ASSESSMENT OF KNOWLEDGE AND ADHERENCE TO MEDICATION: A MIXED METHODOLOGY STUDY AMONG PATIENTS WITH TYPE-2 DIABETES MELLITUS IN PENANG

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Conference Presentations

1- Harith K. Al-Qazaz, Syed A. Sulaiman, Mohamed A. Hassali. Experience and knowledge of diabetic patients about their medications use: a qualitative study among patients attending a university primary care center in Malaysia. [poster presentation] *ACCP conference 2009*, September 26-28, Coex, Seoul, Korea.

2- Al-Qazaz HK, Sulaiman SAS, Hassali MA, Shafie AA, Sandrum S. Diabetes knowledge and its association with glycaemic control in Penang , Malaysia. The 10th Asian Conference in Clinical Pharmacy ACCP, 9-12 July, 2010 Singapore.

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4- Al-Qazaz HK, Hassali MA, Shafie AA, Sulaiman SA, Sundram S. Translation and validation of Michigan diabetes knowledge scale into Malaysian version. ISPOR 4th Asia-pacific conference, 5-7 September, 2010, Hilton Phuket, Phuket, Thailand.

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7- Al-Qazaz HK, Sulaiman SAS, Hassali MA, Shafie AA, Sandrum S. Does Diabetes medication adherence alone influence optimum glycemic control? Results from cross sectional study on diabetic patients in Malaysia. Health Services Research and Pharmacy Practice Conference 5 – 6 May 2011, Norwich, United Kingdom.

LIST OF ABBREVIATIONS

ACCORD	The Action to Control Cardiovascular Risk in Diabetes
ADA	American Diabetes Association
ADVANCE	Action in Diabetes and Vascular disease: preterAx and diamicroN Controlled Evaluation
BMI	Body Mass Index
BP	Blood Pressure
CVD	Cardiovascular Disease
DCCT	Diabetes Control and Complications Trial
DM	Diabetes Mellitus
DSME	Diabetes Self-Management Education
FBS	Fasting Blood Sugar
HDL-C	High Density Lipoprotein Cholesterol
HbA1C	Hemoglobin A1C
LDL-C	Low Density Lipoprotein Cholesterol
MDKT	Michigan Diabetes Knowledge Test
MMAS	Morisky Medication Adherence Scale
MREC	Medical Research and Ethics Committee
NHMS III	Third National Health and Morbidity Survey
TC	Total Cholesterol
TG	Triglyceride
UKPDS	United Kingdom Prospective Diabetes Study
USM	Universiti Sains Malaysia
WHO	World Health Organisation

PENILAIAN TENTANG PENGETAHUAN DAN KEPATUHAN TERHADAP PENGUBATAN: SUATU KAJIAN METODOLOGI BERCAMPUR DALAM KALANGAN PESAKIT DENGAN DIABETES MELLITUS JENIS 2 DI PULAU PINANG

ABSTRAK

Prevalens diabetes mellitus telah meningkat begitu ketara dalam kalangan populasi Malaysia sejak dekad yang lalu. Tambahan pula, pengurusan diabetes yang berkaitan morbiditi sentiasa berdepan dengan cabaran oleh penyedia penjagaan kesihatan. Dalam usaha menyediakan pengurusan penyakit yang optimum, terdapat keperluan bagi mendedahkan pesakit diabetis terhadap pendekatan pengurusan diri diabetes. Walaupun langkah perlu telah diambil untuk meningkatkan kawalan glisemik dalam kalangan pesakit diabetes di Malaysia, namun hasilnya masih belum mencukupi. Kepatuhan terhadap pengubatan, tahap pengetahuan pesakit serta persepsi mereka tentang diabetes masih belum didokumenkan sebaiknya di negara-negara sedang membangun. Kebanyakan usaha intervensi untuk meningkatkan kepatuhan terhadap pengubatan dan amalan pengurusan-diri diserapkan dalam kandungan pendidikan. Intervensi ini berdasarkan andaian bahawa pengetahuan tentang diabetes mungkin memberi kesan terhadap kesedaran pesakit serta mempengaruhi kepatuhan mereka terhadap regimen rawatan. Dalam konteks ini, kajian yang dijalankan di Malaysia tentang diabetes dan kepatuhan terhadap pengubatan adalah agak terbatas. Di samping itu, pengalaman dan persepsi pesakit diabetes tentang penyakit dan pengubatannya tidak banyak ditonjolkan.

Dalam usaha meneroka serta memahami kepercayaan dan pengalaman pesakit, kaedah penyelidikan kualitatif dikira amat berguna. Malahan, ia dapat menjelaskan senario ini dengan lengkap, yang tidak mampu dijelaskan melalui penyelidikan kuantitatif. Justeru, metodologi rentas campuran (kajian kualitatif dan kuantitatif) ini secara prinsipnya bertujuan menilai pengetahuan pesakit tentang diabetes dan juga kepatuhan terhadap pengubatan dan perkaitannya dengan kawalan glisemik.

Dalam usaha meneroka persepsi, pengetahuan dan pengalaman pesakit tentang diabetes, dua belas orang pesakit ditemu bual. Hasil analisis kandungan tema daripada temu bual mengenal pasti empat tema utama: pengetahuan tentang diabetes dan pengubatannya, pengalaman kesan berbahaya daripada pengubatan, isu berkaitan kepatuhan, dan impak daripada perkaitan perubatan dan keluarga terhadap kesejahteraan hidup. Pengalaman kesan berbahaya daripada pengubatan dan penyakit, pengetahuan diabetes, perkaitan pesakit-preskriber, sokongan sosial dan kepercayaan pesakit dan sikap yang wujud untuk memainkan peranan dalam isu kepatuhan pengubatan.

Ujian Pengetahuan Diabetes Michigan (Michigan Diabetes Knowledge Test, MDKT) dan Skala Kepatuhan Pengubatan Morisky (Morisky Medication Adherence Scale, MMAS) digunakan untuk menilai pengetahuan diabetes secara umum dan kepatuhan terhadap pengubatan. Sampel seramai 307 orang pesakit dipilih daripada klinik pesakit luar diabetes di Hospital Pulau Pinang untuk mengesahkan kedua-dua skala ini dari segi versi Malaysia. Suatu prosedur standard "maju-mundur" digunakan untuk menterjemah skala ini ke dalam bahasa Melayu. Kebolehpercayaannya diuji bagi ketekalan dalaman dan kesahihannya disahkan melalui kumpulan yang diketahui dan konvergen, MMAS dan MDKT menunjukkan ketekalan dalaman yang boleh diterima dan kebolehpercayaan ujian-ujian semula. Bahagian kajian ini

merumuskan bahawa kedua-dua MDKT dan MMAS adalah sahih dan boleh dipercayai dan boleh digunakan dalam kalangan pesakit diabetes dalam konteks Malaysia.

Kohort seramai 540 orang pesakit dipilih daripada klinik pesakit luar diabetes di Hospital Pulau Pinang bagi penilaian pengetahuan diabetes, kepatuhan pengubatan, dan kawalan glisemik. Dapatan kajian menunjukkan bahawa 41.8% dan 42.2% daripada pesakit masing-masing mempunyai tahap pengetahuan diabetes dan kepatuhan pengubatan yang rendah. Daripada keseluruhan kohort, hanya 20.8% pesakit mencapai kawalan glisemik yang baik. Perkaitan yang signifikan ditemui di antara tiga pemboleh ubah: HbA1C, pengetahuan diabetes dan kepatuhan terhadap pengubatan. Peramal kawalan glisemik yang baik adalah tahap pengetahuan yang tinggi tentang diabetes dan kepatuhan terhadap pengubatan, dan juga terapi mono bagi pengurusan diabetes.

Justeru, dirumuskan bahawa pengetahuan pesakit tentang diabetes adalah dikaitkan dengan kepatuhan terhadap pengubatan dan kawalan glisemik yang lebih baik. Sehubungan dengan faktor lain yang menpengaruhi kepatuhan terhadap pengubatan dan kawalan glisemik, maka penyedia penjagaan kesihatan sepatutnya memberikan tumpuan terhadap tahap pengetahuan pesakit apabila mempertimbangkan kepatuhan mereka terhadap pengubatan. Usaha keras diperlukan untuk meningkatkan pengetahuan pesakit dan seterusnya kepatuhan terhadap pengubatan dan kawalan glisemik. Hasil kajian ini mengutarakan beberapa cadangan bagi penilaian secara berkala tentang pengetahuan pesakit berhubung dengan kepatuhan pengubatan dan penggunaan program pendidikan untuk meningkatkan keupayaan pengurusan diri pesakit.

ASSESSMENT OF KNOWLEDGE AND ADHERENCE TO MEDICATION: A MIXED METHODOLOGY STUDY AMONG PATIENTS WITH TYPE-2 DIABETES MELLITUS IN PENANG

ABSTRACT

The prevalence of diabetes mellitus had increased tremendously among the Malaysian population during the last decade. Furthermore, managing diabetes related morbidity is always faced with challenges by the healthcare providers. In order to provide optimal disease management, there is a need for diabetic patients to be exposed to diabetes self management approach. Although numerous measures have been taken to improve glycemic control among patients with diabetes in Malaysia, the results are still unfavorable. Adherence to medications, level of knowledge of patients' and the perception they carry about diabetes has not been well documented in developing countries. Most interventions attempted to improve medication adherence and self-management practices were educational in context. These interventions were based on the assumption that knowledge regarding diabetes might affect patients' awareness and influence their adherence to treatment regimen. Within this context, limited studies have been conducted in Malaysia focusing on knowledge towards diabetes and medication adherence. In addition, experiences and perceptions of diabetic patients about the disease and its medications are not highlighted.

In order to explore and understand patients' beliefs and experiences, qualitative research methods found to be useful. It even enlightens the aspects of research which quantitative research alone is unable to uncover, and to explain the complete scenario in the research field. Therefore, this cross-sectional mixed methodology (qualitative

and quantitative study) principally aimed to evaluate patients' knowledge about diabetes as well as medication adherence and its association with glycemic control.

In order to explore patients' perception, knowledge and experience about diabetes, twelve patients were interviewed. Thematic content analysis of the interviews identified four major themes: knowledge about diabetes and its medication, experiences of adverse effects of medication, issues related to adherence, and the impact of medical and family relationships on well-being. Experience of adverse effects of medication and disease, diabetes knowledge, the patient–prescriber relationship, social support and patients' belief and attitudes appeared to play a role in the issue of medication adherence.

The Michigan Diabetes Knowledge Test (MDKT) and the Morisky Medication Adherence Scale (MMAS) were used for the assessment of general diabetes knowledge and medication adherence respectively. A sample of 307 patients was conveniently recruited from the outpatient diabetes clinic at Hospital Pulau Pinang for the purpose of validation of Malaysian versions of these two scales. A standard "forward-backward" procedure was used to translate the scales into the Malay language. Reliability was tested for internal consistency and validity was confirmed using convergent and known group validity. MMAS and MDKT showed acceptable internal consistency and test-retest reliability. This part of the study concluded that both MDKT and MMAS were valid and reliable and can be used among patients with diabetes in the Malaysian setting.

A cohort of 540 patients was conveniently recruited from the outpatient diabetes clinic at Hospital Pulau Pinang for the evaluation of diabetes knowledge, medication adherence and glycemic control. The study findings revealed that 41.8% and 42.2%

of patients respectively had a low level of diabetes knowledge and medication adherence. Of the entire cohort, only 20.8% of patients achieved good glycemic control. Significant associations were found between the three variables HbA1C, diabetes knowledge and medication adherence. Predictors of good glycemic control were a higher level of diabetes knowledge, a higher level of medication adherence and mono therapy for diabetes management.

Therefore, it is concluded that patients' knowledge about diabetes is associated with better medication adherence and better glycemic control. In addition to other factors affecting medication adherence and glycemic control, healthcare providers should pay attention to the level of knowledge held by patients when considering their medication adherence. Extra effort is required to improve patients' knowledge and thus medication adherence and glycemic control. The study results reinforce the recommendations for the periodic assessment of patients' knowledge regarding medication adherence and the use of educational programs to improve the self-management ability of patients.

CHAPTER ONE: INTRODUCTION

1.1 Background of the study

In recent decades, the ability to diagnose and treat by the medical professionals has greatly grown with an increase in medical knowledge and new technologies. However, the effectiveness of this growth is challenged by the requirement of patients to change their behavior. All over the world, there have been rapid changes in disease prevalence. Diabetes mellitus (DM), along with the other chronic diseases such as heart diseases, stroke, cancer, hypertension and mental illnesses, now accounts for 47% of the global health burden of disease and 60% of all deaths (Fincham, 2007).

The prevalence of diabetes is increasing continuously. High levels of its morbidity and mortality is a mounting health problem in the contemporary era. More than 171 million people were affected by diabetes worldwide in 2000 and the prevalence of this disease is estimated to be 366 million in 2030 (Wild *et al.*, 2004). According to Frank Vinicor (the director of the division of diabetes translation at the Centers for Disease Control and Prevention in Atlanta) "every 24 hours, 4,100 new diabetes cases are diagnosed in the U.S., at least 810 people die, 230 undergo amputation, 120 learn they need kidney dialysis or transplant, and 55 go blind" cited from (Beckley, 2006). Type 2 diabetes accounts for about 90% of cases of diabetes and is more likely to occur in developing countries due to a sedentary lifestyle, aging, obesity and poor dietary habits (World Health Organisation, 2009). Diabetes can affect any person of either gender, at any age from any race and socio-economic background, but Asians are affected more than Caucasians (International Diabetes Federation, 2005).

Diabetes epidemic is mainly found in Asia. The prevalence of diabetes in this racially heterogeneous population with different demographical, cultural and socio-economic backgrounds has rapidly increased among urban and younger people (Chan *et al.*, 2009; Ramachandran *et al.*, 2009; Sicree *et al.*, 2006; Wild *et al.*, 2004; Yoon *et al.*, 2006). Countries undergoing substantial economic growth are more likely to show an increased prevalence of diabetes, and epidemiological data from Asian countries has attracted attention to this problem (Ramachandran *et al.*, 2009). The proportion of urbanization in Singapore, Korea, Malaysia, the Philippines and Indonesia will be more than 50% by 2010 (Ramachandran *et al.*, 2009). Urban lifestyles are associated with changes in the level of physical activity and increased diversity of the diet, including animal-based foods along with more unsaturated and total fats and a low intake of fiber. Chronic diseases like diabetes are diet-related and the effect of poor dietary habits is significant to the etiology of these diseases (Chan *et al.*, 2009; Ramachandran *et al.*, 2009). However, Asian populations tend to develop diabetes with a lower degree of obesity and at a younger age, meaning that they suffer longer from complications and die sooner than people from other regions (Ko *et al.*, 1999; Yoon *et al.*, 2006).

1.2 Diabetes in Malaysia

Malaysia is a multiethnic country with a total population of 28.25 million (Department of Statistics Malaysia, 2010). According to the Third National Health and Morbidity Survey (NHMS-3) in Malaysia, the prevalence of type 2 DM in adults aged 30 years and over now stands at 14.9%, increased from 8.3% in 1996, with the highest prevalence among those of Indian ethnicity (National Health and Morbidity

Survey III, 2006). The number of people with diabetes is expected to increase from 1,846,000 in 2010 to 3,254,994 in 2030, and the adjusted prevalence of diabetes (adjusted to the world population) in Malaysia will rise from 11.6% in 2010 to 13.8% in 2030 (International Diabetes Federation, 2009). In the Malaysian Ministry of Health, there is an increasing interest in the increasing prevalence of chronic disease, including diabetes, within the population (Lim and Morad, 2004). This increase in prevalence of diabetes is associated with many factors, including rapid economic growth of the country in the last few decades, urbanization and industrialization which have resulted in more overweight/obese people and a sedentary population (Ismail *et al.*, 2002; Kee *et al.*, 2008; Mustaffa, 2004; Rashid, 2008). A jumping transformation in socioeconomic and demographic status over the last two decades has occurred in Malaysia as a result of massive industrialization and globalization with an improved educational system (Yun *et al.*, 2007). As a result, the standard of living, quality of life, population and the concomitant ageing of the population and reduction in the death rate have improved (Yun *et al.*, 2007). The Malaysian population in the age group of 65 years and above has increased from 4.3 % in 2005 to 4.8 % in 2007 which indicates that the number of Malaysian senior citizens has gradually increased over time compared to the younger group (Yahya *et al.*, 2008). In this age group, around 25% to 30% of people have diabetes or glucose intolerance (Wild *et al.*, 2004).

1.3 Diabetes Care in Malaysia

Diabetes cannot be cured, but can be controlled with combination of medical care, patients education and patient self-management (American Diabetes Association,

2009; Ministry of Health Malaysia, 2009). Multiple diabetes complications (vascular complications) in Malaysian patients with type 2 diabetes have been found to be as high as 38% (Dhanjal *et al.*, 2001; Mafauzy, 2006; Mimi *et al.*, 2003; Ooyub *et al.*, 2004). Out of all the patients who require dialysis in Malaysia, 57% are as a result of diabetic nephropathy (Lim and Lim, 2006) and 55% of patients who suffered from stroke were patients with diabetes (Hamidon and Raymond, 2003; Wong, 1999). Diabetes was the eighth in the list of top ten causes of death by non-communicable diseases, and diabetes also was the fifth most important cause of disability in adjusted life years (Yusoff *et al.*, 2005). Studies on diabetes in Malaysia reported that a large proportion of patients had poor or suboptimal glycemic control and the mean HbA1C was higher than the recommended HbA1C level according to international guidelines (Chuang *et al.*, 2002; Ismail *et al.*, 2001; Ismail *et al.*, 2000; Kamarul Imran *et al.*, 2010; Mafauzy, 2005; Mafauzy, 2006; Mimi *et al.*, 2003; Sulaiman *et al.*, 2004; Tan *et al.*, 2008; Wong and Rahimah, 2004; Yusof *et al.*, 2009).

1.4 General diabetes knowledge

A low level of awareness within the population, among health professionals and a low priority to initiate an appropriate preventive and curative plan have been identified as major issues in the management of diabetes (Ooyub *et al.*, 2004). A low level of diabetes knowledge among patients with diabetes has been identified in other countries (Al Shafaee *et al.*, 2008; Angeles-Llerenas *et al.*, 2005; Bell *et al.*, 1997; Bruce *et al.*, 2003; Caliskan *et al.*, 2006; Gunay *et al.*, 2006; Habib and Aslam, 2003; Kamel *et al.*, 1999; McClean *et al.*, 2001; Murata *et al.*, 2003; Murugesan *et al.*, 2007; Speight and Bradley, 2001; West and Goldberg, 2002). Diabetes self-

management is a cornerstone for the proper management of patients with diabetes, and diabetes education has a role in improving diabetes outcomes (Funnell *et al.*, 2007; Simmons *et al.*, 1994). Diabetes self-management education has shown a positive effect on glycemic control, lipid and blood pressure control in patients with diabetes (Gagliardino and Etchegoyen, 2001; Norris *et al.*, 2001). Knowledge of diabetes is a central part in informed decision making on the pharmacological and non-pharmacological aspects of diabetes management and evaluation of patients needs, and has been recommended to achieve better metabolic control (Al-Adsani *et al.*, 2009; Mensing *et al.*, 2007; Murata *et al.*, 2003). However, modest improvements in glycemic control have been found after educational intervention with diabetes patients (Acik *et al.*, 2004). Improved information from the family physician to patients with chronic diseases has also been recommended to improve medication adherence (Burge *et al.*, 2005; Karaeren *et al.*, 2009). A well-developed educational program is essential for the improvement of medication adherence and diabetes outcomes in terms of glycemic control and an evaluation of the educational needs for patients is essential as a first step.

1.5 Medication adherence

Self-management and health behavior changes play central roles in diabetes care. In order to achieve optimal health, the diabetes patients are usually advised on appropriate diet, exercise, frequent medical examinations (annual eye, foot and kidney examinations). They are also usually prescribed multiple medications to be taken daily. However, this advice, recommendations and behavior must be maintained lifelong. If patients do not properly adhere to these guidelines, their

diabetes is more likely to be poorly controlled with an increased risk of developing further health problems. Christensen and Johnson stated that "*Whether medical intervention requires a patient to follow a prescribed medication regimen, involves making a necessary dietary or other lifestyle change, or simply requires an individual to attend a scheduled appointment or procedure, the patient's adherence is, in virtually all cases, a necessary condition for safe, effective, and efficient treatment*" (Christensen and Johnson, 2002). The success in ensuring a healthy life for patients with diabetes requires a good association between both the health care providers who follow the patient's progress and prescribe the appropriate treatment and the patient who has the responsibility for following recommendations and maintaining behavioral changes.

Generally, medication adherence is considered to be the extent to which patients take medication as prescribed by the health professional (Eraker *et al.*, 1984; Vitolins *et al.*, 2000). One of the most important targets in the management of patients with diabetes is the control of blood glucose by proper adherence to medications. Positive health outcomes and lower mortality among patients with diabetes have been associated with good adherence compared with those patients with poor adherence (Krapek *et al.*, 2004; Rhee *et al.*, 2005b; Simpson *et al.*, 2006). Patients with good adherence to medications were more able to maintain their glycemic control, had lower HbA1c, fewer hospital admissions, an overall reduction in morbidity and mortality and lower medication costs (Hepke *et al.*, 2004; Mahoney, 2008; Piette *et al.*, 2004b; Schectman *et al.*, 2002). Poor adherence is not only a problem among patients with diabetes, but also with other chronic diseases such as hypertension and hyperlipidemia (Dunbar-Jacob and Mortimer-Stephens, 2001; Haynes *et al.*, 2002; Sabate, 2003).

Poor adherence to medications in diabetes found to be a major contributor to poor glycemic control (Balkrishnan *et al.*, 2003). Besides, a strong association has been found between poor adherence and increased health service utilization (Dalewitz *et al.*, 2000). The effectiveness of pharmacological treatment in diseases are mainly dependent on the efficacy of the medication and the rate of adherence to the medication (Epstein, 1984). Previous behavioral studies in patients with diabetes have shown that taking medication can be more easily followed than complying to non-pharmacological treatment such as diet and exercise (Gonder-Frederick *et al.*, 2002). It has been estimated that about 50% of patients were unable to follow their pharmacological treatment regimens properly and failed to obtain the full benefit from their treatment (Roter *et al.*, 1998).

The rate of poor or non-adherence appears to be decreasing from high rates for preventive regimens in asymptomatic patients to low rates for time-limited regimens in acutely ill patients (Horne, 2006). Poor adherence has been linked to an increased frequency of illness, treatment failures, hospitalization and to higher mortality across many clinical populations (Christensen and Johnson, 2002). Poor medication adherence in diabetes has been documented in many research studies and reviews have suggested that a large proportion of patients have difficulty in totally adhering to their medication. A retrospective analysis review concluded that the adherence rate to diabetic medications ranged from 36 to 93% (Cramer, 2004). In a study conducted in Scotland, 69% and 66% of patients were poor adherent to sulphonylureas and metformin respectively (Donnan *et al.*, 2002). A report by the WHO estimated that the average rate of adherence to medication is around 50% among patients suffering from chronic diseases in developed countries, and this is assumed to be lower in developing countries where there is limited access to health

care and medicines (World Health Organization, 2003). It was reported in Nigeria that 39.8% of patients with type 2 DM were poor adherent to their medications (Adisa *et al.*, 2011).

1.6 Research Problems

Diabetes management is lifelong process that requires efforts from diabetic health care providers and patients. However, the patient is the key for successful management and serious complications can result from poor management. Patients must be proficient to successfully manage, maintain lifestyle changes and make daily decisions for their objectives while health care providers have the responsibility to help patients to make the right decision and cope with the difficulties and barriers through education, support and advice (Funnell and Anderson, 2004).

This study has illustrated the following problems:

1- The proportion of good glycemic control constitutes a small percentage among the total patients with diabetes in Malaysia.
2- To date, there have been few academic and empirical published papers regarding knowledge and medication adherence and most of the reviews on this subject have been conducted in Western countries.
3- In Malaysia, there has been a shortage of data on the topic of patients' experience and knowledge about diabetes and its medications among patients with type 2 diabetes.
4- No validated Malaysian tools have been found for the assessment of diabetes knowledge and medication adherence.

5- Little has been published regarding the association of both knowledge and adherence on glycemic control in patients with diabetes.

6- Inconclusive results have been found in previous studies that investigated the association between general diabetes knowledge and medication adherence and their impact on glycemic control.

1.7 Rationale of the study

Diabetes is a growing health problem in Malaysia with a high cost in terms of economics and disability. It is estimated that 3,254,994 people will have diabetes in 2030 in Malaysia compared with the estimate of 1,846,000 in 2010 (International Diabetes Federation, 2009). This increase is due to rapid socio-economic growth, urbanization and changes in dietary habits resulting in an increase in the proportion of the obese and overweight population. The NHMS-3 found that the prevalence of diabetes increased from 8.3% in 1996 to 14.9% in 2006 with a high prevalence of poor glycemic control. Patients with type 2 diabetes frequently do not adhere to their prescribed medications and, consequently, poor glycemic control can result, with an increased incidence of diabetic complications, increased morbidity and mortality and increased health care facilities utilization (Delamater, 2006; Hertz *et al.*, 2005).

Multiple factors have been found to be related to medication adherence, such as patient variables, health status, medications, economic variables and health care provider variables (Balkrishnan *et al.*, 2003). Although numerous measures have been taken to improve glycemic control among patients with diabetes in Malaysia, there is still a lack of good diabetes control. In Malaysia, it is important to explore

the patients' perception about the diabetes, diabetes medications and the interaction between patients and health care providers. It is also imperative to understand the contribution of general diabetes knowledge among patients with type 2 diabetes on their medication adherence behavior to promote better self-care for diabetes. Lack of proper self-management and poor adherence to medications are responsible for the high prevalence of poor diabetes control (Ruggiero *et al.*, 1997; Whittemore, 2000). It has been recommended that diabetes education should be a component of the diabetes management process by the health system (Harris, 1996). Most of the interventions that attempt to improve medication adherence and self-management practice of patients are educational; therefore, for a proper intervention that leads to changes in patient behavior, it is important to first evaluate patient knowledge. Diabetes self-management education must be adjusted to the level of knowledge of the patients and should be culturally sensitive.

1.8 Significance of the study

As a result of the rapidly growing prevalence of diabetes and with the evidence that good glycemic control of diabetes is associated with reduced morbidity, mortality, and disability, diabetes self-management has been considered as an important part of the management of patients with diabetes (American Diabetes Association, 2009). Medication adherence is an important element of diabetes self-management to improve glycemic control and to prevent complications, and a patient's knowledge of diabetes is highly correlated to medication adherence (Okuno *et al.*, 1999). Poor medication adherence may result in worsened outcomes and additional medication regimens to be added to the prescription. Although many studies regarding

medication adherence among patients with diabetes are available, published data on medication adherence and the factors contributing to it in Malaysia is sparse.

It has been recommended by the American Diabetes Association to annually assess diabetes self-management skills of patients and to provide continuous diabetes education (American Diabetes Association, 2009). Diabetes knowledge is required for proper self-management of diabetes (Browne *et al.*, 2002; Coates and Boore, 1996; Norris *et al.*, 2001; Speight and Bradley, 2001), However, little is known regarding the specific skills, knowledge and beliefs needed for the patients to effectively participate in their diabetes management (Heisler *et al.*, 2005). Therefore, the assessment of patient knowledge is important for improving patient outcomes (Rothman *et al.*, 2005). This study will attempt to discover the association between patient knowledge on diabetes and medication adherence.

Many factors and barriers related to medication adherence are noted from previous studies but, in the Malaysian setting, little is known about these factors and how they contribute to the problem of poor glycemic control. It is important to determine the perception of patients and their experience with diabetes and the associated medications for the purpose of evaluating the factors affecting glycemic control. At the end of this study, healthcare professionals and authorities will have a clearer picture of the problem of medication adherence. The results from this study will help to explore patient perceptions of diabetes, identify patients with poor knowledge and adherence and identify patients with poor glycemic control. The results will help in planning educational programs for patients with diabetes and help health care providers to concentrate on those patients with risk factors for poor adherence.

1.9 Research objectives and questions

1.9.1 Objective of the study

Poor glycemic control of diabetic patients is a major public health problem that requires attention. Patients often do not adhere tightly to their prescribed medications. It is important to understand the contribution of factors associated with poor adherence in order to provide better care. Some interventions which have been carried out to improve medication adherence involve an educational program; therefore, this study assumed that knowledge regarding Malaysian patients might affect their awareness in terms of medication use and could consequently influence adherence to a medical regimen. To date, few papers have been published in terms of the assessment of both patient knowledge and medication adherence in type 2 diabetes. Therefore, further exploration of the association between medication adherence and patient knowledge and the effect of both of these factors on glycemic control is needed. The principal purpose of the study was to investigate the medication adherence of patients with diabetes and the general knowledge and the association of both knowledge and adherence on glycemic control. The study findings may provide the healthcare system with a better understanding of the effect of knowledge improvement on medication adherence of patients and consequently on glycemic control.

The specific aims of this study are:

1- To explore the perception and knowledge of diabetic patients on diabetes and thier medications.

2- To understand the factors contributing to medication adherence in Malaysian patients.

3- To translate, validate and assess the psychometric properties of the chosen tools for the assessment of general knowledge and medication adherence.

4- To evaluate general diabetes knowledge and medication adherence among patients with type 2 diabetes

5- To identify the characteristics of the patients who have low level of knowledge, low medication adherence and poor glycemic control

6- To examine the relationship between the general knowledge of patients and their medication adherence with glycemic control

7- To examine the factors affecting the patients to be in a good glycemic control.

1.9.2 Research questions

The study addressed the following questions:

1- Is there a high prevalence of poor medication adherence? What is the percentage of medication adherence in patients with diabetes?

2- Is there a general diabetes knowledge deficiency among patients with type 2 diabetes?

3- Do patients with different degrees of diabetes knowledge adhere differently to their diabetic medication?

4- Which of the two variables (knowledge and adherence), including interaction variables, account for the most variance in predicting HbA1C levels?

5- What is the type and strength of the relationship between patients' characteristics and the other two variables (knowledge and adherence) as well as the outcome (HbA1C)?

1.10 Thesis overview

In this thesis, chapter 2 reviews the literature related to the study with the definition of terms and provides a conceptual framework for the study. A brief discussion of the importance of diabetes knowledge and medication adherence for patients is discussed in depth. The chapter continues with an overview of diabetes knowledge assessment and the tools used for its measurement with an overview of medication adherence assessment and the methods used for its measurement. A thorough review of literature relevant to the study, focusing on at patient knowledge and medication adherence in regards to diabetes and its medications in Malaysia and elsewhere in the world form the bulk of this chapter.

Chapter 3 illustrates the qualitative exploration of patient perceptions and experience of diabetes and its medications. A detailed methodology will be presented for the assessment of qualitative interviews with conveniently sampled patients with diabetes in Penang. The findings from the interviews conducted with patients about their perceptions and experience regarding diabetes and its medications with a discussion and conclusions are also presented in this chapter.

Chapter 4 will illustrate the Malaysian translation of the psychometric validation scales used for the assessment of both general diabetes knowledge and medication

adherence. Detailed methodology, findings and conclusions for the validation of the general diabetes knowledge test used in this study is included.

Chapter 5 illustrates the assessment of general diabetes knowledge and medication adherence and glycemic control as well as their impact on glycemic control. The detailed methodology, findings and conclusions for the assessment of patient knowledge, medication adherence and glycemic control is described.

Chapter 6, the final chapter, includes an overall summary of the study findings, the conclusions of the thesis and along with a set of recommendations for further work.

CHAPTER TWO: LITERATURE REVIEW

2.1 Diabetes mellitus

2.1.1 Definition of diabetes mellitus

Diabetes mellitus (DM) is a common chronic disease characterized by hyperglycemia and other metabolic abnormalities and is mostly due to insulin deficiency, insulin resistance and/or increased hepatic production of glucose (in type 2 diabetes). Diabetes is "a group of metabolic diseases characterized by hyperglycemia and resulting from a defect in insulin secretion, insulin action or both" (American Diabetes Association, 2005). DM occurs when the body fails to absorb glucose due to factors associated with insulin availability or inappropriate insulin action.

2.1.2 Types of diabetes

Genetically, etiologically, and clinically, diabetes is a heterogeneous group of disorders (Koda-Kimble *et al.*, 2009). Based on the etiology of diabetes, there are three main types of diabetes: type 1, type 2 and gestational diabetes. However, other specific types of diabetes also exists such as maturity onset diabetes of the young (MODY) in which these forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age 25 years) and are characterized by impaired insulin secretion with minimal or no defects in insulin action (American Diabetes Association, 2011; The Expert Committee on the Diagnosis Classification of Diabetes Mellitus, 2007). Moreover, latent autoimmune diabetes in adults (LADA), is a subgroup of type 2 diabetes and the patients share many genetic and immunological similarities with type 1 diabetes, suggesting that LADA, like type 1 diabetes, is an autoimmune disease (Naik *et al.*, 2009).

Type 1 diabetes occurs when the insulin-producing cells in pancreas (beta cells) are damaged or destroyed by an autoimmune process resulting in a reduced or impeded insulin production (Atkinson and Maclaren, 1994; Falorni *et al.*, 1995). The exact etiology of type 1 diabetes is not known, but it is believed that a patient's genetic background in the context of a possible infectious trigger leads to the development of the disease (Genuth *et al.*, 2003a; Mayfield, 1998). Type 1 diabetes mostly afflicts individuals around the time of puberty and is treated by insulin, diet and exercise (Franz *et al.*, 2004; Koda-Kimble *et al.*, 2009).

Type 2 diabetes is the most common type of diabetes, occurring in about 90% of diabetic patients. Type 2 diabetes results when the body produces less insulin or when the cells of the body become insensitive to insulin (American Diabetes Association Website). While the incidence of type 1 diabetes is highest in children and around puberty, type 2 diabetes also known as adult onset diabetes (Howlett and Lillie, 2006). However, the incidence of type 2 diabetes in children is also increasing along with the epidemic of childhood obesity (Ludwig and Ebbeling, 2001; Silverstein and Rosenbloom, 2001). Type 2 diabetes has been found to have a strong genetic component with a three-fold higher risk among the siblings of an individual with diabetes (Elbein, 2002).

Gestational diabetes, which is the third main type of diabetes, occurs in about 4% of pregnant women in the US (Engelgau *et al.*, 1995). Like type 1 diabetes, the exact etiology is not well understood, but hormones from the placenta are believed to block the action of insulin in the mother's body (Koda-Kimble *et al.*, 2009). Usually, gestational diabetes is temporary and disappears after the end of the pregnancy; however, an increased risk of impaired glucose tolerance and type 2 diabetes remains and women with gestational diabetes have a 17%-63% risk of developing type 2

diabetes within the next 5-16 years (Ben-Haroush *et al.*, 2004; Hanna and Peters, 2002; Henry and Beischer, 1991).

The fourth type of diabetes, which is secondary to other conditions, consists of diabetes associated with a genetic defect in the function of the beta cells of the pancreas, a genetic defect in the action of insulin, diseases of the pancreas, other genetic syndromes, drug use or chemical exposure (Diabetes Mellitus Information, 2006).

The assessment and discussion in this study is limited to type 2 DM and the term diabetes that subsequently appears in this study refers to type 2 DM.

2.1.3 Diagnosis of diabetes

Diabetes is usually diagnosed when one or more of the usual signs and symptoms of diabetes are present and confirmed by a high level of glucose in a venous blood sample. The recommended criteria for the diagnosis of DM are as follows (American Diabetes Association, 2009; International Diabetes Federation, 2005; Ministry of Health Malaysia, 2009; Rodbard *et al.*, 2007).

1- When there are symptoms of diabetes (polyuria, polydipsia and weight loss) associated with causal (any time of day, with no regard to the last meal) fasting blood sugar (FBS) more than 11.1 mmol/L

2- FBS is equal to or more than 7 mmol/L

3- Two hour postprandial plasma glucose is equal to or more than 11.1mmol/L.

2.1.4 Clinical presentation of type 2 diabetes

Type 2 diabetes is typically diagnosed incidentally during a routine physical examination or when the patient seeks attention for another complaint. This is because symptoms are so mild and their onset so gradual that they can easily be explained away (Koda-Kimble *et al.*, 2009). However, when the patients giving a history of their illness, fatigue, polyuria, and polydipsia are acknowledged (Alberti and Zimmet, 1998; Boron and Boulpaep, 2003; Ganong and Systems, 1995; Koda-Kimble *et al.*, 2009). Weight loss is uncommon, and macrovascular disease is also often evident at diagnosis while the presence of microvascular complications at diagnosis suggests the presence of undiagnosed or subclinical diabetes for 7 to 10 years (Koda-Kimble *et al.*, 2009).

2.1.5 Glycosylated hemoglobin A1C (HbA1C)

HbA1C is a result of the reaction between glucose and hemoglobin in the blood. The hemoglobin is exposed to glucose in the blood and when there is a higher level of glucose, more HbA1C will be formed. HbA1C is an important marker and is an index for glycemic control. HbA1C is considered as the gold standard for the evaluation of diabetes control as it provides an average blood glucose over the preceding two to three months (American Diabetes Association, 2009; Katsilambros and Tentolouris, 2003). The normal level of HbA1C in a non-diabetic person ranges from 3.8-6.4% of the total hemoglobin (Goldstein *et al.*, 2004; Kasper *et al.*, 2005). According to the 2009 American Diabetes Association recommendations, a HbA1C less than 7% is desired for good glycemic control (American Diabetes Association,

2009), while a HbA1C equal to or less than 6.5% was recommended by the American Association of Clinical Endocrinologists (Rodbard *et al.*, 2007).

The target level of equal or less than 6.5% HbA1C for patients with type 2 diabetes is recommended by the Malaysian Clinical Practice Guidelines for the management of type 2 diabetes (Ministry of Health Malaysia, 2009). There is strong evidence that HbA1C should be measured routinely in all patients with diabetes (type 1 and 2) in order to evaluate the degree of glycemic control. Glycemic goal should be based on the results of prospective randomized clinical trials like the Diabetes Control and Complications Trial (DCCT), the United Kingdom Prospective Diabetes Study (UKPDS) and Action in Diabetes and Vascular disease: preterAx and diamicroN Controlled Evaluation (ADVANCE) or based on the guidelines for the management of diabetes (Sacks *et al.*, 2002).

2.1.6 Diabetes complications

There are different forms and types of complications associated with diabetes which vary from acute to chronic in onset and can be classified by the type of tissues or cells where complications occur (Fowler, 2008). Generally, complications are more common in patients who have difficulty in controlling their blood glucose at acceptable levels (Stratton *et al.*, 2000).

2.1.6.1 Acute complications of diabetes

Primary or secondary hypoglycemia is an acute complication of diabetes, which can be severe and sometimes have rapid consequences and multiple causes, depending on the etiology and especially the presence or absence of hyperinsulinemia (Bibergeil, 1988). Diabetic ketoacidosis also is an acute metabolic complication of diabetes resulting primarily from intense insulin deficiency that mostly occurs with type 1 diabetes and occasionally in type 2 diabetes and which is associated with a mortality rate of 10% (Walker *et al.*, 1989). Hyperosmolar non-ketogenic coma results from profound dehydration as a result of fluid loss (pneumonia, burns, stroke or a recent operation) or inadequate fluid intake. It is associated with a greater than 50% mortality rate and is considered a true medical emergency (Walker *et al.*, 1989).

2.1.6.2 Chronic complications of diabetes

The long term complications associated with diabetes can develop in patients with type 2 diabetes which include micro and macro-vascular complications. Macro-vascular complications are responsible for stenosis at the three major arteries which are the coronary, cranial and limb arteries (Nesto, 1988; Pyorala and Laakso, 1983). Micro-vascular complications of diabetes affect the small blood vessels and capillaries resulting in thickening of the basement membrane of the capillaries throughout the body. Among the problems caused by this complications are retinopathy, nephropathy and neuropathy (Cheung and Wong, 2008; King and Brownlee, 1996). Diabetic neuropathy is classified into different types of diabetes complications, in which patients suffer from numbness or irritation at the tips of the limbs with wasting of manual muscles and impaired reflexes. Neuropathy is the most common complication and occurs in 12% of patients at the time of diagnosis and in

25% of patients after 25 years of diabetes (Vinik *et al.*, 2000). Other chronic complications of diabetes includes autonomic neuropathy, diabetic foot disorder, carpal tunnel syndrome, increased susceptibility to infection, poor circulation and poor renal function (Herfindal and Gourley, 2000).

2.1.7 Diabetes management

Diabetes management normally follows the clinical diagnosis with lifestyle modification, pharmacotherapy and patient education to encourage self-care and to achieve glycemic control (Funnell *et al.*, 2009; Funnell *et al.*, 2007; Martin *et al.*, 2005). This involves, in addition to the primary medical evaluation of patients, a variety of strategies to provide adequate education to the patients and considers diabetes self-management education as an integral part of diabetes management with dietary planning, pharmacotherapy and exercise (American Diabetes Association, 2009; Rodbard *et al.*, 2007). For proper implementation of self-management in therapeutic plans, a combination of behavioral strategies to improve self-management requires a multidisciplinary team effort from physicians, pharmacists and nurses (American Diabetes Association, 2009). Teaching self-management is time consuming and requires repeated contact with health care professionals for education, self-monitoring and the assessment of progress. The approach to patients should be individualized, taking into consideration their culture, economic situation, knowledge and beliefs regarding the disease and treatment, response to medication and changes in status over time.

The aim of adequate diabetes management is to reduce the acute and chronic complications of diabetes, principally by maintaining good glycemic control and

controlling the other associated risk factors (hypertension and hyperlipidemia) as much as possible. Diabetes requires lifelong management, which is challenging and sometimes overwhelming for patients who have to manage their diabetes alone or with additional support from family members.

Patients are required to properly adhere to their daily medication intake and to their new lifelong lifestyle modifications. Patients need to adhere to their medication, meal plans, adjust their physical activity, lose weight if they are obese and monitor their blood glucose. For these required activities, patients must acquire knowledge and skills through systematic diabetes education. Traditional diabetes education focused on the transfer of information from health care professionals to patients, which generally does not improve patient behavior or outcomes (Brown, 1992). In order for effective education to be achieved, health professionals need to change their approach to improve all aspects of self-care behavior, including medication adherence and daily self-care. The plan for continuous diabetes management consists of three arms, which are relief of the acute symptoms of diabetes, optimized glycemic control and mitigation of other risk factors for complications and the treatment of the existing complications (Ministry of Health Malaysia, 2009). The available choices for the treatment of diabetes are education, diet, pharmacotherapy and exercise.

2.1.7.1 Diabetes education

Diabetes education is effective for improved clinical outcomes and quality of life and should be provided to all patients with type 2 diabetes regardless of the mode of treatment (Ellis *et al.*, 2004; Gary *et al.*, 2003; Norris *et al.*, 2002). It is important to