient's health or care. There is a growing concern to reform the nursing sector in Egypt to provide healthcare services that meet the patients' needs. The reform process is still being implemented as it aims to increase the number of qualified nurses by improving the quality of university nursing education and by increasing the number of admitted students and to stop secondary school nursing (Ma et al. 2012). However, the reform has faced several obstacles such as financial restrictions and stakeholder resistance (Bossert and El Rabbat 2012).

Nurses have an important role in supporting patients and their families to adjust to the disease and use available healthcare resources effectively to improve their QOL. Thus, supporting patients to engage in their daily activities as far as possible can be achieved by providing self-management programs. Healthcare policy should support nurses by providing continuous development programs, and establishing evidence based infrastructure. Improving people’s health cannot be achieved without continuous support from the national healthcare system. Healthcare policy makers need to develop strategic plans of investment for improving current nurses' performance and equipping them with the needed resources. For example in the one of the developed Western countries, the Scottish Government (2010, p. 41) states that in their healthcare strategy for improving the National Health Service (NHS) in Scotland *'...important changes in culture and approach will be required to ensure that staff are equipped and supported...'*. Therefore continuous upgrading of the healthcare system through staff development and training together with the provision of resources is important for increasing the quality of healthcare services.

The main responsibility of healthcare policy makers is to improve the map of healthcare services to direct healthcare providers' actions and performance, particularly for the care of liver disease patients. Delivering high quality healthcare that produces better health outcomes for patients requires qualified staff with skills and knowledge that makes them competent to deliver high quality care. Ware et al. (2008, p. 3) state that *'clinical investigators evaluating new treatments and technologies and practicing physicians and other providers trying to achieve the best possible patients outcomes began to use the information about functional status, well-being, and other important health outcomes. Policy analysts also began to utilize this information to compare the costs and benefits of competing ways of organizing and financing healthcare services, as did managers of healthcare organisations seeking to produce the best value for each healthcare dollar'.*

In Egypt, the Executive Committee for Accreditation and Quality (ECAQ) was established in 2006, with the aim to update the standards of accreditation, assess and survey facilities, increase quality awareness, provide training, and develop performance improvement projects. Accordingly, a strategic plan was developed in 2006 to improve the quality of healthcare services under the supervision of the ECAQ. However, Professor El Hosseiny, the Head of ECAQ and Consultant for the Egyptian Minister of Health (MOH) reported that many challenges in the application of accreditation standards have been identified. The main problem was staff resistance to change especially in the areas of: (1) working as a team, (2) delivering care as an integrated team and (3) following standard procedures (El Hosseiny 2010).

Furthermore, many cultural problems challenged the ECAQ's aims; such as changing the concept of physician-centred to patient-centred care, accepting the idea of continuous performance evaluation, staff turnover due to the fact that preparing for accreditation requires more effort and problems of staff communication (among doctors, nurses and patients). Therefore, ECAQ asserted that there is still a need for more effort and work to increase the commitment of policy makers and all healthcare providers and to enhance the concept of patient first in healthcare provision (El Hosseiny 2010). It is strongly recommended that healthcare providers, social scientists and policy makers in Egypt work in harmony to improve the national healthcare system, while taking patients', families' and healthcare professionals' experience into consideration, for their mutual benefit.

Although patient-centeredness is one of the ECAQ aims in Egypt (El Hosseiny 2010), the list of national indicators to analyse and evaluate quality of healthcare does not include assessment of patients, family or healthcare professionals' satisfaction. In Scotland, the healthcare quality strategy is built on listening to people's experience of care and using this information to improve healthcare services (The Scottish Government 2010). Thus, a person-centered approach with communication not only between healthcare professionals but also with patients and their family is at the heart of a quality healthcare strategy. Patient reported outcomes, patient experience of access, self-assessed general health and healthcare experience are some of the quality outcomes measures. Thus, peoples' experience was used to develop a quality healthcare strategy generally for NHS Scotland (The Scottish Government 2010), and specifically for liver care (NHS Liver Care 2013)

Involving patients in the processes of decision making during the development of a care plan would help to develop a self-management program that satisfies patients' needs. Patients are the greatest source of information to help healthcare providers to decide whether a goal is achieved. However, patient experience regarding their disease or the medical intervention provided has not been routinely collected in clinical practice (Ware et al. 2008), particularly in public hospitals in Egypt where the majority of patients receive healthcare services.

Continuous ignorance of the psychosocial needs of people with liver cirrhosis may cause them to experience *'stigma and discrimination; lack of adequate healthcare and rehabilitation services; and inaccessible transport, buildings and information'* as reported by WHO in disabilities and rehabilitation (2012b). According to the recommendations of the WHO, governments and authorities have the responsibility to provide services to meet peoples' needs, develop national specific programmes for those who are in need, and adopt a national improvement strategy and action plan. Furthermore, lay people should be involved in the development of services to cover patient needs and expectations, as well as understanding barriers to receiving appropriate care. They should be involved in the design and implementation of programs and strategic plans as lay persons (WHO 2012b).

To enhance the mental health of patients, healthcare providers in Egypt, particularly physicians and nurses, need to be aware of the importance of engaging the patient’s family in the care plan. Social support can influence patients' health outcomes as well as the care plan. In a study of US patients with diabetes or heart failure to assess the influence of family support and family-related barriers to their self-care Rosland, et al. (2010) found that about two-thirds of patients had supportive family involvement in self-care. Patients with high social support were more likely to report high adherence to self-care programs. Therefore, it is highly recommended to enhance the social support to people with liver cirrhosis in Egypt by developing effective intervention programs.

9.8.2 Recommendations for Future Research

Replicating this study with a large sample of patients at different stages of chronic liver disease (non-cirrhosis, compensated and decompensated cirrhosis) using a longitudinal approach to investigate the predictive factors of HRQOL and symptoms experience are needed in order to confirm the hypotheses of the model of Wilson and Cleary (1995) as well as to develop causal relationships. Although this study used quantitative questions, some patients gave qualitative comments to "explain" their answer, which increased the understanding of patients’ suffering. Therefore, a qualitative approach is recommended to explore why cirrhotic patients in Egypt, particularly females, have lower perceived social support and higher severity of some symptoms, such as depression, than men.

The majority of the studies of HRQOL of liver disease patients that were conducted in different countries have a norm-based sample of a healthy population that was used as a comparative group, particularly for SF-36 (Younossi et al. 2001; Hauser et al. 2004; Karaivazoglou et al. 2010). There are also HRQOL databases, which have been used to track liver disease patients' HRQOL (Afendy et al. 2009; Liu et al. 2012). However, the SF-36 has not been tested with the Egyptian general population's HRQOL, which may be less than the norm-based standard in Western countries. Moriarty et al. (2003, p. 2) insisted that *'continuous monitoring of population HRQOL gives public health agencies current health data they need to assess, protect, and promote population health. Tracking population HRQOL over time also helps identify health disparities, evaluate progress on achieving broad health goals, and inform healthy public policy'*. Therefore, there is a need in the near future to create a database in Egypt about the general population's HRQOL and patients' generic and disease specific HRQOL. This should be available for routine clinical care as well as for future research to study and track HRQOL of patients with liver disease and other chronic illnesses.

There are different sources of support: (1) natural or primary support provided by family and (2) professional support provided by healthcare professionals (Lanza and Revenson 1993). Perceived social support from healthcare providers has not been investigated in patients with liver disease or cirrhosis in Egypt or other chronic illnesses. Lindsey et al. (1985) assessed structural and functional social support using the Norbeck Social Support Questionnaire in Egyptian cancer patients. Results showed that no participant reported a healthcare provider; therapist or counsellor in their social network, while only two listed a religious person. This suggests that Egyptian patients may not recognise that healthcare professionals are a source of support. Therefore it may be useful to explore how cirrhotic or liver disease patients in general perceive the availability and adequacy of support from their healthcare provider and the types of social support available. Types of social support in general have been explored in people with other chronic diseases; however, they have not been investigated in patients with liver disease or cirrhosis, particularly in Egypt. Types of support can be helpful in identifying the needed intervention, for example, for a lack of information the healthcare provider may give effective support.

Although the association between social support and physical and mental health has been supported theoretically (Cohen and Wills 1985; Tijhuis et al. 1995; Hlebec et al. 2009) it still needs more empirical investigation in patients with chronic diseases in Egypt, particularly those with liver disease, to understand the mechanisms of social support, and whether types of social support from different sources are associated with HRQOL.

9.9 STRENGTHS AND LIMITATIONS OF THE STUDY

9.9.1 Study Design

This study is cross-sectional, which makes it difficult to report causal relationships between variables. However, Seers and Critelton (2001), and Ligthelm et al. (2007) acknowledged that a well-designed cross-sectional study can play a vital role in supporting evidence-based practice for patient management. Getting information from the population at a single point in time is seen as a reasonable strategy for pursuing descriptive and exploratory research projects (Ruane 2005) in order to develop future hypotheses. However, future longitudinal studies are recommended to identify causal relationships between the studied independent and dependent factors such as social support, symptoms experience and HRQOL.

The cross-sectional nature of this study also made it impossible to explore how patients perceived their health over time to evaluate health transition status. The data for this study were collected between June-August 2011, the same year as the Egyptian revolution (January 2011). Therefore, the results may have been influenced by this as community change can affect an individual's perception of their health, particularly mental health. Therefore, there is a need to repeat this study and to conduct longitudinal research to determine whether there is stability in perceived general health over time and whether the perception of health status is different according to patients' satisfaction with the healthcare they received.

9.9.2 Sample and Sampling Strategy

Although, probability (randomization) sampling is the best way to give every individual a chance to take part in the study and to decrease the chances of sampling errors (Meadows 2003), this method is sometimes impossible when facilities and resources to develop a random table for recruitment is missing. Bruce et al. (2008, p. 139) insisted that *'where time and resources are very short, or there is no structured way of contacting people for a given study, it may be satisfactory to use what is known as a convenience sample'*. A convenience sample is a commonly used method in nursing research because it saves time and money, and is useful in overcoming insufficient resources (Nieswiadomy 2008). The time restriction of the data collection period (three months) and insufficient resources to develop a sampling frame made it impossible to randomly select the participants.

For this reason, a nonprobability (convenience) sampling method was used to recruit the sample.

The convenience sampling method is usually criticised as a limitation in generalising the research findings, because it may not be representative of the general population of interest. However, the current study sample is thought to be representative of people with liver cirrhosis in Egypt. The sample was collected from three specialized well-known hospitals caring for liver disease people, which patients from different regions in Egypt and socioeconomic status attend for treatment. Four hundred and one patients with heterogeneous demographic and socioeconomic status participated in this study. There was an excellent response rate (96.6%), which decreases the chance of selection bias. Specific inclusion and exclusion criteria helped to select the representative sample of patients with liver cirrhosis but without cancer, or advanced hepatic encephalopathy, who may need a different approach of care.

9.9.2.1 Participants' Characteristics

A total of 401 patients with compensated and decompensated cirrhosis were recruited for this study, where 56.6% were females, 63.6% resident in urban areas, 77.3% married, 44.4% housewives, 54.5% illiterate and mean age 53.25 years (22-76 years). In previous liver disease surveys in both Egypt (Darwish et al. 2001; Strickland et al. 2002; Schwarzinger et al. 2004; Basal et al. 2011) and western other countries (Marchesini et al. 2001; Kim et al. 2006; Les et al. 2009) more men were recruited than women because liver disease is reported to be higher among males (WHO 2006). However, this study sample represents cirrhotic patients in Egypt in terms of socio-demographic and medical characteristics.

It was found that most participants in previous Egyptian surveys were males, married, illiterate and between 35-39.6 years (Darwish et al. 2001; Strickland et al. 2002; Schwarzinger et al. 2004). This study is quite different, as the mean age was higher and the number of females larger. This may be because the previous Egyptian studies were conducted only with HCV patients, mainly without cirrhosis and the majority were farmers and manual labourers from rural areas or Upper Egypt (Darwish et al. 2001; Strickland et al. 2002; Schwarzinger et al. 2004). The current study was conducted in Cairo, so the majority of participants came from urban areas, and the participants were patients diagnosed with cirrhosis due to various causes.

In a recent quasi-experimental study of Egyptian patients with liver disease, Abdel-Wahhab et al. (2011) investigated the impact of new medical treatment in two groups of patients: liver cirrhosis and hepatic carcinoma (HCC). The results were similar to the current study; the mean age of the cirrhotic group was 47.8, while the HCC group was 52.3. The percentage of men in the two groups was 42.3% and 44.4% respectively, which is lower than the females. In addition, the number of patients living in urban areas was 61.1% in the liver cirrhotic patients group, which was higher than the patients with hepatic carcinoma (46.2%). In Kalaitzakis et al. (2006) study, the mean age of the cirrhotic Swedish participants was 57.2 and 61% were men. The mean age of non-cirrhotic patients was 48, and 50 for patients with advanced cirrhosis, the majority (67%) were married and women were more than half of the participants (van der Plas et al. 2003). Therefore, this sample is quite representative of cirrhotic patients in terms of socio-demographic characteristics such as age, education, marital status, type of occupation and employment status.

Regarding the medical characteristics of the participants, this study's results showed that comorbidities were common in cirrhotic patients. A number of patients reported one or more medical comorbidities, most often diabetes and hypertension. This study's findings are consistent with previous studies which found that medical comorbidities, such as diabetes mellitus, hypertension…etc. were the most common comorbidities of cirrhotic patients (Marchesini et al. 2001; Kalaitzakis et al. 2006; Firtz and Hammer 2009; Les et al. 2010; Basal et al. 2011). For example, Mabrouk et al. (2012) retrospectively studied HRQOL of patients getting liver transplants and compared them to patients on the waiting list for transplantation. They found that 45.6% of the liver transplant patients had diabetes and 25.2% had hypertension, and in non-transplant patients, diabetes was 48% and hypertension was 28%. These findings suggest that the current study is representative of cirrhotic patients in Egypt and the most common comorbidities are diabetes and hypertension.

According to the report of the Ministry of Health and Population and National Committee for the Control of Viral Hepatitis in Egypt, viral hepatitis is the main cause of liver cirrhosis and is a major health problem facing Egypt (Dalglish 2008). In this study, the common cause of cirrhosis was HCV. Similarly, in a recent study HCV was identified as the major cause of liver cirrhosis (>77%) in liver transplant and no-transplant patients in Egypt (Mabrouk et al. 2012), however, *'Egyptian patients may also be co-infected with Schistosomiasis, a pathogen that also harms the liver and accelerates the course of liver disease'* (Dalglish 2008, p. 9). Also, a group of patients in this study had both viral hepatitis (B or C) and Schistosomiasis.

Although the current study lacked laboratory data to confirm the stage of cirrhosis using the Child-Pugh score, endoscopy reports, ultrasound and/or CT images were used to identify complications such as ascites and varices and medical records were reviewed to find significant comorbidities. Medical comorbidities and number of hospitalizations were self-reported by some patients, because their medical records did not show this data. However, several studies have demonstrated the accuracy and validity of self-reported medical history by patients (Dominguez et al. 2007; Vinay et al. 2011). In conclusion, we argue that the study sample represents cirrhotic patients in Egypt in terms of socio-demographic and medical characteristics.

9.9.2.2 *Setting and Method of Data Collection*

About 100 hospitals in Egypt are prepared to provide healthcare for patients with advanced liver disease, although there are about 400 specialist liver disease hospitals (Dalglish 2008). To recruit a large heterogeneous sample, patients were recruited from three liver disease specialist hospitals in the biggest city in Egypt (Cairo) from different sectors: teaching institute (NHTMRI), teaching hospital (Section 2 in Kaser El-Ani) and private hospital (CDYCDLR).

The majority of the participants (85%) were approached by the researcher. One of my colleagues in the Faculty of Nursing-Cairo University assisted me in recruiting the others. To avoid data collection biases the assistant was trained in the method of recruitment and completing the questionnaire. A training protocol (Appendix 4-17) was developed and there was training on clinical settings with real examples.

The majority of the participants preferred to be interviewed alone. Interviewing the patients without family attendance was helpful to avoid their effect on the patients' perception of their health status. For instance, two of the participants agreed to be interviewed with their relative in attendance and the family member tried to answer on behalf of the patient. For example, when asking the patients item 1 in SF-36 which is related to general health perception, the daughter and wife of these two patients responded rapidly that s/he could not do anything and their health is so poor. Thus, it was observed that the patient's family perceived his/her health status as poor, although the patient perceived it as fair or good. As a result, it was difficult to complete the interview; therefore, it was essential to agree that attending family member avoid responses during the interview. Based on that, it may be useful to conduct future research to find whether or not there is a significant difference between the patients and their families' perception of the patients’ HRQOL.

9.9.3 Quality and Limitations of Instruments

9.9.3.1 Generic HRQOL: SF-36

Over the last few years interest in using generic and disease specific measures of HRQOL has rapidly increased in health research (Bowling 2001). Hauser et al. (2004) recommended that HRQOL should be measured by generic and disease specific instruments. Therefore both disease specific (LDSI-2.0) and generic (SF-36) measures of HRQOL were used in this study for first time.

SF-36 is a short validated generic HRQOL tool in Arabic and can be completed within 20 minutes. Bao et al. (2007) stated that the SF-36 is a cheap and convenient generic HRQOL tool, which can be used in developing countries, to provide complementary and useful clinical data. However, its validity was not tested in liver disease Egyptian patients although it is widely used. Therefore, it was essential to test its psychometric properties in the studied sample. The results confirmed its validity and internal reliability (see section 8.4).

9.9.3.2 Disease Specific HRQOL: LDSI-2.0

LDSI-2.0 is a short tool that can be completed in 10 minutes; it can assess the severity and hindrance of symptoms. LDSI-2.0 was translated into Arabic for this study and its convergent and divergent validity was established among 38 cirrhotic patients in Egypt (Youssef et al. 2012). A further analysis for testing the tool's construct validity using the main sample size (n=401) was done. Factor analysis found that the Arabic LDSI-2.0 is valid and has high internal consistency and reliability. This suggests that the LDSI-2.0 is a feasible tool that can be used in clinical settings (see section 8.2). The LDSI-2.0 has been used before in clinical settings in the Netherlands and its applicability in tracking patients' health status was statistically significant (Gutteling et al. 2008; Gutteling et al. 2008a). However, there is a need for future studies to confirm the psychometric properties of the LDSI-2.0 in different stages of liver disease and its feasibility in clinical practice among people with mixed liver disease stages.

9.9.3.3 Perceived General Health: Item 1 in SF-36

It was planned to investigate the relationship between perceived general health and HRQOL, but because the scale (perceived general health) is an item in the SF-36, it proved to be difficult to expose this relationship. Smith et al. (1999) conducted a meta-analysis study to find the difference between QOL and health status. The standard question "in general, would you say your health is excellent, very good, good, fair or poor?" was the widely used measure to assess the patients' perception of general health (Smith et al. 1999). Item 1 in SF-36 had the same 5 point ordinal scale ranging from excellent to poor. Therefore, it was apparent that item 1 in SF36 was the most appropriate scale to use to assess the general health perception among cirrhotic patients in Egypt. However, because the item is involved in the PCS of the SF-36 it was difficult to include it in the regression analysis as an independent factor to find the association between perceived general health and HRQOL to avoid singularity.

Singularity is a statistical problem that occurs if one independent variable is a combination of another independent variable and entered in the regression analysis, because it will develop poor regression results (Pallant 2007). Therefore, there is a need to develop a valid tool to assess the perceived general health in liver disease patients in Egypt to use in future research.

9.9.3.4 Perceived adequacy of Social Support: MSPSS

No identified studies have assessed perceived social support in liver disease patients using the MSPSS. Hence, this study was the first to use this tool in liver disease and cirrhotic patients to assess their social support perception. The psychometric properties of MSPSS were tested with Arabic immigrant women in the US (Aroian et al. 2010); however, it has not been examined in liver disease patients in Egypt or elsewhere. Hence, it was important to test its validity and internal reliability to check its properties in cirrhotic patients. The findings established that the MSPSS is valid and reliable in cirrhotic patients in Egypt (see section 8.3).

While completing the MSPSS no particular problem related to clarity and understandability was found by participants. For instance, the patients did not ask for further clarification during the completion of the MSPSS and it took less than six minutes to complete. However, future research is required to investigate its retest reliability, which was not examined due to the constraints of time.

Although the MSPSS could explore how patients in this study perceived the available support from different sources: spouse, family and friends, it could not decide the type of available support, and this was the only limitation in MSPSS. Social support has been identified as *'a multi-faceted concept that has been difficult to conceptualise, define and measure'* (Hupcey 1998, p. 1231). Therefore, a recommendation for future research is to evaluate different types of social support using a valid tool combined with the MSPSS, in order to help to recognise some of these patients' needs.

9.10 CONCLUSION

It is important to acknowledge that using a cross-sectional design makes it impossible to determine the direction of causality of any identified associations. However, the study is unique as it is the first study to investigate and explore HRQOL, symptoms experience and perceived social support of liver cirrhotic patients in Egypt. It is the only study to have been conducted among liver cirrhotic patients in the Middle East and particularly in Egypt to evaluate and analyse the factors associated with HRQOL, symptoms experience and perceived social support. Regarding the first aim of this study, results showed that liver cirrhotic patients in Egypt have poor perceived HRQOL in all domains of SF-36. Symptoms severity has been identified as the main factor associated with perceived HRQOL. Therefore, treating symptoms may improve these patients' HRQOL and decrease their physical, psychological and social suffering. Social support was also found to be an important factor associated with perceived symptoms severity and hindrance of symptoms. This suggests that engaging the patients' family in the care plan will decrease these patients' burden and increase their HRQOL.

Regarding the second aim of this study, results showed that liver cirrhotic patients in Egypt have relatively high severity of symptoms. The majority of participants reported one or more of a wide range of symptoms: joint pain, decreased appetite, memory problems and difficulty of using time effectively were some of the most frequent reported symptoms. Joint pain, depression and decreased appetite were the symptoms that influenced their daily activities most. Gender, number of liver cirrhosis complications and perceived social support from spouse associated significantly with symptoms severity as well as hindrance of symptoms. Therefore, healthcare providers should consider these factors during the development of symptoms management programs of cirrhotic patients.

Regarding the third aim, the perceived social support score was relatively high among patients with liver cirrhosis in Egypt, with the support from a spouse rating the highest. Marital status made the strongest contribution, followed by gender, to explain social support. Singles, females, unemployed and elderly patients were more likely to perceive low social support. Therefore, these patients were found to be a vulnerable group who need further attention from healthcare providers to develop a care plan, particularly a self-care program that may need involving the patient's family.

In summary, symptoms are a treatable factor that can be managed; however so far few studies are concerned with developing intervention programs that aim to improve these patients' HRQOL. Hence, there is a need for future studies to alleviate these patients' symptoms in order to improve their HRQOL. This study has contributed to knowledge by finding some of the psychosocial factors that may affect HRQOL of liver cirrhotic people in Egypt. However, there may be other important associated factors, although the regression model could significantly explain the HRQOL. Accordingly, further research in liver cirrhotic patients in Egypt is urgently needed to explore other factors that are associated with or predict perceived HRQOL such as self-efficacy and coping style that have not been investigated before among patients with cirrhosis.

Finally, based on this study results we recommend that for clinical practice and future research:

- Different dimensions of symptom experience should be measured: severity and hindrance.
- Liver disease patients should be regularly assessed for symptom experience to identify treatable symptoms such as depression and decreased appetite.
- Future intervention studies that aim to develop programs to relieve treatable symptoms and enhance social support are recommended.
- Nurses should involve the patient’s family in any plan of care.
- Enhancing social support to people with liver cirrhosis in Egypt by developing effective intervention programs is required.
- Healthcare providers in Egypt, particularly physicians and nurses, need to be aware of the importance of engaging the patient’s family in the care plan.
- Future studies to confirm the psychometric properties of the LDSI-2.0 in different stages of liver disease and its feasibility in clinical practice among people with mixed liver disease stages need to be developed.
- A valid tool to assess perceived general health in liver disease patients in Egypt to use in future research needs to be developed.
- There is a need to design future studies to examine whether the cause of cirrhosis is related to HRQOL by measuring this association using an adequate sample size for each cause and a common classification strategy.

- Further research is recommended to explore additional predictive factors of HRQOL and symptoms experience, such as coping strategy and self-efficacy.
- Longitudinal studies are recommended to identify causal relationships between the studied independent and dependent factors such as social support, symptoms experience and HRQOL
- Future studies are recommended to explore why cirrhotic patients in Egypt, particularly females, have lower perceived social support and higher severity of some symptoms, such as depression, than men.
- There is a need to create a database in Egypt about the general population's HRQOL and patients' generic and disease specific HRQOL. This should be available for routine clinical care as well as for future research to study and track HRQOL of patients with liver disease and other chronic illnesses.
- It may be useful to explore how cirrhotic or liver disease patients in general perceive the availability and adequacy of support from their healthcare provider and the types of social support available.
- There is a need for further studies to investigate the type of social support and its relation with HRQOL among liver cirrhotic patients.
- Testing the mediation effect of social support in the relationship between symptoms experience and perceived HRQOL should be evaluated in future research.

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APPENDICES LIST

Appendix 3-1: Search process

(1) MEDLINE via web of knowledge (search ended at April 2012)

Number of search	Key-terms	Result
# 1	MeSH Heading=((((quality of life *) OR health related quality of life *) OR functional status *) OR health status *) OR well-being *) *Databases=MEDLINE Timespan=All Years Lemmatization=On*	153438
# 2	MeSH Heading=((liver cirrhosis *) OR liver disease *) OR hepatitis *) *Databases=MEDLINE Timespan=All Years Lemmatization=On*	184020
# 3	MeSH Heading=((liver disease *) OR liver cirrhosis *) OR ((hepatits *) NOT fatty liver *) NOT alcohol *)) *Databases=MEDLINE Timespan=All Years Lemmatization=On*	65430
# 4	#1 AND #3 *Databases=MEDLINE Timespan=All Years Lemmatization=On*	<u>309</u>
# 5	MeSH Heading=(((symptom *) OR fatigue *) OR pain *) OR depression *) *Databases=MEDLINE Timespan=All Years Lemmatization=On*	271214
# 6	#5 AND #3 *Databases=MEDLINE Timespan=All Years Lemmatization=On*	<u>259</u>
# 7	MeSH Heading=(((social support *) OR social network *) OR psychosocial support *) OR support system *) *Databases=MEDLINE Timespan=All Years Lemmatization=On*	43627
# 8	#7 AND #3 *Databases=MEDLINE Timespan=All Years Lemmatization=On*	<u>9</u>
# 9	#7 AND #5 AND #3 *Databases=MEDLINE Timespan=All Years Lemmatization=On*	0
# 10	#7 AND #5 AND #3 AND #1 *Databases=MEDLINE Timespan=All Years Lemmatization=On*	0
Total number of papers that reviewed from MEDLINE	<u>309+259+9= 577</u>	

(2) CINAHL and PsycINFO (via Health Source) (search ended at April 2012)

Number of search	Key-terms	Limiters/Expanders	Result
S1	quality of life OR health related quality of life OR functional status OR health status	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	109610
S2	liver disease OR liver cirrhosis OR hepatitis NOT fatty liver NOT alcohol NOT transplantation NOT primary biliary cirrhosis	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	23851
S3	symptom OR fatigue OR pain OR depression	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	538237
S4	social support OR social network OR psychosocial support OR support system	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	93166
S5	S1 and S2	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	461
S6	S2 and S3	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	1711
S7	S2 and S4	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	121
Total number	461+1711+121= 2293		

(3) ASSIA Databases Applied Social Sciences Index and Abstracts

Number of search	Key-terms	Result
S1	su.EXACT(("Alcohol related liver cirrhosis" OR "Liver cirrhosis") OR "Hepatomegaly" OR "Chronic liver diseases" OR ("Cholestasis" OR "Chronic liver diseases" OR "Hepatocellular cancer" OR "Hepatomegaly" OR "Liver diseases" OR "Obstetric cholestasis"))	130148
S2	su.EXACT(("Perceived social support" OR "Social support")) OR su(Support System)	3542
S3	(symptom OR fatigue OR pain OR psychological status OR	49541

	depression)	
S4	health related quality of life or quality of life or health status or functional health or mental health or functional status	50792
S5	S1 AND S4	21
S6	S1 AND S3	33
S7	S1 AND S2	0
Total	21 + 33 = 54	

(4) Search strategy used in Google scholar: search limitations (1990-2012), English study

First search

http://scholar.google.co.uk/scholar?q=quality+of+life+and+chronic+liver+disease+or+hepatitis+C+in+Egypt&btnG=&hl=en&as_sdt=0%2C5&as_ylo=1990&as_yhi=2012

Second search

http://scholar.google.co.uk/scholar?q=fatigue+or+pain+or+depression+and+chronic+liver+disease+or+hepatitis+C+in+Egypt&btnG=&hl=en&as_sdt=0%2C5&as_ylo=1990&as_yhi=2012

Search libraries of these sites in Egypt:

Centre library of Cairo University,

National liver institute,

Academy of Scientific Research and Technology and

Arab Journal of Gastroenterology.

Appendix 3-2: Quality appraisal form

Study	Reporting				External validity (generalisability		Internal validity (bias)					
	1. No. 2. Yes				1. No 2. Unable to determine 3. Yes - not applicable		1. No 2. Unable to determine 3. Yes - not applicable					
	Cleary described the study's aim, hypotheses or research questions	Clearly described the main outcome	Clearly described participants characteristics	Clearly described the key findings	Participants are representative of the entire population	Healthcare resources in setting of data collection representative of the treatment that majority of patients receive	Used valid and reliable measurement	Used appropriate statistical data analysis (e.g. nonparametric methods used for small sample size)	Recruited study and control from the same population	Used appropriate sampling method (e.g. random selection for intervention study)	Reported number and characteristics of participants who lost during follow-up or response rate	Reported power analysis or method of sample calculation

Appendix 3-3:Methodological characteristics of 41 studies investigating HRQOL in liver disease or cirrhotic patients

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Afendy et al. 2009 **USA**	Databases cohort study, Databases cohort sample, USA cohort: 1996-2008, Italian cohort: July-December 1998, self-completion, NA	1103 (number of patients with cirrhosis =69%)	Mean age 54.2±12.0, 40% females.
Arguedas et al. 2003 **USA**	Cross-section, consecutive, January-September 2001, interview, NA	160 patients at liver mixed stage (Child-Pugh A-c), one transplant clinic in university hospital	Mean age 51.7±10, 64% males, 85% Caucasians
Bailey et al. 2009 **USA**	Cross-section, convenience, NA, self-completed in the hospital or by phone, NA	126 patients with chronic HCV, one tertiary centre, 93% response rate	Mean age 53.1±9.4 (27-78), 50.8% females, mean education 14 (7-22) years
Bao et al. 2007 **China**	NA (seems cross-section comparative study), NA, December 2003-February 2006, self-completing, NA	126: 20 chronic HBV, 106 with cirrhosis, two hospitals (out and inpatients)	Cirrhotic patients: Mean age 45.4±7.2, 69% males, mean education 11.3±2.3 years
Basal et al. 2011 **Egypt**	Cross-section, Convenience, June-December 2010, interview, NA	200 patients with HCV: 27 Child-A, 173 Child-B, three clinics in three regions: Tanta, Assuite, Monofia	39% aged 50-60 years, 71.5% males, 73.5% were married, the sample was divided into males and females: 56.6% of men and 63.2% of women lived in rural area, 39.2% of men were farmer, 36.8% of women were housewives, above 51% of both their income was not enough. 33.6% males and 42.1% females had secondary school education, 56.6% males and 63.2% females live in rural area.

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Bianchi et al. 2005 **Italy**	NA, (seems cross-section), consecutive, January-December 2002, self-report and interview to check completion, NA	165 cirrhotic patients, one university hospital	age 37-87 years (median 65), 51.5% males
Dan et al. 2006 **USA**	Databases cohort study (Retrospective survey), cohort sample completed the questionnaires between 1997-2005 during clinic visit, self-completion, NA	140 patients at mixed disease stage (38% had cirrhosis)	Mean age 49.4±11.2, 42% females,
Fritz and Hammer 2009 **Australia**	NA (seems cross-section), consecutive, December 2001- December 2002, self-reported, NA	75 cirrhotic patients, one tertiary centre (out and inpatient)	Mean age 57±1.4 (24-82), 42 males, 91% secondary education or above, 17 working, 36 benison
Girgrah et al. 2003 **Canada**	NA (seems cross-section, NA, July 1998-December 1999, self-reported, NA	30 patients with cirrhosis, liver clinic of the general hospital	Mean age 54±4, 93.3% males
Gutteling et al. 2006 **Netherlands**	NA (seems cross-section survey), cohort samples were selected from databases and received questionnaires by emails. October-February 2000, self-report, NA	1175 patients at mixed disease stages, Dutch liver patient association (DLA)	Age 48±12, 42.3% males
Haag et al. 2008 **Germany**	Prospective (seems cross-section), consecutive, NA, self-completed, NA	204 patients with chronic liver disease (100 had cirrhosis), two tertiary centres (outpatient)	Mean age 52.7±13.9, 51% men, 100% Caucasians
Hauser et al. 2004 **Germany**	NA (seems cross-section), consecutive, August 2002-August 2003, self-completed during outpatients visit or hospital stay, YES (biopsychosocial model of HRQOL in chronic gastrointestinal disease, did not mention how it was applied), NA	88 patients with chronic HCV at mixed stage, one tertiary referral centre	Mean age 48.6%±14.6, 50% females, 70.5% with partner, 20.7% unemployed, 18.4% housewives or houseman, 39.8% in work, 52.3% were regular smokers, 25.0% had ≥ 2 alcoholic drink/day.
Hilsabeck et al. 2005 **USA**	NA (seems cross-section), consecutive, NA self-report, NA	94 (38 with cirrhosis), one tertiary liver care centre	Mean age 46.2±7.6, 57 males, 68% married, mean education 13.4 ±2.4 years, 78% married, 72%

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
			Caucasians, 61% genotype 1
Hsu et al. 2009 Canada	NA (seems cross-section/Comparative study, convenience, 1st January 2006—1st June 2007, self-completion, NA	271 patients with chronic HCV, 197 non-cirrhosis, 17 CC, 57 DC, a tertiary care clinic (five hospitals)	Mean age 49.7±8.6, 62.4% males, 51.3% married, 89.7% white ethnicity, 20.3% lower high education
Jover et al. 2005 Spain	Cross-section, consecutive, January 2001-September 2002 administer by doctors, NA	46 with cirrhosis (20 alcoholic cirrhosis)	Mean age 58.8±9 (41-73), 69.5% men
Kalaizakis et al. 2006 Sweden	Cross-section, consecutive, NA, self-completion, NA	128 patients with cirrhosis, one university hospital (in and outpatient), 90% response rate	Mean age 57.2±11.5, 61% males
Kalaizakis et al. 2008 Sweden	Cross-section, consecutive, NA, NA	156 with cirrhosis, one gastroenterology clinic (in and outpatient), 87% response rate	Alcoholic cirrhosis (n=55): age 60±8, 78%males,76% outpatients, HCV cirrhosis (n=32): age 54±7, 72% males, 84% outpatients, cholestatic cirrhosis (n=29): age 54±4, 69% males, 86% outpatients
Karaivazoglou et al. 2010 Greece	Cross-section, consecutive, May 2004-Septamber 2006, self-reported, NA	84 patients viral hepatitis, HBV=45 and HCV=39, one hepatology unit	Mean age 46±16.7 (19-78), 65.5% men, mean of education 8.8±4.4 years,
Kim et al. 2006 Korea	Cross-section survey, NA (seems consecutive), September 27-November 25 2003, interview, NA	129 cirrhotic patients (82.2% HBV), two university hospitals (in and outpatients clinics), 77.2% response rate	Mean age 53.6±9.28, 80.6% men, 90.7% married, 67.5% had higher education 50.4% unemployed

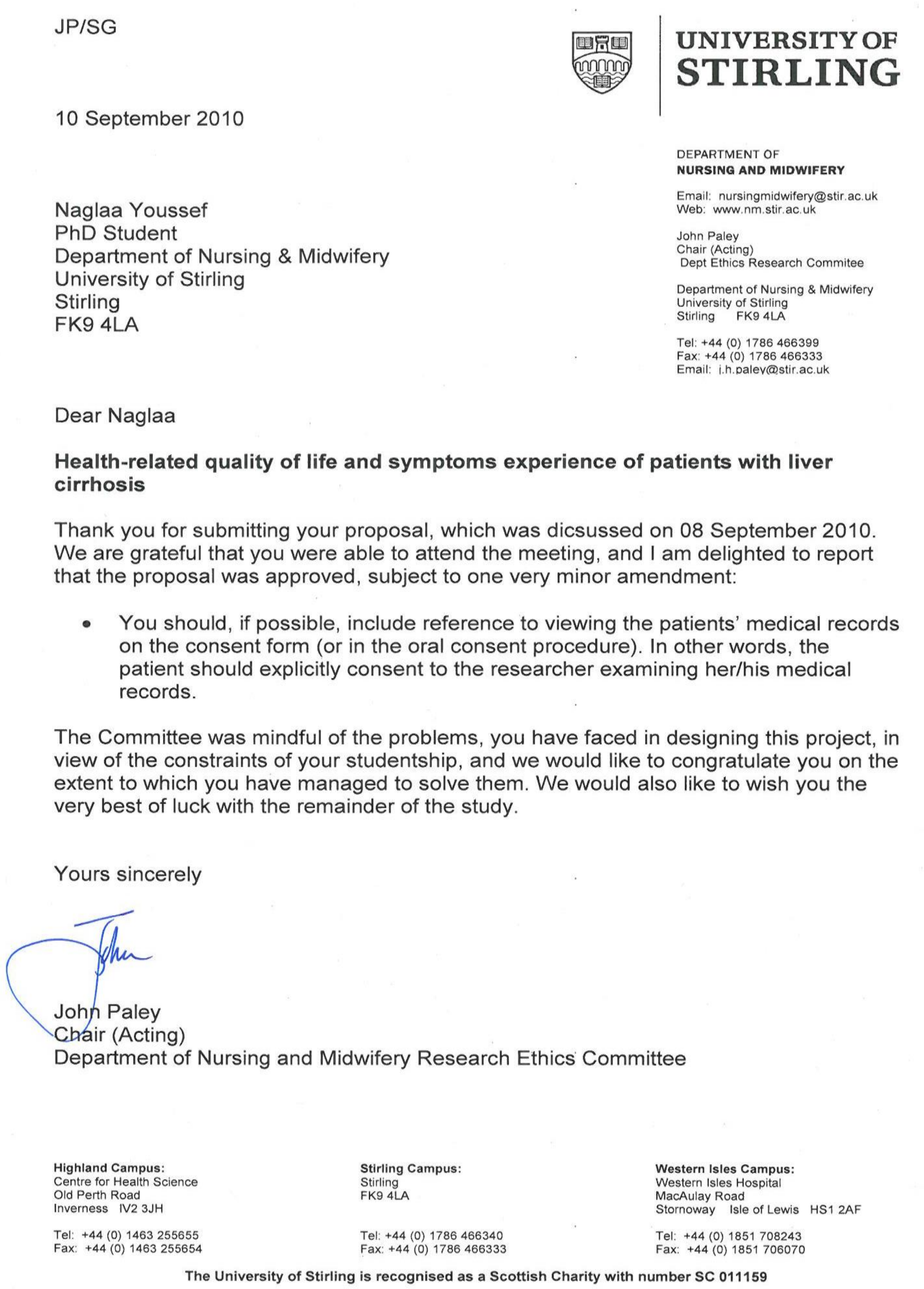
Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Les et al. 2010 **Spain**	Cross section, consecutive, 2004-2007, self-completion, NA	212 with cirrhosis, one tertiary clinic (outpatient)	Mean age 61.5±10.9, 74% males
Liu et al. 2012 **Japan**	Databases cohort study / stratified random sample from the main data in databases, Data available from a cross-sectional survey from 2008-2009 in databases, self-completing, NA	HCV group=312 for unmatched comparison. HCV group after developing matching with control group they become= 306, national survey	306 HCV patients: mean age 60.64.±12.08, 44.38% females, 73.70% married, 46.93% college education, 46.82% employed, 57.45% had national insurance
Marchesini et al. 2001 **Italy**	Cross-sectional survey, Recruiting all patients who regular fellow up in outpatient clinic through 6 months, till December 1998, self-completion and interview to avoid missing data, NA	544 with cirrhosis, tertiary clinic (in and outpatients)	Age 50±11, , 64% males, 51% had primary school
Moyer et al. 2003 **Michigan**	Survey, consecutive, October 1999-May 2000, self-completing, NA	214 with HCV : 91 say not knowing, 123 divided into optimists (79.6%) and pessimists (6.5%), one tertiary university clinic (outpatient),	Mean age 46.9±7.9, (20-69), 59.3% males, 69.9% married.
Schwarzinger et al. 2004 **Egypt**	Cohort survey, NA (seems convenience), May-December 2002, interview, NA	146 HCV, Community, response rate 78%	Participants were not aware of their HCV status, mean age 39.6%±12.3, 43.1% females, 86.3% married, 74.7% farmers, 60.3% illiterate
Singh et al. 1997 **USA**	Prospective: 100 days for all participants, 18 months for patients after transplantation, consecutive, 1991-1994, self-completion, NA	81 with cirrhosis waiting for transplantation, one newly liver transplant centre	Median age 47 (22-68 years), 80 males
Sobhonslidsuk et al. 2006 **Thailand**	Cross-section, NA (seems consecutive), 1st January -30th June 2004, self-completion and interview with illiterate, NA	250 patients with chronic liver disease, 23.6% Child-A, 22.4% Child-B/C, gastroenterology clinic	Mean age 49.1±8.5, 64% males, 29.8% single, 26.4%, unemployed, 36.6%.reported financial burden

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Sumskiene et al. 2006 Lithuania	Survey, NA, 2001-2002, NA, NA	131 with cirrhosis different causes, one gastroenterology clinic (inpatient)	Age: 17.6% <40years, 51.1% 40-60 years, 31.3% > 60 years. 51.9% men
Svirtlih et al. 2008 Serbia	Prospective (seems cross-section) study, consecutive, January 2005-December 2006, self-completion, NA	227 patients with chronic liver disease (43 cirrhosis)	Mean age 39±11.3 (16-66 years), 64.3%
Bondini et al. 2007 USA	Retrospective, cohort sample, NA, self-completing, NA	128 patients from Databases with viral hepatitis: B =68, C=60 and PBC=18	HBV: mean age 44.2±12.9, 35% females, 29% cirrhosis HCV: mean age 47.3±8.3, 31% females, 38% cirrhosis PBC: mean age 57.9±9.6, 100% women
Taliani et al. 2007 Italy	Prospective (6 months follow up), consecutive divided into three groups, NA structured interview and self-completing (based on type of data), NA	264: patients with recent diagnosis of HCV and divided into three groups: untreated, treated and did not respond and treated and relapsed (cirrhosis was in 5 untreated and 2 in treated), 14 academic centres at 8 cities	Mean age 43.8±11.4 (20-69), 64.4% males
Teixeira et al. 2005 Brazil	Cross-section, NA , NA, self-completion, NA	103 (63 cirrhotic and 40 non-cirrhotic)	Cirrhotic group: age 46±9.2, men 64.4%, Non cirrhotic group: age 37±10.8, males 60%
Teixeira et al. 2006 Brazil	Survey (6 month follow up only for the group was on antiviral therapy), July 2001-May 2003, administer by physician, NA	120 (5 had cirrhosis), on hospital (outpatient)	Mean age 38.6±11 (20-62), 63.3% males

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Teuber et al. 2008 **Germany**	Cross-section, NA, self-completion, NA	215 chronic hepatitis C (16.7% severe fibrosis or cirrhosis), on university hospital (outpatient), power of sample calculated (at least 200 required)	Mean age 46.7±13.4 (19-79), 57% men, disease duration 6±5.6 (1-32 years)
Toda et al. 2005 **Japan**	NA, NA, answered the questionnaires during clinical visit, NA	117, chronic viral hepatitis (45.3% cirrhosis), one hospital (outpatient)	Age 50 year 19%, 50-59 year 28%, >60 year 53%,
van de Plas et al. 2003 **Netherlands**	Survey, selected from databases of liver disease association and received email to complete the tools, October 2000, self-completion, NA	1175 cohort sample of patients with chronic liver disease. 489 non-cirrhosis, 391 CC, 84 DC, Dutch liver patient association (DLA), 80% response rate	G1: non-cirrhosis (489) , mean age 48±12, 43.8% males, 73.9% married G2: CC (391), mean age 49±14, 41.4% males, 75.1% married G3: DC, mean age 50±12, 42.9% males, 67.9%. married
van der Plas et al. 2004 **Netherlands**	Survey, consecutive, patients received questionnaire by email, October 2000, self-completed, NA	1175: 42.5% non-cirrhotic 34% CC, 7.3% DC, 16.2% liver transplant, DLA	Mean age48±12, 57.7% males, 74% married. 90.7% secondary or higher education,
van der Plas et al. 2007 **Netherlands**	Observational study, patients received questionnaire by email, October 2000, self-completed, NA	918 patients with mixed stages and causes of disease (48.7% non-cirrhosis, 42.1%) CC, 9.2% DC), DLA, about 80% response rate	Mean age 49±13, 58.5% women, 74.5% married, 52.4% secondary education of above

Author/country	Design, Sampling method, Year of data collection, Method of data collection, theoretical framework	Sample size, Setting	Demographic characteristics of the participants
Wilson et al. 2010 **USA**	Cross-section, consecutive, 2004-2005, self-completing, NA	65 of patients had HCV, 39% grade IV fibrosis, one gastroenterology clinic (outpatient).	66% males, 55% married,
Wunsch et al. 2011 **Poland**	NA, consecutive, January September 2008, self-completion, NA	77 with cirrhosis, one tertiary clinic (in and outpatient)	Mean age 52.8±13.1, (22-84 y), 61% males,
Younossi et al. 2001 **USA**	Cross-section, convenience, August 1997-February 1999, self-completion, NA	353 patients with different causes of liver disease, 35% Child-A, 61.6% Child-B/C, cirrhosis, one liver disease clinic,	G1 chronic viral hepatitis (n=133), mean age 46±9, 64.7% males G2 chronic cholestatic (n=126), mean age 54±11, 30.2% males, G3 Hepatocellular disease (n=94), mean age 52±13, 59.6% males
Zandi et al. 2005 **Iran**	Quasi-experimental study control, Longitudinal cases register method random assignment to divide the sample into 20 control and 20 study groups, 2002, NA	40 with cirrhosis, one hepatitis centre,	Experimental group: mean age 40.8±12.5/(18-65), 50% males, 85% married, 90% primary, secondary and higher education, 40% work: laborer, 30% employee, 20% housewife

Appendix 4-1: Ethical approval of DREC



JP/SG

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DEPARTMENT OF
NURSING AND MIDWIFERY

Email: nursingmidwifery@stir.ac.uk
Web: www.nm.stir.ac.uk

John Paley
Chair (Acting)
Dept Ethics Research Commitee

Department of Nursing & Midwifery
University of Stirling
Stirling FK9 4LA

Tel: +44 (0) 1786 466399
Fax: +44 (0) 1786 466333
Email: j.h.paley@stir.ac.uk

10 September 2010

Naglaa Youssef
PhD Student
Department of Nursing & Midwifery
University of Stirling
Stirling
FK9 4LA

Dear Naglaa

Health-related quality of life and symptoms experience of patients with liver cirrhosis

Thank you for submitting your proposal, which was dicsussed on 08 September 2010. We are grateful that you were able to attend the meeting, and I am delighted to report that the proposal was approved, subject to one very minor amendment:

- You should, if possible, include reference to viewing the patients' medical records on the consent form (or in the oral consent procedure). In other words, the patient should explicitly consent to the researcher examining her/his medical records.

The Committee was mindful of the problems, you have faced in designing this project, in view of the constraints of your studentship, and we would like to congratulate you on the extent to which you have managed to solve them. We would also like to wish you the very best of luck with the remainder of the study.

Yours sincerely

John Paley
Chair (Acting)
Department of Nursing and Midwifery Research Ethics Committee

Highland Campus:
Centre for Health Science
Old Perth Road
Inverness IV2 3JH

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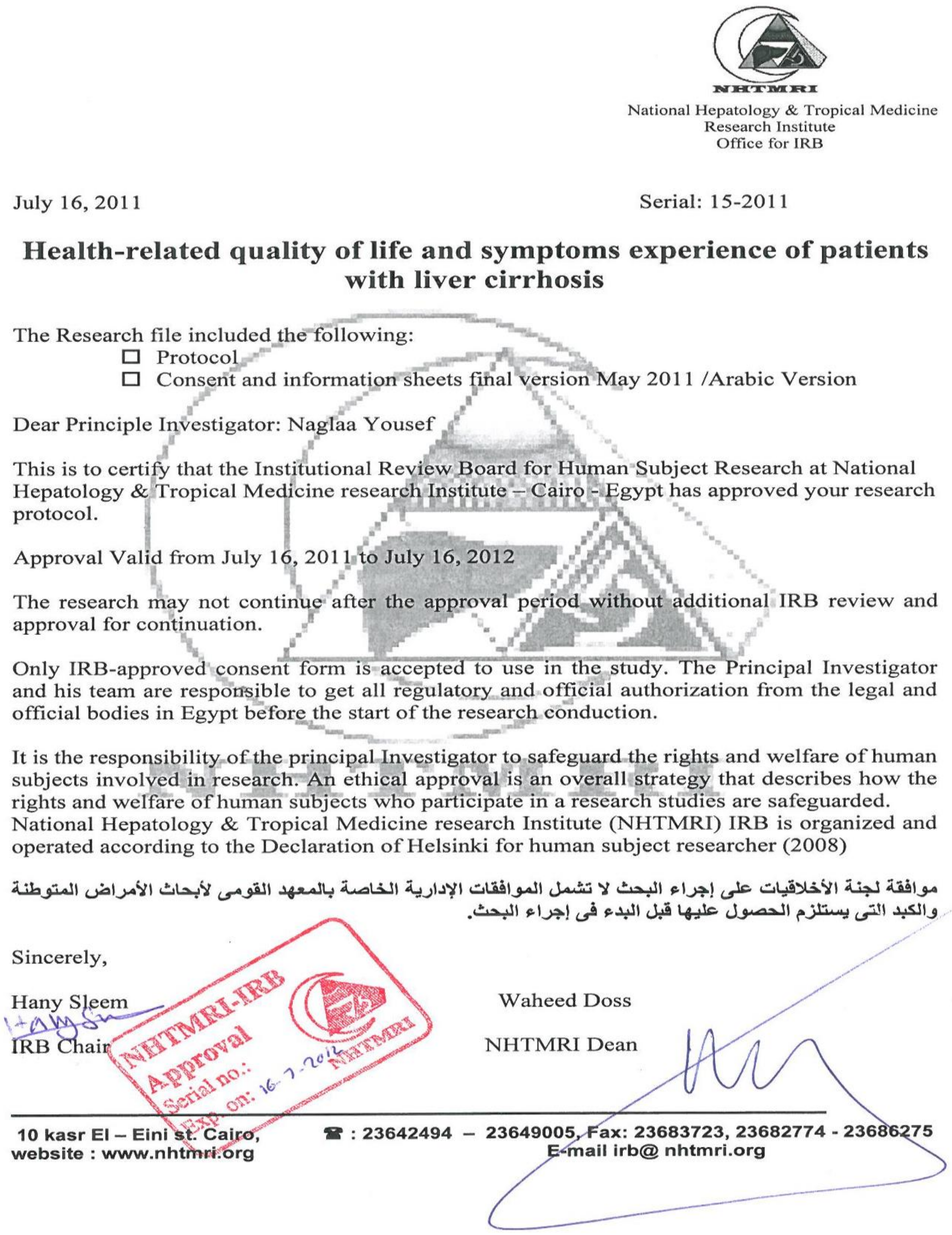
Stornoway Isle of Lewis HS1 2AF

Tel: +44 (0) 1851 708243
Fax: +44 (0) 1851 706070

The University of Stirling is recognised as a Scottish Charity with number SC 011159

Appendix 4-2: Ethical approval of the NHTMRI in Egypt



NHTMRI
National Hepatology & Tropical Medicine
Research Institute
Office for IRB

July 16, 2011 Serial: 15-2011

Health-related quality of life and symptoms experience of patients with liver cirrhosis

The Research file included the following:
- ☐ Protocol
- ☐ Consent and information sheets final version May 2011 /Arabic Version

Dear Principle Investigator: Naglaa Yousef

This is to certify that the Institutional Review Board for Human Subject Research at National Hepatology & Tropical Medicine research Institute – Cairo - Egypt has approved your research protocol.

Approval Valid from July 16, 2011 to July 16, 2012

The research may not continue after the approval period without additional IRB review and approval for continuation.

Only IRB-approved consent form is accepted to use in the study. The Principal Investigator and his team are responsible to get all regulatory and official authorization from the legal and official bodies in Egypt before the start of the research conduction.

It is the responsibility of the principal Investigator to safeguard the rights and welfare of human subjects involved in research. An ethical approval is an overall strategy that describes how the rights and welfare of human subjects who participate in a research studies are safeguarded. National Hepatology & Tropical Medicine research Institute (NHTMRI) IRB is organized and operated according to the Declaration of Helsinki for human subject researcher (2008)

موافقة لجنة الأخلاقيات على إجراء البحث لا تشمل الموافقات الإدارية الخاصة بالمعهد القومى لأبحاث الأمراض المتوطنة والكبد التى يستلزم الحصول عليها قبل البدء فى إجراء البحث.

Sincerely,

Hany Sleem
IRB Chair

Waheed Doss
NHTMRI Dean

NHTMRI-IRB
Approval
Serial no.:
Exp. on: 16-7-2012
NHTMRI

10 kasr El – Eini st. Cairo, ☎ : 23642494 – 23649005, Fax: 23683723, 23682774 - 23686275
website : www.nhtmri.org E-mail irb@ nhtmri.org

Appendix 4-3: Information sheet (The main study-English)

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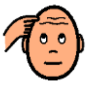
1. Title of research study

Health-related quality of life and symptoms experience of patients with liver cirrhosis in Egypt

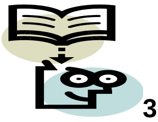
2. Invitation for taking part in research study

Would you like to take part in a research study?



Before you decide, it is important for you to understand why the research is being done and what it will involve.

Please take time to read/understand the following information sheet carefully and discuss it with the researcher or others if you wish. Please ask if there is anything that is not clear or if you would like more information.



3. Introduction about liver cirrhosis:

Liver cirrhosis is a chronic disease that leads to impaired liver functions as a result from fibrosis and scarring formation. Till now there is no definite management for curing patients from cirrhosis. Patients have only to keep taking prescribed medications and follow up with their doctor to prevent disease complications and stop cirrhosis to progress.

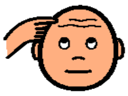
4. Background about the study research:

This study is part of a research project for my PhD study.

This research is looking at what patients with liver cirrhosis think about their health status and what symptoms that they have and how these symptoms affect their daily activities and social life.

The research is funded by the Egyptian government and is part of my PhD study which I am doing at Department of Nursing and Midwifery, University of Stirling, UK.

The study will be conducted for three years



It is up to you to decide whether or not to take part.

5. What will happen to the participants?

I am interested in exploring what patients with liver cirrhosis think about their health status and what are symptoms that they have and how these symptoms affect their daily activities and social life.

Therefore, I will interview a sample of patients (at least 200) with liver cirrhosis disease to complete the following four questionnaires:

1) A background questionnaire that contains questions such as where you live, whether you work and your medical history with liver disease.

2) A questionnaire to assess if you experience any symptoms associated with your liver disease and how these may affect your everyday activities.

3) A questionnaire to assess what you think about your health status.

4) A questionnaire to assess what you think about your family support.

I will interview you for about one hour and this will take place in the hospital before or after consultation with the consultant (for out-patient) or in the patients' room (for admitted patients).

If you like, you can ask a relative or friend to be present during the interview.

I just will take notes about what you are saying to complete the questionnaires.

There will be a private room for conducting the interview to maintain privacy.

You can ask me to stop to take a rest at any point during the interview.

6. Volunteer participation

If you would like to participate you will be asked to sign a consent form. You will be given a copy of the signed consent form to keep.

If you change your mind at any time about being involved, you can tell me to stop and you can withdraw from the study and withdraw your consent without having to say why.

Stopping will not affect your care.

7. Results of the study and confidentiality

The results of the study will be collected together and written in my PhD thesis (report) which will be ready in 2012. You will not be identified in the report.

All data will be kept confidential and I will make sure that you cannot be identified from any data collected. I will put a code, not your name, on the questionnaire. Also, nobody can see your medical records except me to collect your medical data. All your personal information will be stored in a locked filing cabinet and will be treated as confidential.

I hope that this study will explore what patients with liver cirrhosis think about their health status and what symptoms they have and how these symptoms affect their daily life. This will help healthcare providers in the future to develop appropriate intervention programs to decrease symptoms severity and improve patients' health status.

8. Medical research ethical approval

The Research Ethics Committee (REC) in Department of Nursing and Midwifery, University of Stirling, UK has examined the proposal and has raised no objections from the point of view of medical ethics. The research also has been approved by responsible institutes in Egypt whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

If you would like to talk to someone about the study, please contact Prof. Khairia Elsawy on 0102572350 (professor of nursing in Faculty of Nursing, Cairo University) who will be happy to discuss it with you.

Thank you for taking time to consider taking part in this study. If you would like to find out more about it, please contact me.

Naglaa Fathy Afifi Youssef
PhD student, Department of Nursing and Midwifery
University of Stirling - United Kingdom
I can be contacted in any of the following ways:
☎ **Telephone**: 0181725189; I am available all the day.
💻 **Email**: nagla.elshamy@gamil.com

Appendix 4-4: Information sheet (The main study-Arabic)

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وثيقة إعلام للمشاركة فى دراسة-بحثية

صفحة معلومات للمشاركين في البحث

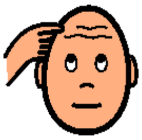
1. عنوان الدراسة

نوعية الحياة الصحية و خبرة الآعراض لمرضى التليف الكبدى بمصر

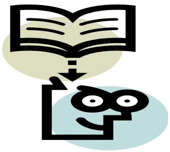
2. دعوة للمشاركة في الدراسة:

يدعوك الباحث للمشاركة في هذه الدراسة البحثية

هل تود المشاركة فى هذه الدراسة البحثية؟



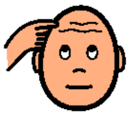
رجاء إستغرق وقتا كافيا لدراسة هذه المعلومات ولا تتردد في توجيه أي اسئلة للباحث إذا ماكان هناك أي شئ غير واضح لك.



3- مقدمة للمريض:

تليف الكبد هو مرض نتج عن تحول خلايا الكبد الطبيعية الى الياف و تكون ندبات مما ينتج عنه خلل فى اداء الكبد لوظائفه بصورة طبيعية. حتى الان ليس هناك علاج جذرى لمرض التليف الكبدى. العلاج الحالى يعتمد على المتابعة الدورية مع الطبيب و اخذ الادوية الموصوفة من قبل الطبيب المعالج لتقليص فرص تطور المرض و تقليل المضاعفات و الاعراض المصاحبة للمرض.

4. شرح موجز للدراسة التي ستجري والغرض من اجرائها



هذه الدراسة هى جزء من مشروعى البحثى المقدم للحصول على درجة الدكتوراة

هذا البحث يهدف الى معرفة مفهوم مريض التليف الكبدى عن حالته الصحية و الاعراض التى يعانى منها و شدة هذه الاعراض و مدى تاثرها على انشطة المريض اليومية و على حالته الاجتماعية.

و لك الحرية فى الاختيار بالموافقة او الرفض للمشاركة فى الدراسة

5. وصف البحث:

عدد المشاركين فى البحث على الاقل 200 مريض من مرضى التليف الكبدى فى مصر. سيتم اختيار المشاركين الذين تنطبق عليهم شروط المشاركة من العيادات الخارجية و الاقسام الداخلية.

سوف يتم مقابلة المرضى المشاركين فى هذه الدراسة مره واحدة فقط :

اثناء هذه المقابلة سيقوم الباحث بملىء الأستمارات البحثية (عدادهم اربع استمارات. مدة المقابلة بالتقريب ساعة و سيكون مكان المقابلة داخل المستشفى

سيكون موعد المقابلة بلاتفاق مع المريض (قبل او بعد الاستشارة الطبية او فى يوم آخر داخل المستشفى)

المطلوب من المشارك طوال فترة الدراسة هو الموافقة على المشاركة فى الدراسة ثم الاجابة على الاسئلة المطروحة.

يمكنك أن تطلب مني أن أتركك لتأخذ قسطا من الراحة في أي لحظة خلال المقابلة.

هذه الدراسة البحثية هى دراسة خارجية بتمويل من الحكومة المصرية للحصول على الدكتوراه من جامعة استرلنج باللملكة المتحدة البريطانيه.

مدة الدراسة 3 سنوات

6. وصف الهدف النهائي للبحث:

الهدف من هذه الدراسة هو معرفة نوعية الحياة الصحية و شدة الاعراض التى يعانى منها مرضى التليف الكبدى فى مصر ومدى تاثيرها على انشطة المريض اليومية و على حالته

7. الاشتراك التطوعي:

يمكن للمريض عدم الاشتراك او الانسحاب من الدراسة في اي وقت بدون ابداء اسباب و دون أن يؤثر ذلك علي علاجه أو علاقة مع الاطباء المعالجين او الممرضات.

8- حماية بيانات:

لن يستخدم اسم المريض وسوف يشار اليه برمز وستظل هويته غير معلنة في ايه نتائج ولكن سوف يسمح لفريق البحث (الباحث الاساسى فقط) في الإطلاع علي الملف الطبى.

9- نتائج الدراسة:

نتائج الدراسة سوف يتم تجمعها و كتابتها فى رسالة الدكتوراة التى سوف تكون جاهزة للمناقشة بعام 2012

اتمنى هذه الدراسة ان تساعد فى كشف اسباب معانة مرض التليف الكبدى مع المرض حتى تساعد معطى الرعاية الصحية (الطبيب و الممرضة) ايجاد طرق علاجية لتخفيف معانتهم.

10- لجنة أخلاقيات البحث العلمى:

هذا البحث تمت الموافقة عليه من قبل لجنة أخلاقيات البحث العلمى بكلية التمريض- جامعة استرلنج, اسكتلند, المملكة المتحدةالبريطانية والتي تدقق بأن كل الشروط التي تتعلق بسلامتك وحقوقك محترمة و محفوظة طول مدة الدراسة. وقد أعطيت الموافقة علي هذا البحث بتاريخ 2010/9/8

11- يمكنك الإتصال بالباحث:

في حالة احتياجك لمعرفة المزيد عن الدراسة و مناقشاتها يمكنك الاتصال بدكتورة مها صلاح (كلية التمريض-جامعة القاهرة) على هذا الرقم 0120818383

او بالباحث

اسم الباحث: نجلاء فتحى عفيفى يوسف

طالبة دكتوراة, قسم التمريض-جامعة استرلنج-المملكة المتحدة البريطانية

الهاتف: 0165501154

وقت الأتصال: يمكنك الاتصال فى اي وقت

البريد الالكترونى: nagla.elshamy@gmail.com

إذا وافقت علي الإنضمام الي هذا البحث سوف تعطى الباحث موافقة كتابية بالموافقة على المشاركة و لديك الحق في الاحتفاظ بنسخة من هذه الوثيقة بعد أن توقعها.و يمكنك الاتصال برقم الهاتف السابق في اى وقت اذا ما كانت لديك اسئلة

شكرا" لمشاركتك فى هذه الدراسة

Appendix 4-5: Informed consent (The main study-English)

UNIVERSITY OF
STIRLING

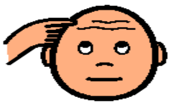
DEPARTMENT OF
NURSING AND MIDWIFERY

The study title: “Health-related quality of life and symptoms experience of patients with liver cirrhosis in Egypt”

Please answer the following questions with yes (√) or no (X) to be sure you understood the content of the information sheet.

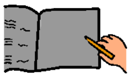
I have read/informed well the information sheet ☐

I have had the chance to ask questions and talk about the research study ☐



I have been informed and understand it is voluntary participation ☐

I have been informed that I can withdraw from the study at any time without saying why ☐

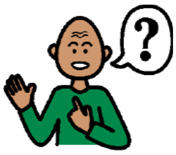


I have been informed and understand the data and my confidentiality will be protected ☐

I agree to see my medical document ☐

I have taken copy of the informed consent ☐

I am happy to take part in the above study ☐



Do you have any other question before giving your consent ☐

Participant's name:…………………...........Signature:………………………..
[by a person independent of the research]……………………………………
To be used if participant is unable to sign because of physical disability……:
Name:……………………………………Signature:…………………………..
Name of person taking consent:………………………Signature:…………………
Date:…………………………………….

Appendix 4-6: Informed consent (The main study-Arabic)

UNIVERSITY OF STIRLING

DEPARTMENT OF
NURSING AND MIDWIFERY

وثيقة قبول (موافقة) على الاشتراك فى دراسة بحثية

عنوان الدراسة البحثية

نوعية الحياة الصحية و خبرة الاعراض لمرضى التليف الكبدى بمصر

من فضلك اجب على هذه الاسئلة بنعم (√) او لا (x) للتاكد من انك قد فهمت كل المعلومات الخاصة بالبحث

لديك الحق في الاحتفاظ بنسخة من هذه الوثيقة بعد أن توقعها.

أعلمت بشكل صحيح بالدراسة البحثية المقترحة. ☐

إستلمت نسخة من صفحة معلومات المريض. ☐

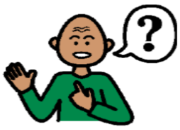
اتيحة لى الفرصة للاستفسار عن الدراسة
اوافق على ان تطلع على ملفى الطبى ☐

اعلمت بان إشتراكي تطوعي تماماً ولدي الحق في سحب موافقتي في أي وقت بدون أبداء تفسير ☐
ولن يوثر ذلك علي علاقتي مع طبيبي المعالج او الممرضة.

اعلمت بان البيانات والمعلومات التي ستجمع منى اوعني ستكون سرية ويتم التصرف فيها طبقا لقانون حماية المعلومات الخاصة بالآشخاص فيما يتعلق بالبيانات الشخصية. ☐

أوافق علي المشاركة في الدراسة البحثية التى تحت عنوان
نوعية الحياة الصحية و خبرة الاعراض لمرضى التليف الكبدى بمصر ☐
والمسجلة بقسم التمريض- جامعة استرلنج بالمملكة المتحدة البريطانية

إستلمت نسخة من وثيقة الموافقة (قبول الاشتراك) ☐



هل هناك اى سوال تود الاستفسار عنه قبل اعطاء الموافقة ☐

أسم المريض: ....

توقيع المريض: ....التاريخ: / /

أسم وكيل المريض فى حالة عدم القراءة والكتابة: ....

توقيع وكيل المريض: ....التاريخ: / /

توقيع الباحث: ....التاريخ: / /

هذه الوثيقة أعدت مع الاخذ في الاعتبار لكلا من:

إعلان الرابطة العالمية والمتبني من مؤتمر الجمعية الطبية العالمية الثامن عشر الذي عقد بهلسنكي بفنلندا في يونيو 1964. والذي روجع اعوام 1975؛ 1983؛ 1989 ؛ 1996 وفي السادس من اكتوبر 2000 www.wma.net(في ادنبرة اسكتلندا, 2008 (اعلان هلسنكى
سبتمبر CPMB/ICH/35/951997 للمارسة السريرية الجيدة ICH-GCPتوجيهات
التوجيهات الاخلاقية العالمية للبحث الطبي الحيوي المتضمن ادمين مجلس للمنظمات العالمية من العلوم
(جنيف عام 1992 والذي روجع عام 2002 CIOMSالطبية-)
: التوجيهات العلمية للجنة الاخلاقية لمراجعة البحوث الطبية الحيوية (WHOمنظمة الصحة العالمية)
جنيف عام 2000.

Appendix 4-7: Background data sheet (English)

Participants' Code……………………….

Place of data collection (Setting)
1. Outpatient 2. Inpatient

A. Individual characteristics (Socio-demographic data and economic status)

Age: …………………

Gender:
1. Male 2. Female

Marital status
1. Single 2. Married. 3. Widowed 4. Divorced

Educational level:
1. Illiterate
2. Can read and write
3. Primary or preparatory school
4. Secondary school or Diploma
5. Higher education

Place of residence:
1. Rural
2. Urban

Socio-economic status:

Type of work/job
1. Employee 2. Worker 3. Housewife 4. Farmer

Current employment status
1. Employed 2. Unemployed

Reason for unemployment
2. The liver disease……………………..
3. Other ………………………………………………

House occupied
1. Own 2. Rented

Who pay for your medications? --------------------------------

B. Medical and clinical data

Complication of liver disease that you have in year 2010-2011:
1. Splenomegaly
2. Ascites
3. Oesophageal varices without bleeding
4. Oesophageal varices with bleeding
5. Encephalopathy
6. Other ………………..

Disease stage/severity

1. Compensate cirrhosis 2. Decompensate cirrhosis

Cause of liver disease ……………….

Note: These data from the patients' medical records

Previous hospital admission due to liver disease:

1. No
2. Yes
    1. Number of admission……………………………..
    2. Cause of hospital admission………………………..

Comorbidity

1. Number of comorbidity…………………………..
2. Types of comorbidity: 1. 2. 3.

Appendix 4-8: Background data sheet (Arabic)

استبيان البيانات الديموجرافية و الطبية

كود المريض المشارك بالبحث:...................

مكان تجميع البيانات

1. عيادة خارجية   2. اقسام داخلية

اولا" البيانات الديموجرافية

السن-----------------

النوع/الجنس؟

1 . ذكر   2. أنثى

الحالة الاجتماعية

1. اعزب (لم يسبق لى الزواج)   2 . متزوج   3. أرمل   4. مطلق   5. مهجوره

مستوى التعليم

1. أمى (لا يمكن القراءة والكتابة)
2. يمكن القراءة والكتابة فقط (ابتدائيه – اعداديه)
3. المدارس الثانوية أو الدبلوم
4. التعليم العالي
5. اجابه اخرى...

مكان الاقامة (المحافظة)...

1. ريف   2. حضر

الحالة الاجتماعية والاقتصادية

نوع العمل

الوظيفة...

ا الحالة الوظيفية

1. تعمل   2. لا تعمل

سبب عدم العمل

مرض الكبد 2. اسباب أخرى (ربة منزل- على المعاش..

هل تملك المنزل الذي تعيش فيه؟ 1. نعم   2. لا

من الذي يدفع لك ثمن ألادوية ؟

1. انا   2. الاقارب او الاهل   3. قرار على نفقة الدولة
4. انا و التأمين (النص بالنص او كله)   5. ذكاة او جمعيات خيرية..

ثانيا. البيانات الطبية

ما هي المضاعفات الناجمة عن مرض الكبد ألتى يعانى منها المريض خلال عام2010 -2011؟

1. تضخم الطحال
2. استسقاء
3. دوالي المريء النزيف
4. مرض الكبد الدماغى
5. الصفراء

ما هي شدة / مرحلة تليف الكبد؟

1 تليف الكبد تعويضى
2. تليف الكبد غير تعويضى

سبب مرض الكبد (فيرس س, ب, بلهارسيا.....................................)

ملحوظة: هذه البيانات من ملف المريض الطبى

هل سبق لك دخول المستشفى بسبب مرض الكبد؟

1. لا
2. نعم

ما هو عدد مرات دخولك المستشفى بسبب مرض الكبد؟ ....

اسباب دخول المستشفى فى كل مرة"؟ مثال على ذلك النزيف ....

ما هي الأمراض الأخرى التي تعاني منها؟

1..2....................................3....................................

Appendix 4-9: SF-$36v_2$ (English)

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please tick the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

		Yes, limited a lot ▼	Yes, limited a little ▼	No, not limited at all ▼
a	<u>Vigorous activities</u>, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b	<u>Moderate activities</u>, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c	Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d	Climbing <u>several</u> flights of stairs	☐ 1	☐ 2	☐ 3
e	Climbing <u>one</u> flight of stairs	☐ 1	☐ 2	☐ 3
f	Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g	Walking <u>more than a mile</u>	☐ 1	☐ 2	☐ 3
h	Walking <u>several hundred yards</u>	☐ 1	☐ 2	☐ 3

i	Walking <u>one hundred yards</u>	☐ 1	☐ 2	☐ 3
j	Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health</u>?

		All of the time ▼	Most of the time ▼	Some of the time ▼	A little of the time ▼	None of the time ▼
a	Cut down on the <u>amount of time</u> you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	<u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Were limited in the <u>kind</u> of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Had <u>difficulty</u> performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?

		All of the time ▼	Most of the time ▼	Some of the time ▼	A little of the time ▼	None of the time ▼
a	Cut down on the <u>amount of time</u> you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	<u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Did work or other activities <u>less carefully than usual</u>	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

Not at all ▼	Slightly ▼	Moderately ▼	Quite a bit ▼	Extremely ▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
▼	▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼
a Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f Have you felt downhearted and low?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

[1]11. How TRUE or FALSE is <u>each</u> of the following statements for you?

		Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a	I seem to get ill more easily than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

صحتك وعافيتك

يستفسر هذا الاستبيان عن آرائك في صحتك. ستساعد هذه المعلومات على تتبع ما تشعر به ومدى قدرتك على القيام بأنشطتك المعتادة. ***شكرًا لك على ملء هذا الاستبيان!***

برجاء وضع علامة ☒ في المربع الذي يحدد إجابتك أفضل تحديد وذلك لكل سؤال على حدة.

1. بصفة عامة، هل يمكنك القول أن صحتك:

ممتازة	جيدة جدًا	جيدة	متوسطة	معتلة
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. بالمقارنة بالسنة الماضية، كيف تقيّم صحتك بصفة عامة في الوقت الحالي؟

أفضل كثيرًا الآن من السنة الماضية	أفضل إلى حد ما الآن من السنة الماضية	تقريبًا مثلما كانت السنة الماضية	أسوأ إلى حد ما الآن من السنة الماضية	أسوأ كثيرًا الآن من السنة الماضية
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. تتناول الأسئلة التالية الأنشطة التي قد تمارسها خلال أي يوم من أيامك العادية. هل صحتك الآن تقيّد من ممارستك لهذه الأنشطة؟ إذا كانت الإجابة بنعم، فإلى أي مدى؟

	نعم، تقيّدها كثيرًا	نعم، تقيّدها قليلاً	لا، لا تقيّدها إطلاقًا
	▼	▼	▼
ا أنشطة قوية، مثل العدو ورفع الأشياء الثقيلة والمشاركة في الرياضات المجهدة	☐ 1	☐ 2	☐ 3
ب أنشطة متوسطة، مثل تحريك منضدة أو دفع مكنسة كهربائية أو السباحة أو ركوب دراجة	☐ 1	☐ 2	☐ 3
ج رفع بقالة أو حملها	☐ 1	☐ 2	☐ 3
د صعود السلم لعدة طوابق	☐ 1	☐ 2	☐ 3

ه صعود السلم لطابق واحد .... ☐ 1 .... ☐ 2 .... ☐ 3

و الانحناء أو الركوع أو الميل .... ☐ 1 .... ☐ 2 .... ☐ 3

ز السير لما يزيد عن كيلومتر .... ☐ 1 .... ☐ 2 .... ☐ 3

ح السير عدة مئات من الأمتار.. ☐ 1 .... ☐ 2 .... ☐ 3

ط السير مائة متر .... ☐ 1 .... ☐ 2 .... ☐ 3

ي الاستحمام أو ارتداء الملابس.. ☐ 1 .... ☐ 2 .... ☐ 3

4. خلال الأسابيع الأربع الماضية، كم من الوقت مررت بأي من المتاعب التالية في عملك أو في أي أنشطة يومية معتادة أخرى نتيجة لحالتك الصحية البدنية؟

طوال الوقت	معظم الوقت	بعض الوقت	قليل من الوقت	لم يحدث
▼	▼	▼	▼	▼

ا تخفيض الوقت الذي تقضيه في العمل أو
غيره من الأنشطة. .... ☐ 1 .... ☐ 2 .... ☐ 3 .... ☐ 4 .... ☐ 5

ب أنجزت أقل مما تود .... ☐ 1 .... ☐ 2 .... ☐ 3 .... ☐ 4 .... ☐ 5

ج حدث انحصار في نوعية العمل
أو غيره من الأنشطة. .... ☐ 1 .... ☐ 2 .... ☐ 3 .... ☐ 4 .... ☐ 5

د لاقيت صعوبة في أداء العمل أو
غيره من الأنشطة (مثلاً، بذلت فيه
جهدًا إضافيًا)... ☐ 1 .... ☐ 2 .... ☐ 3 .... ☐ 4 .... ☐ 5

5. خلال الأسابيع الأربع الماضية، كم من الوقت مررت بأي من المتاعب التالية في عملك أو في أي أنشطة يومية معتادة أخرى نتيجة لأي مشكلات نفسية (مثل الشعور بالاكتئاب أو القلق)؟

	طوال الوقت	معظم الوقت	بعض الوقت	قليل من الوقت	لم يحدث
	▼	▼	▼	▼	▼
ا تخفيض الوقت الذي تقضيه في العمل أو غيره من الأنشطة	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
ب أنجزت أقل مما تود	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
ج أديت العمل أو غيره من الأنشطة بعناية أقل من المعتاد	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

6. خلال الأسابيع الأربع الماضية، إلي أي مدي أثرت حالتك الصحية البدنية أو مشاكلك النفسية على أنشطتك الاجتماعية العادية مع أسرتك أو أصدقائك أو جيرانك أو التجمعات التي تنتمي إليها؟

لم يحدث أثر مطلقًا	حدث بدرجة طفيفة	حدث بدرجة متوسطة	حدث بدرجة كبيرة	حدث بدرجة كبيرة جدًا
▼	▼	▼	▼	▼
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

7. ما مقدار الألم البدني الذي شعرت به خلال الأسابيع الأربع الماضية؟

لا شيء	طفيف جدًا	طفيف	متوسط	حاد	حاد جدًا
▼	▼	▼	▼	▼	▼
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

8. خلال الأسابيع الأربع الماضية، كم أثر الألم على عملك المعتاد (بما في ذلك كل من عملك خارج المنزل وأعمال المنزل)؟

لم يحدث أثر مطلقًا	حدث بدرجة طفيفة	حدث بدرجة متوسطة	حدث بدرجة كبيرة	حدث بدرجة كبيرة جدًا
▼	▼	▼	▼	▼
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

9. هذه الأسئلة تتناول شعورك و كيفية سير الأمور معك خلال الأسابيع الأربع الماضية. نرجو أن تجيب على كل من الأسئلة التالية بالإجابة الأقرب إلى طريقة شعورك. كم المدة خلال الأسابيع الأربع الماضية...

	طوال الوقت	معظم الوقت	بعض الوقت	قليل من الوقت	لم يحدث
	▼	▼	▼	▼	▼
ا هل كنت تشعر أنك مليء بالحيوية؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ب هل كنت عصبيًا جدًا؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ج هل كنت تشعر أنك مغتم لدرجة أنه لا شيء يستطيع أن يسعدك؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
د هل كنت تشعر بالهدوء والسكينة؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ه هل كان لديك كثير من الطاقة؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
و هل كنت تشعر بالحزن والاكتئاب؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ز هل كنت تشعر بأنك منهك القوى؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ح هل كنت سعيدًا؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
ط هل كنت تشعر بالإرهاق؟	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. خلال الأسابيع الأربع الماضية، كم من الوقت أثرت حالتك الصحية البدنية أو النفسية في أنشطتك الإجتماعية (مثل زيارة الأصدقاء أو الأقارب إلخ)؟

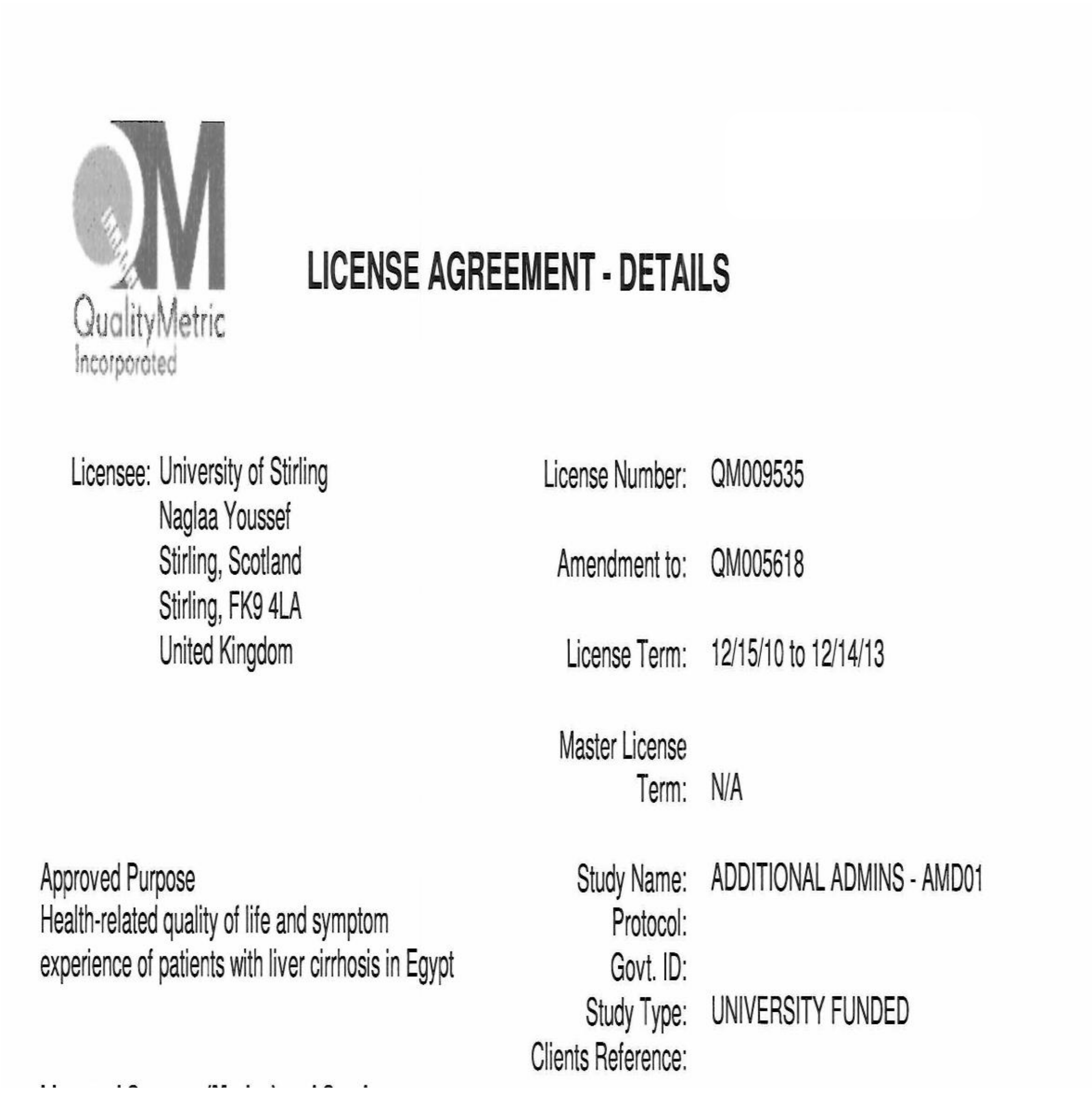
طوال الوقت	معظم الوقت	بعض الوقت	قليل من الوقت	لم يحدث
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐5

11. ما مدى صحة أو خطأ كل من العبارات التالية بالنسبة لك؟

	صحيح تمامًا	صحيح غالبًا	لا أعرف	خطأ غالبًا	خطأ تمامًا
	▼	▼	▼	▼	▼
ا يبدو أنني أمرض بصورة أسهل قليلاً من الآخرين	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
ب صحتي جيدة مثل صحة أي شخص أعرفه	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
ج أتوقع أن تسوء صحتي	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
د صحتي ممتازة	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

شكرًا على الإجابة على هذه الأسئلة!

Appendix 4-11: Permission of QualityMetric Incorporated



QualityMetric
Incorporated

LICENSE AGREEMENT - DETAILS

Licensee: University of Stirling
Naglaa Youssef
Stirling, Scotland
Stirling, FK9 4LA
United Kingdom

License Number: QM009535

Amendment to: QM005618

License Term: 12/15/10 to 12/14/13

Master License Term: N/A

Approved Purpose
Health-related quality of life and symptom experience of patients with liver cirrhosis in Egypt

Study Name: ADDITIONAL ADMINS - AMD01
Protocol:
Govt. ID:
Study Type: UNIVERSITY FUNDED
Clients Reference:

QualityMetric

AMENDMENT TO LICENSE AGREEMENT

Effective Date: August 9, 2011

Amendment Number: QM009535
Amendment To: CT125808 / OP007621 / QM005618

Licensee Name: University of Stirling
Licensee Address: Stirling, Scotland
Stirling, Scotland
FK9 4LA

Approved Purpose: Health-related quality of life and symptom experience of patients with liver cirrhosis in Egypt
Study Name: ADDITIONAL ADMINS - AMD01
Protocol:
Gov ID:
Study Type: UNIVERSITY FUNDED

Therapeutic Area: Procedures and Therapies

This Amendment to License Agreement (the "Amendment") is entered into as of the Amendment Date, by and between QualityMetric Incorporated ("QM") and Licensee.

The following term(s) of the License are modified as indicated below:

License fee: $59.40
Total Administrations: Add 108 administrations to original license for licensed total of 438
Term: No change from original license
Licensed Surveys: No change from original license
Other Change: N/A

Except as expressly modified by this amendment, all terms and conditions of the License shall continue in full force and effect without change.

EXECUTED, as of the Effective Date, by the duly authorized representatives as set forth below.

[QM]
QualityMetric Incorporated
Signature:
Name: Martha Bayliss
Title: VP Operations
Date: 12 SEPT 2011

[Licensee]
University of Stirling
Signature: Nag
Name: Naglaa Youssef
Title: PhD student
Date: 9/9/2011.

Appendix 4-12: Method of interpreting outcome of SF-36v$_2$, adapted from (ware and Gandek 1998 and Ware et al. 2000)

Score under the average NBS (50)	**Norm-based standard (NBS)** **Domains & Component summary**	**Score above the average NBS (50)**
Difficult in performing different types of physical activities due to health limitation	1 **Physical functioning (PF)**	Performing different levels of physical activities without health limitation
Difficult in performing work or daily activities because of physical health problems	2 **Role limitation due to physical problems (RP)**	Performing work or daily activities without physical health problems
Experience severe pain and extremely difficult in performing daily activities due to pain	3 **Bodily Pain (BP)**	No pain or experience of limitation in activities due to pain
Report general health as poor	4 **General Health (GH)**	Report general health as excellent
Feeling tired and worn out all of the time	5 **Vitality (VT)**	Feeling of full happiness and energy all of the time
Frequent difficult in performing social activities due to physical and emotional problems	6 **Social Functioning (SF)**	Performing social activities without limitation result from physical or emotional problems
Difficult in performing work or daily activities because of emotional health problems	7 **Role Limitation Due To Emotional Problems (RE)**	Performing work or daily activities without emotional problems
Feeling nervous and depression all of the time	8 **Mental Health (MH)**	Feeling peaceful, calm and happy all the time
Experience limitation in self-care, physical, social and role activities, feeling severe body pain, tiredness and perceived poor general health	**Physical Component Summary (PCS)**	No physical health problems, limitations, feeling high energy, excellent general health perception
Feeling psychological distress, social and role activities limitation due to due to emotional problems and perceived poor general health	**Mental Component Summary (MCS)**	No psychological distress, no problems in performing usual social and role activities due to emotional problems and perceived excellent general health

Appendix 4-13: LDSI-2.0 (English)

Item		
1A	To what extent in the past week: did you have itch?	Not at all ☐☐☐☐☐ To a high extent
1B	To what extent in the past week: has itch hampered you in your work or daily activities	Not at all ☐☐☐☐☐ To a high extent
1C	To what extent in the past week: has itch hampered you in your sleep?	Not at all ☐☐☐☐☐ To a high extent
2A	To what extent in the past week: did you have joint pain?	Not at all ☐☐☐☐☐ To a high extent
2B	To what extent in the past week: has joint pain hampered you in your work or daily activities?	Not at all ☐☐☐☐☐ To a high extent
3A	To what extent in the past week: did you have pain in the right upper belly?	Not at all ☐☐☐☐☐ To a high extent
3B	To what extent in the past week: has pain in the right upper belly hampered you in your work or daily activities?	Not at all ☐☐☐☐☐ To a high extent
4A	To what extent in the past week: were you sleepy during the day?	Not at all ☐☐☐☐☐ To a high extent
4B	To what extent in the past week: has sleepiness hampered you in your work or daily activities?	Not at all ☐☐☐☐☐ To a high extent
5A	To what extent in the past week: did you worry about the impact your liver disease may have on your home/family situation?	Not at all ☐☐☐☐☐ To a high extent
5B	To what extent in the past week: did you worry about the impact your liver disease may have on your home/family situation, hamper you in your work or daily activities?	Not at all ☐☐☐☐☐ To a high extent
6A	To what extent in the past week: did you have a decreased appetite?	Not at all ☐☐☐☐☐ To a high extent
6B	To what extent in the past week: did decrease appetite hamper you?	Not at all ☐☐☐☐☐ To a high extent
7A	To what extent in the past week: did you feel depressed due to your disease?	Not at all ☐☐☐☐☐ To a high extent
7B	To what extent in the past week: did depression due to your disease hamper you in your work, daily activities and/or social contacts?	Not at all ☐☐☐☐☐ To a high extent

8	To what extent in the past week: were you afraid that possible liver disease complications would develop?	Not at all ☐☐☐☐☐ To a high extent
9A	To what extent in the past week: did your skin turn yellow?	Not at all ☐☐☐☐☐ To a high extent
9B	To what extent in the past week: did yellowness of your skin hamper you in your work, daily activities and/or social contacts?	Not at all ☐☐☐☐☐ To a high extent
EXTRA ITEMS		
10	Since I have a liver disease I have difficulty remembering things. For example: things, which happened recently, where I have left things and appointments I have made.	Not at all ☐☐☐☐☐ To a high extent
11	Due to my liver disease my personality has changed.	Not at all ☐☐☐☐☐ To a high extent
12	My liver disease is a hindrance to my financial affairs. For example: with respect to mortgaging or insuring.	Not at all ☐☐☐☐☐ To a high extent
13	My liver disease forces me to use my time differently than I really want.	Not at all ☐☐☐☐☐ To a high extent
14	My sexual interest has decreased since I know I have a liver disease.	Not at all ☐☐☐☐☐ To a high extent
15	My sexual activity has decreased since I know I have a liver disease.	Not at all ☐☐☐☐☐ To a high extent

Appendix 4-14: MSPSS (English)

Items	Very Strongly Disagree	Strongly Disagree	Mildly Disagree	Neither agree nor disagree	Mildly Agree	Strongly Agree	Very Strongly Agree
1. There is a special person who is around when I am in need	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
2. There is a special person with whom I can share my joys and sorrows	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
3. My family really tries to help me	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
4. I get the emotional help and support I need from my family	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
5. I have a special person who is a real source of comfort to me	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
6. My friends really try to help me	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
7. I can count on my friends when things go wrong	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
8. I can talk about my problems with my family	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
9. I have friends with whom I can share my joys and sorrows	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
10. There is a special person in my life who cares about my feelings	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
11. My family is willing to help me make decisions	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐
12. I can talk about my problems with my friends	1 ☐	2☐	3☐	4☐	5☐	6☐	7☐

Appendix 4-15: MSPSS (Arabic)

نحن مهتمين عن شعورك تجاه البيانات التالية. اِقْرَأْي كلّ بيان بعناية. أَشيِري إلى كيف تَشعرين حول كلّ بيان.

ضعي دائرة حول رقم واحد (1) إذا كنتَ لا توافقين
ضعي دائرة حول رقم اثنين (2) اذا كنت محايدة
ضعي دائرة حول رقم ثلاثة (3) اذا كنت توافقين.
ضعي دائرة حول رقم (99) اذا كان لا ينطبق عليك (ارملة، مطلقة، او منفصلة)

	لا توافقين	محايدة	توافقين	لا ينطبق
	1	2	3	99
1. زَوْجي بجانبي عندما أكون محتاجة له.................................	1	2	3	99
2. أشاركَ فَرحتي و أحزاني مع زَوْجي..................................	1	2	3	99
3. تُحَاوِلُ عائلتي (سوى زَوْجي) أن تُسَاعِدَني....................	1	2	3	
4. أحصل على المساعدة العاطفيّة و الدعم الذي اِحْتَاجَه من عائلتي (سوى زَوْجي)	1	2	3	
5. زَوْجي هو مصدر حقيقي للراحة ليّ.................................	1	2	3	99
6. يُحَاوِلُ أَصْدِقائي مساعدتي..	1	2	3	
7. أَعْتَمِدَ على أَصْدِقائي عندما تسوء الامور معي......................	1	2	3	
8. أَتَحَدَّثَ عن مشاكلي مع عائلتي (سوى زَوْجي)......................	1	2	3	
9. عندي أَصْدِقاء أشاركَ فَرحتي و أحزاني معهم......................	1	2	3	
10. يَهْتَمُّ زَوْجي بمشاعري...	1	2	3	99
11. عائلتي (سوى زَوْجي) راغبة أن تُسَاعِدَني لاتخاذ قَرَارَات.........	1	2	3	
12. أَتَحَدّث عن مشاكلي مع أَصْدِقائي..................................	1	2	3	

Appendix 4-16: Permission to use MSPSS

(1) Professor Aroian permission

From: Karen Aroian <karoian@mail.ucf.edu>
Sent: 28 June 2010 15:10
To: Naglaa Youssef
Subject: Re: Multidimensional scale of perceived social support in Arabic
Attachments: MSPSS.docx

Naglaa,

You have my permission to use the Arab version but be sure to credit Dr. Zimit as the author of the original version. Also, please note, we adapted the Arab version so that special person on the original is "husband" on the Arab version. This should meet your needs but I want to make sure you are informed. I also want the Arab version to be properly referenced to me (Aroian) and for you to let me know how it performed in your study. The Arab version is attached. RE: time to complete the measure; my guess is 10 minutes at the most. Best wishes.

Karen
Karen Aroian, Professor
Karen Aroian karoian@mail.ucf.edu

(2) Professor Zimet permission

From: Zimet, Gregory D <gzimet@iupui.edu>
Sent: 17 January 2012 01:32
To: Naglaa Youssef
Subject: RE: Permission to use MSPSS

Dear Naglaa Youssef,

You have my permission to use the MSPSS in your research.

I hope your research goes well.

Sincerely yours,
Gregory D. Zimet, PhD
Professor of Pediatrics & Clinical Psychology
Section of Adolescent Medicine
Indiana University School of Medicine
Health Information & Translational Sciences
410 W. 10th Street, HS 1001
Indianapolis, IN 46202
USA
Phone: +1-317-274-8812
Fax: +1-317-274-0133
e-mail: gzimet@iupui.edu

Appendix 4-17: Training protocol for data collection assistant

1. Contents outlines of the protocol
2. Introduction
3. Process that was used to identify data collection assistant
4. What criteria that data collection assistant should have to be eligible for helping?
5. Objectives of training data collection assistant
6. The main objectives of these training sessions
7. Content that will cover
8. Tips to keep the team work
9. Objectives of the training program and how it will achieve
10. List of documents
11. Interview procedures

The document content is available but to save space it was not attached. Then you can ask the researcher to obtain it

Appendix 5-1: Permission for LDSI-2.0 tool to be translated into Arabic

(1) Doctor Robert A. de Man permission

From: R.A. de Man [r.deman@erasmusmc.nl]
Sent: 21 May 2010 21:40
To: Sally Wyke
Cc: 'b.hansen@erasmusmc.nl'; Naglaa Youssef; Ashley Shepherd
Subject: Re: Permission to translate and use LDSI 2.0

Dear dr. Wyke,
The LDSI has not been translated in arabic.
The questionaire is in the public domain so we give you permission to use it and wish you lots of succes with the planned studies.
Kind regards,
sincerely yours,
Robert A. de Man

Appendix 5-2: Information sheet (Pilot study-English)

UNIVERSITY OF
STIRLING

DEPARTMENT OF
NURSING AND MIDWIFERY

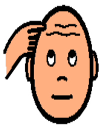
1. Title of research study

Pilot study to test the Arabic liver disease symptoms questionnaire

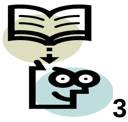
2. Invitation for taking part in research study

Would you like to take part in a pilot research study?

Before you decide, it is important for you to understand why the pilot study is being done and what it will involve.



Please take time to read/understand the following information sheet carefully and discuss it with the researcher or others if you wish. Please ask if there is anything that is not clear or if you would like more information.



3. Introduction about liver cirrhosis:

Liver cirrhosis is a chronic disease that leads to impaired liver functions as a result from fibrosis and scarring formation. Till now there is no definite management for curing patients from cirrhosis. Patients have only to keep taking prescribed medications and follow up with their doctor to prevent disease complications and stop cirrhosis to progress.

4. Background about this pilot study:

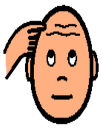
This pilot study is looking at testing the use of a questionnaire that has been translated into Arabic from English. I want to see if the questionnaire is easy to use or if during translation the questions are unclear for the Arabic speaker.

The pilot study is part of my PhD study research which I am doing at the

University of Stirling in the UK. The research study is funded by Egyptian government.

The research study will be conducted for three years.

It is up to you to decide whether or not to take part.



5. What will happen to the participants?

This is a pilot study to test a liver disease symptom questionnaire that is used for assessing the symptoms among patients with liver disease and how these symptoms affect these patients' daily activities and their social life. This questionnaire has recently been translated from English to Arabic in order to assess health-related quality of life and symptoms experience of patients with liver cirrhosis in Egypt.

I am interested in finding out whether the questionnaire is easily understood by participants and whether all the questions are clear.

Therefore, I will interview a sample of at least 30 patients with liver cirrhosis

I will ask questions to find out your thoughts about this questionnaire. Also, I will complete three questionnaires:

1) A background questionnaire that contains questions such as where you live, whether you work and your medical history with liver disease.

2) A questionnaire to assess if you experience any symptoms associated with your liver disease and how these may affect your everyday activities.

3) A questionnaire to assess what you think about your health status.

I will interview you for about one hour and this will take place in the hospital before or after consultation with the consultant (for out-patients) or in the patients' room (for admitted patients).

I need to interview you again for approximately 20 minutes to complete one of the questionnaires that mentioned before within the next three days after the first interview. You have the ability to refuse to attend the second interview.

If you like, you can ask a relative or friend to be present during the interview.

I just will take notes about what you are saying and complete the questionnaires.

There will be a private room for conducting the interview to maintain privacy.

You can ask me to stop to take a rest at any point during the interview.

6. Volunteer participation

If you would like to participate you will be asked to sign a consent form. You will be given a copy of the signed consent form to keep.

If you change your mind at any time about being involved, you can tell me to stop and you can withdraw from the study and withdraw your consent without having to say why.

Stopping will not affect your care.

7. Results of the study and confidentiality

The results of the study will be collected together and written in my PhD thesis (report) which will be ready in 2012. You will not be identified in the report.

All data will be kept confidential and I will make sure that you cannot be identified from any data collected. I will put a code, not your name, on the questionnaire. Also, nobody can see your medical records except me to collect your medical data. All your personal information will be stored in a locked filing cabinet and will be treated as confidential.

8. Medical research ethical approval

The Research Ethics Committee (REC) in the Department of Nursing and Midwifery, University of Stirling, UK has examined the proposal and has raised no objections from the point of view of medical ethics. The pilot study also has been approved by responsible institutes in Egypt whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

If you would like to talk to someone about the study, please contact Prof. Khairia Elsawy on 0102572350 (professor of nursing in Faculty of Nursing, Cairo University) who will be happy to discuss it with you.

Thank you for taking time to consider taking part in this study. If you would like to find out more about it, please contact me.

Naglaa Fathy Afifi Youssef
PhD student, Department of Nursing and Midwifery

University of Stirling - United Kingdom

I can be contacted in any of the following ways:

☎ **Telephone**: 0181725189; I am available all the day.

💻 **Email**: nagla.elshamy@gmail.com

Appendix 5-3: Information sheet (Pilot study-Arabic)

UNIVERSITY OF
STIRLING

DEPARTMENT OF
NURSING AND MIDWIFERY

وثيقة إعلام للمشاركة فى دراسة بحثية تجريبية

صفحة معلومات للمشاركين في البحث

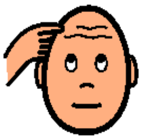
1. عنوان الدراسة

دراسة تجريبية لاختبار استبيان مؤشر أعراض مرض الكبد 2.0 المترجم الي العربيه

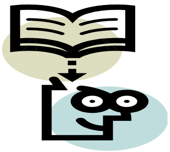
2. دعوة للمشاركة في الدراسة:

يدعوك الباحث للمشاركة في هذه الدراسة البحثية

هل تود المشاركة فى هذه الدراسة البحثية؟

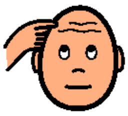


رجاء إستغرق وقتا كافيا لدراسة هذه المعلومات ولا تتردد في توجيه أي اسئلة للباحث إذا ماكان هناك أي شئ غير واضح لك.



3- مقدمة للمريض:

تليف الكبد هو مرض نتج عن تحول خلايا الكبد الطبيعية الى الياف و تكون ندبات مما ينتج عنه خلل فى اداء الكبد لوظائفه بصورة طبيعية. حتى الان ليس هناك علاج جذرى لمرض التليف الكبدى. العلاج الحالى يعتمد على المتابعة الدورية مع الطبيب و اخذ الادوية الموصوفة من قبل الطبيب المعالج لتقليص فرص تطور المرض و تقليل المضاعفات و الاعراض المصاحبة للمرض.



4. شرح موجز للدراسة التي ستجري والغرض من اجرائها

هذه الدراسة التجريبيه هى جزء من مشروعى البحثى المقدم للحصول على درجة الدكتوراة

هذه الدراسة التجريبية تهدف الى معرفة ما إذا كانت الاستبيان المسمي "مؤشر أعراض مرض الكبد 2.0 " التي تم ترجمتها من الانكليزية الى العربية يسهل فهمها من قبل المشاركين في الاستبيان وأيضا ما إذا كانت جميع الأسئلة واضحة.

يتم استخدام ا الاستبيان لتقييم الأعراض التي يعاني منها مرضي تليف الكبد وكيف تؤثر هذه الأعراض علي

أنشطتهم اليومية وحياتهم الاجتماعية.

و لك الحرية فى الاختيار بالموافقة او الرفض للمشاركة فى الدراسة

5. وصف البحث:

عدد المشاركين فى البحث على الاقل 30 مريض من مرضى التليف الكبدى فى مصر. سيتم اختيار المشاركين الذين تنطبق عليهم شروط المشاركة من العيادات الخارجية و الاقسام الداخلية.

سوف يتم مقابلة المرضى المشاركين فى هذه الدراسة مرتين :

في المقابله الاولي: سيقوم الباحث بملىء الأستمارات البحثية

هناك ثلاثة استبيانات سيتم ملئها:

1) استبيان البيانات الديموجرافيه مثل التاريخ المرضى, السن.
2) استبيان لتقييم الأعراض المصاحبة لمرضي الكبد وكيف تؤثر على نشاطاتهم اليومية.
3) استبيان لتقييم ما رأيك في صحتك

مدة المقابلة بالتقريب ساعة و سيكون مكان المقابلة داخل المستشفى

سيكون موعد المقابلة بلاتفاق مع المريض (قبل او بعد الاستشارة الطبية او فى يوم آخر داخل المستشفى)

المطلوب من المشارك طوال فترة الدراسة هو الموافقة على المشاركة فى الدراسة ثم الاجابة على الاسئلة المطروحة و رائيك حول هذا الاستبيان.

في المقابله الثانيه: سيقوم الباحث بملىء استماره بحثية واحده, مدة المقابلة بالتقريب 20 دقيقه و سيكون مكان المقابلة داخل المستشفى و سيكون موعد المقابلة بلاتفاق مع المريض

يمكنك الاتشارك في المقابله الثانيه

إذا أردت ، يمكنك ان تطلب من قريب أو صديق ليكون حاضرا خلال المقابلة.
سوف اكتب ملاحظات حول ما تقوله ولا استكمال الاستبيانات.

وسيكون هناك غرفة خاصة لإجراء المقابلة للحفاظ على خصوصية المريض المشارك

يمكنك أن تطلب مني أن أتركك لتأخذ قسطا من الراحة في أي لحظة خلال المقابلة.

هذه الدراسة البحثية هى دراسة خارجية بتمويل من الحكومة المصرية للحصول على الدكتوراه من جامعة استرلنج باللملكة المتحدة البريطانيه.

مدة الدراسة 3 سنوات

6. وصف الهدف النهائي للبحث:

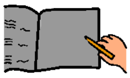
الهدف من هذه الدراسة التجريبية هو معرفة ما إذا كانت اداة الاستبيان "مؤشر أعراض مرض الكبد 2.0 " التي تم ترجمتها من الانكليزية الى العربية يسهل فهمها من قبل المشاركين في الاستبيان وأيضا ما إذا كانت جميع الأسئلة واضحة.

7. الاشتراك التطوعي:

يمكن للمريض عدم الاشتراك او الانسحاب من الدراسة في اي وقت بدون ابداء اسباب و دون أن يؤثر ذلك علي علاجه أو علاقته مع الاطباء المعالجين او الممرضات.

8- حماية بيانات:

لن يستخدم اسم المريض وسوف يشار اليه برمز وستظل هويته غير معلنة في ايه نتائج ولكن سوف يسمح لفريق البحث (الباحث الاساسى فقط) في الإطلاع علي الملف الطبى.



9- **نتائج الدراسة:**

نتائج الدراسة سوف يتم تجمعها و كتابتها فى رسالة الدكتوراة التى سوف تكون جاهزة للمناقشة بعام 2012

10- **لجنة أخلاقيات البحث العلمى:**

هذا البحث تمت الموافقة عليه من قبل لجنة أخلاقيات البحث العلمى بكلية التمريض- جامعة استرلنج, اسكتلند, المملكة المتحدةالبريطانية والتي تدقق بأن كل الشروط التي تتعلق بسلامتك وحقوقك محترمة و محفوظة طول مدة الدراسة. وقد أعطيت الموافقة علي هذا البحث بتاريخ 2010/9/8

11- يمكنك الإتصال بالباحث:

في حالة احتياجك لمعرفة المزيد عن الدراسة و مناقشاتها يمكنك الاتصال بدكتورة خيرية الصاوئ على هذا الرقم 0102572350 او بالباحث
اسم الباحث: نجلاء فتحى عفيفى يوسف
طالبة دكتوراة, قسم التمريض
جامعة استرلنج, المملكة المتحدة البريطانية
الهاتف:0181725189
وقت الأتصال: يمكنك الاتصال فى اي وقت
البريد الالكترونى: Nagla.elshamy@gmail.com

إذا وافقت علي الإنضمام الي هذا البحث سوف تعطى الباحث موافقة كتابية بالموافقة على المشاركة و لديك الحق في الاحتفاظ بنسخة من هذه الوثيقة بعد أن توقعها.و يمكنك الاتصال برقم الهاتف السابق في اى وقت اذا ما كانت لديك اسئلة

شكرا" لمشاركتك فى هذه الدراسة

Appendix 5-4: Informed consent (Pilot study-English)

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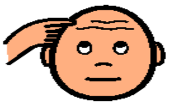
NURSING AND MIDWIFERY

Pilot study to test the Arabic liver disease symptoms questionnaire

Please answer the following questions with yes (√) or no (X) to be sure you understood the content of the information sheet.

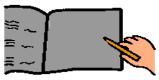
I have read/informed well the information sheet ☐

I have had the chance to ask questions and talk about the research study ☐



I have been informed and understand it is voluntary participation ☐

I have been informed that I can withdraw from the study at any time without saying why ☐

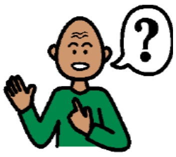


I have been informed and understand the data and my confidentiality will be protected ☐

I have taken copy of the informed consent ☐

I am happy to take part in the above pilot study ☐

I am happy to take part in the second interview in the above pilot study ☐



Do you have any other question before giving your consent ☐

Participant's name:……………………..........Signature:………………………..
To be used if participant is unable to sign
Name:……………………………………Signature:…………………………..
Name of person taking consent:………………………Signature:………………………..
Date:…………………………………….

Appendix 5-5: Informed consent (Pilot study-Arabic)

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DEPARTMENT OF
NURSING AND MIDWIFERY

وثيقة قبول (موافقة) على الاشتراك فى دراسة بحثية تجريبية

عنوان الدراسة البحثية تجريبية

دراسة تجريبية لاختبار استبيان مؤشر أعراض مرض الكبد 2.0 المترجم الي العربيه

من فضلك اجب على هذه الاسئلة بنعم (√) او لا (x) للتاكد من انك قد فهمت كل المعلومات الخاصة بالبحث

لديك الحق في الاحتفاظ بنسخة من هذه الوثيقة بعد أن توقعها.

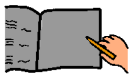
أعلمت بشكل صحيح بالدراسة البحثية المقترحة. ☐

إستلمت نسخة من صفحة معلومات المريض. ☐

اتيحة لى الفرصة للاستفسار عن الدراسة ☐

اعلمت بان إشتراكي تطوعي تماماً ولدي الحق في سحب موافقتي في أي وقت بدون أبداء تفسير أو اسبا
ولن يوثر ذلك علي علاقتي مع طبيبي المعالج او الممرضة. ☐

اعلمت بان البيانات والمعلومات التي ستجمع منى اوعني ستكون سرية ويتم التصرف فيها طبقا لقانون
حماية المعلومات الخاصة بالآشخاص فيما يتعلق بالبيانات الشخصية ☐

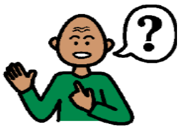


أوافق علي المشاركة في الدراسة البحثية التى تحت عنوان
دراسة تجريبية لاختبار استبيان مؤشر أعراض مرض الكبد 2.0 المترجم الي العربيه
والمسجلة بقسم التمريض- جامعة استرلنج بالمملكة المتحدة البريطانية ☐

☐

أوافق علي المشاركة في المقابله الثانيه
اوافق على ان تطلع على ملفى الطبى

إستلمت نسخة من وثيقة الموافقة (قبول الاشتراك) ☐



هل هناك اى سوال تود الاستفسار عنه قبل اعطاء الموافقة ☐

أسم المريض: ....
توقيع المريض: .... التاريخ: / /
أسم وكيل المريض فى حالة عدم القراءة والكتابة:...
توقيع وكيل المريض: ....التاريخ: / /
اسم الباحث:..
توقيع الباحث:....................................التاريخ: / /

هذه الوثيقة أعدت مع الاخذ في الاعتبار لكلا من:

إعلان الرابطة العالمية والمتبني من مؤتمر الجمعية الطبية العالمية الثامن عشر الذي عقد بهلسنكي بفنلندا في يونيو 1964. والذي روجع اعوام 1975؛ 1983؛ 1989 ؛ 1996 وفي السادس من اكتوبر 2000 في ادنبرة اسكتلنداwww.wma.net

سبتمبر CPMB/ICH/35/951997 للمارسة السريرية الجيدة ICH-GCPتوجيهات

التوجيهات الاخلاقية العالمية للبحث الطبي الحيوي المتضمن ادمين مجلس للمنظمات العالمية من العلوم الطبية CIOMS1993 (جنيف عام)

منظمة الصحة العالمية : التوجيهات العلمية للجنة الاخلاقية لمراجعة البحوث الطبية الحيوية جنيف عام 2000.

Appendix 5-6: List of committee members

Reviewers	**Experience and speciality**	**Department**
Prof. Sharazad Ghazies	Dean of Faculty of Nursing Prof. of Medical-Surgical Nursing (Adult nursing)	Faculty of Nursing, British University, Egypt
Prof. Kairia El-Sawia	Prof. of Medical- Surgical Nursing (Adult nursing)	Medical Unit, Faculty of Nursing, Cairo University, Egypt
Dr. Naglaa Zayd	Lecturer of Tropical Medicine, Consultant of Hepatology and Gastroenterology, Researcher	Department of Tropical Medicine Gastroenterology and Liver Diseases, Kasr El Aini, Egypt Faculty of Medicine, Cairo University, Egypt
Ali Alshraifeen	PhD student in the UK	School of Nursing, Midwifery and Health, University of Stirling
Nahla Hassan	MPhil student in the UK	School of Languages, Cultures and Religions, University of Stirling

Appendix 5-7: Guidance sheet for assessing face and content validity of the LDSI-2.0

The questionnaire of Liver disease symptom Index 2.0 (LDSI-2.0) has been translated from English to Arabic to use among patients with liver disease in Egypt. I would like to know your feedback about the questionnaire (LDS1-2.0) to what extent the English and Arabic versions are similar and its items appropriate to Egyptian people. Please read each question in the following table and answering it by giving your point of view during comparing between the two versions (Arabic and English Copies) by selecting from that scale:

1. Strongly agree 2. Agree 3. Disagree 4. Strongly disagree

LDSI's items	**Is the translation similar in two versions?**	**The item has to be modified?** **How? write your notes**	**Is the item valid to the target cultural context (Egypt)?** i.e.it gather information about symptoms among patients with liver disease in Egypt	**Is the concept valid in the target culture (Egyptian)?** i.e. depression, pain, within the tool	**Is the phrasing clear in Arabic and English versions?**	**Additional comment**

Appendix 5-8: Observation sheet to evaluate feasibility of the Arabic LDSI-2.0

Participant's code: **Date:**

1. How long did it take to complete the LDSI-2.0 from the patient? (Administration time)
    - ○ 0-5 minutes
    - ○ 6-10 minutes
    - ○ 11-15 minutes
    - ○ 16-20 minutes
    - ○ 20 minutes +
2. Write **(√)** if the answer is Yes or write **(X)** if the answer is No

Tools' items	**Difficult and Missing items**					**Researcher's comment**
	Did patient provide a specific answer?	Did patient give an open ended answer?	Researcher asks: What do you mean by this answer? **(in case the patients gave open ended answer)** Did patient give a miss understood answer again?	Did patient need clarification?	Did patients cannot understand the item completely?	

Appendix 5-9: LDSI-2.0 (Arabic)

مؤشر أعراض مرض الكبد 2.0

استبيان

هذا الاستبيان يستفسر عن شدة الاعراض التى تشعر بها و تعانى منها و الى اى مدى هذه الاعراض تؤثر على عملك او انشطتك اليومية او الاجتماعية. سوف تقوم بتحديد الإجابة التي تنطبق عليك. جميع الاسئلة متصلة بالاسبوع الماضي.

على سبيل المثال :

البند 1 : إلى أي مدى في الاسبوع الماضي: شعرت بألم؟

0 لم يحدث على الإطلاق	1	2	3	4 إلى حد كبير

البند 2 : إلى أي مدى في الاسبوع الماضي: أعاقك الألم في عملك أو فى أنشطتك اليومية ؟

0 لم يحدث على الإطلاق	1	2	3	4 إلى حد كبير

مؤشر أعراض مرض الكبد 2.0	**لم يحدث على الإطلاق 0 ☐☐☐☐☐ 4إلى حد كبير**
(1أ) إلى أي مدى في الأسبوع الماضي: عانيت من حكة / هرش بجسمك؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(1ب) إلى أي مدى في الأسبوع الماضي: اعاقتك الحكة /الهرش بجسمك في عملك أو أنشطتك اليومية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(1ج) إلى أي مدى في الأسبوع الماضي: اعقتك الحكة /الهرش بجسمك اثناء النوم؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(2أ) إلى أي مدى في الأسبوع الماضي: عانيت من ألم في المفاصل؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(2ب) إلى أي مدى في الأسبوع الماضي: اعاقك ألم المفاصل في عملك أو فى أنشطتك اليومية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(3أ) إلى أي مدى في الأسبوع الماضي: عانيت من ألم في الجانب العلوي الأيمن من البطن؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(3ب) إلى أي مدى في الأسبوع الماضي: اعاقك ألالم في الجانب العلوي الأيمن من البطن في عملك أوفى انشطتك اليومية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(4أ) إلى أي مدى في الأسبوع الماضي: كان النوم يغلبك أثناء النهار؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(4ب) إلى أي مدى في الأسبوع الماضي: اعاقك النوم أثناء النهار في عملك أوفى أنشطتك اليومية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(5أ) إلى أي مدى في الأسبوع الماضي: كنت قلقاً بشأن تأثير مرض الكبد الذي تعاني منه على الوضع العائلى/ اسرتك؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(5ب) إلى أي مدى في الأسبوع الماضي: أعاقك القلق *(القلق من تاثير مرض الكبد على حياتك العائلية)* في عملك أو فى أنشطتك اليومية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(6أ) إلى أي مدى في الأسبوع الماضي: كان لديك ضعف فى الشهية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(6ب) إلى أي مدى في الأسبوع الماضي: أعاقك ضعف الشهية الذي تعاني منه؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(7أ) إلى أي مدى في الأسبوع الماضي: شعرت بالاكتئاب *(الحزن الشديد)* بسبب مرضك؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(7ب) إلى أي مدى في الأسبوع الماضي:	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير

أعاقك الاكتئاب بسبب مرضك في عملك، أنشطتك اليومية و/أو علاقاتك الاجتماعية؟	
(8) إلى أي مدى في الأسبوع الماضي: شعرت بالخوف من احتمال تطور مضاعفات مرض الكبد؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(9أ) إلى أي مدى في الأسبوع الماضي: تغير لون جلدك الى الاصفر (*صفراء*)؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(9ب) إلى أي مدى في الأسبوع الماضي: أعاقك اصفرار لون جلدك في عملك، أنشطتك اليومية و/أو علاقاتك الاجتماعية؟	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(10) *بسبب أنك تعاني من مرض الكبد فإنك تجد صعوبة في تذكر الأشياء ، على سبيل المثال: الأشياء التي وقعت حديثاً، وكذلك الأماكن التي تركت فيها الأشياء والمواعيد التي اتفقت عليها.* (*الى اى مدى منذ ان اصبت بمرض الكبد اصبحت تنسى*)	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(11) الى اى مدى تغيرت شخصيتك (*طباعك*) بسبب مرض الكبد.	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(12) الى اى مدى يمثل مرض الكبد الذي تعاني منه إعاقة لشئونك المالية (*مثال: مصاريف البيت*).	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(13) الى اى مدى مرض الكبد الذي تعاني منه يجبرك على استغلال وقتك بطريقة مختلفة عما تريده في الواقع (*يمنعك من استغلال وقتك*)	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(14) الى اى مدى قل اهتمامك/ رغبتك للعلاقة الزوجية (*الجنسية*) منذ علمك بانك تعاني من مرض كبدي.	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير
(15) الى اى مدى قل نشاطك/ممارستك للعلاقة الزوجية (*الجنسية*) منذ علمك بانك تعاني من مرض كبدي	لم يحدث على الإطلاق ☐☐☐☐☐إلى حد كبير

هل هناك اى اعراض اخرى تعانى منها؟

ما هى؟---

و الى اى مدى شدتها؟---

و الى اى مدى أعاقتك في عملك، أنشطتك اليومية و/أو علاقاتك الاجتماعية؟---------------------