A Study to Explore the Causes of Higher Notification of Tuberculosis in Adult Females in the Province of Khyber Pakhtunkhwa, Pakistan

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Doctor of Philosophy

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School of Health Sciences

LIST OF CONTENTS

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LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AFG	Afghanistan
JID	Journal of Infectious Diseases
AJPH	American Journal of Public Health
BHU	Basic Health Unit
BTB	Bovine tuberculosis
CDR	Case detection rate
DHO	District Health Officer
DHQ	District Headquarter Hospital
DOTS	Direct Observed Therapy Short Course
DPT	Diphtheria, pertussis and tetanus
EMR	Eastern Mediterranean Region
EPI	Expanded Programme on Immunisations
ERS	Electronic Reporting System
ESR	Erythrocytes sedimentation rate
EXTB	Extra Pulmonary Tuberculosis
GAVI	Global Alliance for Vaccines and Immunisation
GPs	General Practitioners
HBCs	High Burden Countries
HND	Higher Notification Districts
KPK	Khyber Pakhtunkhwa
LHW	Lady Health Worker
LND	Lower Notification Districts
MBBS	Bachelor of Medicine Bachelor of Surgery
MCH	Mother and Child Health
MD	Doctor of Medicine

MDG	Millennium Development Goals
MDR	Multi drug resistant
TB	Mycobacterium tuberculosis
ND	Notification Districts
NGO	Non-governmental Organisation
NIMS	Northern Institute of Medical Sciences
NTCP	National Tuberculosis Control Programme
NWFP	North West Frontier Province
PRISMA-P	Preferred Reporting Systematic reviews and Meta-analysis Protocol
PKR	Pak Rupees
PPs	Private Practitioners
PTB	Pulmonary Tuberculosis
RHC	Rural Health Centre
TB	Tuberculosis
TSR	Treatment Success Rate
UNHCR	United Nations High Commission for Refugees
WHO	World Health Organisation

The University of Manchester

Muhammad Aziz **PhD: November 2015**

ABSTRACT

A Study to Explore the Causes of Higher Notification of Tuberculosis in Adult Females in the Province of Khyber Pakhtunkhwa (KPK), Pakistan.

Background: Tuberculosis (TB) continues to be major cause of death for adult females in Pakistan, which ranks as the fifth highest country in the world with a TB burden. Globally, TB occurrence, morbidity and mortality is higher in males. However, the notification of TB in Khyber Pakhtunkhwa (KPK) and Balochistan is higher in females as compared to males. This study aims to explore the risk factors associated with the higher notification of TB in women in KPK province of Pakistan.

Aim : To explore the reasons behind the variation of Tuberculosis Notification between males and females in the province of Khyber Pakhtunkhwa (KPK), Pakistan.

Objectives:

1. To describe the epidemiological characteristics of confirmed TB cases in KPK by age, gender and geographical location between 2002 and 2010.
2. To determine the risk factors associated with TB in the province of KPK.
3. To assess the knowledge of new diagnosed TB patients.
4. To evaluate the level of knowledge, attitude and practice of physicians working in TB diagnostic centres (TDCs) in KPK.

Methods:

1. We retrospectively collected data for all registered TB patients between 2002 and 2010 using data from the National TB Control Programme (NTCP) in KPK, Pakistan. We analysed the data to show the distribution of TB by age, gender, type of disease, geographical location and treatment outcome.
2. We carried out a cross-sectional study from 1st July 2012 to 30th September 2012, identifying newly diagnosed TB patients from ten districts (five high notification and five low notification districts) in PKP to determine the risk factors associated with the diagnosis of TB and knowledge assessment of TB patients in higher versus lower notification districts.
3. We carried out a cross sectional study of a sample of general practitioners in these districts to assess their knowledge and management of TB cases.

Results: Through a descriptive analysis of nationally collected data, we confirmed that female patients in KPK were at a higher risk of contracting TB compared to males. We determined that the majority of female patients in higher notification districts were illiterate, unemployed, poor and living in households of low socioeconomic status when compared to women from low notification districts. A strong association was noted for the interaction between education and gender (OR = 0.16), suggesting that more educated women were around 6 times less likely to be in a higher notification area (1/0.16) compared to a low notification area. It was also observed from the logistic regression model that income level (*OR = 0.42*), anaemia (*OR = 0.45*) and unemployment (*Or = 0.23*) were also associated with being in a high notification district in the province of KPK. Lower notification districts with female gender were used as reference category for the model. Finally, knowledge of general practitioners about the treatment, follow up and complications of TB was poor.

Discussion: Our results suggest that differences in socio-economic factors are implicated in the differential notification of TB between men and women and between high and low notification districts. Poor knowledge of physicians in the treatment and management of TB may also be a contributory factor. This has implications for the future management of TB control programs in these areas and in Pakistan more generally.

DECLARATION

I undertake that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Muhammad Aziz

COPYRIGHT STATEMENT

ACKNOWLEDGEMENT

I would like to thank everyone who has helped and supported me during my PhD study in Manchester. First of all, I would like to thank to the committee members who were more than generous with their expertise and precious time. I am particularly grateful for their support when both of my supervisors left the University in second year of my PhD. The committee identified my current supervisor with both a public health and clinical background, which was very important for my study. I would like to express my deep appreciation to my supervisor Professor Aneez Esmail, who accepted me in the middle of my PhD. His critical review, inputs and constructive comments moved me forward and enabled me to complete my PhD thesis. I will never forget your kind support during the hard and tragic time I passed through from August to December 2013. I am also thankful to my co supervisors Professor Mark Woodhead and Dr David Baxter for their valuable inputs and advice. I would also like to thank Professor Sara O'Brien who was my main supervisor at the start of my PhD and for her assistance in creating a strong foundation for my study. I would like to thank my postgraduate administrators Christine Burns, Tasleem Hanif and Amina Saeed for helping and supporting me throughout my study in the University of Manchester.

I would like to thank Dr Catherine Reed, Programme Director of Postgraduate Courses in Public Health and Mr Stewart Taylor, MPH e-learning Technologist, University of Manchester for their support and cooperation and giving me access to online MPH courses of Epidemiology, Biostatistics, Evidence Based Practice, Qualitative Research methods and Health System in Low Income Countries. These courses helped me a lot in completion of my research project.

I am also thankful to David Springate, Statistical Research Assistant, Primary Care Research Group, Institute of Population Health, University of Manchester, for helping me in the development of the logistic regression model.

I would like to thank Dr Malek Shah, Manager, Scholarship Division and Brother Shaharuqul Haq, Scholarship Officer at the Islamic Development Bank Scholarship Programme for financing my PhD and who supported me during my PhD.

I am also thankful to Dr Abdul Latif and Dr Ubaid Hussain, Project Directors, and Dr Maqsood Ali, Project Manager, TB Control programme Khyber Pakhtunkhwa for their cooperation and support. I am also thankful to all the Executive District Officers Health (EDOH) and District TB Control Officers for their continuous and outstanding support during the field work. I am also thankful to all the Medical Technicians, Lady Health Workers and Area Supervisors for their efforts towards the successful completion of the data collection project.

On a personal note, I would like to thank to all those TB patients who participated in this study and who made this study possible.

I must also acknowledge all my friends, teachers, trainers and librarians who assisted, advised and helped me throughout my PhD. I am also grateful for the generous support of my friend Dr Salik Javeed for proof reading, feedback and constructive comments.

Finally, this was an enormous PhD research project with extensive financial and technical requirements. Therefore, I am sincerely thankful to the financial support of the Islamic Development Bank, Jeddah, Saudi Arabia for the award of the PhD scholarship for my research. I would also like to thank The University of Manchester for financing parts of this PhD and the Provincial TB Control Programme KPK for providing technical support, which helped me particularly in the successful completion of the data collection phase

DEDICATION

First of all, I am grateful to dedicate this thesis to my parents, without their support, encouragement and constant love I could not have completed this PhD.

Secondly, I would like to dedicate this thesis to my teachers Mr Muhammad Neem, Mr Abdul Salm, Mr Gul Zaman, Prof Mehfoz Jan Abid, Prof Zia-ur-Rehman and Abdul Raouf, who were involved in my previous education and I acknowledge that their enthusiasm and support is one of the reasons why I am here today and submitting my thesis for PhD.

Finally, I dedicate this work and special thanks to my wife and children who suffered a lot during my studies, particularly when I was away for field study. I believe that without your cooperation, engagement and patience, I could not have completed this milestone.

CERTIFICATE OF APPROVAL

This is to certify that the work presented in this thesis "A Study to Explore the Causes of Higher Notification of Tuberculosis in Adult Females in the Province of Khyber Pakhtunkhwa, Pakistan" submitted by Dr Muhammad Aziz was carried out by the candidate under my supervision. The information obtained from other sources has been duly acknowledged in the thesis.

University of Manchester
November 2015

Prof Aneez Esmail
Supervisor

THE AUTHOR

I have completed a two years Master's degree in Public Health (MPH) in 2009 from Abasyn University, Peshawar, Pakistan, charted by the Government of Pakistan and recognised by the Higher Education Commission (HEC) of Pakistan. I graduated from Ayub Medical College Abbottabad, Pakistan in 2006, in medicine (MBBS), which is recognized by the HEC and Pakistan Medical & Dental Council (PMDC) Islamabad.

Before starting my PhD I was working as a medical doctor at the United Nations High Commission for Refugees (UNHCR) and was an assistant professor in the Department of Community Health Sciences & Research at Northern Institute of Medical Sciences, (MINS College of Medicine), an institution that is involved in the areas of medical education and research.

I am interested in the research aspects of community health sciences (Public Health) and health care delivery management systems. This interest developed during my MBBS and MPH endeavours under the supervision of Prof Zia-ur-Rehman and Dr Irfan who were based in Ayub Teaching Hospital Abbottabad and Abasyn University Peshawar. My MPH dissertation was titled ‘EPIDEMIOLOGY OF DOG BITE CASES ATTENDING THE ACCIDENT & EMERGENCY DEPARTMENT OF AYUB TEACHING HOSPITAL, ABBOTTABAD’ which sought to study the epidemiological characteristics of dog bite injuries, the knowledge, attitude and practices of the subjects regarding dog bites. This work contributed towards providing reliable data to the national institute of health (NIH) in Pakistan regarding dog bite injuries.

In 2007, on annual tuberculosis day, I participated in a training workshop organised by the National TB Control Programme (NTCP). During the presentation, Dr Ghafor, the programme manager of NTCP showed us a slide describing the differential notification of males (42%) and females (58%) with respect to TB. He further explained that the notification of Tuberculosis is higher in males globally and nationally. However, in Khyber Pakhtunkhwa, there was a higher female notification rate compared to males. He posed the question, "Can I have anyone amongst you to investigate scientifically the causes of this higher notification". This sparked my interest and I started collecting information about the problem. In 2008, I completed the preliminary background work and submitted a research proposal on the issue to the Islamic Development Bank (IDB) for 3 Years PhD Merit Scholarship. I was given the award in 2009. After securing the scholarship, I applied to study for a PhD to several

UK universities and received offer letters from the University of Warwick, University of Leicester, Imperial College London and the University of Manchester. Before, accepting the offers, I visited all the above universities and chose the University of Manchester.

University Positions

Peer Mentor for the School of Community Based Medicine 2011-12

Postgraduate Student Representative (PGR) 2011-12

(See Appendix 14.6 on page 222)

My Training & Development in the University of Manchester

Unit Code	Title	Event Date	Event Venue	Hours
FMHSS2401	Graduate Teaching Assistants/Demonstrator Training	13/03/2012	STDU, 2nd Floor, Humanities Bridgeford Street Building	7
FMHSS1202	Research Ethics Application: University & NHS	29/11/2011	Room 3.204, University Place	4
FMHSS1302	Introduction to Statistics using SPSS	15/11/2011	room 4.2, Roscoe Building	12
FMHSS1021	Mini First Year Workshop	03/11/2011	Room 4.38, Simon Building	4
FMHSS2105	Getting the most out of research conferences	14/10/2011	Hanson Room, Humanities Bridgeford Street Building	4
FMHSS1100	Academic Writing in English	12/10/2011	2.03, Mansfield Cooper Building	27
FMHSS2101	Communicating your Research with the Public	06/10/2011	Room 4.38, Simon Building	3
MEDN62212	Health System in Low Income Countries	2011-12	MPH e-Learning Technology	150
MEDN63121	Qualitative Research Methods	2011-12	MPH e-Learning Technology	150
MEDN60991	Fundamentals of Epidemiology	2011-12	MPH e-Learning Technology	150
MEDN60982	Biostatistics	2011-12	MPH e-Learning Technology	150
MEDN60041	Evidence Based Practice	2011-12	MPH e-Learning Technology	150
FMHSS1106	Communicate with Confidence	09/09/2011	G306A/B, Jean McFarlane Building	3
FMHSS1102	Introduction to Effective Presentation Skills	08/02/2011	Room 4.50, Simon Building	6
FMHSS1301	Critical analysis of research papers	03/02/2011	Room 1.010, Roscoe Building	4
FMHSS2303	Systematic Review Training	12/01/2011	Room 4.2, Roscoe Building	7
FMHSS2300	Effective Publications: Taking the sting out of peer review	10/12/2010	Room 5.206, University Place	4
FMHSS1100	Academic Writing in English	13/10/2010	Room 3A, Simon Building	30
FMHSS	An Introduction to Statistical Modelling with Stata	28/09/2010	Room 2.825, Stopford Building	48
FMHSS1010	First Year: Introduction to Research Speed PhD and MD Course	23/09/2010	Day 1 & 2: Room 1.010, Roscoe Building	10

LIST OF PUBLICATIONS AND CONFERENCE PROCEEDINGS

44th World Conference on Lung Health, Organised by the International Union against Tuberculosis and Lung Diseases (The Union), Paris France 30 October-03 November 2013 (**Poster Presentation**) Title: Are women at higher risk of TB? An epidemiological study of prevalence and risk factors for TB in Khyber Pakhtunkhwa, Pakistan (Appendix 14.5 on page 216).

45th World Conference on Lung Health, Organised by the International Union against Tuberculosis and Lung Diseases (The Union), Barcelona Spain 28 October-01 November 2013 (**Poster Presentation**) Title: Gender and tuberculosis: A prospective study exploring risk factors for higher notification of tuberculosis (TB) in adult women in Khyber Pakhtunkhwa (Appendix 14.5 on page 216).

First Islamic Development Bank (IDB) Scholar's Scientific Conference, University of Cambridge UK 22 May 2014 (**Oral and Poster Presentation**) Title: Did you know, women are at higher risk of Tuberculosis in Khyber Pakhtunkhwa (KPK), Pakistan? An epidemiological study of prevalence and risk factors for TB in KPK, Pakistan (Appendix 14.5 on page 216).

6th International Conference on Health Care and Life Sciences Research (ICHLSR), Imperial College London, 18-19 September 2015 **(Oral and Poster Presentation**) Title: Tuberculosis in Adult Women: A systematic Review of Gender Differences in Tuberculosis Notification in the province of Khyber Pakhtunkhwa, Pakistan (Appendix 14.5 on page 216).

Faculty PGR Showcase: Faculty of Medical and Human Sciences, School of Medicine, University of Manchester 09 April 2014 (**Poster Presentation**) Title: Are women at higher risk of TB? An epidemiological study of prevalence and risk factors for TB in Khyber Pakhtunkhwa, Pakistan (Appendix 14.5 on page 216).

CHAPTER 1: INTRODUCTION

1.1 Introduction

Tuberculosis (TB) continues to be a major cause of morbidity in adult females in Pakistan, which globally ranks as the fifth highest country with a TB burden (1-3). Tuberculosis was affirmed as a major worldwide health problem in 1993 by the World Health Organisation (WHO) because of concerns about the alarming development of multi-drug resistant tuberculosis. The WHO has developed a series of initiatives which includes an extensive programme of Direct Observed Therapy Short Course (DOTS). The DOTS programme has now become the recommended treatment approach not only for the detection and cure of TB, but also as a means of global tuberculosis control. However, despite implementation of the DOTS programme across Pakistan, the disease remains uncontrollable. One of the criticisms of the WHO's approach is that it is not gender aware and there is emerging evidence of the differential impact of risk of infection, progression of disease, case fatality and access to treatment which is mediated by gender difference. For example, according to TB data reported to the National Tuberculosis control programme (NTP) in Pakistan, the notification of TB has been higher in females when compared to men in the province of Khyber Pakhtunkhwa (KPK), Pakistan since 2000 (4). In the status of TB drug resistance, Abu-Amero has argued that this has also led to a negligence of the gender aspects of TB in relation to research and control of the disease (5).

Globally, TB case notification is higher in males as compared to females but in KPK female patients are at a higher risk of TB than male patients (6).This study, therefore, aims to explore the risk factors associated with higher notification of TB in women in KPK province of Pakistan with a view to identifying areas where supplementary action could be provided to strengthen the planning, administration and

implementation of the National TB Control Programme (NTP). In addition, this study will explore the knowledge and practice of general practitioners (GPs) in the province of Khyber Pakhtunkhwa as it relates to the diagnosis and treatment of TB. This is important because GPs are the main group of healthcare professionals who are responsible for the diagnosis and management of TB in many parts of Pakistan. The purpose of this study will be to understand and explain gender differences in the notification and treatment of TB.

1.2 Burden of Tuberculosis

Tuberculosis (TB) was declared a global emergency in 1993 by WHO (7). Efforts were subsequently made to expand partnerships and bring all stakeholders on board in order to promote effective control of the disease, and recognise correlation of socioeconomic conditions with new cases of TB (8-10).

Some of the highest areas of TB incidence are areas of Africa, Asia and Latin America where the gross national product (GNP) is low (3)(11). An estimated eight million people are infected with TB each year, 95% of those living in developing countries. Globally it is estimated that nearly 2 million people die each year from TB and its associated complications (12).

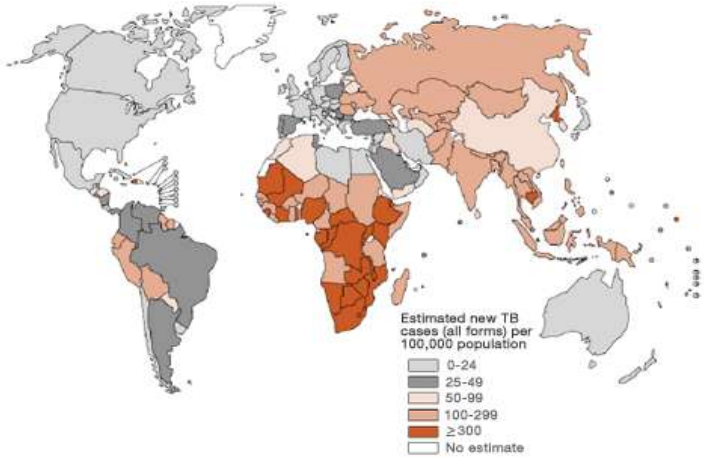
1.2.1 Global Burden

In 2012, the WHO estimated that there were 8.6 million cases of TB globally. This is equivalent to 122 cases per 100,000 of population. In the same year, 1.3 million people died because of this curable disease (13).

An expert group, commissioned by the WHO, has prepared estimates of the number of cases which were categorized by age and gender as part of an update to the

Global Burden of Disease study (14). This showed that the 35% of all cases of TB were attributed to women, giving an estimated number of 3.3 million cases worldwide.

Figure 1: Global Distribution of TB (New TB Cases) in 2007 (15).



In terms of distribution, the largest numbers of TB occurrences in 2012 were in Asia (58%) and Africa (27%). The Americas had the lowest reported incidents, accounting for 3% of all cases (13). The 22 high burden countries (HBCs), which included Pakistan, accounted for 81% of all estimated cases worldwide. China and India together, accounted for 26% of all cases, with India contributing to 21% of cases and representing one-fifth of all TB cases globally (16)**[**Table 1**].**

Table 1: Five Higher TB Occurrence States in 2009 (15)

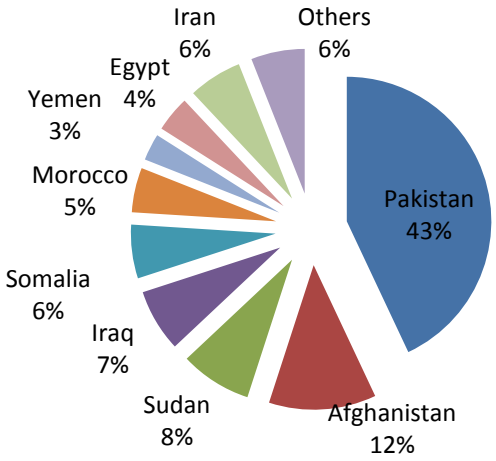
State	Cases	Population in 1000	Incidence Rate
India	2.4 million	1,236,687	176
China	1.1 million	1,377,065	73
South Africa	0.60 million	52,386	1000
Indonesia	0.50 million	246,864	185
Pakistan	0.50 million	179,160	231

1.2.2 **Regional Burden**

Nine out of twenty countries of the WHO Eastern Mediterranean Region (EMR), contributed to total of 94% of TB cases in the region. Pakistan has the highest

prevalence of patients (43%), while Yemen has the lowest (3%). Figure 2 shows TB burden by country in the EMR. However Gillini and Seita in an article about the control and epidemiology of TB in the EMR region suggested that TB data for Pakistan and Afghanistan had probably been underestimated because of the low detection rate in the two countries (17).

Figure 2: TB Burden in the Eastern Mediterranean Region (18)



1.2.3 National Burden of TB in Pakistan

In terms of TB incidence, Pakistan was ranked number one among the high burden countries (HBCs) in the EMR in 2013 and ranked fifth worldwide. According to the WHO, Pakistan's estimated tuberculosis incidence for all forms of the disease is 330/100,000 and for sputum positive TB cases the rate is 80/100,000 population per year (1)(12). Despite this high incidence, TB remains one of the neglected areas for health investment. Figures show that Pakistan's expenditure on health as percentage of GDP (2.2%) is significantly lower than neighbour countries such as Afghanistan (7.6%), Iran (5.7%) and India (4.2%) (19). In 2014, Pakistan spent 114 million US$ on TB of which 30% was donated by international organisations. This lack of investment may be one of the reasons why the prevalence of TB in Pakistan contributes nearly 44% of the total tuberculosis burden in the Eastern Mediterranean Region. Data from the WHO also shows that TB is responsible for 5.1% of the total national disease burden in

Pakistan with a significant impact on socio-economic status of the population (20). TB treatment in Pakistan is free but indirect costs such as travel to health facilities and loss of income may cause socio-economic problems for low earning families. TB commonly occurs in the most productive age group of 15 to 45 years, considered to be the most economically active (19). Although DOTS was introduced in Pakistan in 1995, it was only in 2000 that the Ministry of Health began its wider implementation. It was probably as a result of the national implementation of DOTS through the NTP that the detection rate of TB and DOTS coverage doubled (21). However, despite this increase in DOTS population coverage, from 24% in 2001 to nearly 63% in 2003, the positive case detection rate has remained low with only 17% in 2003. This suggests that many patients do not have access to DOTS even within the designated DOTS areas because the TB burden remains high (22).

1.2.4 **Tuberculosis in Khyber Pakhtunkhwa**

More than half (22,000) of the estimated 40,000 TB patients who registered with 214 public investigative and 1,029 management centres in 24 districts across the Khyber Pakhtunkhwa province in 2009 were females. Two-hundred fifty eight (n = 258) of these females were reported to have died of TB in the Khyber Pakhtunkhwa and Federally Administered Tribal Areas (FATA) (23). Over a nine year period, the notification of new sputum positive (NSS +ve) cases remained higher in females of KPK comparing to data reported from Punjab, Sindh and Pakistan, where the notification was higher in males. Similarly, figures from Balochistan province also showed higher notification of females as compared to males from 2002 to 2010 (6)[Table 3][Table 3].

Table 2: Comparison of Gender Differences of TB (NSS+ve) Case Notification of KPK with other Provinces in Pakistan from 2002-2010(6)

Year	Pakistan			KPK			Punjab			Sindh			Balochistan		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
2002	6521	6725	**13246**	1239	1720	**2959**	1011	917	**1928**	3029	2372	**5401**	347	512	**859**
2003	9820	9504	**19324**	1907	2492	**4399**	1985	1720	**3705**	4634	3431	**8065**	391	585	**976**
2004	15113	14520	**29633**	2465	3422	**5887**	3962	3459	**7421**	6851	5224	**12075**	783	1076	**1859**
2005	23661	23086	**46747**	3473	5081	**8554**	9039	7986	**17025**	8915	7140	**16055**	1168	1552	**2720**
2006	33461	31126	**64587**	4278	5776	**10054**	16188	13998	**30186**	10646	8166	**18812**	1367	1976	**3343**
2007	45123	42442	**87565**	5029	6838	**11867**	25405	22523	**47928**	12006	9582	**21588**	1564	2094	**3658**
2008	50587	48341	**98928**	5308	7209	**12517**	30374	27558	**57932**	12253	10030	**22283**	1519	2040	**3559**
2009	51974	49354	**101328**	5547	7572	**13119**	31199	27963	**59162**	12517	10193	**22710**	1368	1908	**3276**
2010	53033	51444	**104477**	6191	7945	**14136**	31478	28644	**60122**	12775	11274	**24049**	1474	2147	**3621**

Table 3:Percentages of Gender Differences of TB (NSS+ve) Case Notification of KPK with other Provinces in Pakistan from 2002-2010 (6)

Year	Pakistan		Punjab		Sindh		Balochistan		KPK	
	M(%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
2002	49.23	50.77	52.44	47.56	56.08	43.92	40.40	59.60	41.87	58.13
2003	50.82	49.18	53.58	46.42	57.46	42.54	40.06	59.94	43.35	56.65
2004	51.00	49.00	53.39	46.61	56.74	43.26	42.12	57.88	41.87	58.13
2005	50.62	49.38	53.09	46.91	55.53	44.47	42.94	57.06	40.60	59.40
2006	51.81	48.19	53.63	46.37	56.59	43.41	40.89	59.11	42.55	57.45
2007	51.53	48.47	53.01	46.99	55.61	44.39	42.76	57.24	42.38	57.62
2008	51.14	48.86	52.43	47.57	54.99	45.01	42.68	57.32	42.41	57.59
2009	51.29	48.71	52.73	47.27	55.12	44.88	41.76	58.24	42.28	57.72
2010	50.76	49.24	52.36	47.64	53.12	46.88	40.71	59.29	43.80	56.20

1.3 Summary

This chapter has briefly examined TB at global, regional, national and local levels. It shows that the TB burden in Pakistan is the greatest in the EMR. Data from KPK province shows that this burden seems to fall disproportionally on women. In part, local disease trends reflect health service utilization, which will be discussed in the next chapter.

CHAPTER 2: HEALTH SERVICES IN PAKISTAN

2.1 Introduction

The goal of this section is to highlight the health services and infrastructure in Pakistan to give a better understanding of the study area. The geography of Pakistan and Khyber Pakhtunkhwa state will also be described.

2.2 Demography of Pakistan

According to WHO 2010 report the estimated population of Pakistan is about 180 million, making it the world`s sixth most populated country with a 1.95% population growth rate. The literacy rate of females (36.0%) is significantly lower than males (63.0%) (23).

Figure 3: Age Structure of Pakistan's Population (24)

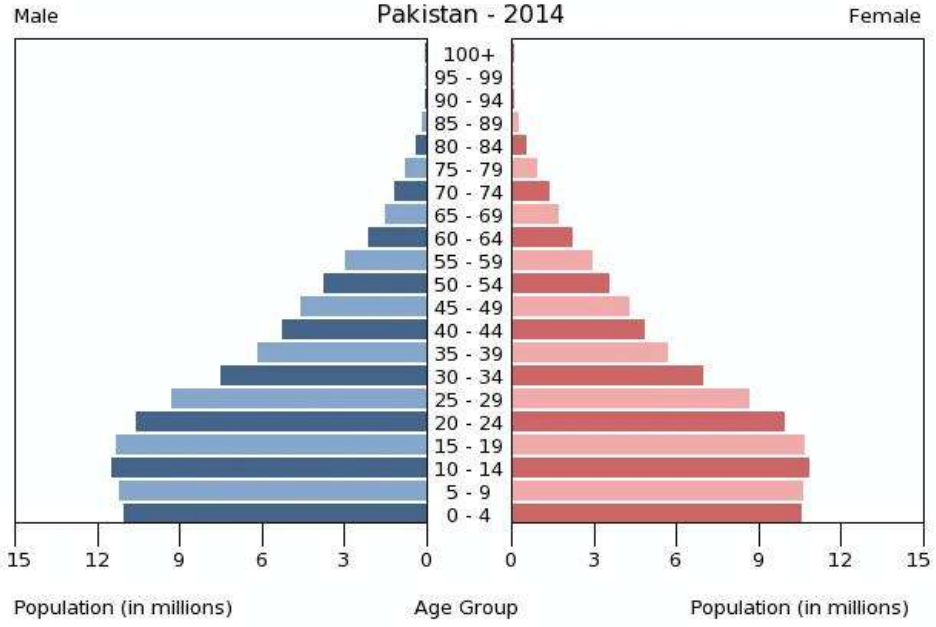


Figure 3 shows the age and gender structure of Pakistan's population. Horizontal axis shows gender distribution of the population and vertical axis represents the age groups of the population.

Table 4: Pakistan's National Age Structure (25)

Age Group	Total (%)	Rural (%)	Urban (%)
0-14	43.40	45.06	40.09
15-44	42.14	40.15	46.15
45-64	10.93	10.98	10.83
≥ 65	3.53	3.81	2.93

Table 4shows the distribution of urban and rural population of Pakistan by different age groups.

Table 5: Sex Ratio of Pakistan (25)

Sex Ratio per 100 Females			
Age Group	**Total (%)**	**Rural (%)**	**Urban (%)**
0-14	108.0	102.9	110.6
15-44	92.8	90.6	96.6
45-64	97.0	93.2	106.1
≥ 65	127.8	136.4	113.3
Overall	101.6	100.4	103.9

Table 6: Pakistan Demographic Summary (26)

Description	Figures
Population	1,822,143,000 estimated 2013
Growth rate	2.03
Birth rate (estimated births/1000)	27
Death rate (estimated deaths/1000)	7.86
Deaths due to tuberculosis (per100,000 population)	69
Literacy total (Male, Female)	49.90 (63.00, 36.00)
Unemployment	7.4
Life Expectancy	65.6
Gross national income per capita (PPP int $)	$4,920

Table 6 shows the WHO latest Pakistan's demographic data about population, literacy, unemployment and gross national income.

2.3 Geography of Pakistan

Pakistan, located in the north-western part of the South Asia, became an independent state as a result of the division of British India on August 14, 1947. After the Indo-Pakistani War of 1947-48, Pakistan annexed Azad (Free) Kashmir. The north-east part of the subcontinent where the majority of the population were Muslims also became part of Pakistan as East Pakistan. Hence, East and West Pakistan were separated by 1,600 km of Indian Territory. In December 1971, East Pakistan became the independent state of Bangladesh (25).

Figure 4: Map of Pakistan (25)

Pakistan has four provinces Punjab, Sindh, Khyber Pakhtunkhwa and Baluchistan. The total land area of Pakistan which occupies a position of great geostrategic importance is estimated about 803,940 square kilometres (310,401 sq mi).

It occupies a great geostrategic importance as it borders with Afghanistan (2,430 km) in the west, China (523 km) in the northeast, India (2,912 Km) on the east and the Arabian Sea (1,064 km) on the south. The estimated population of Pakistan is about 1,822,143,000 with 2.7% growth rate. This makes it in the top ten of the world population growth rate (27).

2.4 Geography of Khyber Pakhtunkhwa

Khyber Pakhtunkhwa (KPK) is the third largest populated province of Pakistan. The total land area of KPK is about 74,251 square kilometres (28,773 sq mi). Peshawar, Abbottabad, Mardan, Bannu, Dera Ismail Khan, Dir, Swat and Chitral are the main districts and the main cities are Bannu, Kohat, Haripur, Mansehra, Peshawar, Mardan, and Abbottabad (28).

Table 7: Distribution of KPK Population According to Rural /Urban Ratio, Sex Ratio and Area by District in 1998 Census (29)

District	Area		Population		Urban Proportion	Rural Proportion	Sex Ratio	Growth Rate (1981-98)
	sq.kms	%	000s	%	%	%	Males per Hundred Females	% per Annum
NWFP	**74521**	**100**	**17736**	**100**	**16.88**	**83.12**	**105**	**2.82**
Abbottabad	1967	2.64	881	4.97	17.93	82.07	100	1.82
Bannu	1227	1.65	676	3.81	7.04	92.96	107	2.81
Battagram	1301	1.75	307	1.73	-	100.00	107	-0.58
Buner	1865	2.50	506	2.85	-	100.00	100	3.86
Charsadda	996	1.34	1022	5.76	18.86	81.14	108	2.88
Chitral	14850	19.93	319	1.80	9.61	90.39	103	2.52
D.I.Khan	7326	9.83	853	4.81	14.75	85.25	111	3.26
Hangu	1097	1.47	315	1.78	20.42	79.58	96	3.25
Haripur	1725	2.31	692	3.90	11.95	88.05	100	2.19
Karak	3372	4.52	431	2.43	6.47	93.53	96	3.26
Kohat	2545	3.42	563	3.17	27.00	73.00	101	3.25
Kohistan	7492	10.05	473	2.67	-	100.00	124	0.09
Lakki	3164	4.25	490	2.76	9.57	90.43	104	3.16
Lower Dir	1583	2.12	718	4.05	6.18	93.82	98	3.42
Malakand	952	1.28	452	2.55	9.55	90.45	107	3.36
Mansehra	4579	6.14	1153	6.50	5.32	94.68	98	2.40
Mardan	1632	2.19	1460	8.23	20.21	79.79	107	3.01
Nowshera	1748	2.35	874	4.93	25.96	74.04	109	2.90
Peshawar	1257	1.69	2019	11.38	48.68	51.32	111	3.56
Shangla	1586	2.13	435	2.45	-	100.00	106	3.27
Swabi	1543	2.07	1027	5.79	17.45	82.55	101	2.96
Swat	5337	7.16	1258	7.09	13.83	86.17	106	3.37
Tank	1679	2.25	238	1.34	15.00	85.00	109	3.13
Upper Dir	3699	4.96	576	3.25	3.98	96.02	103	2.76

Table 7 shows the distribution of rural and urban populations of KPK by districts, where Battagram, Buner, Kohistan, and Shangla districts are 100 % rural residence.

Key to text colour in table:

■ = Districts out of Research Area

■ = Districts with Lower Female TB Notification

■ = Districts with Higher Female TB Notification

Figure 5: Map of Khyber Pakhtunkhwa (30)

The region differs in its natural features. The southern part is mostly dry and rocky while the northern part mostly consists of woodlands and green plains. The typical weather in this region varies from hot summers to freezing winters. In spite of these large variations in weather, agriculture is both viable and it plays an important role in the regional economy.

Kalam, Upper Dir, Naran and Kaghan are all known for their magnificent mountainous landscape and tourism remains an important component of the local economy. Swat was called "the Switzerland of the east" by Queen Elizabeth II during her visit to the Yusafzai state of Swat in 1961 (31).

Figure 6: Queen Elizabeth II visit to Swat in 1961(31).

Figure 6 shows Queen Elizabeth II with Price Philip, Miangul Jehanzeb Khan (Wali-e-Swat) and Qudratullah Shahab (Urdu writer and bureaucrat)

According to the 1998 census report, the population of KPK is 17,734,645 (of whom 52% are males and 48% are females). There are approximately 1.5 million Afghan refugees living in the province. Two-thirds of the population are classified as Pashtuns who make the largest ethnic group in the area (32).

2.5 Healthcare in Pakistan

The development of the health services in Pakistan can be traced to policy developments implemented at the time of partition. The Health Survey and Development Committee, popularly known as the Bhore Committee, reported in 1946 that the future state of Pakistan should assume full responsibility for all preventive measures and treatment necessary for the health protection of the population (33). Recent policy developments have resulted in attempts to provide a range of comprehensive services by the State and attention has also been paid to the distribution

of medical benefits and the ability to pay for health care irrespective of a person's economic situation. Politically, the state ascribes to the notion that health care is a fundamental right which should be available to all irrespective of ability to pay (25).

The health care delivery system in Pakistan can be classified into three categories: primary, secondary and tertiary care.

2.5.1 Primary Healthcare

Basic health unit (BHU) and rural health centre (RHC) are primary healthcare facilities mostly providing preventive care for immunisation such as for polio and TB. Family planning and maternal and child health services are also available in primary healthcare facilities.

2.5.1.1 *Basic Health Unit*

The basic health unit (BHU) was created in 1980 and established by the government during 1985-86 in every union council. Lady health workers (LHWs) linked to BHUs reinforce the health system at community level, where BHUs are the main upward referral centres for rural and district health hospitals. The government also decided to provide clinics and medical supplies in all larger union councils in 1991-92.

Staff at BHUs consists of a medical doctor, medical technician, health technician, vaccinator, midwife and LWH. BHUs provide health services for 5000 to 10000 of the population. BHUs have morning out-patients department (OPD) from Monday to Friday between 0800 to 1500 hours (33-34). The total annual budget of the BHU is around 1.33 million Pakistani Rupees (USD 133,000; 1 US$= 100 Pak Rupees at the time of writing) (35).

2.5.1.2 *Rural Health Centre*

There was a significant urban rural divide with fewer government-supported services in the rural areas. The country's second five-year plan (1960-65) required the establishment of 150 rural health centres (RHC) over a period of five years in West Pakistan alone. By December 2000, this number had increased to 572 RHCs (35).

In the same way that BHUs, are organised, RHCs also provide preventive services. RHCs not only provide health services to a population of 25000 to 50000 but are also focal points for community and health authorities for meeting and training of health personnel. The staffing of RHCs consist of senior medical officer, medical officer, women's medical officer, medical technicians, midwifes and LHWs (34)(36).

2.5.2 Secondary Healthcare

Tehsil headquarter hospitals (THQ) and district headquarter hospital (DHQ) are secondary healthcare facilities, providing primary curative health services for outpatients and inpatients.

2.5.2.1 *Tehsil Headquarter Hospital*

These are located in the centre of Tehsils providing preventive, promotive and primary curative services for 100,000 to 150,000 residents. THQ are the first level referral facilities for RHCs and BHUs. They are equipped with morning OPDs as well as 24-hour emergency and ambulance services. THQ also have 40 to 60 bedded facilities for inpatients divided to children, surgical and medical wards. All THQs have operative and diagnostic facilities that include medical laboratory and radiology equipment. Personnel in THQ consist of medical superintendent (MS), specialist doctors, medical officers, nurses, medical technicians, midwives and other supportive staff (34).

2.5.2.2 *District Headquarter Hospital*

DHQ hospitals are located in every district, providing curative care to half to one million residents. DHQs are secondary level referral facilities for THQs, RHCs and BHUs. They have both morning and evening OPD with 24-hour ambulance services. DHQs are125 to 250-beded facilities divided into children's, surgical, medical, orthopaedic, cardiology and maternity wards. DHQ hospitals also have dental, intensive care units and operating theatres (OT). Personnel in DHQ consist of MS, specialist doctors, medical officers, dental surgeon, pharmacist, medical technicians, OT technicians, nurses, Medico legal officer (MLO), midwives and other supporting staff (36).

2.5.3 **Tertiary Healthcare**

Tertiary healthcare hospitals (THC) are mainly located at the centre of provinces or big cities, providing specialised consultative care with more advanced diagnostic facilities. Patients usually referred to THC from DHQs, THQs, RHCs and BHUs. Teaching hospitals are an example of highly skilled tertiary care level treatment hospitals in Pakistan (37). Teaching hospitals are mainly curative with medical education, research and training facilities. THCs have bedding capacity ranging from 600 to 1200, with specialised obstetrics and gynaecology, cardiology, surgical, medical, paediatric, skin, orthopaedics and 24-hour emergency units. THCs also have advanced diagnostic and waste management services. Tertiary care hospitals provide advanced treatment services such as plastic surgery, angiography, angioplasty, coronary artery bypass etc. Both morning and evening outpatient clinics are available for outpatients and inpatients in THCs. Personnel in THC consists of MS, deputy medical superintendents, casualty medical officers (CMOs), specialist doctors, medical officers,

trainee medical officer, house officers, medical technicians, OT technicians, nurses, managers, medical directors and other supporting staff.

Table 8 shows that Punjab and Khyber Pakhtunkhwa provinces have better health services than Sindh and Baluchistan (38).

Table 8: Provincial Comparison of Health Services in Pakistan (38)

Health Facility	Provinces				Total
	PUNJAB	SINDH	KPK	Baluchistan	
DHQs	28	11	15	18	**72**
THQs	57	44	10	0	**111**
Dispensaries	1,006	309	623	652	**2590**
TB Centres	46	1	24	9	**80**
MCH	404	41	112	76	**633**
RHCs	307	119	100	58	**584**
BHUs	2,494	781	1,135	432	**4,842**
Total	**4,342**	**1,306**	**2,019**	**1,245**	**8,912**

Source: Economic Survey of Pakistan (2012-13)

2.6 Public Health Services

The BHUs provide medicinal and preventive services for between 5,000 to 10,000 people. Rural health centres (RHCs) provide extensive outpatient services but inpatient services are usually limited to short-term observation and treatment for people who do not require transfer to a higher-level facility. RHCs serve about 25,000 to 50,000 people and are staffed by about 30 individuals including doctors and paramedics. Each RHC has approximately 10-20 beds and X-ray, laboratory, and minor surgery facilities (34).

Tehsil (sub-district) headquarter hospitals provide limited inpatient and outpatient services. They serve between 100,000 and 300,000 people with 40 to 60 beds and other services such as X-ray, laboratory and surgery facilities. The district

headquarter hospitals serve between half to one million people and provide a range of specialist care in addition to basic hospital and outpatient services. They typically have about 125-250 beds.

All health services in the district are controlled by the District Health Officer (DHO). All Tehsil Headquarter hospitals managers and first-level care facilities give their reports to their DHO. Consultant surgeons head the district headquarter hospitals who along with DHOs report to the Director General of Health at the provincial level. The Provincial Secretary of Health is directly responsible for the tertiary care hospitals.

2.7 Private Health Services

There are more than 20,000 small office-based clinics for general practitioners in the private health sector in Pakistan. These include more than 300 maternity homes called Mother and Child Centres (MCH), about 340 dispensaries for outpatient primary healthcare facilities, and more than 450 diagnostic laboratories. With regards to small to medium sized hospitals, there are also more than 500 units with 30 beds per hospital. These small to medium-sized hospital generally cater to low risk patients and are equipped with basic obstetric, surgical and diagnostic procedures. Most of these private health services are concentrated in urban areas. Large rural hospitals tend to be run by nongovernmental organisations (NGOs) [Table 9].

Table 9: A Comparison of the Public and Private Sector Health Care System in Pakistan (39)

PUBLIC SECTOR		PRIVATE SECTOR	
Facility	**Number**	**Facility**	**Number**
Hospitals	1,270	Hospitals	106
Dispensaries	5,382	Small hospital	520
RHCs	550	General practitioners	20,000
BHUs	5,404	Maternity homes	300
MCH Centres	696	Dispensaries	340
TB Clinics	285	Diagnostic Laboratories	450
Total hospital beds	101,173 (1,786 persons / bed)	NGOs	254

Table 9 shows the summary of health services and human resource in health sector of Pakistan.

2.8 The Expanded Programme on Immunisation (EPI) in Pakistan

Pakistan became part of the accelerated health programme in 1983 after 5 years of EPI launch by the WHO in 1978. The programme was evaluated and commended by an international commission in 1984 after it successfully achieved an immunisation coverage of about 95 percent of children between the ages 2 to 5 years old (40-41). Initially, only smallpox, BCG, diphtheria, tetanus and pertussis were included in the vaccination programme. The programme gradually evolved and six diseases were chosen on the basis of high burden of disease and the availability of well-tried vaccines at an affordable price. These currently include tuberculosis, diphtheria, neonatal tetanus, whooping cough (pertussis), poliomyelitis and measles However, following these initial successes, the coverage for vaccination has decreased dramatically. Current estimates suggest that immunisation has dropped to 54 percent, with the coverage for vaccination of pregnant women with tetanus toxoid even lower. This indicates weaknesses in the

EPI programme. There is evidence that the decrease in vaccination coverage may result in poor BCG vaccination in KPK (41).

In response to the situation, the government took a number of steps to further improve EPI services by accessing funds from the Global Alliance for Vaccines and Immunisation (GAVI). Additional resources were targeted at training additional staff to facilitate vaccination, improved surveillance, introduction of new vaccines (e.g. hepatitis B vaccine) and provision of cold chain equipment (42). The Pakistan EPI has also taken up the challenge of eradicating poliomyelitis by immunising every child in the country; however, it is still unsuccessful in achieving polio eradication. According to the WHO, 81 cases of polio were recorded in Pakistan during 2013. The WHO imposed travel restrictions necessitating polio vaccination for all Pakistani residents intending to travel abroad (43).

Table 10: Pakistan EPI Childhood Immunisation Plan (42)

Antigen	**Age**				
	At Birth	**6 weeks**	**10 weeks**	**14 weeks**	**9 months**
TB	BCG				
Polio		OPV 1	OPV 2	OPV 3	
Diphtheria ,tetanus, pertussis		DTP 1	DTP 2	DTP 3	
Hepatitis B		HB 1	HB 2	HB 3	
Measles, Mumps, Rubella					MMR

2.9 National Tuberculosis Control Programme

In 2003, the World Health Organisation (WHO) re-emphasised the importance of TB as a global emergency declaring that tuberculosis (TB) was a threatening disease for mankind (40). Pakistan was identified as one of the countries with significant problems in relation to TB. The government of Pakistan declared TB as a national emergency after recognising it as a major public health problem. Pakistan recently

passed a resolution through its national assembly reiterating its commitment to control and subsequently eliminating the disease as one of its Millennium Development Goals (44). Thereafter, Pakistan has implemented a programme aimed at facilitating the prevention of TB. The National TB Control Programme Pakistan (NTCP) was created and is now running as the largest health programme in the public sector across Pakistan. In this regard, the Ministry of Health initiated the National TB Programme to curb the spread of TB through enhancing public and private sector health facilities (1).

The overall objective of NTCP is to reduce mortality, morbidity and disease transmission so that TB is no longer a public health problem. NTCP and the Ministry of Health developed a comprehensive strategy for control of tuberculosis in the country with the focus on expansion and consolidation of Directly Observed Treatment Short Course (DOTS) services in the country. The national programme was successful in establishing a country-wide network of laboratory services, providing free diagnostic and treatment services at 5,000 public health facilities and engaging the private sector to further enhance the quality of TB services. The programme was able to achieve the Millennium Development Goals (MDG) output indicators by detecting 70% of TB cases in the country and treating 85% of them, suggesting that Pakistan was now well on track to reach MDG targets by 2015 (45).

The public education campaign associated with this programme of TB control was extensive. Posters identifying "Free services for diagnosis and treatment of TB available here" were affixed on all TB centres across the country in order to empower TB patients to demand their rights to free treatment and diagnosis. And to ensure proper monitoring, a well-coordinated surveillance system was put in place for prompt response to drug or chemical shortages in these centres. It is because of interventions such as these that the case detection rate (CDR) and treatment success rate (TSR) for

TB have increased from 70% to 74% and from 88.% to 91.%, respectively. CDR and TSR are the two key indicators that have been used to measure the burden of TB (46).

2.10 Summary

Chapter 2 has explored the geography, health services structure and the role of national TB control programme in the control of TB in Pakistan. Chapter 3 presents a detailed literature review exploring risk factors of TB with particular relevance to Khyber Pakhtunkhwa.

CHAPTER 3: LITERATURE REVIEW

3.1 Introduction

Mycobacterium Tuberculosis (TB) is a serious public health threat globally and particularly in developing countries (47). Among the 22 high burden countries, Pakistan ranks 5th with a diagnosis of about 420,000 new cases every year (48). Globally, case notification is higher in males as compared to females but in Khyber Pakhtunkhwa (KPK) the rate of notification is much higher in females (6). There is similar data reported from Afghanistan, where 68.50% new sputum positive patients were female (49).

To explore the causes of gender differences in notification of TB, it is essential to identify potential risk factors, evaluate patients and physician's knowledge of, diagnosis of and treatment of TB. Existing literature can help us to understand and interpret the results of different studies and utilise these findings to inform the theoretical basis of my proposed research.

3.2 Aim of the Literature Review

A literature review in the context of this project is aimed at assessing the factors associated with the increased notification of TB in women and exploring the range of methodologies available to investigate and explore the risk factors.

The review also contributes to developing a theoretical base for my research identifying key areas for data collection (Social and Epidemiological Risk factors, Patients and Physicians Knowledge).

3.3 Methodology of Literature Review

3.3.1 Systematic Review

Comprehensive analysis of the existing literature is required for identification of possible risk factors and evaluation of knowledge, perception, diagnosis and treatment of TB. To examine the issue of higher notification of TB in females, I looked at literature from a variety of sources (Global, Regional, National and Local). This helped me to identify global and regional differences - and allowed me to compare national and local studies - so that I could identify the different variables that would be used for the data collection.

3.3.2 Search Strategy

Ultimately there are three types of time dimension in research: cross-sectional (collecting data at a single point in time), longitudinal (more than one point in time) or retrospective (asking about previous data and comparing it to now). For the literature review I chose the retrospective method for looking back at what was previously known so that I could then go on to compare it to what I found in the interview stage. I was later able to bring them together in my discussion of results. Relevant literature was identified through covering key theoretical papers and review articles on risk factors for Tuberculosis including gender issues. Databases accessed were MEDLINE, EMBASE and Global Health, through the OvidSp interface focusing on literature published between January 2000 and February 2015. These dates were in a convenience range, as they marked the National TB Control Programme range up to the end date of my research project. The websites of specific journals, including the Journal of Infectious Diseases and American Journal of Public Health (AJPH) were used to locate references cited in articles (mostly review articles). Additionally, the websites of the World Health Organisation (WHO), the National Tuberculosis Control Programme (NTCP) and the

Department of Health, Pakistan, were used to find related reports. Finally, theses and documents held by universities and important unpublished review documents were also searched for grey literature. Data were extracted from the selected 85 research articles for tabulation, comparison and synthesis.

The search strategy sought material evaluating epidemiology and gender differences, risk factors, patient knowledge and general practitioners' knowledge of TB in Pakistan and Khyber Pakhtunkhwa. Key words "Tuberculosis or TB", "risk factors", "adult female or females", "Pakistan" and "Khyber Pakhtunkhwa or NWFP" were used to search at the national level. I also used key words "China", "India", "Iran", and "Afghanistan" for available studies to compare the situation of the disease at the regional level [Table 11].

3.3.2.1 *Search Strategy for Objective 1*

The first search aimed to identify papers and reports describing the epidemiology of Tuberculosis in Pakistan and Khyber Pakhtunkhwa previously known as NWFP. Key words "Tuberculosis or TB", "Epidemiology", "Pakistan" and "Khyber Pakhtunkhwa or NWFP" were used for the specific search at national level. I also used key words "China", "India", "Iran", and "Afghanistan" for available studies to compare the situation of the disease at the regional level. From the above search strategy, 34 potentially relevant published articles, globally, regionally, nationally and locally were identified [Table 11-Table 12].

3.3.2.2 *Search Strategy for Objective 2*

The second search sought material evaluating risk factors for TB in adult females in Pakistan and Khyber Pakhtunkhwa. Key words "Tuberculosis or TB", "risk factors", "adult female or females" "Pakistan" and "Khyber Pakhtunkhwa or NWFP" were used to search at the national level. I also used key words "China", "India", "Iran",

and “Afghanistan” for available studies to compare the situation of the disease at the regional level. From the above search strategy, 24 potentially relevant published articles, globally, regionally, nationally and locally were identified [Table 11-Table 12]

3.3.2.3 ***Search Strategy for Objective 3***

The third search sought material evaluating the knowledge, attitude, awareness and treatment seeking behaviour in TB patients. Using the terms “tuberculosis”, “TB”, “Knowledge”, “Attitude” and “Patient” as key words yielded 11 potentially relevant published articles globally, regionally, nationally and locally [Table 12].

3.3.2.4 ***Search Strategy for Objective 4***

The fourth search was to address the awareness, opinion and management of TB amongst family physicians. Using the terms “Tuberculosis”, “TB”, “Knowledge”, “Attitude,” “doctors”, “General Practitioner”, “GPs” and “Family Physician” as key words yielded 16 potentially relevant published articles globally, regionally, nationally and locally [Table 12].

Table 11: Search Strategy and Terms

Search Group	**Search Terms**			**Justification -** To limit results to papers relating	**Rationale**
"Epidemiology of TB"	Tuberculosis/TB AND Epidemiology	Combined with (AND)	China, India, Iran, Afghanistan OR	Regionally	In choosing these terms I endeavoured to fully define the terminology for the review and maintain consistency in interpretation
			Pakistan OR	Nationally	
"Risk Factors for Adult TB Patient"	Tuberculosis/TB AND Risk Factors Adult Female/s		NWFP OR Khyber Pakhtunkhwa	Locally	
"Knowledge, attitude, awareness and treatment seeking behaviour among the TB patients"	Tuberculosis/TB AND Knowledge OR Attitude OR Awareness OR Patients		China, India, Iran, Afghanistan OR	Regionally	
			Pakistan OR	Nationally	
			NWFP OR Khyber Pakhtunkhwa	Locally	
"Assessment of Awareness, manner and management of TB amongst Family Physicians"	"Tuberculosis" AND "Knowledge" OR "Attitude" OR "Awareness" OR "GPs" OR "Doctors" OR "Family Physicians"		China, India, Iran, Afghanistan OR	Regionally	
			Pakistan OR	Nationally	
			NWFP OR Khyber Pakhtunkhwa	Locally	

Table 11 on page 58 shows in detail what, search terms were used for each task with a justification and rationale. Searches were limited to references about empirical research or review articles.

The results of all these searches were exported into a database using Reference Manager. Then, the titles and abstract of each reference were read carefully to decide which papers should be reviewed critically. Therefore, the following criteria were used to identify relevant papers for review:

3.4 Inclusion Criteria

- Empirical research or a systematic review relevant to the epidemiology and risk factors for TB.
- Articles published in English
- Knowledge, Attitude, Awareness and Treatment seeking behaviour in TB patients-related papers.
- Assessment of learning, approach and management of TB amongst family physicians-related papers.

3.5 Exclusion Criteria

- The research involved a case report or case series
- Involved bovine Tuberculosis (BTB) or did not differentiate TB from BTB infection.
- Research involved individuals at higher risk of TB because of underlying disease (for example, research on subjects with lung cancer or HIV/AIDS).

3.6 Summary of Literature Selection

The systematic review identified 4,630 screen citations. Of the total, 2530 studies were yielded by MEDLINE search, EMBASE search yielded 1155 and GOLBAL HEALTH 730 articles. Additionally, from the websites of WHO, NTCP, MOH and online journals (JID, AJPH) a further 250 articles were identified.

3067 articles were excluded as not relevant to the research area because they did not meet inclusion criteria; for example several focused on children and young people. Further review of the articles by reading the titles and abstracts, resulted in removal of a further 749 articles as not relevant. After reading full text articles, 154 studies were considered eligible on the basis of our inclusion criteria. Finally, after removing the duplicate articles 85 studies were identified for the literature review [Figure 7] (PRISMA Check list available as appendix 14.8 on page 235)

Figure 7: PRISMA Flow Diagram

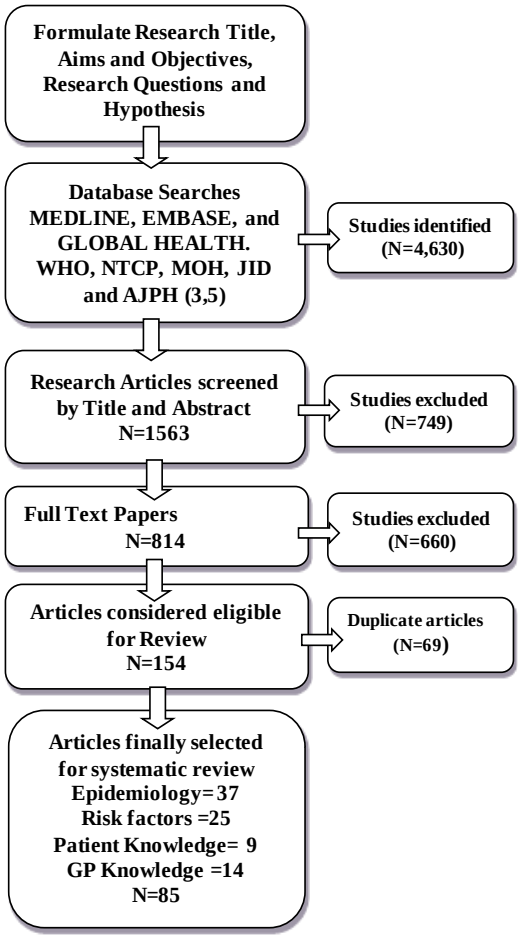


Table 12: Findings from the Different Search Strategies

Task	Database	Global	Regional				National	Local	Total
			China	India	Iran	Afg*			
Search Strategy	Medline	17	6	7	5	3	9	3	50
	Embase	15	7	6	3	1	4	5	41
	Global Health	13	6	4	2	2	7	3	37
	WHO/NTCP/Other	10	2	1	2	1	7	3	26
	Total Searched Articles	55	21	18	12	7	27	14	154
	Total After Duplication	27	12	10	7	5	16	8	85
1	TB Epidemiology	11	4	3	3	3	5	5	34
2	Risk Factors for TB Patients	6	3	3	2	2	6	2	24
3	Articles Related to Knowledge of TB Patients	4	2	2	1	0	2	0	11
4	Publication Related to Review of GPs Knowledge about TB	6	3	2	1	0	3	1	16
Afg*; Afghanistan									

The four different search strategies identified the following relevant papers: 34 on the epidemiology of TB, 24 on the risk factors for TB, 11 on patient knowledge about TB and 16 on GPs' knowledge about TB.

Table 13: Summary Table of the Literature describing Gender Differences of TB in Pakistan

Author Name (Year)	Aim	Study Design or Methodology	Study Subjects and Recruitment Methodology	Key Findings	Critical Observations
Khadim *et al* (2003) (50)	Factors affecting TB control: Decision making in the household level	Cross Sectional Study	100 (M=56, F=44) Newly registered TB patients in the Rawalpindi TB Centre between Jan to Feb 2002 included in the study. A questionnaire filled by every 5th adult participant in the serial.	Health awareness, easy accessibility to health care facility qualified heath care provider play important role National TB Control	No statistical methodology mentioned in the study, however detail diagrammatic presentation makes the study unique
Vermund *et al* (2009) (19)	Highlights TB burden and importance of research in Pakistan	No study design	no	Budget for research activities in Pakistan is very low	This is an article which provides comprehensive exploration of the diseases and importance of research in the region especially in Pakistan
Ullah *et al* (2008) (51)	To identify trends in the Extra Pulmonary TB incidence in NWFP.	Prospective study	525 (m=176, f=349) Study subject recruited as per submission of the biopsy for TB	Women are at higher risk of Extra Pulmonary TB than male in NWFP	Very well written paper .The results provide some support for our study hypothesis
Rizvi *et al* (2003) (52)	To identify age related differences in the clinical presentation of TB	Prospective study	67 (M=35, F=32)	Dyspnoea in elderly and upper lobe infiltration are common symptoms of TB	Statistical software or methodology used is unclear, however clear and detail statistical analysis done.
Israr (2003) (53)	Is the Ministry of Health fully prepared to implement an effective DOTS programme in Pakistan?	Descriptive Study	12 (M=6, F=6)	Information and communication system of the Health care system of Pakistan is very poor for effective control of TB	Although, sample size of the study is very small it explored very important area of research (DOTS).
Shah *et al* (2003 (54)	Prevalence of Pulmonary TB in Karachi Juvenile Jail, Pakistan	Cross Sectional Study	386 male	Results showed that prevalence of TB among the prisoners was 3.9%	Single centre study and limited to male patients only. Insufficient training of the technicians with language barriers Targeting the neglected group of the community where all the risk factors present in single premises.
Rao and Sadiq, (2002)(55)	Recent trends in the radiological presentation of Pulmonary TB in Pakistani adults	Descriptive Study	150 (M= 77, F=73) All newly diagnosed TB cases with x ray chest were included in the study.	Atypical pattern of TB increasing diagnosing delay	Study adopted strong descriptive study design. But limited to single centre

Muynck *et al* (2001)	TB Control in Pakistan: Critical analysis of its implementation	Literature review	Literature review	NTP facing very serious technical and managerial weakness, with strong political interventions. Research based activities should be promoted and importance should be given to those areas where data gaps are present	A retrospective study, limited to previous research articles Comprehensive critical analysis of the NTCP and ministry of health in Pakistan
NTCP Report, 2006 (56)	Reporting annual activities of National TB Control Programme	Annual Report	National report	A total of 11362 New Smear Positive, 4816 New Smear Negative, 1063 Extra Pulmonary and 148 Re-treatment were notified in 2006. Pakistan achieved 100% DOTS coverage in 2005 and sustained. Treatment Success Rate was reported 85% in 2006. Additionally, 700 health professionals including doctors, medical and laboratory technicians were trained	Provincial data of TB regarding the new cases and gender distribution were missing.
NTCP Report, 2007 (57)	Reporting annual activities of National TB Control Programme	Annual Report	National report	Incidence of TB in Pakistan 177/100,000. TB responsible for 5.1% of the total national morbidity burden in Pakistan.	On the basis of case notification Pakistan ranks 6th amongst the high burden countries globally in 2007.
NTP Report, 2008 (21)	Free TB Pakistan: Current status and the way forward	Annual report	National report	NTP achieving its aims and objectives as per planning. Incidence of TB in Pakistan increased from 177/100,000 to 181/100,000 in 2008. But the global ranking of Pakistan improved from 6th to 8th, which reflects the NTCP activities of fighting against TB in Pakistan	Annual report of NTCP based on population of 1998 where there is huge increase in the last 10 years. Well written report highlights the key components in TB epidemiology and control in Pakistan. Too many figures and discussing the achievements of the programme but didn't report weak areas of the programme.
NTCP Report, 2009 (44)	Reporting annual activities of National TB Control Programme	Annual Report	National report	A total of 267,491 new cases, including 101,887 sputum positive were reported in 2009. Incidence rate was 181/100,000.	A detailed report having the data of all four provinces and reporting that more female patients were notified in Balochistan. But the report missed the gender notification of TB in KPK which was also higher in females.
NTP Report, (2010) (45)	UPSCALING TUBERCULOSIS CARE AND CONTROL Epidemiology of TB in KPK	Annual Report	National report	Incidence of TB in Pakistan 231/100,000 269,290 new TB cases (all types) were notified during 2010. Of these, 104,263 cases were SS+, these figure are higher as compared to last year.	A detailed report of TB burden in Pakistan but data regarding foreign nationals with TB is missing. The report showed that female notification was significantly high in some Balochistan but missed KPK in reporting.
NTCP Report, 2012 (2)		Annual report	National report	Incidence rate was reported 177/100,000. Pakistan jumped to 5th in global ranking with 55% of total burden of TB disease in EMR	This was the first comprehensive and detailed report of NTCP. More TB patients were reported as compared to 2011. Report also

				region. A total of 269,265 TB patients were reported in 2012, of these 104,238 cases were sputum positive.	highlighted the issue of multi drug resistant TB in Pakistan. Health services in Pakistan also reported in 2012. The report also showed the summery of notified cases from 2001 to 2012.
NTCP Report, 2013 (1)		Annual Report	National report	Pakistan jumped to A total of 298,446 new cases notified during 2013, compared to 273,097 in 2012, with an incidence of 264/100,000. Pakistan ranks 5th globally in term of TB burden.	In-spite of 100 % DOTS coverage achieved in 2005, still 27 deaths were reported in 2013 from a disease which is curable. Pakistan share about 65% of total TB burden in EMR region in 2013, comparing to 55% in 2012.
WHO Report (2006)	Gender and Tuberculosis	Report of research and training in Tropical diseases	Multi Countries Study	Males are at higher risk than females in India and Bangladesh (neighbouring countries of Pakistan)	Comprehensive study exploring the burden of TB in the region, but surprising to see that two high burden countries in the region (China and Pakistan) were not reported ,
WHO Report, 2007 (18)	Global Tuberculosis Control SURVEILLANCE, PLANNING, FINANCING	Annual Report	Worldwide population	Report showed that Pakistan one of three countries spending less half of the available funds on TB in 2007. A total of 1.6 million people died of TB, including 195 000 patients infected MDR-TB a serious problem in HBC	Report provides key information about TB worldwide for the year 2007.
WHO Report, 2008 (58)	Global Tuberculosis Control SURVEILLANCE, PLANNING, FINANCING	Annual Report	Worldwide population	A total of 2.5 million new sputum positive cases were reported in 2008. Survey of knowledge, attitude and practice (KAP) were carried in 13 high burden countries. Pakistan ranks 8th globally for TB burden.	The report was based on data from 2006 mainly, not 2007 or 2008. However, it still it has a lot of new information about the global TB burden.
WHO Report, 2009 (15)	Global Tuberculosis Control Epidemiology, Strategy , Financing	Annual Report	Worldwide population	A total 9.27 million new cases notified in 2009, compared to 9.24 million in 2008. 80% of TB occurs in 22 high burden countries, including Pakistan. In 2009, total budget available in 22 HBCs was US $ 2.2 billion for TB.	A detailed analysis of the global TB burden and provides key information for planning and policy making.
WHO Report, 2010 (14)	Global Tuberculosis Control	Annual Report	Worldwide population	A total of 9.4 million new TB cases reported in 2010. Pakistan secured funding for survey in 2008 but due to security concerns the survey still has not been implemented.	Data reported in WHO TB report for 2010 was not as comprehensive as reported in 2008, 2007 and 2006.
WHO Report, 2011 (20)	Global Tuberculosis Control	Annual Report	Worldwide population	A total of 8.8 million TB cases reported in 2011, these figures were less as compared to 2010 (9.4 million). China and India both share 40% of the total TB burden.	The report showed the TB burden in detail globally. Most importantly, the number of cases decreased in 2011 as compared to 2010.

WHO Report, 2013 (13)	Global Tuberculosis Control	Annual Report	Worldwide population	In 2013, 8.6 million TB cases reported globally, where about 450 000 patients developed MDR-TB and of those about 170 000 people died. National survey on drug resistant carried out in Pakistan. In 2013 WHO reported 1:1 Male to female ratio for TB in Pakistan.	A detailed report for the global TB burden, which highlights MDR-TB and its threat in developing courtiers.
WHO Report, 2014 (12)	Global Tuberculosis Control	Annual Report	Worldwide population	In 2014, the numbers of notified TB patients were increased to 9 million, compared to 8.6 million in 2013. TB treatment success rate was reported 86% for new TB patients in 2014.But still 1.1 million people died from TB alone.	The report described reliable data on the global TB burden.
WHO Report, 2015 (59)	Global Tuberculosis Control 20th Edition	Annual Report	Worldwide population	A total of 9.4 million TB cases were reported in 2015, of those 5.4 million men, 3.2 million women and 1.0 million were children. WHO recommends that detection and treatment gaps must be addressed to reduce the TB burden. About 190,000 people died from MDR-TB in 2014. The report highlights that national scurvies identified gender differences in TB and should be investigated	The 2015 global report for TB is the first report that has a separate section (Section 4) on gender differences in TB, which provides reliable data for policy making.
Nassaji *et al* 2014 Afghanistan (60)	To evaluate demonstration of acid fast bacilli in tissues section showing typical histopathological features of tuberculosis in patients with EPTB using ZN staining method.	Cross Sectional Study	A total of 226 patients, of those 46.5% (105) were male and 53.5% (121) female were diagnosed with TB.	More female patients were reported as compared to female.	A well written Study with abstract, background, method, results and discussions. Limitations of the study were missing.
Fader *et al*, 2010 Afghanistan (61)	To describe the epidemiology of EPTB in Afghanistan.	Retrospective Study	118 (male to female ratio = 2:1)	The average age of males at the time of diagnosis was 32.2 years and of females 31.1 years.	A study which showed that female patients in Afghanistan were at a higher risk for TB than males.
Khan & Laaser, 2002 Afghanistan (62)	Burden of Tuberculosis in Afghanistan: Update on a War-stricken Country Ibrahim	Tuberculosis control programme	Health services review	Incidence of TB in Afghanistan 278/100,000. Number of death reported in 2001 15,000. Male to female distribution 30/70. DOTS coverage 10%.	The paper based on the data collected in Pakistan not in Afghanistan by NGO working for the control of TB in Afghan refugees camps.

Roya Alavi-Naini, 2007 Iran (63)	To reveal the gender differences in treatment of TB	Cross Sectional Study	A total of 2,284 of TB patients were registered, of those 1375 (60.2%) females and 909 (39.8%) were males.	Of the total (2,284), majority 1205 (f= 726, m= 479) were sputum positive, 552 (f= 331, m= 221) sputum negative and 527 (f= 318, m= 209) were reported extra pulmonary TB.	Figures in the study showed that all form of TB were more common in females as compared to males. It is a large sample size study but the study design and recruiting methodology of patients was not clear.
Chaha , 2005 India (64)	A review of Tuberculosis epidemiology in India.	Review Article	Medline, Medscape and AIDSLINE databases were searched. Reports also collected from NTP and other websites	TB situation was reported worse in rural areas. India accounts 20% of the global TB burden with estimated 1.8 million TB cases every year.	Gender distribution of TB was not reported.
Viney *et al*, 2011 Global (65)	The Epidemiology of Tuberculosis in Pacific Island Countries and Territories	Retrospective study	A total of 1544 TB cases were notified (male/female = 1.0 /0.8	Of the total, 73% (1105) were pulmonary and 27% (409) were extra-pulmonary. Of all pulmonary TB cases, 52% (575) were sputum positive and 48% (530) were negative.	Multi country study with reliable data, which provides key information about TB globally.
Kakchapati *et al*, 2010 Nepal (66)	Model incidence of TB between 2003 and 2008 in Nepal.	Retrospective study	A total of 198,719 cases reported between 2003-2008, of those 127,979 (64.4%) were male and 70,740 (35.6%) were female.	Epidemiological findings demonstrate that tuberculosis incidence rates are higher for males compared to females. Rural areas were also reported with higher incidence compared to urban.	Study showed the gender difference in the incidence of TB in Nepal.
Kadivar *et al* 2001 Iran (67)	The study aim to evaluate the epidemiology of TB in Afghans in southern Islamic Republic of Iran.	Descriptive Epidemiological Study	A total of 1026 of new sputum positive (NSS +ve) patients were reported, of those 371 where were Afghans. (male= 56%, female= 44%)	Results showed that 66.8% of cases were aged 15-44 years. Pulmonary TB (74.9%) was more common than Extra Pulmonary (24.1%). The incidence of TB was 92.2 (2000), 88.2 (2001) and 63.5 (2002) per 100,000 population	The occurrence of TB in Afghanistan is higher in females as compared to male, but the results of the research reported more males than females, which is not similar to the results in Afghanistan.
Dogar *et al*, 2012 Pakistan (6)	The aim of the study was to see whether gender differences are evenly distributed across the country or vary by geographies, to enable effective targeting of TB control strategies.	Cross Sectional Study	Study carried out on NTCP notified cases between 2001 to 2010	A total of 571,958 new smear sputum (NSS) positive cases were reported between 2001 and 2010. Of those 51% (292,551) were males and 49% (279,407) were females. However, the notification of TB cases in females was higher in KPK (MFR= 0.70:1.00) and Balochistan (MFR= 0.68:0.78), compared to Punjab (MFR= 1.12:1.00) and Sindh (1.27:1.00).	This study reported a reliable data and initiated on the basis of our preliminary study carried out on the 10 years NTCP data in KPK in 2011. Results of this study confirmed the findings of our study for objective one that female patients are at higher risk for TB in the province of KPK, Pakistan.

Table 14: Summary Table of the Literature of Risk Factors for Tuberculosis

Author Name (Year)	Aim	Study Design or Methodology	Study Subjects and Recruitment Methodology	Key Findings	Critical Observations
Akhtar and Rathi, 2009 (68))	To identify risk factors for TB	Cross Sectional Study	385 (m=205, f=180) Cases identified from TB clinic register in Umerkote	Household contact of TB exposure is more significant and need attention	Study is limited to single centre and methodology for recruitment is also unclear. However research highlighted an important issue of house contact of TB patients in Pakistan.
Soomro and Qazi, 2009 (69)	To Compare Factors Associated with Relapsed TB in Male and Females	Cross Sectional Study	100 (m=62, f=38) All patients with relapse were included in the presented to out patients department of Civil Hospital in Hyderabad.	Significant variations observed between male and females	It is a study with small sample size and limited to single centre. However, the research results are valuable focusing on social and potential risk factors, such as overcrowding and HB level
Aziz *et al*, 2008 (70)	To assess the risk for family member of TB patients contacts as compared to non contacts.	Cross Sectional Study	200 participants recruited as household's member having active Pul. TB.	Results showed that household contacts of TB patients are at higher risk than non contacts	Methodology for selection of study subject is missing. Similarly gender of participants was not described in the study. Furthermore, Lahore is a large city so selection of house hold is unclear. Method for statistical analysis described in detail.
Javaid *et al*, 2008 (71)	To identify drug resistance to anti TB drugs in NWFP, Pakistan.	Cross Sectional Study	199 (m=53, f=66) All newly diagnosed TB patients in 7 centres of NWFP	Women are at higher risk than male in NWFP for MDR	The study does not explain the ratio of drug resistance by gender. Multi centres study with significant results
Hussain *et al*, 2003 (72)	To identify risk factors for latent TB infection in prisoners of NWFP.	Cross Sectional Study	425 164- Peshawar 83- Haripur 90-D.I. Khan 54-Kohat	High level of latent TB infection need urgent attention from NTP	Gender aspects of the participants ignored in the study. While some of the participants from risk group were found missing from screening. It is a multi-centres study covering the entire province. The study also recommends further research for the diagnosis of TB in high risk groups.
Rizvi *et al*, 2003 (52)	To differentiate the pattern of pulmonary TB in younger and older patients	Prospective Study carried out from Dec 1999 to May 2000	67 Young 36 Elderly The two groups divided below 60 for younger and above 60 for older and recruited all the study subjects in this age groups between the study duration	COPD is more common risk factor in elder patients	It is unclear that which statistical software or methodology was used in the study. However, the results were presented clearly

Liefooghe and Muynck , 2001 (73)	To identify different factors which Tuberculosis management	Semi structured questionnaire based study having both qualitative and quantitative approach	563 (44% = male, 56%=female) Patient recruited on the basis of sputum positive test and above 15 years of age	Majority of the patients were in the most productive age (15-45), Illiterate patients have high defaulter rate. Irregular use of anti TB drugs is a significant risk factor	It is a study of small sample size, limited to single district. Study design not clear, abstract have no results and organised as like a conclusion
Sharma *et al* 2010, India (74)	To examine the trend in gender gap in the prevalence of TB over the year	Survey	A total of 4,91,000 of covered population nearly half were female.	Of the total 74% were belong to rural and 27% were from urban area. Significant gender difference was noted in rural areas 98/ 100,000 v 176/100,000 ($P<0.05$).	Clear study design was not mentioned and recruiting of ample size was unclear as well. However, the study showed gander differences in rural and urban areas and relevant to our study as 75% of the KPK population living in rural areas.
Davies, 20005 (9)	Risk Factors for Tuberculosis	Review article	Literature review	Malnutrition, young age, socioeconomic, indoor air pollution, alcohol and health system issues were identified as main risk factors for TB.	Well search literature review, identified main risk factors responsible for Tb disease. In our study we also assume some of these risk factors for higher notification of TB in KPK.
Sabawoon and Sato, 2012 Afghanistan (49)	To explore Sex Difference in Tuberculosis in Afghanistan	Retrospective Study of TB records	A total of 9,949 NSS +ve were reported, of those 31.5% (3,131) were males and 68.5% (6,818) were females.	Female patients in Afghanistan who were aged 15 through 44 years, were twice more likely have TB than males. Similarly, females in Afghanistan stay for long time inside in homes with poor ventilation and lighting (i.e., away from sunlight that quickly kills tubercle bacilli)	Retrospective study based on the data of NGOs and TB control programme The geographical and cultural situation of Afghanistan is similar to the province of KPK, where we conducted our research. Therefore findings of this study were very relevant and important to our results

Table 15: Summary Table of the Literature on Patient's Knowledge about Tuberculosis

Author Name (Year)	Aim	Study Design or Methodology	Study Subjects and Recruitment Methodology	Key Findings	Critical Observations
Mushtaq *et al*, 2011 (75)	To Explore inequities in knowledge, attitude and practices regarding TB among the urban and rural populations.	Cross sectional Study	1080 (Urban=432, Rural=648) Male=76.2% Female=23.3% Two out 35 distracts in Punjab were randomly selected. Five Union council two from urban and three from rural were further selected randomly. From each Tehsil two villages selected for interviewing 18 indivisibles	In the rural population knowledge regarding TB was deficient.	Unavailability of female staff for interviewing females. Repetition of study previously published with same results in 2010. However, it is important study, comparing TB in both urban and rural communities.
Samera *et al*, 2008 (76)	To assess the level knowledge of TB patients regarding TB	Hospital based cross sectional study	301 (m=160, f=141) Hospital based study, all TB patients attending the setting from May to July 2006 recruited for the study.	Awareness about TB was very deficit in TB patients contributing to delay in diagnosis of TB	It is study limited to only two centres
Khan *et al*, 2006 (77)	To assess the knowledge of patients with TB about their disease and misconceptions regarding TB	Cross Sectional Study	170 (m=92, f=78) Patients above 16 years having TB now or in past were recruited for the study, seeking treatment in two hospitals.	Misconceptions about TB were widespread in Pakistani Patients.	Limited to a single city only, but covered both the Government and Private health facilities.
Ali *et al*, 2003 (78)	To explore the level of knowledge regarding TB amongst patients and their families	Descriptive cross sectional survey based study	203 (m=131, f=72)	Knowledge about TB in both patients and their family was deficit and larger population based studies should be conducted	Findings limited to only one centre where the awareness level is high as compared to other areas Health education should be a part of such studies in future TB patients and their families members were the most affecting people, so important area for research
Agboatwalla *et al*, 2003 (79)	To assess the knowledge and attitude about TB in rural and urban community of Sindh Provence of Pakistan	Cross Sectional descriptive study	754 (m=385, f=369) One urban and rural site in Karachi were selected randomly for interviewing 100 household each	Overall Knowledge of TB was deficient in rural females.	Selection of urban and rural sites in methodology was not mentioned. However, the approach of interviewing the study subjects, male by male and female by female was very appropriate. Similarly, is very important research focusing on gender perspective of knowledge about TB

Table 16: Summary Table of the Literature on Physician's Knowledge about TB

Author Name (Year)	Aim	Study Design or Methodology	Study Subjects and Recruitment Methodology	Key Findings	Critical Observations
Ahmed *et a*l, 2009 (80)	To assess the knowledge, attitude and practices of private GPs regarding TB DOTS	Questionnaire based survey	22 PPs Participant recruited from a TB DOTS workshop having medical graduation	High gaps in the diagnosis and treatment of TB through DOTS observed	It is single distract study limited to male private General practitioners only. Similarly, clear study design is not mentioned in methodology.. However, this is the first survey in the rural area of Sindh, Pakistan
Shehzadi *et al*, 2005 (81)	To assess the knowledge of GPs in NWFP and Northern Areas of Pakistan regarding the management of TB	Cross Sectional Survey	88 GPs were recruited from Gilgit, Hunza, Skardu, Abbottabad and Peshawar	Sever deficiencies were seen in the treatment of TB by GPs in NWFP.	The methodology for sampling and recruiting of GPs is not clear in the study. Similarly, the study limited to only male GPs. However, the study highlights the important area of research (GP's Knowledge) in six distracts of NWFP.
Hussain *et al* (2005) (82)	To evaluate the knowledge of PPs regarding TB management	Cross Sectional Study	53 GPs recruited who fulfilled the inclusive criteria for the study	Research observed significant deficit of knowledge regarding TB management amongst PPs	A study of small sample size, limited to male PPs, however the statistical analysis of data and the tabulated presentation is very good. Most importantly, it was an unique research strategy for assessing the knowledge of GPs by experimental approach by acting as TB patient
Shah *et al*, 2003 (83)	To determine the knowledge of private GPs towards diagnosis, treatment and follow up of pulmonary TB in 2 large cities of Pakistan.	Descriptive Cross sectional Survey.	245(m=197, f=48) FPs were selected from Rawalpindi and Lahore cities of Punjab, Pakistan, working in Govt health care facilities with basic degree in medicine.	The study showed that the knowledge and practices of GPs were not in line with National TB Control Programme guidelines.	Study limited to only 2 cities of Pakistan. Majority of Pakistani population were receiving treatment in Government Hospital, so it is the strength of the study that research performed in public health care. Similarly, study covered all the basic components of TB management i.e. diagnosis, treatment and follow up.
Khan and Hassain 2003 (84)	To assess the practice of prescription of doctors working in the private teaching hospital of Pakistan	Cross sectional study	120 GPs out of 141GPs participated in the study	Some of the Doctors in the private teaching hospital prescribing TB drugs below recommended dose.	This is also a single centre study limited to only male doctors.
Khan, 2003 (85)	To evaluate the knowledge and practices of private GPs regarding the diagnosis and treatment of Pulmonary TB.	Questionnaire Survey	120 GPs All the GPs working in Karachi were invited to join a workshop on health practices and during that workshop questionnaire distributed and collected for the study	It has been found that the knowledge and practices among Private GPs were unsatisfactory	Study covered only a single city of the country with no clear study design. Questionnaire of the study described in detail with important variables and meet the gender aspect of research. However, it is not mentioned how many male or female were included in the study.
Rizvi and Hussain, 2001 (86)	To investigate the knowledge, attitude and practices pertaining to TB among family physicians.	A questionnaire based study.	150 Family Physicians 30 FPs from each five districts of Karachi were selected randomly	There are many misunderstandings about the transmission of TB and BCG vaccinations.	The writing standard of the study is very bad repeating study questions. Similarly, reference section is not according to the standard guidelines. Focus on GPs without Post Graduate qualification

CHAPTER 4: FINDINGS OF THE SYSTEMATIC REVIEW "TUBERCULOSIS IN PAKISTAN"

Tuberculosis (TB) is one of the most rapidly re-emerging infectious diseases globally and is having a significant impact on the health burden in Pakistan. The national incidence of TB is 177/100,000 which means that Pakistan is ranked 5th in the High Burden Countries (HBC) worldwide. Pakistan ranks first with 43.0% share of the total TB burden in the Eastern Mediterranean Region (40). National TB Control Programme (NTCP) reported that TB contributes a 5.1% share to the overall morbidity burden in Pakistan (1)(4)(19).

The population of Pakistan is 182.2 million the sixth largest in the world - the annual growth rate is 2.7%. About 70.0% of the total population lives rurally. The province of Khyber Pakhtunkhwa is identified as an area where the notification rate of Tuberculosis is reportedly higher in female than male - a situation which is contrary to the gender distribution of TB at the national level (6)(21). Similar data are also reported from Afghanistan, where female notification of TB was also higher in female patients (49). Sharma *et al* in a survey of 90,000 households in India found that prevalence of TB in males is higher than females (74). Similarly, data reported from the TB Control Programme Shanghai China by Shen *et al* also described that the notification of male TB patients was significantly higher than female (87).

4.1 Epidemiology of TB in Pakistan

4.1.1 Introduction

The main source of information about TB in Pakistan is the National Tuberculosis Control Programme (NTCP) which started in 2001, with the annual reports for 2001 to 2013 describing the disease epidemiology in detail (1)(4)(21). NTCP

is a national organisation working with aid agencies and partner organisations for the eradication of TB in Pakistan: it also has branches responsible for TB control at the provincial level.

The control strategy involves co-ordinating the Primary Health Care (PHC) system, District Headquarter Hospitals (DHQs), Rural Health Centres (RHCs) and Basic Health Units (BHUs); in addition there are currently 23 tertiary heath care hospitals in Pakistan working within the NTCP for the diagnosis and treatment of TB patients (36). At collecting district level, the TB Control Officer (TBCO) is responsible for reporting all newly diagnosed TB patients' data to NTCP provincial office on a monthly basis. All the TBCO have extensive training on data reporting and therefore the data is highly reliable.

According to the 2014 WHO report annual disease incidence in Pakistan is 275/100,000, which is higher than Afghanistan (189/100,000), China (70/100,000) and India (171/100,000) (12). The notification of new TB cases of all forms was 298,446 in 2013, compared to 273,097 in 2012. In 2013 newly reported sputum positives and sputum negative cases were 111,682 and, 118279 respectively. Additionally 52,646 new extra pulmonary cases (EPTB) were registered in 2013. Multi Drug Resistant TB (MDR-TB) is a serious public health issue with 1,570 new cases reported in 2013, compared 210 in 2010. The total burden of MDR-TB in Pakistan is about 9,900 (1). According to WHO 0.9% of TB patients in Pakistan have co-infection with HIV (88).

Directly observed treatment short course (DOTS) coverage increased from 50.0% in 2002 to 100% national coverage in 2005. Treatment success rate has increased from 67.0 % to 91.0% in the last 10 years, which is higher than Afghanistan (88%) and India (89%) in the region (89). Nevertheless, the mortality rate remains unacceptably high at 37/100,000. The NTP spends 19.0% of its budget on first line

drugs, 20.0 % for laboratory and equipment costs, and 6.6% for NTP staffing costs out of a US$65 million total budget in 2007 (21).

Vermund *et al* reported that Pakistan spends 0.8% of its GDP on health care, which is about 50.0% less than Bangladesh and Sri Lanka. Health care research expenditure is also very limited in Pakistan because of high state expenditure on defence (22.0%). The report identifies the need for further research to eradicate TB from Pakistan (19).

4.1.2 Age and Gender

Age and gender are the two important variables in TB research, because the age of patients plays an important role in the state economy. Globally, it is recognised that notification of TB is higher in males as compared to females (90-92). However, figures show that younger female patients in developing countries are at a higher risk of TB than males of the same age (93). According to National TB Control Programme, TB case notification was higher in young female patients of Khyber Pakhtunkhwa and Balochistan as compared to Punjab and Sindh, where notification of male patients was higher when compared to females (6)(94). Seventy five percent of identified TB cases occurred amongst the economically active population (15-45 years), which is a substantial economic burden at both the individual and state level (19). In a study of 386 male inmates of a Juvenile prison in Karachi, Shah *et al* reported that nearly two thirds of TB patients (n=239, 61.9%) were aged 17 to 18 years. Overall disease prevalence was 3.9% which was significantly higher than the estimated 1.1% in the general Pakistani population (54). A similar study of male inmates in five prisons in the North West Frontier Province found that of 425 prisoners, 204 (48.0%) had latent TB infection, as determined by Mantoux testing and of these just over a quarter (n=111, 26.0%) were aged 18 to 26 years (72).

Rizvi *et al* in a prospective study carried out in two teaching hospitals in Karachi, reported that among 67 TB patients with a mean age of 30.6 years, just over half (n=35, 54.0%) were male: among older patients whose mean age was 65.9 year, a similar proportion were male (86). Khadim *et al* reported similar findings from a small cross sectional study carried out in Rawalpindi , where among one hundred TB patients, just over half (n=56, 56.0%) were male . The authors identified the need for larger population-based studies to explore risk factors for TB in Pakistan (50). Khan *et al* studied the awareness of 170 TB hospitalised patients about their illness – more than half (54.2%) were male (77). In a two-hospital chest clinic out-patient based cross sectional study, Samera *et al* recruited 301 participants of whom 160 (53.0%) were males (76). In a descriptive cross sectional study, Akhtar and Rathi reported that out of 385 study subjects, 53.2% were males and 46.8% were females (68). Somooro and Qazi using a cross sectional study design looked at 100 patients with reactivated/ re-infection TB in the Hyderabad DHQ Hospital between August and November 2008 and found that 62.0% were males (95). In a very recent study, Mushtaq *et al* compared knowledge and behaviour about TB infection in urban and rural communities in Punjab province: among the 1080 participants, just over three quarters were male (75). Therefore, the evidence for the predominance of TB in men is substantial.

In contrast to these findings, Dogar *et al* in a recent study about gender differences in TB in Pakistan reported higher case notification for females in the province of KPK as compared to males (6). These results are reliable, as it was conducted by NTCP in four provinces of Pakistan, similar to our descriptive study in KPK between 2002 and 2010. Ullah. *et al* in a recent prospective study carried out on TB patients at the Lady Reading Hospital Peshawar, KPK also found that of 525 patients diagnosed with extra-pulmonary TB (EPTB), nearly two thirds (n=349, 66.5%) were female (51). Research data from this small study suggested that risk factors for this

higher female incidence was related to the male dominant culture, multi parity, poor nutritional status, lack of awareness about TB, overcrowding and the low female literacy rate in the area. Most patients (70.1 %, n=369) were diagnosed with TB in their most productive age (15 to 45 years). The authors concluded that women were at higher risk of TB than males particularly during the reproductive age. Moreover, a recent study by Khattak *et al*, aimed to identify the number of sputum positive cases among PTB patients, women were found to be at higher risk of TB than males in KPK. Out 104 patients, 57.40% (n=60) were female and 61.52% were between the age 20 and 50 (96). Bassali *et al* reported that males were more commonly infected with TB in Egypt, Iraq and Yemen, while in Pakistan and Iran females were diagnosed in larger number as compared to males (97). These results provide evidence for the study hypothesis that females in the province of KPK are at higher risk for TB than males. Therefore, it is very important to investigate the causes of this higher notification in females, because women are mainly responsible for looking after children and families in KPK.

4.1.3 **Educational Status**

Educational status is the level of literacy attained by an individual by attending school, college or university. In Pakistan, there are religious institutions (Madrassa), which also provide education to the community. Literacy rates in general in Pakistan are higher in males than females (98). Several studies have reported that literacy levels are directly related to the incidence of Tuberculosis. Shah *et al* reported that more than half (n=239, 59.1%) of patients with TB in a juvenile prison were uneducated (54). Similar findings were reported by Hussain *et al* in a cross sectional study carried out to assess the risk factors for TB in KPK, where just over half (57.0%) of their study subjects were uneducated (illiterate) with a further third (34.0%) only receiving primary education (72). Similar results were reported by Akhter *et al* who found that the

majority (n=277, 71.9%) of participants who were randomly selected from the TB patient register maintained by the Umerkot AntiTuberculosis Association clinic were categorised as uneducated (68). Similar results were reported by Somooro and Oazi who found that 58.1% males and 68.4% females were uneducated (95). Samera *et al* explored the relationship between knowledge and the delay in the diagnosis and treatment of Tuberculosis. Of the 301 recruited patients, just under three quarters (71.0%, n=213) were uneducated (76). Agboatwalla *et al* compared literacy levels connected to TB in urban and rural settings – people were eligible to enter the study provided they had lived in the area for ≥ 6 months. They interviewed 754 participants and found that more than three quarters (78%) of respondents from rural areas were uneducated compared with only 51.0% in urban areas (79). Due to poverty, problems in transportation and cultural barriers, we would expect these results from rural areas.

Somewhat contradictory results were reported by Khan *et al* who found that just under a quarter (24.1%) were classified as illiterate with 10.0% having either a degree or postgraduate qualification – this is almost certainly explained by the study design which recruited nearly two-thirds (65.9%) of patients from a private hospital (77). Similar results were found in a study by Mushtaq *et al* of villages in the Punjab – of the 1080 participants, the majority (n=648, 60%) were from rural areas. Their research compared knowledge and behaviour about TB infection in urban and rural communities in Punjab province, and reported that only 25.5% from rural and 16.3% from urban areas were classified as uneducated (75).

4.1.4 **Socio-Economic Status**

Socio-economic status (SES) is characterised by the economic and social position of an individual based on income, education and employment. Soomro and Qazi reported that nearly three quarters (71.2%) of the patients with TB in their study

were classified as low income (i.e. having a monthly income of less than 5,000 Pak Rupees) – this compares with the national average of 7,685 Pak Rupees (95). Khan *et al* in a study of TB knowledge awareness in 170 hospital attendees in Karachi reported that just under half (46.5%) of their patients were classified as having a low income (77). Mushtaq *et al* compared TB in urban and rural communities of Punjab province and found that more than half (59.3%) of rural community cases had a low income (75). This means that the majority of patients in rural areas of Pakistan are classified as having low income. Since 75% of KPK population live in rural areas, low income level could be one of the risk factors for this higher notification of TB in females in KPK.

4.1.5 **Ethnic Origin**

The majority of patients with TB in the reviewed studies were Pakistani – Shah *et al* determined that of 386 single male inmates 92.5% (n = 357) were Pakistani and 7.5 % (n = 29) were foreign nationals: unfortunately at the national level, NTCP do not report the TB incidence of foreign nationals living in Pakistan (54). There are about 0.6 million registered Afghan refugees living in KPK, but they have a separate parallel programme for TB diagnosis and treatment. Therefore, we can assume that ethnic origin has no association with higher female notification of TB in KPK.

4.1.6 **Summary**

The papers reviewed in this section have suggested that male rates for reported TB notification in Pakistan are higher than KPK female rates. Research regarding gender and TB in KPK is very limited. However, available published studies and data from National TB Control Programme have described the higher notification rates of TB in women, supporting the premise of this thesis that reasons behind the variation in TB notification in parts of Pakistan require further investigation. Socio-economic factors are likely to explain the differential notification rates that we wish to investigate.

4.2 Risk Factors for Disease Acquisition

4.2.1 Introduction

TB is a major cause of death accounting for 7% of all causes of mortality (99). NTCP data suggests that overall males were more likely to be affected than females in Pakistan. However, there were several studies that pointed to a higher case notification of females than males in the province of KPK (6)(92)(96). In this section I will discuss the main risk factors for TB disease acquisition in Pakistan. The majority of females in Pakistan are unemployed and living as housewives in joint family system (where entire family of brothers, sisters and parents live together in a single house even after marriages and children) (100). Therefore, I have assumed that household contact, overcrowding, malnutrition, smoking and male dominant culture are potential risk factors for Tuberculosis in Khyber Pakhtunkhwa.

4.2.2 Disease Risk Factors

4.2.2.1 *Household Contact*

Akhtar *et al* explored the role of household contact as a risk factor for acquiring TB in the Umerkote distract of Sindh. Out of 385 study subjects, more than half (56.0%) reported living in the same bedroom as someone with TB. The authors reported that nearly half (n=184, 47.8%) of all children with TB were most likely infected as the result of a contact in the family (the mother or father) having active disease. More females (8.8%) than males (7.3%) also claimed they had acquired their TB from their married partner (68).

In a cross sectional study of TB patients seen at the Hyderabad DHQ hospital between August and November 2008, Soomro and Qazi determined that 26 (68.4%)

female cases reported household contact with a TB patient as a possible source for their infection (95).

Shah *et al* identified 15 cases of TB in Karachi out of 386 single male inmates – in this case control study a family history of TB was significantly more likely to be associated with confirmed disease (adjusted OR 7.78, 95% CI = 1.12 – 62.48) (54).

Recently, Aziz *et al* in study of 200 people selected from the family members of TB patients identified household contact as a major risk factor for developing TB (as determined by a positive Mantoux test); the authors suggested that a household contact, where there was an index case with active disease, was nearly 13 times more likely ($p<0.01$) to have a positive Mantoux test than controls drawn from households without such a case (70). The majority of females are unemployed, spending most of the time inside the home. This suggests that if there are undiagnosed or female patients in the home with active TB, the risk for TB occurrence will increases in females. Therefore, I consider that the time spent by patients outside of the home is one of the variables for my study.

4.2.2.2 ***Overcrowding***

When more people are living in a single house where limited space is available to them, as compared to a WHO standard, this is referred to as overcrowding. The WHO recommends a floor space area with 11 or more square metres for two persons, 9 to 10 or more square metres for 1.5 persons and 7 to 9 or more square metres for one person, while children 1 to 10 years counted 0.5 unit and babies under 12 months are not included (101-102). Several studies have explored the role of overcrowding as a risk factor for Tuberculosis. In a cross sectional study conducted by Soomro & Qazi in the Department of Medicine in DHQ hospital Hyderabad between August and November 2008 on TB patients, all the participants of the study reported living in overcrowded

housing, (defined as more than two persons of different genders sleeping in the same room) (95). Similar findings were reported by Javid *et al* in a cross sectional prevalence study of drug resistance in NWFP and suggested that almost all (n=110, 92.4%) the culture positive patients were from overcrowded families (71). Shah *et al* studied the transmission of Tuberculosis in 386 prisoners in Juvenile prisons in Karachi and reported that overcrowding was the main risk factor for disease acquisition (54). From the above evidence, it therefore concluded that overcrowding is also one of the most important risk factors for Tuberculosis and may be responsible for higher notification of TB in female patients in KPK.

4.2.2.3 ***Smoking***

Smoking is one of the main risk factors of Tuberculosis. Smoking not only increases the risk for TB in smokers but children and other family members exposed to passive smoking are also at a risk of TB (103). Three studies have looked at the role of smoking and occurrence of TB. Soomro & Qazi reported that more than half (58.0%, n = 38) of males with TB reported that they smoked – this was considerably higher than the corresponding figure for females (21.1%, n = 8, p= 0.01) (95).

Hussain *et al* studied latent TB in prisoners; they randomly recruited 425 participants from five main provincial prisons. One hundred and sixty four (38.6%) were from Abbottabad, 19.5% (n = 83) from Haripur, 21.1% (n = 90) from D.I Khan, 12.7% (n = 54) from Kohat and 8.0% (n = 34) were from Mardan. The authors reported that more than half (53.0%) of the participants were smokers with 29.0% (n = 77) saying that they smoked between 1 and 5 cigarettes daily (72). In another study (Shah *et al* 2003) in Karachi showed that 42.6% (n = 164) of the participants with suspected TB were smokers; these results are similar to the findings of Khan *et al* who reported that 40.0% males and 8.0% females in Pakistan smoke regularly (54)(77).

4.2.2.4 *Malnutrition*

Malnutrition is a condition caused by lack of proper nutrition or not having enough food to eat. Malnutrition was identified as a major risk factor for TB by Soomro and Qazi in a cross sectional research study focusing on gender differences in relapse patients. One hundred relapse cases were included in the study, with more males (38 out of 62, 61.3%) than females (18 out of 38, 47.4%) reporting malnutrition as a risk factor for disease acquisition (95). Research conducted in India reported that malnutrition is not only a risk factor for TB but better diet also plays an important role in the treatment of TB (104). Malnutrition is mainly associated with poverty and it is evident from the literature review that the majority of TB patients in Pakistan belong to a low income group. Therefore, malnutrition in my study will also be assessed by asking questions about eating meat on daily, weekly and monthly basis.

4.2.3 Cultural Risk Factors

4.2.3.1 *Male Dominant Culture*

Ullah *et al* in a prospective study carried out in LRH (Lady Reading Hospital) on 525 patients, found that 66.5% (n = 349) female and 33.5% (n = 176) males were diagnosed with Extra Pulmonary Tuberculosis (EPTB). The authors suggested that the higher incidence of TB in the region was due to the male dominant culture, where males have a higher priority than females – thus it is common practice in Pakhtuns' families – for example, males are served food earlier than females, and male children have a higher standard of health, education and emotional care as compared to females (51). In a local study of urban and rural differences in KPK, Rahman *et al* also reported that male gender is dominant in making decisions and in the social life (105).

4.2.3.2 *Summary*

Articles reviewed in the literature review showed that overcrowding, malnutrition, household contact and cultural restraints were main risk factors for TB in KPK.

4.2.4 Knowledge Based Risk Factors

4.2.4.1 *Patient's Knowledge about TB*

4.2.4.1.1 Introduction

This section will consider patient awareness and knowledge about TB – particularly the signs and symptoms of TB, transmission and prevention of TB, stigmatisation about TB and urban and rural differences in disease occurrence.

4.2.4.1.2 Signs and symptoms of TB

In a very recent study, Mushtaq *et al* compared the knowledge, attitude and training about TB in patients: a total of 1080 (urban 66.2%, rural 63.4%) respondents above 20 years were recruited randomly from two districts of Punjab Province. Just under two thirds of all respondents reported that cough was the main symptom of pulmonary tuberculosis, with significantly fewer in each group (*53.5% urban and 36.1% rural, p=0.001, 95% CI, 1.59 – 2.61*) correctly identifying that a cough lasting three or more weeks was the more accurate indication of pulmonary TB (75). Lack of knowledge about signs and symptoms of TB may lead to delay in the diagnosis and treatment. This is potentially therefore a very important study because it included both rural and urban populations but the research was limited to only two districts of Punjab province.

In a hospital based cross sectional study, Samera *et al* looked at the relationship between knowledge of TB and time to diagnosis and treatment. Three hundred and one patients presenting to the outpatient departments for chest diseases at Nishter Hospital Multan and Bethania Hospital Sialokot were recruited to the study. The researchers found that of those who presented within 20 days of onset of illness, 63.0% were aware that cough was a principal feature of TB, compared with only 37.0% in those patients who presented after 20 days – these observed differences were statistically different, p= 0.007 (76).

Khan *et al* studied knowledge of TB among 170 TB patients at out-patients department (OPD), attending two different hospitals in Karachi. The percentage of patients able to identify the signs and symptoms of disease were as follows: cough (83.5%), fever (54.7%), chest pain (24.7%) and blood in sputum (24.7%) (77). The study was limited to Aga Khan and Jinnah hospitals in Karachi. Aga Khan is a private teaching hospital and the majority of people coming for treatment belong to a high income group. It is highly likely that the sample of patients in this study is not representative of the overall population of Karachi.

4.2.4.1.3 Urban and Rural differences

Mushtaq *et al* in cross sectional study carried out in two districts, explored the knowledge and behaviour patterns about TB in urban and rural communities of Punjab province. Due to a generally higher level of education, the urban population were more aware about TB. Two out of 35 distracts in Punjab were randomly selected. Five Union Councils, two from urban and three from rural areas were randomly selected for this study. From each Tehsil (sub district), two villages were selected for interviewing 18 individuals, yielding a total of 1080 participants. The majority (n=648, 60.0%) of the

study subjects were recruited from rural as compared to urban areas (n=432, 40.0%) (75).

A study of 754 female subjects reported that 76.5% of urban dwellers compared with 57.7% of rural dwellers correctly identified that cough (of any duration) was the main symptom of TB. Furthermore, urban women were more informed about TB than rural women with 47.8% reporting that the lungs were involved in TB infection compared with 13.3% of rural females ($p<0.05$) (79). In a local study, results showed that people living in rural areas were significantly ($p = <0.05$) illiterate as compared to urban population in KPK (105).

4.2.4.1.4 Transmission and prevention of TB

Agboatwalla *et al* conducted research on gender and urban/ rural differences in knowledge about TB. In a questionnaire-based study, 51.0% of the 754 participants were male. The authors reported that just over three quarters of females from rural areas were classified as illiterate compared with 51.0% of urban-based females: in addition, female respondents from rural areas (24.5%) were less likely to report that TB was spread from TB patients through coughing and sneezing than urban living females (38.9%) - these observed differences were statistically significant ($p= 0.004$) (79).

In another cross sectional study of knowledge about TB transmission in two districts of Punjab Pakistan, just over four out of five (80.8%) of urban participants randomly selected from the community, correctly identified that TB was spread by the respiratory route (droplet nuclei generated by coughing and sneezing) compared with 68.5% of rural participants – this observed difference was statistically significant ($p<0.001$) (75).

Similarly, results explored knowledge about TB in patients and their relatives: more males (n=131, 65.0%) were interviewed than females (n=72, 35.0%).They

reported that more than four out of five participants (n=166, 82.0%) were aware that TB was a communicable disease and that just over half (n=110, 54.0%) said that it was spread through respiratory droplets (78).

4.2.4.1.5 Stigmatisation about TB

Results from the research conducted in two districts of Punjab (Nankana Sahib and Bahawalnagar) showed that stigmatisation (shame or disgrace associated with TB) was a common cause of delay in the diagnosis and treatment of both urban (83.6%) and rural (71.5%) patients – this observed difference was statistically significant ($p<0.001$) (75). Samera *et al* also identified stigma in 40.0 % of the educated population and suggested that patients due to shame and fear of being rejected by the community do not inform even their family members about TB. This can result in delay in diagnosis and treatment (76). These results are similar to the research conducted by Khan *et al* in Karachi who reported that just over two fifths (n=70, 41.0%) of the 170 in-patients studied did not tell relatives they had TB because of the stigma associated with the disease (77).

4.2.4.1.6 Summary

The literature on patients' knowledge about Tuberculosis is very limited. In Khyber Pakhtunkhwa, I could not identify any research on the knowledge of TB patients. However, there were several studies carried out on patients' knowledge in Pakistan. It is evident from the results of studies included in the literature review that patients' knowledge regarding TB is very limited, especially in rural communities. Since nearly 75 % of KPK population live in rural areas, it is a reasonable assumption that patients from rural districts of KPK have poor knowledge of TB and should be investigated for the association between knowledge and higher notification of TB in females.

4.2.4.2 *Physicians' Knowledge about the disease*

4.2.4.2.1 Introduction

In this section I will review the studies that have explored General Practitioners' awareness of the signs and symptoms of TB, approaches to diagnosis, and the appropriate treatment and follow-up of patients – the physicians studied were drawn from either Government or private hospitals.

4.2.4.2.2 Signs and Symptoms of TB

Ahmed *et al* looked at the knowledge of male Private Practitioners (PPs) providing health care services in the District of Thatta, a rural area of Sindh. Of the 100 PPs who took part in the study, half (50.0%) reported they regularly treated patients with TB: 22 private practitioners (PPs) were included in a more detailed study. The authors reported that 68.0% of respondents correctly identified that a cough for ≥ 3 weeks was the main symptom of TB, with 32.0% saying that cough, together with haemoptysis, weight loss and an elevated temperature – particularly in the evening – were additional disease features (80).

Shah conducted research to assess the level of knowledge and practices among PPs in the two cities of Punjab, Lahore and Rawalpindi. Two hundred and forty five PPs were randomly selected – 80.0% (n=197) were males: 59.2 % (n= 145) were from Lahore and the remainder from Rawalpindi. Of the total, 17.0% of PPs in Rawalpindi and 14.0% in Lahore were reported to have a postgraduate qualification. Fifty eight per cent of PPs and 41.0% from Rawalpindi and Lahore respectively reported that they had provided TB services for between 1 and 5 patients in the last quarter before the study. Assessing the knowledge regarding TB, only one PP reported having a cough above 3 weeks as a major symptom of the disease, while 45.0% said a cough with haemoptysis were the main sign and symptom of TB. The authors commented on the small number

of postgraduates who were able to describe a cough lasting for longer than 3 weeks as a major symptom of TB (83). Studies above were limited to the assessment of private practitioners' knowledge and conducted in single district. Similarly, Ahmed *et al* evaluated the knowledge of male PPs only.

Khan *et al* explored the knowledge and practices of PPs around the diagnosis and treatment of Tuberculosis using a questionnaire-based methodology and conducted from May to September 2002 in Karachi. A total of 141 registered PPs were identified within a two km circle of the central private health facility from where the research study was carried out. All the participants were asked to join a workshop about Tuberculosis management and requested to complete the study questionnaire: only 85.1% (n=120) PPs participated in the study by completing the questionnaire. The researchers reported that nearly all participants (95.0%, n=114) knew that cough was a major symptom of TB, whilst 86.7 % (n=104) also said that fever and weight loss (74.2 %, n= 89) were features of the disease (84).

In another cross sectional study about the knowledge and practices of 150 private practitioners treating between seven and ten TB patients monthly in Karachi, the authors reported that more than half (55.0%) of PPs said they suspected tuberculosis on the basis of respiratory symptoms including a prolonged cough, haemoptysis, productive sputum and chest pain (86).

4.2.4.2.3 Diagnosis of TB

Research conducted on 100 private practitioners in the Thatta District, a rural area of Sindh, found that the majority (86.0%, n=19) advised that diagnosis of TB required a combination of tests including a chest X-ray, erythrocyte sedimentation rate (ESR) and complete blood count (CBC), but only 14.0% (n=3) correctly identified the need for sputum microscopy (80).

Shah *et al* reported that 80.0% of PPs made the diagnosis of TB and started treatment on the basis of a clinical history, Chest X-Ray, ESR and CBC (termed "self diagnosis and management"), without referral to a TB centre although the latter are responsible for treatment at the district level. Eleven per cent said they made the diagnosis of TB as above but referred the patients to the district TB centre for confirmation and treatment, and 8.0% sent the patient directly to the TB centre. Very few PPs (2.0%, n=5) had their own diagnostic facilities, and only two PPs were able to examine sputum for Acid Fast Bacilli. Only one out of 245 PPs advised sputum microscopy alone for the diagnosis of TB, while 45.0% mentioned combination of Chest X-Ray, ESR and sputum examination (83). In another study Khan noted that just over half (55.0%) of PPs used a "self diagnosis and management" approach to TB with 21.0% saying they referred patients to the TB centre. More than half 58.3 % (n=70) PPs reported they diagnosed TB on the basis of sputum examination and 20.0% (n=24) by X-ray chest (84). Similar observations were made by Rizvi and Hussain, who studied the diagnostic skills of 150 General Practitioners (GPs) treating on average 7 to 10 TB patients monthly in Karachi. They noted that for the diagnosis of TB only 21.0% PPs suggested sputum examination and 15.0% a Chest X-Ray (86). Hussain *et al* carried out a cross-sectional study to assess the diagnostic capability of PPs. The authors reported that only one out of fifty three PPs advised on the need for sputum examination for the diagnosis of TB, with liver function tests and an ESR being advised by 5.7% and 11.3 % of PPs respectively (82).

Shehzadi *et al* using a cross sectional research study design investigated the knowledge and practices of GPs in NWFP and Northern areas in 2003. Eighty eight study subjects were recruited by convenience sampling from Gilgit, Hunza, Abbottabad, Haripur and Peshawar. The majority (87.5%, n=77) reported having attended chest X-Ray interpretation classes during their medical training. More than three quarters

(77.3%) stated that their approach to management was based on "self diagnosis and management" without referral to a TB centre. The authors also reported that only 43.3% (n=38) identified sputum examination and 21.6% (n=19) Chest X-Ray as the two principal investigation tools of choice for the diagnosis of TB (81).

It was suggested previously that patients living in rural areas belong to low income groups. WHO recommends sputum microscopy for the diagnosis of TB. Unnecessary diagnostic tests may increase the financial burden on poor TB patients and delays the diagnosis and treatment as well (89).

4.2.4.2.4 Treatment of TB Patients

Research conducted on 100 PPs in the Thatta District, a rural area of Sindh, found that just under three fifths prescribed the correct treatment regimen for the continuation and 73.0% for the intensive phase. TB treatment takes six months where the first two months is called intensive phase and the rest of the four months is known as the continuation phase (80).

In another study of assessment of GP's knowledge in NWFP and Northern areas about the management of TB patients, when asked to write a prescription for a 60 kg new adult TB patient, only 35.2% (n=31) prescribed an accurate combination and dosage of drugs for the intensive phase and 29.5 % (n= 26) for the second phase of the treatment The authors reported that just over two-thirds (68.8%, n=60) said that the same treatment regimen should be given to pregnant women, with 10.2% (n=9) advising a termination of pregnancy, and 8.0% (n=7) suggesting that treatment should be discontinued (81). Even fewer PPs (3.7%, n=2) were able to write a correct prescription as per NTP guidelines in a cross sectional study carried out by Hussain *et al*. Just under three quarters (70.0%) PPs prescribed medicine additional to TB treatment – for example Ciprofloxacin (82).

The majority of PPs working in Lahore and Rawalpindi also failed to follow the NTP guidelines for TB treatment Shah *et al* reported that 68.0% advised a combination of four drugs, while 15.0% chose three separate drugs for TB treatment (83). It is surprising that 87.0% of the GPs did not differentiate management for initial and continuation phases, while only 6.0% mentioned a two month required period for the first phase of TB treatment.

Khan *et al* explored the prescribing practices of PPs in the Aga Khan University hospital in Karachi. They reported that the majority (79.0%) of PPs prescribed four drugs for the initial phase of TB treatment as per NTP guidelines although just under a half prescribed less than the recommended dose of Pyrazinamide (43.0%) and Ethambutol (48.0%) (84). Similar findings were reported in a questionnaire based research conducted from May to September 2002 in Karachi by Shah, who suggested that just over a quarter (26.7%) of PPs did not follow the recommended regimen of four drugs in the first phase of TB treatment with 35.0 % (n=42) also prescribing an incorrect regimen for the second phase. The study also found that of the 102 participants, 20.0% prescribed a lower than recommended dose of Rifampicin with 49.0% prescribing for longer than the recommended duration (83).

A study of practice assessment of 150 GPs treating 7 to 10 TB patients monthly in Karachi, reported that only 23.0 % (n=34) prescribed the correct treatment regimen for TB with 29.0% of GP failing to answer this question. This highlights deficiencies in the treatment of TB by GPs. Replying to the duration of treatment, 24.0% reported 12 months and above which is alarming because of the potential for causing MDR-TB (86).

Poor diagnosis and treatment knowledge are therefore important factors responsible for the delay in the diagnosis and treatment of TB patients.

4.2.4.2.5 Directly Observed Treatment Short Course

Directly observed treatment short course (DOTS) has been recommended as a treatment strategy for TB since 1993, when TB was affirmed as a global emergency. Several studies have explored the knowledge and practices of medical practitioners regarding TB DOTS in Pakistan. In District Thatta province of Sindh (rural area), researchers explored the knowledge of 100 PPs in relation to TB DOTS. Half (50.0%) of the PPs reported treating TB patients but no physicians identified their practice as following recommended DOTS strategy. Furthermore, few knew how to trace defaulters, because they never maintained TB patients' records (80). Shah *et al* found similar findings in a research project to assess the level of knowledge and practices of PPs in two major cities of Punjab. Out of 245 PPs, nobody advised treatment under DOTS (83).

In 2005, Pakistan achieved 100% DOTS coverage nationally (1). Further, due to the lady health worker (LHW) programme the implantation of DOTS at village level become more effective. However, my own observations suggest that the use of LHW in rural and remote areas of Pakistan still needs improvement

4.2.4.2.6 Follow up of TB Patients

In a rural area of Sindh (District Thatta), Ahmed *et al* (2009) explored the knowledge of 100 PPs about TB patient follow-up. Half (50.0%) reported treating TB patients, but only 40.0% followed the patients for the duration of treatment. The majority (n=19, 86.0%) never advised sputum examination at end of the second, fifth and seventh months (80). Similar findings were reported by Shah *et al* who conducted research to assess the level of knowledge and practices among PPs in Lahore and Rawalpindi. Slightly more than three quarters (76.0%) preferred a chest X Ray for the assessment of TB, whereas WHO only recommend sputum examination at the end of

second, fifth and seventh months (83). Khan *et al* also identified that only 35.0% (42/120) of doctors were aware that sputum examination is the most useful test in follow up (84).

National TB control programme recommends follow up at the end of the second, fourth and sixth month for sputum negative and fifth and seventh month for sputum positive patients (106). It is one of the most important components of TB DOTS programme and negligence in follow up may lead to multi drug resistance TB (MDR-TB).

It is evident from the above studies that physicians' knowledge is limited about diagnosis and treatment of TB. However, the majority of the respondents in the studies reviewed were private practitioners. Research conducted in seven countries including Pakistan, showed that delay in the diagnosis and treatment was significantly higher in private clinics (97). TB patients in Pakistan prefer public facilities (TDCs, BHUs, RHCs and Hospitals) for free diagnosis and treatment of TB. National TB control programmes have TB diagnostic and treatment centres (TBDCs) for the diagnosis and treatment of TB patients in KPK. Therefore, it is important to evaluate the knowledge of physicians working in those TBDCs about the diagnosis and treatment of TB.

4.3 Summary of the Literature Review

Chapter 4 has explored the literature in relation to the epidemiology, and risk factors for tuberculosis in the Pakistan (See Table 13 and Table 14 on pages 63-68). Patient's knowledge and treatment seeking behaviour of TB was also discussed in this section. (See Table 15 and Table 16 on pages 70 and 71)

Finally the awareness and practices of private and public practitioners regarding TB management was explored in detail and the results identified a number of serious gaps in knowledge and practices

CHAPTER 5: METHODOLOGY

5.1 Introduction

This chapter will describe and explain the research methodology, aims and objectives of the study. Research questions and methods for each objective will be discussed. The process of data collection, data collection instrument, ethical consideration and data entry will also be discussed.

5.2 Aim of the Study

To explore the reasons behind the variation of Tuberculosis Notification between males and females in the province of Khyber Pakhtunkhwa (KPK), Pakistan.

5.3 Objectives of the Study

1. To describe the epidemiological characteristics of confirmed TB Cases in Khyber Pakhtunkhwa by age, gender, nationality, geographical location and disease type for 2002 to 2010.
2. To explore risk factors for newly diagnosed laboratory confirmed TB disease in all adult patients in KPK from July 01, 2012 to September 30, 2012.
3. To estimate the level of knowledge about TB in adult TB patients in KPK from July 01, 2012 to September 30, 2012.
4. To evaluate the level of knowledge, attitude and practice of Physicians working in TB diagnostic centres (TDCs) in KPK.

5.4 Research Questions

Keeping in view the aims and objectives, the issues and questions were discussed in detail with the supervisory team and I settled on the following four research questions around which I shaped the study design:

1. What are the Epidemiological Characteristics of Confirmed TB cases in KPK?
2. What are the risk factors for TB in adult patients in higher versus lower notification districts within KPK**?**
3. What do adult TB Patients in KPK know about their disease?
4. What are the levels of knowledge, attitude and practice about TB for Physicians working in TBDCs in KPK?

5.5 Hypothesis

On the basis of these research questions the following four hypotheses were developed:

1. The notification of TB in female patients is higher than males in the province of KPK.
2. Socio-economic issues are the most important risk factors for higher notification of TB in females in the province of KPK, Pakistan.
3. Females of KPK are less knowledgeable than males regarding Tuberculosis.
4. General practitioners' knowledge of TB in respect of diagnosis, treatment and monitoring is not satisfactory in the province of KPK.

5.6 Methodology for Objective One

5.6.1 Study Setting and Target Population

KPK is one of the provinces in Pakistan and is divided into 26 districts for administrative purposes. According to the 1998 census, the population of KPK is 17.7 million (29). The executive district officer health (EDOH) is the person who is in charge of health-related projects in the entire district. The district TB control officer (DTCO) is responsible for the diagnosis, treatment, management and case reporting activates at district level for National TB Control Programme (NTCP). There are 225 TB diagnostic

centres (TBDC) in KPK (107-108). Patients who present to all 225 TB diagnostic centres in KPK for diagnosis and treatment were reported to NTCP on monthly, quarterly and annual basis by DTCO. The study population included all registered patients who reported for treatment to NTCP from 2002 to 2010 in KPK.

5.6.2 Study Design

Through a retrospective study, I performed a detailed preliminary quantitative analysis of existing NTCP confirmed TB admission records to identify trends in TB outcomes according to age, gender, location, nationality, disease type, diagnostic tests and the post treatment cure rate using NTCP data from 2002 to 2010. The data helped me in identifying epidemiological characteristics for confirmed TB cases in Khyber Pakhtunkhwa.

5.6.3 Data Collection

The National TB Control programme (KPK) collected data from all districts of Khyber Pakhtunkhwa on regular basis through the DTCO. Specific WHO TB data collection instruments have been used for data collection (Copies attached as Appendix-14.7 on page 226). Monthly data received from district TB control officer between 2001 and 2009 were entered by NTCP data operators into a Microsoft Access© database especially designed for NTCP KPK. In 2009 an electronic reporting system (ERS) was developed for recording data of TB patients in KPK.

Data related to Objective One was obtained through analysing the NTCP Microsoft Access© database data for TB patients from 2002 to 2009. Data for 2009 to 2010 was retrieved from the ERS database of NTP. Access to the database was provided by the NTCP IT department with a valid user name and password. The data was

analysed and tabulated to show the distribution of TB by age, gender, type of disease, geographical area, cure rate, default rate, death rate.

5.6.4 Data Quality

The data presented was checked for accuracy and entirety. To identify any deficiencies in the data, I visited the NTP Office and district TB control offices of five districts - Abbottabad, Bannu, Dir (lower), Kohistan and Peshawar. TB registers of the selected districts were then manually checked to verify the NTP data for confirmation.

5.6.5 Analysis

Study Data from 2002 to 2010 were exported to Microsoft Excel 2007 which was then used to aggregate and tabulate the results. Patients' age, sex, region, type of disease and treatment outcome were tabulated. Statistical analyses were carried out using SPSS 22.

5.6.6 Ethics

The ethics committee of the Provincial Tuberculosis Control Programme Khyber Pakhtunkhwa approved this study and agreed for the additional support with regard to field work in 2013. Authorisation was acquired to conduct the study and communicated with the EDOs (H) of all districts oh KPK. (Copy of the NTCP permission letter is attached as appendix 14.2 on page 196).

5.7 Methodology for Objectives Two and Three (Study Design)

5.7.1 Study Setting and Target Population

For the purpose of data collection ten districts were selected, five from higher and five from lower notification areas. (See Table 17 below) These districts were identified as higher and lower TB case notification regions through the earlier descriptive study using the NTCP data from 2002 to 2010, in respect of gender difference of TB in KPK. Five TDCs were further selected randomly from each district for the recruitment of study subjects. All confirmed adult TB patients presented to each TDC between 1 July 2012 and 30th September 2012, were included in the study.

Table 17: Five Higher and Five Lower Notification Districts of KPK

Higher Case Notification Districts	Lower Case Notification Districts
Kohistan	Karak
Battagram	Kohat
Chitral	Mardan
Buner	Nawshera
Upper Dir	Malakand

Key to text colour in table:

■ = Districts with Lower Female TB Notification

■ = Districts with Higher Female TB Notification

5.7.2 Study Design

A case control study was chosen to explore the reasons behind the variation in case notification of TB patients in KPK. Participants registered to higher case notification districts (Kohistan, Battagram, Chitral, Buner and Upper Dir) were marked as case group and patients reported to lower case notification districts (Karak, Kohat, Mardan, Nawshera and Malakand) were noted as control group for the study.

5.7.3 **Sample Size**

The results from objective one showed that a total of 221,051 TB patients were reported in KPK between 2001 and 2010. Therefore, dividing this figure by nine (years) would suggest that on average 24,561 TB patients notified annually and 2,047 monthly in KPK during 2001 to 2010. As there are 225 TDCs in KPK, by dividing this monthly figure by the total number of TDCs, on average nine patients reported to each TDC monthly. By excluding cases below 15 years of age, relapsed patients (i.e. those who had taken full course of TB treatment in the past and were declared cured or treatment completed but re-infected), transferred in (had taken TB drugs and had been transferred from another TDC), treatment failure (smear positive patients who had taken TB drugs for five months or more) and treatment default (had taken TB drugs for a certain period then interrupted for two or more months) cases I expected to receive five patients monthly to each TDC. As in each district there were five TDCs, the anticipated sample size was calculated as 375 (five patients from each TDC monthly multiplied by twenty five TDCS in each group and multiplied by three months) new adult TB patients from higher (Case Group) and 375 from lower notification regions (Control Group) from 1st July 2012 to 30th September 2012. All newly diagnosed TB patients confirmed by sputum microscopy in the selected 50 TDCs from ten districts were recruited between 1st July and 30th September 2012.

5.7.3.1 ***Inclusion Criteria***

- All adult newly diagnosed male and female TB patients confirmed by sputum microscopy, because I believed that defaulted or previously treated patients would be more knowledgeable than newly diagnosed ones due to their lived experience of treatment. (‘Defaulted’ are those cases who do not complete their

treatment), ('previously treated' are those treated but not cured or who are re-infected).

- All adult patients permanently living in the TDC area of the district. I include those patients because it was possible for community health workers (CHWs) to trace and meet the patients at their home for confirmation of data.
- Willingness of subjects to take part in the research, because patients have a right to accept or reject the interview with the assurance that their right to receive health care will not be affected by the decision.

5.7.3.2 *Exclusion Criteria*

- Patients below the age of 15 years were excluded from the study.
- Referred or transferred patients from other TDCs or districts (Those who were diagnosed in other centres or other districts).

5.7.4 Date Collection Tools

Structured questionnaires were used for data collection using face to face interviews with patients attending the TDC. A questionnaire was used because it made data capture relatively straightforward. The questionnaire was developed in Epi Info 7© software developed by the Centre for Disease Control in the USA (109). The advantage of using Epi Info© was that, it automatically created a database for analysis of inputted data. A further consideration in using a questionnaire was because research by Saunders, Lewis and Thornhill (110) suggested that if study subjects are illiterate, planned and then administered questionnaires are the best choice for information collection in research.

The research tool was divided into four sections:

5.7.4.1 *Baseline Data*

Variables included in this section provided information about case n^{o}, date of registration, name, gender, age, height, weight, type of TB and district of residence. Age, height and weight were used for body mass index (BMI) calculation.

5.7.4.2 *Demographic Data*

This section contained demographic information of patients, such as educational status, marital status, economic status, number of family members, number of rooms, type of fuel of using for cooking, eating meat interval etc.

5.7.4.3 *Risk Factors*

Questions explored past medical history and some potential risk factors. These variables were mainly past and positive family history for TB, associated diseases, smoking etc.

5.7.4.4 *Knowledge of TB*

To assess the level knowledge of TB patients, questions were included to find data about the cause, transmission and spread of TB. Questions were also asked about the most common symptom of TB, duration, cost, and consequences of incomplete treatment (copy of questionnaires attached as Appendix 14.4 on page 205).

5.7.5 Validity of Data Collection Tool

The degree to which a data collection tool measures what is supposed to be measured is called validity. The spectrum of validity is mainly dependent on three points: the structure of the questionnaire, the purpose of the questionnaire and the population which will be investigated. For the reliability, I validated the questionnaire using the following main methods:

5.7.5.1 *Content Validity*

After selecting different variables, based on the literature review, a structured data collection tool was developed. Initially, content validity was achieved through detailed discussion with PhD students (a primary expert group) who were working in the same research field. This had the benefit of being able to discuss the tool with other researchers and 'test it out' prior to the formal pilot (111).The questionnaire was then discussed with a secondary expert group (the supervisory team) for further content validity.

5.7.5.2 *Concurrent Validity*

The structure of my questionnaire was mainly based on the variables extracted from the literature review. Therefore, it could be argued that the validity of the variables was already established. However, due to the addition of extra questions proposed by expert groups, further validity testing of the questionnaire was advised by supervisory team.

5.7.5.3 *Piloting the Questionnaire*

For final validation of the data tool, I tested the questionnaire on 50 medical technicians recruited from selected TDCs of ten districts in KPK before and after the training sessions in each district. All medical technicians were trained and the

questionnaire was discussed with them in detail. In addition, after completion of training sessions, 5 patients were randomly selected from each district (total of 50) and medical technicians were asked to conduct face to face interviews to test the questionnaire practically. The purpose of this activity was mainly to achieve validity and:

- To pilot test the questionnaires for data collection.
- To estimate the time duration for data collection.
- To estimate the level of difficulty for words or terms used in questionnaires for medical technicians.
- To increase their understanding of the field work.
- To pilot test the questionnaires for data collection in respect of patients' point of view.
- To develop the questionnaire for final approval.

5.7.6 **Data Collection**

5.7.6.1 ***Face to face interview***

Since the majority of the population of KPK are illiterate, therefore face to face interview was the chosen method for data collection. Before interview, all patients were informed in detail about the research activity and verbal consent was obtained. All confirmed new TB patients were interviewed by trained medical technicians in selected TDCs between 1st July 2012 and 30th September 2012. To provide flexibility and confidentiality, medical technicians ensured that all interviews were conducted in a safe and private place. All female patients were interviewed in the presence of LHWs.

5.7.6.2 *Double Data Entry Strategy*

Area supervisors were trained to use Epi Info 7© for data entry on a weekly basis. To avoid and minimise human error during the data entry process, a double data entry strategy was adopted. Both male and female area supervisors entered the same data separately on an identical Epi Info-7© database. At the same time, I also entered data separately on a weekly basis using the same Epi Info 7© database. As a result of this, two data sets were created. After completion, 55 different discrepancies were found, which were reconciled by confirming against the original questionnaires.

5.7.6.3 *Analysis*

Data was collected through pre-coded questionnaire and analysed using Epi Info 7© software. Chi-square tests were used for comparisons between two groups. Multiple logistic regression was used to test for the simultaneous involvement of several factors that might influence the higher notification of tuberculosis in females in the province of Khyber Pakhtunkhwa, Pakistan. A P value < 0.05 was considered statistically significant. For the determination of relative risks (RRs), confidence intervals and standard errors, Stata© software was used.

5.7.7 Ethical Approval

5.7.7.1 *Ethics Committees*

We sought and received approval for conducting this research from the National Tuberculosis Control (NTCP) Khyber Pakhtunkhwa. (A copy of approval is attached as Appendix 14.2 on page 196).

We also obtained ethical approval from the Committee on Ethics of Research on Human Beings at The University of Manchester to conduct the study (See Appendix 14.1 on page 194 for the copy of Ethical approval).

5.7.7.2 *Informed Consent*

Obtaining consent from the patients was problematic because of the high levels of illiteracy. We agreed with the ethics committee that patients will be verbally consented and that the medical technicians and LHWs were specifically trained to ensure that patients were not coerced into taking part.

We did not anticipate any problems in relation to obtaining the information because the questionnaire was primarily asking about knowledge and socio-economic factors, much of which was already collected as part of the health surveillance carried out by the NTCP (See appendix 14.4 on page 205).

5.7.7.3 *Confidentiality*

NTCP already follow the guidelines set by the World Health Organisation (WHO) regarding ethics and health safety within their premises. Staff who were carrying out this research were already subjected to the requirements for confidentiality regarding patient data, public safety and ethics. Additional training was provided to all the research staff specific to our research project with specific emphasis being given to consent and confidentiality

5.8 Methodology for Objective Four

5.8.1 Research Plan

One of the reasons that more women were diagnosed with TB could be related to the diagnosis and treatment carried out by physicians working in the primary health care setting. Understanding physicians' knowledge, attitude and practice will be critical to understanding why women have a higher notification of TB. We therefore carried out a cross sectional study targeting the general practitioners of selected TDCs. Delay in diagnosis and treatment increases the chance of spreading infection to healthy family

members. As in KPK, the majority of females are not working and they remain at home. This suggests that a case of active TB in an untreated woman may increase the chance of further TB infections in other women.

5.8.2 Study Setting and Target Population:

TDCs that were previously selected for data collection in objective two and three were included in this part of the study. All general practitioners working in the TDCs that form the sample for this study were asked to fill in a questionnaire which explored their knowledge, attitude and practice in relation to treating female patients. This part of the study objective was completed between 1st August 2012 and 30th September 2012 and was carried out by the principal investigator.

5.8.3 Study Design

A cross-sectional study design, using a pre-structured questionnaire was chosen to assess the knowledge of physicians working in the TDCs in KPK.

5.8.4 Sample Size for Objective Four

All practitioners working in the selected TDCs previously being used for data collection for objective two and three were included in the study. Fifty general practitioners were interviewed for Objective Four.

5.8.5 Date Collection Tools

Face to face interview was chosen for data collection using a pre-structured questionnaire.

I prepared a questionnaire with both open and closed questions. The tool was divided into two sections.

5.8.5.1 *Demographic Data.*

Variables included in this section provided demographic information of doctors such as, name, gender, age, medical school attended, qualification, duration of service etc.

5.8.5.2 *Knowledge of TB*

To estimate the level of knowledge and understanding of TB in general practitioners working in TDCs, several questions were asked (Questionnaire attached as Appendix 14.4 on page 205).

5.8.6 Data Collection

A structured questionnaire was used for data collection with written consent. Districts visits were arranged according the availability of doctors and appointments were scheduled for data collection. Data was collected by the main investigator through face to face interview.

5.8.7 Dual Data Entry

Data was entered into Epi Info 7© on daily basis. Dual data entry method was obtained to eliminate human error during data entry process.

5.8.8 Analysis

Statistical analysis was carried out using the Epi Info© software (version 7) Chi-square test was used for statistical significance. A p-value <0.05 was measured to be statistically important.

5.8.9 Ethics

Ethical approval was also obtained for this part of the study (see page 104.)

5.9 Summary

Chapter 5 has described my research methodology. It includes my study aim, objectives and research questions. I have explained both the construction and methods for my four main research surveys. The structure of data collection tools, pilot study for testing those questionnaires and data collection in the field study were also described in this chapter.

CHAPTER 6: RESULTS - DESCRIPTIVE EPIDEMIOLOGY

6.1 Introduction

The study of disease incidence, prevalence and demographic factors (age, gender and geographic area) is called descriptive epidemiology. Differences in the occurrence and frequency of disease in respect of demographical factors may help in identifying the causes of a disease.

The descriptive epidemiology of TB patients in the province of KPK between 2002 and 2010 provides important data regarding the disease burden. Assessing this data may help in planning for the data collection phase relevant for objectives two, three and four.

6.2 TB Patients Registration from 2002 to 2010

In Khyber Pakhtunkhwa 221,051 total TB patients were registered between 2002 and 2010 in the provincial Tuberculosis control programme [Table 18]. Major differences were noted in figures and rates of TB cases reported in each district of the province. A large number of cases were reported in Peshawar (5763, 16.81%) followed by Mardan (3060, 8.93%) and Nawshera (2117, 6.18%). The lowest number of TB cases were reported in Tank (471, 1.37%) followed by Upper Dir (679, 1.98%). About an equal number of cases were reported from Hungo (2.25%), Karak (2.28%) and Malakand (2.37%). Similar figures were notified from Bannu, Shangla, Kohat, and Swabi, Swat, Abbottabad with 3.65%, 3.68%, 3.69% and 4.93%, 5.05%, 5.12% respectively [Table 18, , Figure 9].

Six out of twenty four districts accounted for 52% of total TB patients registered in the province of Khyber Pakhtunkhwa from 2002 to 2010: Peshawar

(16.81%), Mardan (8.93%), Nawsheara (6.18%), Mansehara (5.12%) and Abbottabad (5.35%) ([Figure 8, Figure 9].

Four distinctive trends can be seen in the registration of TB patients from 2002 to 2010. There was a 69.00% increase reported in registration of new TB cases between 2002 and 2003. Subsequent to this, there was a decline noted in the annual increase in case notification between 2003 and 2005 (31.52%, 37.50%) when compared to the period from2002 to2003. Fluctuations in the annual notification percentages can be seen from 2005 to 2009 (i.e., 8.69%, 15.35%, 1.33% and 10.97%). The decrease in annual case notification during 2005 and 2009 could be possibly due to 100% DOTS coverage achieved in 2005. In 2009-2010 the annual TB patients registration decreased by -0.71% [Figure 8, Figure 9].

Table 18: Annual Case Notification of TB by Districts in KPK, 2002-2010

No	District	2002	2003	2004	2005	2006	2007	2008	2009	2010	Total
1	Abbottabad	0	740	1120	1191	1572	1733	1521	1908	1756	**11541**
2	Bannu	0	493	405	675	832	1116	1255	1281	1251	**7308**
3	Battagram	0	0	53	417	338	495	644	691	697	**3335**
4	Buner	74	446	446	548	610	704	727	718	832	**5105**
5	Charsadda	19	359	714	1101	1081	1369	1488	1773	1502	**9406**
6	Chitral	159	881	814	719	770	948	887	904	841	**6923**
7	DI Khan	911	482	661	1107	1100	1461	1294	1288	1422	**9726**
8	Hangu	0	0	0	229	225	282	469	573	772	**2550**
9	Haripur	0	767	829	1032	1149	1175	1147	1116	862	**8077**
10	Karak	0	0	0	303	471	515	625	770	782	**3466**
11	Kohat	0	68	360	622	770	1005	971	1131	1265	**6192**
12	Kohistan	0	0	15	431	425	415	520	683	720	**3209**
13	Lakki Marwat	0	0	125	654	582	858	897	1075	1034	**5225**
14	Lower Dir	0	142	398	819	990	977	1093	1116	1124	**6659**
15	Malakand	0	30	310	464	498	632	610	703	813	**4060**
16	Mansehsra	0	437	1669	1329	1653	1617	1583	1945	1832	**12065**
17	Mardan	1307	1172	1977	2421	2231	2937	2735	3087	3060	**20927**
18	Nowshera	819	984	991	1362	1350	1546	1738	2115	2117	**13022**
19	Peshawar	2616	3546	3734	4312	4701	5647	5381	5917	5763	**41617**
20	Shangala	0	0	45	844	916	904	890	1228	1260	**6087**
21	Swabi	83	768	829	1036	1307	1334	1591	1636	1690	**10274**
22	Swat	2022	2009	1917	1987	2087	2028	1926	1729	1730	**17435**
23	Tank	0	0	21	262	331	381	407	458	471	**2331**
24	Upper Dir	0	213	372	618	624	620	709	676	679	**4511**
Total KPK		**8010**	**13537**	**17805**	**24483**	**26613**	**30699**	**31108**	**34521**	**34275**	**221051**

Figure 8: Annual Case Notification from 2002 to 2010

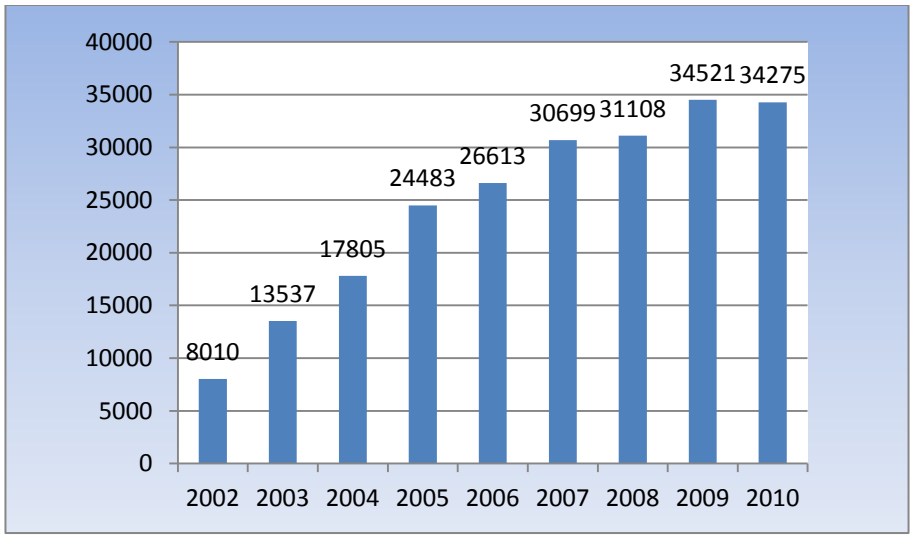
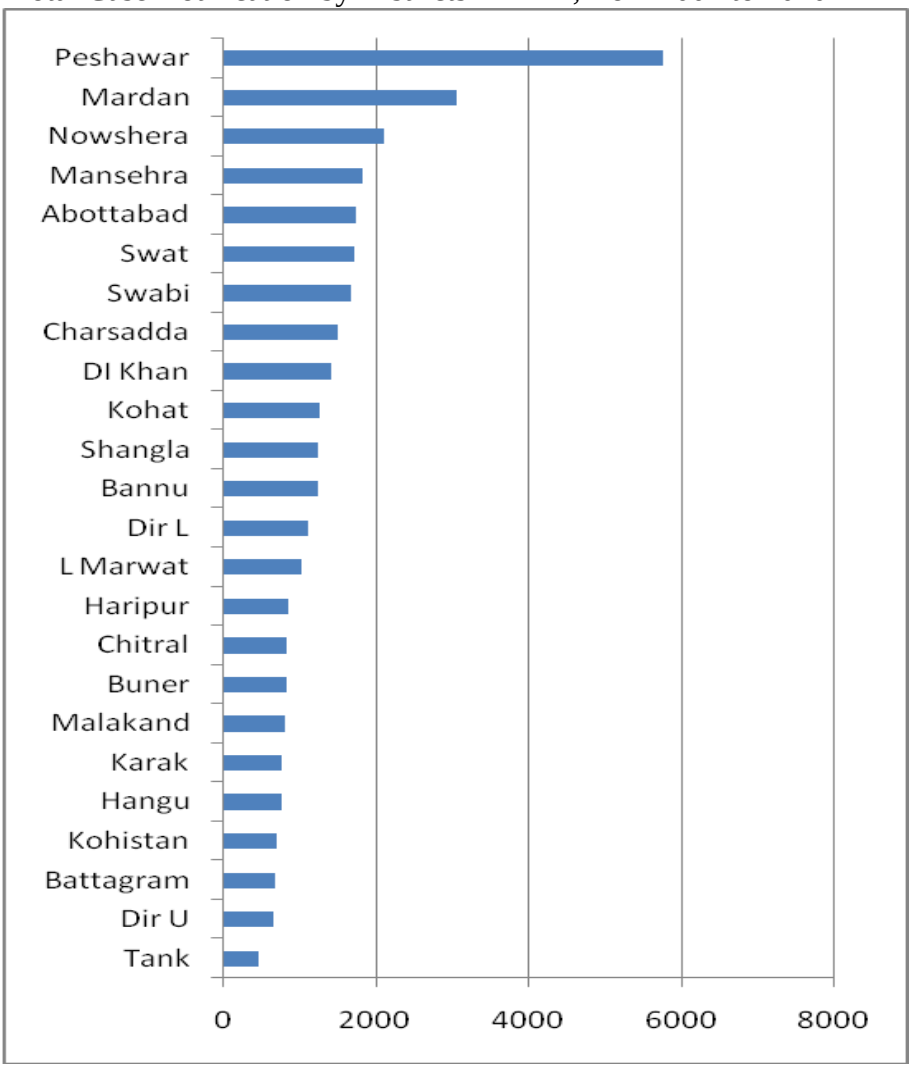


Figure 9: Total Case Notification by Districts in KPK, from 2002 to 2010



6.3 Annual Incidence of TB in KPK

The incidence rate of TB remained unchanged from 2002 to 2010, with an incidence of 177/100,000. The DOTS programme initiated in KPK in 2002 with 85% population coverage increased to 100% in 2005. Between 2002 and 2005, the number of registered TB patients increased by about 3.00% annually. The total annual TB patient registration decreased by 1.54% on average between 2005 and 2009. The reason behind this decrease may be due to 100 % population coverage by the DOTS programme in KPK (See Table 18 on page 111). There was a reported decline of 1% in the success rate (number of patients successfully completed treatment with or without bacteriological success) from 2002 to 2003 which then gradually increased annually to

95% in 2010. The data also shows a fluctuation in the cure rate (number of patients with bacteriological evidence of success after treatment completion); initially the cure rate decreased by 2% between 2002 and 2003. However, between 2003 and 2004, the cure rate rose to 82%. This was followed by a decline of 2% between 2004 and 2006. Between 2006 and 2010 the cure rate increased gradually and reached a maximum of 89% (See Similarly, the number of deaths increased from 17 to 385 from 2002 to 2006 and then deceased gradually to 219 in 2010 (See Figure 11 on page 114).

Table 19: Incidence of TB from 2002 to 2010 in KPK, Pakistan

Year	Population In millions	Total Cases	Pop Under DOTS %	Incidence Rate	Total Pulmonary	Total Ext. Pulmonary	Success Rate %	Cure Rate %	Default Rate %	Failure Rate %	Death Rate %
2002	20.46	8,010	85	177	5,892	2,118	86	79	9	1	1
2003	20.56	13,537	85	177	9,727	3,810	85	77	9	1	2
2004	20.56	17,805	85	177	13,229	4,576	89	82	6	1	2
2005	20.75	24,483	100	177	17,329	7,154	90	81	4	1	3
2006	21.16	26,613	100	177	19,203	7,410	92	80	3	1	2
2007	21.59	30,699	100	177	21,919	8,780	93	84	2	1	2
2008	22.02	31,108	100	177	22,601	8,507	93	85	2	1	2
2009	22.46	34,521	100	177	24,669	9,852	94	88	1	1	2
2010	25.23	34,275	100	177	23,762	10,513	95	89	1	1	2

Figure 10: Cure and Success Rates of TB in KPK, 2002-2010

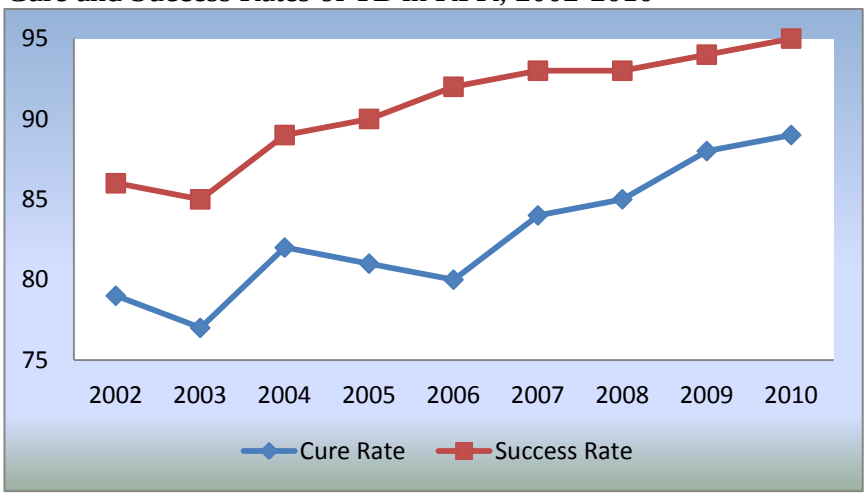
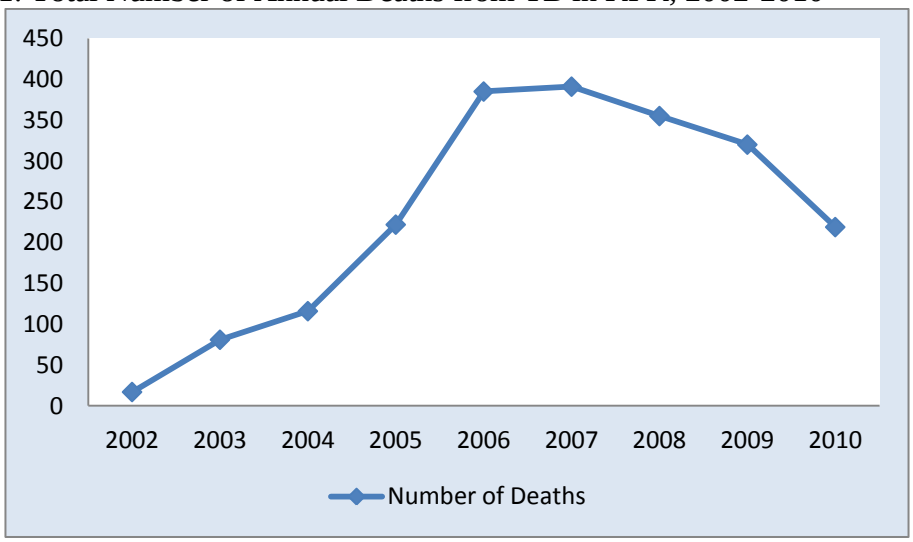
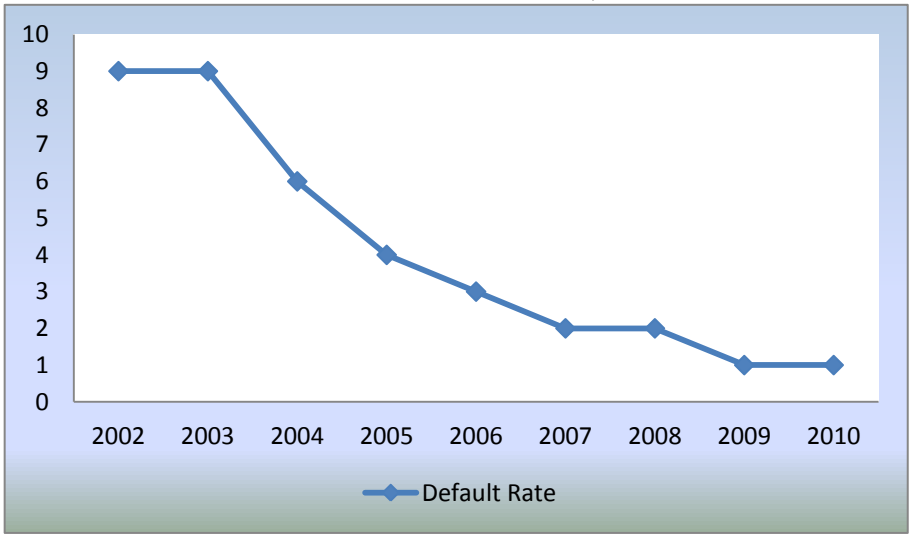


Figure 11: Total Number of Annual Deaths from TB in KPK, 2002-2010



Three major trends can be seen for the default rate from the data reported between 2003 and 2010. Firstly, between 2002 and 2003 the default rate remained stable at 9%. Secondly, a gradual decline to 2% reported between 2003 and 2007. Finally, the default rate remained stable from 2% to 1% between 2007 and 2010 (See Figure 12 below). The increase in cure rate and decrease in the number of deaths between 2006 and 2010 may be due to the DOTS programme achieving full population coverage in 2005.

Figure 12: Annual Default Rate of TB Patients in KPK, 2002-2010



6.4 Distribution of TB Patients by Age and Gender

From 2002 to 2010, 221,051 TB patients registered with the NTP in the province of KPK, Pakistan. Table 20 on page 116 describes the male and female distribution of TB patients in the specified period, contributing 43.78% and 56.22 % respectively to the registered population. A higher number of female patients registered throughout the reported period when compared to males. The differences in gender distribution were statistically significant. (*Chi-Square=29.74, p= <0.0001*). Between 2002 and 2009, there was a gradual increase in the number of TB cases reported both in males (3428 to 15269) and females (4582 to 19252). Between 2009 and 2010, the number of male TB patients increased from 15269 to 15473, while the number of female patients decreased from 19269 to 18802 (See Figure 13 on page 116).

6.5 Classification of TB in Patients

Tuberculosis can be classified into pulmonary TB (PTb) and extra pulmonary TB (EXTb). NTP data from 2002 to 2010 showed that 71.60% (158331) were PTb and 28.40% (62720) were EXTb. EXTb patients increased from 2118 to 10513 between 2000 and 2010 while, PTb cases increased from 5892 to 24669 between 2002 and 2009 with a decline noted from 24669 to 23762 between 2009 and 2010 (See Figure 14 on page 116).

Table 20: Distribution of TB Patients by Gender and Type of Disease, 2002-2010

Year	Pulmonary TB			Extra Pulmonary TB			TOTAL		
	Male (%)	Female (%)	Total	Male (%)	Female (%)	Total	Male (%)	Female (%)	Total
2002	2517 (42.7)	3375 (57.3)	**5892**	911 (43.0)	1207 (57.0)	**2118**	3428 (42.8)	4582 (57.2)	**8010**
2003	4203 (43.2)	5524 (56.8)	**9727**	1652 (43.4)	2158 (56.6)	**3810**	5855 (43.3)	7682 (56.7)	**13537**
2004	5628 (42.5)	7601 (57.5)	**13229**	2051 (44.8)	2525 (55.2)	**4576**	7679 (43.1)	10126 (56.9)	**17805**
2005	7246 (41.8)	10083 (58.2)	**17329**	3188 (44.6)	3966 (55.4)	**7154**	10434 (42.6)	14049 (57.4)	**24483**
2006	8335 (43.4)	10868 (56.6)	**19203**	3391 45.8)	4019 (54.2)	**7410**	11726 (44.1)	14887 (55.9)	**26613**
2007	9355 (42.7)	12220 (55.8)	**21919**	3922 44.7)	5202 (59.2)	**8780**	13277 (43.2)	17422 (56.8)	**30699**
2008	9813 (43.4)	12788 (56.6)	**22601**	3819 (44.9)	4688 (55.1)	**8507**	13632 (43.8)	17476 (56.2)	**31108**
2009	10715 (43.4)	13954 (56.6)	**24669**	4554 (46.2)	5298 (53.8)	**9852**	15269 (44.2)	19252 (55.8)	**34521**
2010	10669 (44.9)	13093 (55.1)	**23762**	4804 (45.7)	5709 (54.3)	**10513**	15473 (45.1)	18802 (54.9)	**34275**

Figure 13: Distribution of TB Patients by Gender, 2002-2010

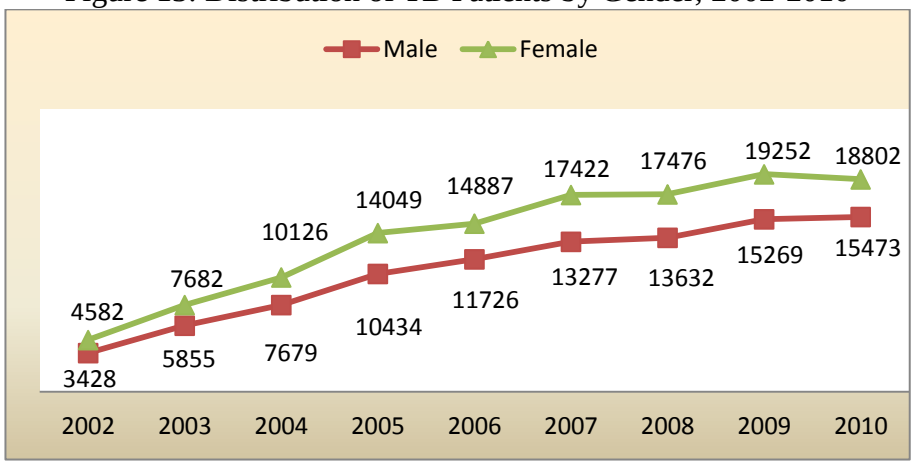
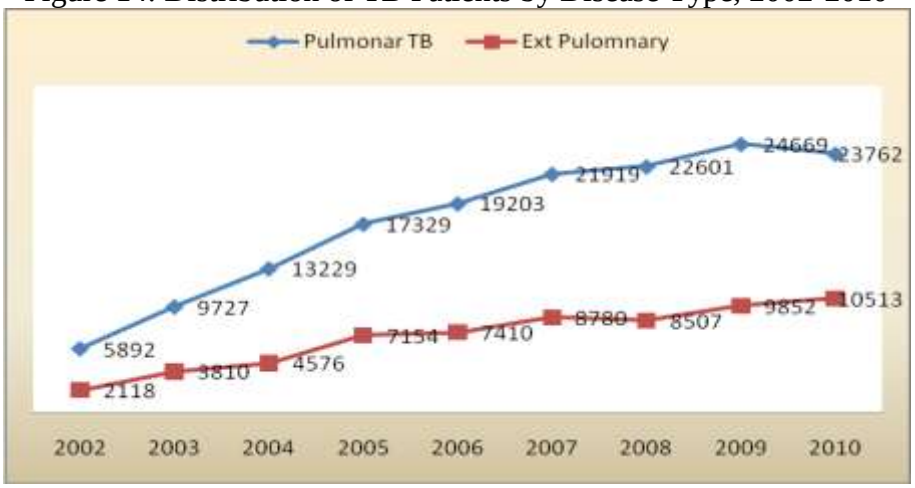


Figure 14: Distribution of TB Patients by Disease Type, 2002-2010



6.6 Notification of New Sputum Positive Cases by Age Structure

Table 17 shows the registered number of sputum smear positive TB patients between 2002 and 2009 (See Table 20 on page 116). Case notification reports suggested approximately 50% annual increase in the number of TB patients from 2002 to 2006.The biggest number (74.511%) of patients registered annually were between 15 to 44 years of age, the most productive age of life. Males contributed 30.65% and females 43.86% of this group. Figure 15 shows that greatest gender difference was in the 14-24 age group. In the over 65 age group the incidence of TB was greater in males compared to females (See Figure 15 on page 118).

Table 21: Notification of Smear Sputum Positive Cases by Age Structure in KPK, 2002-2009

Age/Sex	**0-14**		**15-24**		**25-34**		**35-44**		**45-54**		**55-64**		**65 & >**		**TOTAL**		
Year	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**Total**
2002	52	164	401	554	289	388	172	304	129	157	116	93	80	60	**1239**	**1720**	**2959**
2003	88	204	548	774	415	543	247	355	230	279	219	208	160	129	**1907**	**2492**	**4399**
2004	93	310	759	1067	509	754	343	448	244	358	252	293	279	209	**2479**	**3439**	**5918**
2005	151	523	993	1531	724	1121	468	716	347	494	396	405	394	291	**3473**	**5081**	**8554**
2006	222	591	1223	1671	872	1249	585	787	482	593	415	492	481	389	**4280**	**5772**	**10052**
2007	221	635	1392	2110	1007	1374	651	898	559	724	545	567	653	530	**5028**	**6838**	**11866**
2008	225	634	1508	2185	1028	1555	616	895	601	782	581	631	750	526	**5309**	**7208**	**12517**
2009	242	572	1543	2416	1100	1593	686	994	599	767	646	668	725	571	**5541**	**7581**	**13122**

The average mean age for males was 36.63 and for females 32.71 between 2002 and 2009 (this was calculated by multiplication of mean age of every age set according to annual cases, adding the figures of all age sets and dividing by total annual cases registered in that year).

Figure 16 on page 118 shows the population pyramid of all smear positive TB patients reported to NTP between 2002 and 2010

Figure 15: Distribution of New Smear Positive Cases by Age Structure

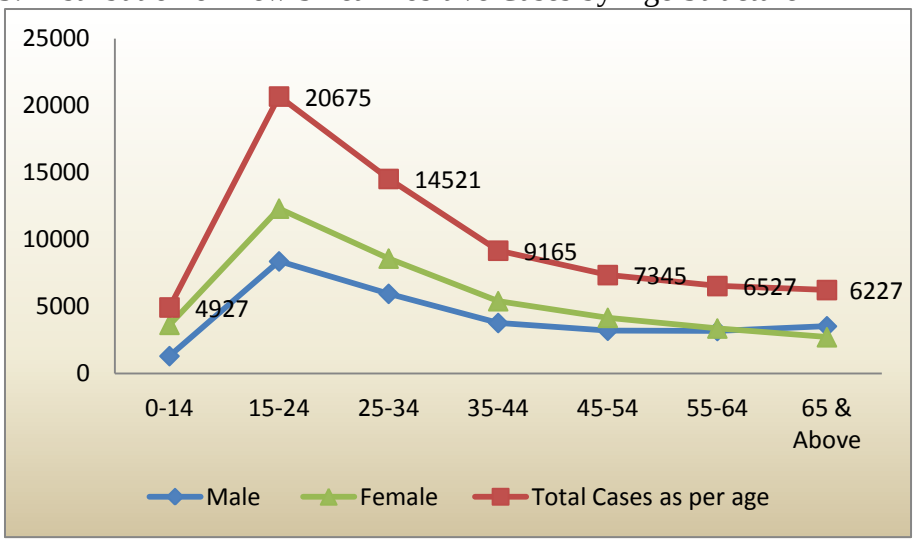


Figure 16: Population Pyramid of New Sputum Positive Cases, 2002-2010

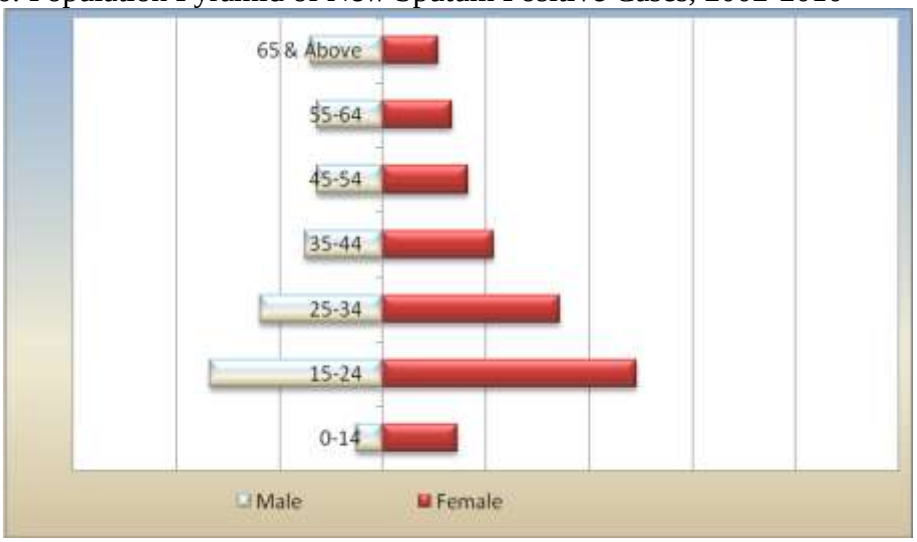


Table 22 on page 119 shows the gender distribution of TB cases by districts from 2002 to 2010. Of the total new sputum positive cases (n=69,387), 42.16 % were males and 57.84% females. The majority of districts reported a higher incidence of TB in female patients as compared to males. Only four districts were identified where males were at higher risk than females: Karak 2007 (m=79, f=75), Kohat 2003 (m=15, f=12), Nawshera 2003 (m=216, f=210) and Shangla 2004 (m=16, f=12).

Table 22: Notification of New Cases by Gender and District, 2002-2010

No	District	2002		2003		2004		2005		2006		2007		2008		2009		G.Total		
		M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Total
1	**Abbottabad**	0	0	82	79	187	221	232	306	397	432	394	533	362	521	379	572	2033 (43.28)	2664 (56.72)	**4697**
2	**Bannu**	0	0	76	81	36	47	69	102	140	167	254	339	307	385	313	411	1195 (43.82)	1532 (56.18)	**2727**
3	**Battagram**	0	0	0	0	3	7	40	96	30	71	44	109	55	150	69	121	241 (30.31)	554 (69.69)	**795**
4	**Buner**	14	19	47	78	47	76	83	133	83	190	103	214	108	237	99	205	584 (33.64)	1152 (66.36)	**1736**
5	**Charsadda**	3	5	44	47	89	94	103	155	131	167	217	286	228	279	275	343	1090 (44.20)	1376 (55.80)	**2466**
6	**Chitral**	6	16	81	154	85	167	94	229	79	161	69	190	90	179	90	191	594 (31.58)	1287 (68.42)	**1881**
7	**DI Khan**	127	175	96	121	131	220	213	403	245	293	341	471	234	331	250	365	1637 (4076)	2379 (59.24)	**4016**
8	**Hangu**	0	0	0	0	0	0	43	53	24	35	38	65	58	111	101	118	264 (40.87)	382 (59.24)	**646**
9	**Haripur**	0	0	121	157	183	246	223	326	255	366	210	295	242	305	261	315	1495 (42.56)	2010 (57.35)	**3505**
10	**Karak**	0	0	0	0	0	0	48	50	65	**95**	**79**	75	120	125	154	166	466 (47.70)	511 (52.30)	**977**
11	**Kohat**	0	0	**15**	**12**	65	67	128	131	132	183	214	181	154	201	205	252	913 (47.06)	1027 (52.94)	**1940**
12	**Kohistan**	0	0	0	0	1	2	23	88	39	131	34	117	44	136	49	193	190 (22.17)	667 (77.83)	**857**
13	**Lakki Marwat**	0	0	0	0	16	23	123	147	132	147	99	162	150	177	133	161	653 (44.42)	817 (55.58)	**1470**
14	**Lower Dir**	0	0	15	22	35	61	78	124	127	194	155	199	163	197	171	183	744 (43.16)	980 (56.84)	**1724**
15	**Malakand**	0	0	2	5	33	43	45	41	73	84	90	107	123	158	165	204	531 (45.27)	642 (54.73)	**1173**
16	**Mansehsra**	0	0	32	50	150	177	147	220	305	477	308	460	282	354	334	472	1558 (41.35)	2210 (58.65)	**3768**
17	**Mardan**	228	244	145	162	362	391	302	389	285	293	450	532	486	563	501	546	2759 (46.93)	3120 (53.07)	**5879**
18	**Nowshera**	168	191	216	210	163	262	237	294	249	262	240	288	319	377	422	449	2014 (46.93)	2333 (53.67)	**4347**
19	**Peshawar**	453	637	504	602	557	768	584	721	732	918	788	1008	786	1028	755	995	5159 (43.59)	6677 (56.41)	**11836**
20	**Shangala**	0	0	0	0	**16**	**12**	114	135	121	192	120	139	103	151	108	184	582 (41.72)	813 (58.28)	**1395**
21	**Swabi**	17	24	119	192	102	212	141	290	265	342	223	330	286	457	273	481	1426 (37.99)	2328 (62.01)	**3754**
22	**Swat**	223	409	293	492	186	287	291	454	251	359	395	466	423	486	248	386	2310 (40.89)	3339 (59.11)	**5649**
23	**Tank**	0	0	0	0	2	2	57	81	85	119	90	155	92	135	95	138	421 (40.06)	630 (59.94)	**1051**
24	**Upper Dir**	0	0	19	28	30	54	55	113	35	94	73	117	92	167	91	130	395 (35.97)	703 (64.03)	**1098**
Total KPK		1239	1720	1907	2492	2479	3439	3473	5081	4280	5772	5028	6838	5307	7210	5541	7581	29254 (42.16)	40133 (57.84)	**69387**

Kohistan district showed the greatest gender difference with females constituting 77.80% of the cases compared to 22% for males. Another five districts, Battagram (m=30.30%, f=69.70%), Chitral (m=31.60%, f=68.40%), Buner (m=33.60%, f=66.40%), Upper Dir (m=36.00%, f=64.00%) and Swabi (m=38.00%, f=62.00%) also reported statistics which showed that women accounted for more than 60% of the total TB cases. Karak (m=47.70%, f=52.30%), Kohat (m=47.10%, f=52.90%), Mardan (m=46.90%, f=53.10%), Nawshera (m=46.30%, f=53.70%) and Malakand (m=45.30%, f=54.70%) are the districts of KPK where number of female registrations were in lower than to the other districts (See Figure 17 and Figure 18on page 120 and 121).

Figure 17: Distribution of TB Patients by Gender and District, 2002-2010

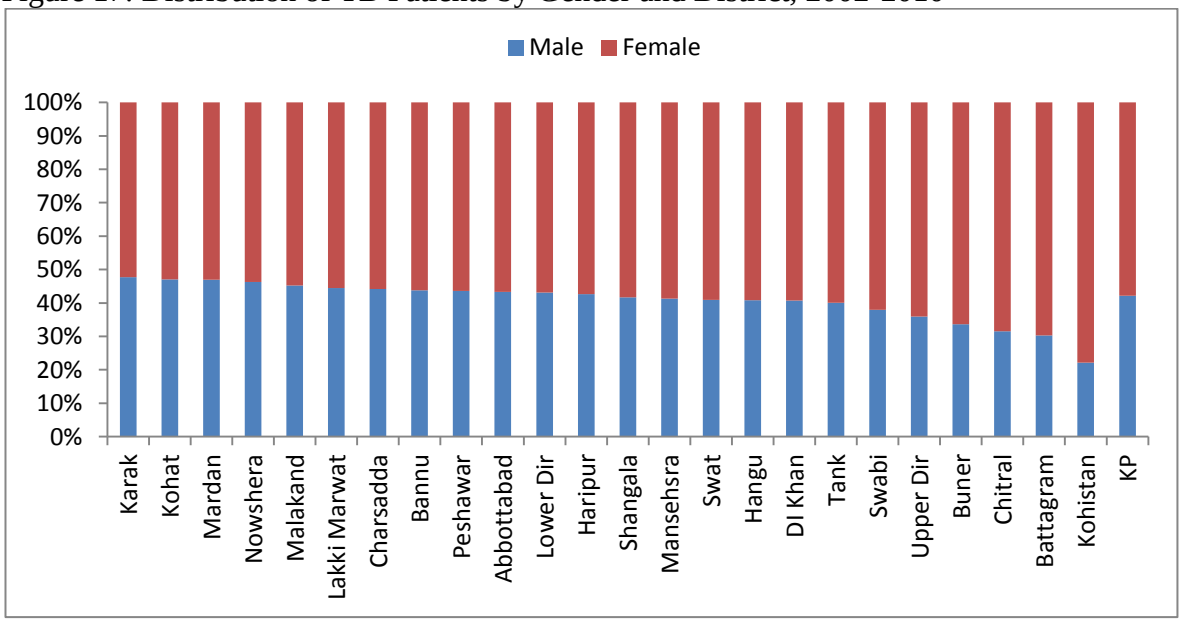
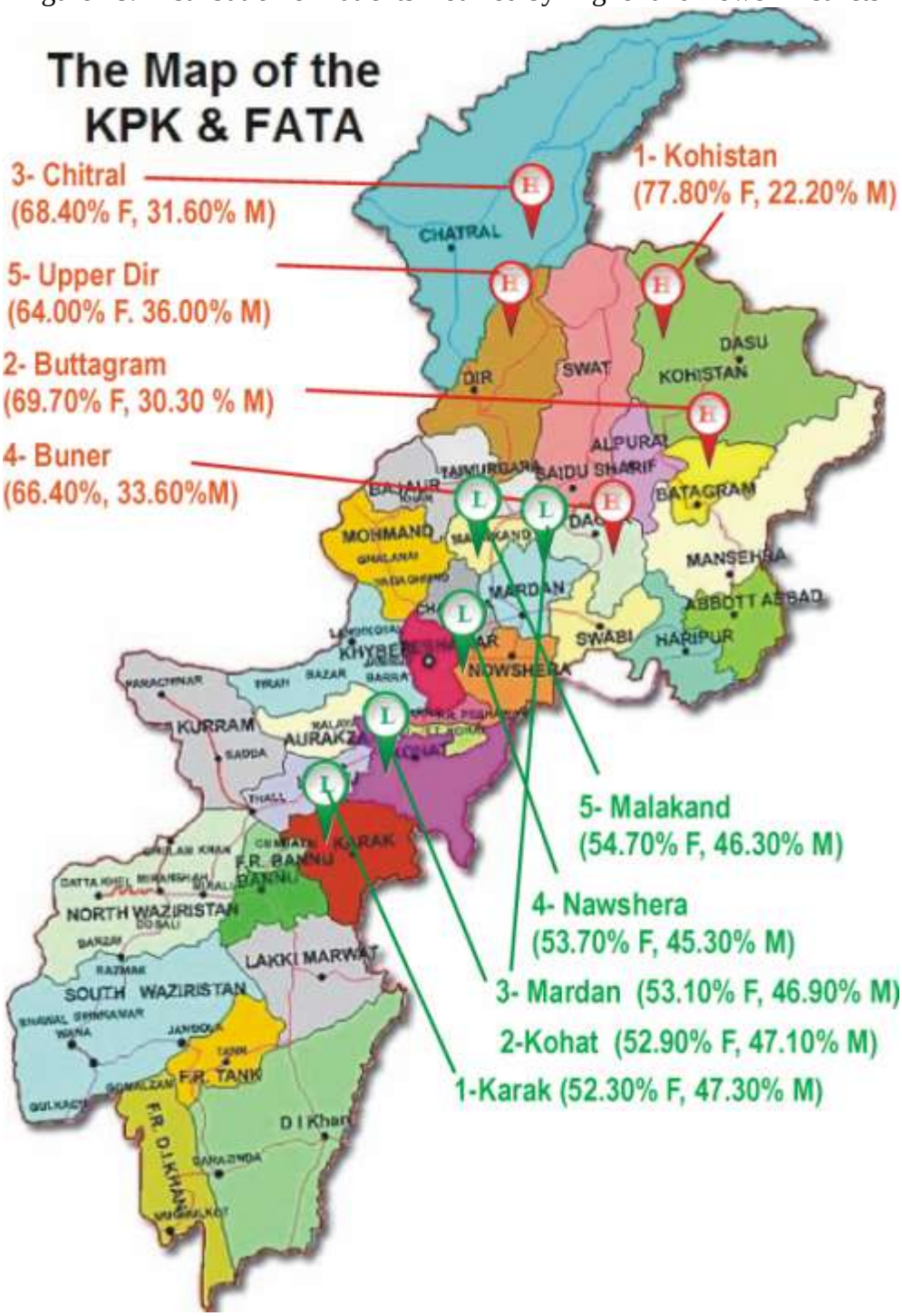


Figure 18: Distribution of Patients Notified by Higher and Lower Districts



6.7 Summary

Chapter 6 has described the descriptive epidemiology of TB patients in the province of Khyber Pakhtunkhwa, Pakistan from 2002 to 2010. Results in this chapter confirmed that notification (and hence incidence rate) of female patients was greater than male patients.

CHAPTER 7: RESULTS - RISK FACTORS

7.1 Introduction

This chapter describes the results of selected risk factors responsible for the higher notification of Tuberculosis in the province of Khyber Pakhtunkhwa (KPK). The results relate to field study carried out in KPK, and compare the risk factors for higher versus lower notification districts identified in Chapter 6.

A total of 914 new patients were diagnosed as confirmed TB cases during the period 1st July 2012 to 30th September 2012 in ten selected districts of KPK. Of the 914 study subjects, 129 were children under 15 years and were excluded from the study. The results therefore relate to 785 patients who were interviewed as part of the study.

The data were inputted using the Epi Info version7© developed by the Centre for Disease Control for epidemiological field analysis. Both Epi Info© and SPSS 22© were used for analysing the data. The relevant findings are presented in tabulated form with frequencies, percentages, mean, median and standard deviation. Chi-squire tests and multiple logistic regressions were used to examine correlation between selected variables.

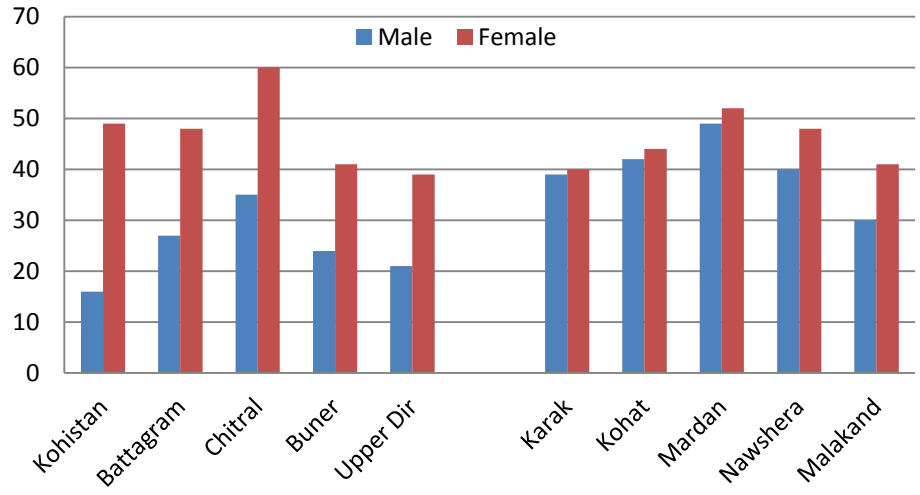
7.2 Distribution of Patients by Districts

785 participants were diagnosed as confirmed TB patients during the 3 months period between 1st July 2012 and 30th September 2012. Of those registered, 41.15 % (323) were males and 58.85 % (462) females. Table 20 shows the distribution of cases by district and gender in the higher notification districts compared to the lower notification districts. Significant gender differences were noted in TB cases from higher notification districts (Chi-Square= 3.29). In Kohistan 75.38% (65) of notified cases were females. Similarly, in Battagram, Chitral, Buner and Upper Dir, about 65% patients were females [Table 23].

Table 23: Distribution of Patients by Districts

Districts		Male (n=323)		Female (n=462)		Total (n=785)	
		Frequency	%	Frequency	%	Frequency	%
Higher	Kohistan	16	24.62	49	75.38	65	8.28
	Battagram	27	36.00	48	64.00	75	9.55
	Chitral	35	36.84	60	63.16	95	12.10
	Buner	24	36.92	41	63.08	65	8.28
	Upper Dir	21	35.00	39	65.00	60	7.64
Lower	Karak	39	49.37	40	50.63	79	10.06
	Kohat	42	48.84	44	51.16	86	10.96
	Mardan	49	48.51	52	51.49	101	12.87
	Nawshera	40	45.45	48	54.55	88	11.21
	Malakand	30	42.25	41	57.75	71	9.04

Figure 19: Gender Differences in TB Notification in Higher and Lower District



7.3 Age Distribution of Patients

The mean age of the participants was 33.86 years with a standard deviation of 16.19. The ages of the youngest and oldest patients were 15 and 85 years respectively. More than three-quarters (76.94%) of notified cases were below 45 years of age [Table 24].

Table 24: Distribution of Patients by Age

Age Group	Frequency	Percent
15 - <30	394	50.19%
30 - <45	210	26.75%
45 - <60	86	10.96%
60 - <75	77	9.81%
75 - <90	18	2.29%
TOTAL	**785**	**100.00%**

7.4 Educational Status of Notified Cases in Higher versus Lower Notification Districts

The level of education was determined by self reports of level of schooling of notified cases. Table 22 shows that 79.30% of females were illiterate in higher notification districts compared to 38.00% in lower notification districts. Gender differences show that 29.30% of males completed high school education in lower districts compared to only 7.20% females in higher notification districts. The percentage of women who completed high school education in low notification districts was 29.8% compared to 7.2% in high notification districts (Male versus female in higher districts; Chi-Square=70.34, p= <0.001) [Table 25].

Table 25: Educational Status of Patients by Higher against Lower Notification Districts

Education Level	Higher (n=360)		Lower (n=425)		Total (%)
	Male (%)	Female (%)	Male (%)	Female (%)	
Illiterate	44 (35.80)	188 (79.30)	82 (41.00)	86 (38.20)	400 (51.00)
Madrassa	5 (4.10)	3 (1.30)	0 (0.00)	12 (5.30)	20 (2.50)
Primary	23 (18.70)	26 (11.00)	41 (20.50)	37 (16.40)	127 (16.20)
High School	36 (29.30)	17 (7.20)	63 (31.50)	67 (29.80)	183 (23.30)
Secondary	11 (8.90)	2 (0.80)	8 (4.00)	19 (8.40)	40 (5.10)
Graduation	1 (0.80)	0 (0.00)	4 (2.00)	3 (1.30)	8 (1.00)
Post Graduation	3 (2.40)	1 (0.40)	2 (1.00)	1 (0.40)	7 (0.90)

Male vs female in Higher; *Chi-Square=70.34, p= <0.001*
Male vs female in Lower; Chi-Square=0.19, p= <0.663

7.5 Distribution of Patients by Family Size in Higher versus Lower Notification Districts

Table 26 shows that more than half (57.07%) of notified cases were living in overcrowded houses with 7-12 family members with little difference between high and low notification districts. Surprisingly, 24.45% of notified cases were living in severely overcrowded houses. The mean family size was 10 members per family with a range of 1 to 40 (SD 4.77). There was no significant difference noted in family sizes between higher and lower notification by districts (Chi-Square=2.27, df= 3 p= 0.519) [Table 26].

Table 26: Distribution of Notified Cases by Family Size in Higher and Lower Notification Districts

Family Size	Higher (n=360)		Lower (n=425)		Total (n-785)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
01-06	68	18.89%	93	21.88%	161	20.51%
07-12	204	56.67%	244	57.41%	448	57.07%
13 -20	74	20.56%	76	17.88%	150	19.11%
≥21	14	3.89%	12	2.82%	26	3.31%

Chi-Square=2.27, df= 3 p= 0.519

7.6 Distribution of Patients by Income

To explore the level of poverty, participants were asked to identify approximate monthly family income. On the basis of household income, patients were divided into three groups. (Severely poor= < 5,000 Pak Rupees, Poor or Low Income= < 10,000 Pak Rupees, High Income or Economically Stable = > 20,000 Pak Rupees, 1 US$= 102 Pak Rupees). Table 26 shows that nearly two thirds (63.18%) of notified cases were living below the poverty level, earring less than $100 a month. Only, 11.21% of notified cases were noted to be economically stable. These data need to be interpreted with caution because 30.09% of females were not sure about their monthly household income [Table 27].

Table 28 shows that 41.77% females in higher notification districts were living in severe poverty compared to 26.67% of the females in the lower notification districts. Thirty per cent of female notified cases in lower notification districts were economically stable compared to 10.84% in higher notification districts. The monthly income of female participants in higher notification areas was significantly different from the monthly income of female participants in lower notification areas (Higher versus lower; Chi Square = 27.54, p=<0.001, df = 4, p=<0.001) [Table 28].

Table 27: Income Distribution of Notified Cases by Gender

Monthly Income Level (Pak Rupees) 1 US $ = 102 PKR	Male (n=323)		Female (n=462)		Total (n=785)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
≤ 5000	100	30.96%	159	34.42%	259	32.99%
≤ 10000	126	39.01%	111	24.03%	237	30.19%
≤ 20000	26	8.05%	38	8.23%	64	8.15%
≥ 30000	9	2.79%	15	3.25%	24	3.06%
Not Sure	62	19.20%	139	30.09%	201	25.61%

Male versus Female; Chi Square = 23.77, p=<0.001Table 28: Income Distribution of Notified Cases in Higher and Lower Notification Districts

Monthly Income Level (Pak Rupee) 1US $ = 102 PKR	Higher			Lower			Total (%)
	Male (%)	Female (%)	Total	Male (%)	Female (%)	Total	
< or 5000	38 (30.89)	99 (41.77)	137	62 (31.00)	60 (26.67)	122	259 (32.99)
< or 10000	46 (37.40)	42 (17.71)	88	80 (40.00)	69 (30.67)	149	237 (30.19)
< or 20000	14 (11.38)	5 (2.11)	19	12 (6.00)	33 (24.67)	45	64 (8.15)
> or 30000	4 (3.25)	3 (1.27)	7	5 (2.50)	12 (5.33)	17	24 (3.06)
Not Sure	21 (17.07)	88 (37.13)	109	41 (20.50)	51 (22.67)	92	201 (25.61)
TOTAL	123	237	360	200	225	425	**785**

Higher versus lower; Chi Square = 27.54, p=<0.001
Male versus female in higher; Chi Square = 40.94, p=<0.001
Male versus female in lower; Chi Square = 13.19, p=0.01

7.7 Distribution of Notified Cases by Age of the Youngest Child

One of the risk factors that we were keen to explore was the impact of having young children on the notification rate in women between high and low notification districts. This may give us an indication of nutritional status of notified cases. Our data showed that 38.60% male and 61.40% female notified cases were married. Of those who were married, 22.85% of notified cases in higher notification districts had a child who was less than a year old compared to 15.08% in lower notification districts., The differences between high and low notification districts were not significant.

Table 29: Distribution of Notified Cases by Age of the Youngest Child

Youngest Child Age	Higher (n=302)		Lower (n=303)		Total (n=605)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
1-3 Months	24	7.95%	22	7.26%	46	7.60%
6-12 Months	45	14.90%	24	7.92%	69	11.40%
1-2 Years	97	32.12%	62	20.46%	159	26.28%
3-4 Years	30	9.93%	64	21.12%	94	15.54%
5-10 Years	16	5.30%	42	13.86%	58	9.59%
Above 10 Years	63	20.86%	69	22.77%	132	21.82%
No Child	27	8.94%	20	6.60%	47	7.77%

Higher vs. lower; Chi-Square= 5.48, p=0.091

7.8 Distribution of Notified Cases by Type of Fuel Used for Cooking

The type of fuel used for cooking may be an indication of poverty and also of the environment. The later may also be a risk factor for TB as discussed in Chapter 3 Table 30 on page 129 shows that the vast majority (80.38%) of notified cases were using firewood as the main source of fuel for cooking. In higher notification districts, 95.00% (342) of the notified cases were using firewood compared to 68.00% (631) in lower notification districts. There were also marked differences in relation to the use of

gas for cooking. The differences between notified cases in high and low notification districts in type of fuel used was significant (Chi-Square=81.14, p=<0.001) [Table 30].

Table 30: Distribution of Notified Cases of Fuel Used for Cooking.

Fuel	Higher (n-=360)		Lower (n=425)		Total (n=785)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Firewood	342	95.00%	289	68.00%	631	80.38%
Gas	18	5.00%	125	29.41%	143	18.22%
Other	0	0.00%	9	2.12%	9	1.15%

Higher vs. lower; Chi-Square=81.14, p=<0.001

7.9 Distribution of Patients by House Type

Table 31 shows that more than three quarters (76.11%) of notified cases high notification districts were living in mud houses, with 11.76% living in brick houses. This compares to 46.86% of cases living in mud houses and 21.8% in low notification districts. These differences were significant (*chi-square=30.26, OR=3.049, p=<0.001*) [Table 31].

Table 31: Distribution of Notified Cases by House Type

House Type	Higher (n-=360)		Lower (n=425)		Total (n=785)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Mud House	274	76.11%	199	46.82%	473	60.25%
Bricks House	42	11.67%	93	21.88%	135	17.20%
Stones House	2	0.56%	15	3.53%	17	2.16%

Chi-square=30.26, p=<0.001

7.10 Distribution of Notified Cases by Amount of Time Spent Outside the House.

The amount of time spent outside the home may be a risk factor for TB because it could reflect on issues such as Vitamin D deficiency and also on the level of emancipation of women – the suggestion being that women who spent more time at home were not given the freedom to take part in activities outside the home. Forty eight

per cent of women indicated that they were going out for at least one hour in a 24 hours period, with 33.98% going out for 2 to 5 hours. In contrast, 60.3% of men indicated that they spent 6 to 8 hours outside the home with 20.12% indicated that they spent more than nine hours in 24 hours. Only 3.72% of men reported that they were staying out for at least one hour. These differences were significant (*Chi-Square=133.1, df = 3, p=<0.001*) [Table 32].

Table 32: Gender Distribution of Notified Cases by Amount of Time Spent Outside the Home

Hours spent outside the home	**Male (n=323)**		**Female (n=462)**		**Total (n=785)**	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
0 to 1	12	3.72%	222	48.05%	234	29.81%
2 to 5	51	15.79%	157	33.98%	208	26.50%
6 to 8	195	60.37%	79	17.10%	274	34.90%
≥ 9	65	20.12%	4	0.87%	69	8.79%

Chi-Square=133.1, p=<0.001

Table 33 shows that there was a difference in time spent outside the home between men and women living in high compared to low notification districts. These differences were significant (Chi-Square= 44.92, p=<0.001).

Table 33: Distribution of Notified Cases by Amount of Time Spent Outside the Home between High and Low Notification Districts

Stay Out Time	**Higher (n=360)**			**Lower (n=425)**			Total (%)
	Male (%)	Female (%)	Total	Male (%)	Female (%)	Total	
0 to 1	6 (4.88)	142 (59.92)	148	6(3.00)	80 (35.56)	86	234 (29.81)
2 to 5	15 (12.20)	77 (32.49)	92	36(18.00)	80 (35.56)	116	208 (26.50)
6 to 8	83 (67.48)	18 (7.59)	101	112(56.00)	61 (27.11)	173	274 (34.90)
≥ 9	19 (15.45)	0 (0.00)	19	46(23.00)	4 (1.78)	50	69 (8.78)

Chi-Square= 44.92, p=<0.001

7.11 Summary Table of Gender Differences and Risk Factors for TB (Model-1)

Table 34 summarises the risk factors for TB by gender. In addition to the risk factors discussed in the preceding paragraphs, the table also includes data on the occurrence of anaemia and weight. There were significant gender differences as exemplified by the odd ratio for all the listed variables. This was the first stage in developing a logistic regression model for assessing the different contribution of the variable to the notification of TB.

Table 34: Gender Difference and Risk Factors for TB (Model-1)

Variables	Male n(%)	Female n(%)	OR	95% CI		p-vale
				Lower	Upper	
Education						
Uneducated	126(31.8)	270(68.2)	2.088	1.562	2.792	<0.001
Educated	197(50.6)	192(49.4)				
Districts						
Higher	123(38.08)	200(61.92)	0.584	0.44	0.78	<0.001
Lower	237(51.30))	225(48.70)				
Income Status						
[1]Low Income	162(35.2)	298(64.8)	1.806	1.352	2.412	<0.001
[2]High Income	161(49.5)	164(50.5)				
HB Level						
[3]Anaemic	14(31.9)	299(68.1)	2.398	1.792	3.208	<0.001
[4]Non-Anaemic	183(52.9)	163(47.1)				
BMI						
[5]Underweight	65(25.1)	194(74.9)	2.873	2.068	3.992	<0.001
[6]Non-underweight	258(49.0)	268(51.0)				
Age						
Younger <45	220(36.4)	384(63.6)	2.305	1.644	3.231	<0.001
Older ≥45	103(56.9)	78(43.1)				
Marital Status						
Married	235(38.6)	374(61.4)	1.591	1.136	2.23	<0.007
Unmarried	88(50.0)	88(50.0)				
TB Type						
Pulmonary	260(41.5)	366(58.5)	1.082	0.7588	1.544	0.731
Extra Pulmonary	63(39.6)	96(60.4)				
Family Size						
Ideal Family <5	32(35.2)	59(64.8)	0.7252	0.4577	1.149	0.171
Overcrowded ≥5	291(41.9)	403(58.0)				
Family Type						
Joint Family	295(42.7)	396(57.3)	1.756	1.101	2.801	0.016
Separated Family	28(29.8)	66(70.2)				
Cooking Mood						
Indoor	243(41.5)	343(58.5)	1.054	0.7595	1.462	0.756
Outdoor	80(40.2)	119(59.8)				

[1] Low Income = ≤ 10,000 Pak Rupees/month
[2] High Income = ≥ 20,000 Pak Rupees/month
[3] Anaemic = HB < 12.00gm/dl (Women), HB <13 gm/dl (Men)
[4] Non-Anaemic = HB > 12 gm/dl (Women), HB > 13gm/dl (Men)
[5] Underweight = BMI < 17.5
[6] Underweight = BMI < 17.5

7.12 Summary Table of Risk Factors for TB Notification by High and Low Notification Districts. (Model-2)

Table 35: Differences in Risk Factors for TB Notified Cases between Low and High Notification Districts

Variables	Higher n(%)	Lower n(%)	OR	95% CI		p-vale
				Lower	Upper	
Education						
Uneducated	228(57.6)	168(42.4)	2.642	1.99	3.53	<0.001
Educated	132(33.9)	257(66.1)				
Income Status						
[7]Low Income	246(53.5)	214(46.5)	2.128	1.59	2.85	<0.001
[8]High Income	114(35.1)	211(64.9)				
HB Level						
[9]Anaemic	201(45.8)	238(54.2)	0.993	0.75	1.32	0.962
[10]Non-Anaemic	159(46.0)	187(54.0)				
BMI						
[11]Underweight	135(51.1)	129(48.9)	1.377	1.02	1.85	0.035
[12]Non-underweight	225(43.2)	296(56.8)				
Age						
Younger <45	278(46.0)	326(54.0)	1.03	0.74	1.44	0.87
Older ≥45	82(45.3)	99(54.7)				
TB Type						
Pulmonary	268(45.0)	327(55.0)	0.873	0.63	1.21	0.417
Extra Pulmonary	92(48.4)	98(51.6)				
Family Size						
Ideal Family <5	37(41.1)	53(58.9)	0.804	0.51	1.25	0.340
Overcrowded ≥5	323(46.5)	372(53.5)				
Persons Living/room						
Ideal Family <5	55(35.9)	98(64.1)	0.602	0.42	0.87	0.006
Overcrowded ≥5	305(48.3)	327(51.7)				
Family Type						
[13]Joint Family	308(44.6)	383(55.4)	0.648	0.42	1.00	0.052
[14]Separated Family	52(55.3)	42(44.7)				
Cooking Mood						
Indoor	24(41.8)	341(58.2)	0.525	0.38	0.73	<0.001
Outdoor	115(57.8)	84(42.2)				

[7] Low Income = ≤ 10,000 Pak Rupees/month
[8] High Income = ≥ 20,000 Pak Rupees/month
[9] Anaemic = HB < 12.00gm/dl (Women), HB <13 gm/dl (Men)
[10] Non-Anaemic = HB > 12 gm/dl (Women), HB > 13gm/dl (Men)
[11] Underweight = BMI < 17.5
[12] Underweight = BMI < 17.5
[13] Joint Family = A cultural system of living of all family members including married brothers and parents together in a single house.
[14] Separated Family = A family living without their family members (Brothers and sisters) in separate house after marriage

Table 35 shows that the significant differences between low and high notification districts were related to education level, income, BMI, overcrowding, family type and whether cooking was carried out indoors or outdoors.

7.13 Summary Table of Multiple Logistic Regression

The variables listed in Table 34 and 32 that were statistically significant were combined in a logistic regression model in order to assess the contribution of the variables to the notification of TB in high notification districts. The reference category was low notification Multi-variable analysis was performed using stata software by logistic regression with groups of Variables i.e. gender, employment, income status, anaemic status, age, stays out of home time and meat eating.

Notification = *Gender* + *Education* + *Employment* + *Income* + *Anaemia* + *Age* + *Stays out time* + *Meat eating* + *Family size* + *(Gender X Education)* + *(Gender X Employment)* +……

The results are presented in Table 35. For gender there is a highly significant effect with women having an odds ratio of 8.7, suggesting that they have nearly 9 times higher odds of being in a high notification area than men.

A strong association was noted for the interaction between education and gender (*OR = 0.16*), suggesting that more educated women were around 6 times less likely to be in a higher notification area (1/0.16) compared to a low notification area. It was also observed from the logistic regression model that income level (*OR = 0.42*), anaemia (*OR = 0.45*) and unemployment (*Or = 0.23*) were also associated with being in a high notification district in the province of KPK. Lower notification districts with female gender were used as reference category for the model.

Table 36 shows that female patients in lower notification districts were six times (1/0.16) less likely to be educated when compared to females in high notification districts (*OR= 0.16, p=<0.001)*. Similarly, women in lower notification districts were four times (1/0.23) less likely to be employed as compared to women in higher notification districts (*OR= 0.23, p=<0.05*). Female participants in lower notification districts were almost 2.5 times less likely (1/0.42) to have high income as compared to female patients in higher notification districts (*OR= 0.42, p=<0.05*). Similarly, older female patients ($\geq$ 45 years) were 2.8 times (1/0.35) less likely to be in lower notification districts than females in higher notification districts (*OR= 0.35, p=<0.05*) [Table 36].

Table 36: Summary Table of Multiple Logistic Regressions

Variables	Estimate	Std err	Z	Odds ratio	lower CI	Upper CI	p-value
(Intercept)	1.7566	1.1598	1.5146	5.7928	0.60	56.25	0.12988
[15]*****Female**	**2.1644**	**0.3919**	**5.5230**	**8.7097**	**4.04**	**18.78**	**0.00000**
Educated	0.3218	0.2741	1.1739	1.3796	0.81	2.36	0.24042
Employed	0.2512	0.2809	0.8943	1.2855	0.74	2.23	0.37115
High Income	0.0863	0.2542	0.3393	1.0901	0.66	1.79	0.73438
[16]****Non-anaemic**	**0.7164**	**0.2537**	**2.8240**	**2.0470**	**1.25**	**3.37**	**0.00474**
≥ 45 Years	0.4031	0.2886	1.3969	1.4964	0.85	2.63	0.16246
*****Female: Educated**	**-1.8059**	**0.3646**	**- 4.9527**	**0.1643**	**0.08**	**0.34**	**0.00000**
[17]***Female: Employed**	**-1.4290**	**0.7145**	**- 1.9999**	**0.2395**	**0.06**	**0.97**	**0.04551**
***Female: High Income**	**-0.8611**	**0.3477**	**- 2.4765**	**0.4226**	**0.21**	**0.84**	**0.01327**
***Female: Non-Anaemic**	**-0.7932**	**0.3405**	**- 2.3296**	**0.4524**	**0.23**	**0.88**	**0.01983**
Female: ≥ 45 Years	**-1.0276**	**0.4168**	**- 2.4652**	**0.3578**	**0.16**	**0.81**	**0.01369**

[15] ****; p = <0.0001*
[16] ***; p = 0.001*
[17] *8; p = 0.01*

7.14 Summary

In this chapter, the analysis has explored different risk factors responsible for gender differences in TB in higher and lower notification districts of KPK.

The gender difference between higher and lower notification districts was found to be statistically significant. Similarly, the majority of female patients in higher notification districts were found to be illiterate, unemployed, poor and living in low socioeconomic status.

Finally, the multivariable analysis determined a highly significant effect with women having an odds ratio of 8.7 showing that they have nearly 9 times higher odds of being in a high notification area than men. The other largest effect is for the interaction of gender and education with more educated women being around 6 times less likely to be in a higher notification area.

CHAPTER 8: RESULTS - PATIENTS' KNOWLEDGE

8.1 Introduction

This chapter describes the results to estimate the level of knowledge in relation to TB of newly diagnosed TB patients comparing patients in higher against lower notification districts.

8.2 Gender Distribution of Patients by Higher and Lower Notification Districts

Of the total 323 male participants, 38.08% (123) were registered from higher and 61.92% (200) from lower notification districts. Similarly, of the total of 462 female participants, 51.30% (237) were registered from higher and 48.70% (225) from lower notification districts. The differences in gender distribution between high and low notification districts were significant (Chi-Square=13.38, p=<0.001) [Table 37].

Table 37: Gender Distribution of Patients in Higher and Lower Notification Districts

Case Status	Male		Female		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Higher	123	38.08%	237	51.30%	360	45.86%
Lower	200	61.92%	225	48.70%	425	54.14%
TOTAL	**323**	**100.00%**	**462**	**100.00%**	**785**	**100.00%**

Chi-Square=13.38, p=<0.001

8.3 Distribution of Patients by Urban and Rural Residence

The data in Table 38 shows that the majority 86.62% (680) of the participants were living in rural areas. Twenty three percent of (53) female participants from lower notification districts replied that they were living in towns compared to 9.28% (22) in higher notification districts. These differences were significant (*Chi-Square=13.03, p=<0.001*).

Table 38: Distribution of Patients by Urban and Rural Residence in Higher and Lower Notification Districts

Urban-Rural	Higher		Lower		Total (%)
	Male (%)	Female (%)	Male (%)	Female (%)	
Township/ Town- Urban	9 (7.32)	22 (9.28)	21 (10.50)	53 (23.56)	105 (13.38)
Village- Rural	114 (92.68)	215 (90.72)	179 (89.50)	172 (76.44)	680 (86.62)
TOTAL	123	327	200	225	785

Chi-Square=13.03, p=<0.001)

8.4 Knowledge of Patients about the Causes of TB

When asked questions about the cause of TB, almost half of the participants provided the correct answer. However a large number of male (42.11%, n = 136) and female participants (57.58%, n = 266) were unaware of the causes of TB. There were significant differences between male and female patients in the higher and lower notification districts (Chi-Square= 21.40, df= 3, p= <0.001). Similarly, the differences between men in the high and low notification districts regarding the cause of TB were not significant (Chi-Square= 0.92, df= 3, p= 0.819). However, when I compared the results of women between high and low notification districts, I noted a highly significant difference (Chi-Square= 96.23, df= 3, p= <0.001) [Table 39].

Table 39: Knowledge of Patients about the Causes of TB by Gender in High and Low Notification Districts

Cause of TB	Male		Total	Female		Total
	Higher (%)	Lower (%)		Higher (%)	Lower (%)	
Germs Bacillus Bacteria Mycobacterium	67 (54.47)	101 (50.50)	168	35 (21.21)	130 (87.79)	165
Hard Work	7 (5.69)	9 (4.50)	16	16 (6.75)	12 (5.33)	28
Hereditary	0 (0.00)	3 (1.50)	3	2 (0.84)	1 (0.44)	3
Don't Know	49 (39.84)	87 (43.50)	136	184 (77.64)	82 (36.45)	264
TOTAL	**123**	**200**	**323**	**237**	**225**	**462**

Male versus female: Chi-Square= 21.40, p= <0.001

Male versus male: Chi-Square= 21.40, p= <0.001

Female versus female: Chi-Square= 96.23, p= <0.001

8.5 Knowledge of Patients about the Transmission of TB

Table 40 summarises the results of the responses regarding the transmission of TB. The majority of male and female patients 61.69% (285) replied correctly in relation to knowledge about the transmission of TB. However, 35.28% (163) of female patients and 24.46% (79) male patients did not know that TB is a transmittable disease. Significant differences were noted between men and women in the higher and lower notification districts regarding knowledge about the transmission of TB (Male versus Female: Chi-Square=10.46, df= 2, p= 0.005, Male versus Male: Chi-Square=11.36, df= 2, p= 0.003, Female versus Female: Chi-Square= 68.41, df= 2, p= <0.001) [Table 40].

Table 40: Knowledge of Patients about the Transmission of TB by Gender in High and Low Notification Districts

TB Transmission	Male		Total	Female		Total
	Higher (%)	Lower (%)		Higher (%)	Lower (%)	
Yes	98 (79.67)	134 (67.00)	232	98 (41.35)	187 (83.11)	285
No	7 (5.69)	5 (2.50)	12	9 (3.80)	5 (2.22)	14
Don't Know	18 (14.63)	61 (30.50)	79	130 (54.85)	33 (14.67)	163
TOTAL	123	**200**	**323**	**237**	**225**	**462**

Male versus female: Chi-Square= 10.46, p= 0.005

Male versus male: Chi-Square=11.36, p= 0.003

Female versus female: Chi-Square= 68.41, p= <0.001

8.6 Knowledge of Patients about the Spread of TB

Nearly two-thirds of the participants were unaware as to how TB was spread. Almost an equal proportion of male (31.89%) and female (30.95%) patients correctly reported that infectious droplet was the main cause of TB spread. There were no significant differences reported in the knowledge about the spread of TB between men and women (Chi-Square= 2.59, df= 4, p= 0.629). Similarly, the differences between men in the high and low notification districts regarding the spread of TB were not significant (Chi-Square= 7.39, df= 4, p= 0.117). However, when I compared the results for women between high and low notification districts, I noted a highly significant difference (Chi-Square= 27.58, df= 4, p= <0.001) [Table 41].

Table 41: Knowledge of Patients about the Spread of TB by Gender in High and Low Notification Districts

TB Spread	Male		Total	Female		Total
	Higher (%)	Lower (%)		Higher (%)	Lower (%)	
Infectious droplet spread	46 (37.40)	57 (28.50)	103	50 (21.10)	93 (41.33)	143
Sharing Food	18 (14.63)	26 (13.00)	44	41 (17.30)	28 (12.44)	69
Smoking	1 (0.81)	11 (5.50)	12	6 (2.53)	3 (1.33)	9
Hard Work	4 (3.25)	5 (2.50)	9	4 (1.69)	10 (4.44)	14
Don't Know	54 (43.90)	101 (50.50)	155	136 (57.38)	91 (40.44)	227
TOTAL	123	**200**	**323**	**237**	**225**	**462**

Male versus Female: Chi-Square= 2.59, p= 0.629

Male versus Male: Chi-Square= 7.39, p= 0.117

Female versus Female: Chi-Square= 27.58, p= <0.001

8.7 Knowledge of Patients about the Signs and Symptoms of TB

Over 40% of males (45.82%) and females (41.34%) correctly reported that having a cough of more than three weeks duration was the most common symptom of TB. However, 13.31% male and 15.58% female participants still believed that fever was the most common symptom of TB. There was a significant difference reported regarding the knowledge of the signs and symptom of TB within females patients between higher and lower districts (Chi-Square= 24.50, df= 3, p= <0.001) [Table 42].

Table 42: Knowledge of Patients about Signs and Symptoms of TB by Gender in High and Low Notification Districts

TB Sign	Male		Total	Female		Total
	Higher (%)	Lower (%)		Higher (%)	Lower (%)	
Cough more than 3 weeks	56 (45.53)	92 (46.00)	148	72 (30.38)	119 (52.88)	191
Fever	21 (17.07)	22 (11.00)	43	46 (19.41)	26 (11.56)	72
Chest pain	7 (5.69)	13(6.50)	20	11(4.64)	8 (3.56)	19
Don't Know	39 (31.71)	73 (37.50)	112	108 (45.57)	72 (32.00)	180
TOTAL	123	**200**	**323**	**237**	**225**	**462**

Chi-Square= 24.50; df 3; p= <0.001

8.8 Knowledge of Patients about Drug Resistance of TB

Only 10.82% (50) of female and 13.31% (43) of male patients correctly reported that multi drug resistant (MDR) TB is the main complication of incomplete and inappropriate TB treatment. There was a significant difference noted between the knowledge of female patients regarding MDR TB in higher and lower notification districts (Chi-Square= 27.48, df= 3, p= <0.001). However, the difference in knowledge regarding MDR TB between male participants in higher and lower notification districts was not significant (Chi-Square= 4.31, df= 3, p= 0.230) [Table 43].

Table 43: Knowledge of Patients about Drug Resistance of TB by Gender in High and Low Notification Districts

Complications of TB	Male		Total	Female		Total
	Higher (%)	Lower (%)		Higher (%)	Lower (%)	
Drug Resistance TB	13 (10.57)	30 (15.00)	43	10 (4.22)	40 (17.78)	50
Prolong Disease	17 (13.82)	40 (20.00)	57	27 (11.39)	32 (14.22)	59
Death	18 (14.63)	29 (14.50)	47	57 (24.05)	31 (13.78)	88
Don't Know	75 (60.98)	101 (50.50)	176	143 (60.34)	122 (54.22)	265
TOTAL	123	**200**	**323**	**237**	**225**	**462**

Female: Chi-Square= 27.48, p= <0.001

Male: Chi-Square= 4.3, p= 0.230

8.9 Overall Knowledge of TB Patients

To assess the level of knowledge of TB patients, the scores for the knowledge questions were summated. The overall score was obtained by adding up all the correct answers. A mean score was calculated with patients having a score below the average classified as having poor knowledge and those with a score above the average being classified as having satisfactory knowledge. It can be seen from the data in Table 44 that female patients in lower notification districts were five times more knowledgeable than female patients in higher districts (Chi-Square=62.87, p= <0.001) [Table 44].

Table 44: Overall Knowledge of TB Patients by Gender in High and Low Notification Districts

Knowledge of TB patients	**Male**		**Total (%)**	**Female**		**Total (%)**
	Higher (%)	**Lower (%)**		**Higher (%)**	**Lower (%)**	
Poor	69 (56.10)	126 (63.00)	195 (63.37)	195 (82.28)	106 (47.11)	301 (65.15)
Satisfactory	54 (43.90)	74 (37.00)	128 (39.63)	42 (17.72)	119 (52.89)	161 (34.85)
TOTAL	**123**	**200**	**323**	**237**	**225**	**462**

Female: Chi-Square= 62.87, p= <0.001

8.9.1 Patients' Knowledge about the Cause, Symptoms, Transmission and Spread of TB

Five questions were asked to assess the knowledge of patients regarding the causes, symptoms and transmission of TB. Of the female patients (462), 78.79% (130) in the Lower notification districts and 21.21% (35) in the higher notification districts replied correctly that germs, bacteria or mycobacterium cause TB. A significant difference was noted between the knowledge of females in lower and higher notifications districts about the causes of TB (Chi-Square=92.99, OR= 7.90, 95% CI= 5.06-12.33, p= <0.001). Table 45 summarises the results of patient's knowledge about the causes and spread of TB and shows that female patients in lower notification districts were more informed than female patients living in notification districts [Table 45].

8.9.2 Patients' Knowledge about the Treatment and Complications of TB

Table 46 summarises the responses to questions about the knowledge of TB patients in relation to perceptions, treatment and complications of TB. The majority, of patients (79.83% (95) in higher notification districts were unaware that TB treatment is free. Similarly, 68.10% (111) female participants in higher notifications districts were ignorant about how to take TB drugs.

Table 46 shows that female patients in higher notifications districts were more ignorant than females in lower notification districts regarding the duration, treatment and follow up of TB [Table 46].

Table 45: Summary of Responses of the Participants Regarding Causes, Symptoms and Spread of TB by Gender in High and Low Notification Districts

Questions	Male		Female		OR	Chi-Square	95% CL	p-value
	Higher	Lower	Higher	Lower				
Knowledge about cause, symptoms, transmission and spread of TB								
What germ causes TB? (Germ, Bacteria, Mycobacterium)					0.85 7.90	0.48 92.99	0.54-134 5.06-12.33	0.488 <0.001
Correct	67(39.88)	101(60.12)	35(21.21)	130(78.79)				
Incorrect	56(36.12)	99(63.87)	202(68.01)	95(31.99)				
Do you know the most common symptom of TB? (Cough, Cough more than 3 weeks)					1.0192 2.5727	0.0086 24.1115	0.65-1.60 1.76-3.76	1.000 <0.001
Correct	56(37.84)	92(62.16)	72(37.70)	119(62.30)				
Incorrect	67(38.29)	108(61.71)	165(60.89)	106(39.11)				
Do you know TB is Curable diseases? (Yes)					0.73 2.89	0.93 19.82	0.38-1.39 1.79-4.67	0.428 <0.001
Correct	107(39.19)	166(60.81)	166(45.86)	196(54.14)				
Incorrect	16(32.00)	34(68.00)	71(71.00)	29(29.00)				
Do you think TB is transmittable disease? (Yes)					0.52 6.98	6.05 85.17	0.30-0.88 4.52-10.77	0.015 <0.001
Correct	98(42.24)	134(57.76)	98(34.39)	187(65.61)				
Incorrect	25(27.47)	66(72.53)	139(78.53)	38(21.47)				
How TB is spread? (Infectious Droplet)					0.67 2.63	2.78 22.11	0.41-1.07 1.75-3.97	0.110 <0001
Correct	46(44.66)	57(55.34)	50(34.97)	93(65.03)				
Incorrect	77(35.00)	143(65.00)	187(58.62)	(132(41.38)				

Table 46: Summary of Responses of the Patient's Knowledge about Treatment and Complications of TB by Gender in High and Low Notification Districts

Questions	Male		Female		OR	Chi-Square	95% CL	p-value
	Higher	Lower	Higher	Lower				
Knowledge about treatment and complications of TB patients?								
What is the minimum duration of TB Treatment? (6 Months)					1.0088 2.4921	0.0015 23.197	0.64-1.58 1.71-3.62	0.530 <0.001
Correct	60(37.97)	98(62.03)	86(39.45)	132(6055)				
Incorrect	63(38.18)	102(61.82)	151(61.89)	93(38.11)				
How you will take TB medicines? (Once a Day)					1.3103 2.9309	1.0985 28.451	0.79-2.17 1.96-4.38	0.299 <0.001
Correct	87(36.40)	152(63.60)	126(42.14)	173(57.86)				
Incorrect	36(42.86)	48(57.14)	111(68.10)	52(31.90)				
Do you know TB diagnosis and treatment is free? (Yes)					1.0008 5.6030	0.0000 52.233	0.57-1.76 3.41-9.21	0.554 <0.001
Correct	99(38.08)	161(61.92)	142(41.40)	201(58.60)				
Incorrect	24(38.10)	39(61.90)	95(79.83)	24(20.17)				
Do you know about follow up of TB?					0.6667 3.5609	0.7386 9.1367	0.26-1.69 1.49-8.51	0.466 0.003
Correct	9(47.37)	10(52.63)	7(24.14)	22(75.86)				
Incorrect	(114(37.50)	190(62.50)	230(53.12)	203(46.88)				
What is the main complication of incomplete or inappropriate TB treatment? (Multi drug resistance TB)					1.4932 4.9081	1.2957 21.985	0.75-2.99 2.39-10.08	0.312 <0.001
Correct	13(30.23)	30(69.77)	10(20.00)	40(80.00)				
Incorrect	110(39.29)	170(60.71)	227(55.10)	185(44.90)				

Figure 20: Correct Responses of Female Patients about the Causes, Symptoms and Spread of TB

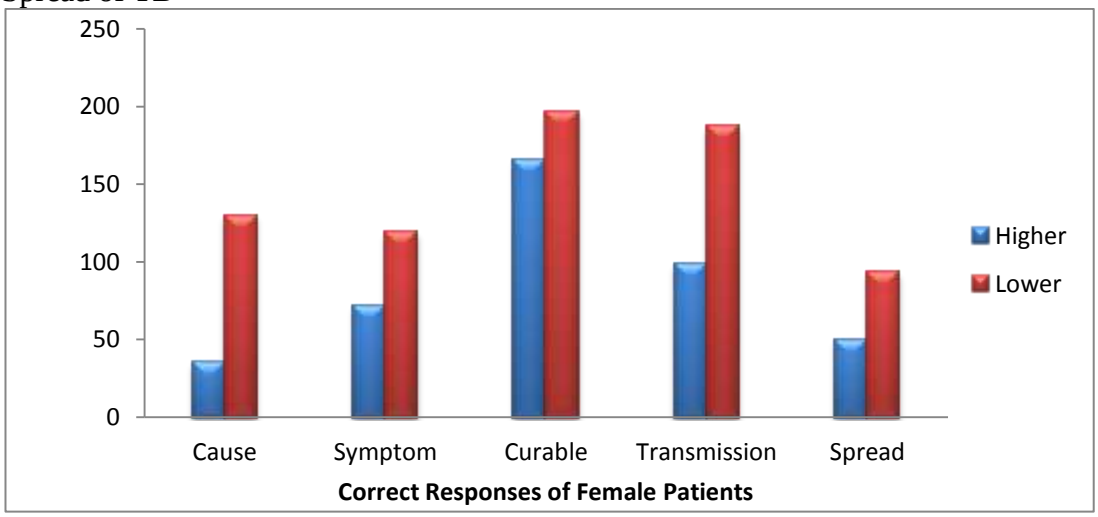


Figure 20 shows the summary of correct responses of female patients in higher and lower notifications districts regarding the causes, symptoms and transmission of TB.

Figure 21: Correct Responses of Female Patients about the Treatment, and Complications of TB

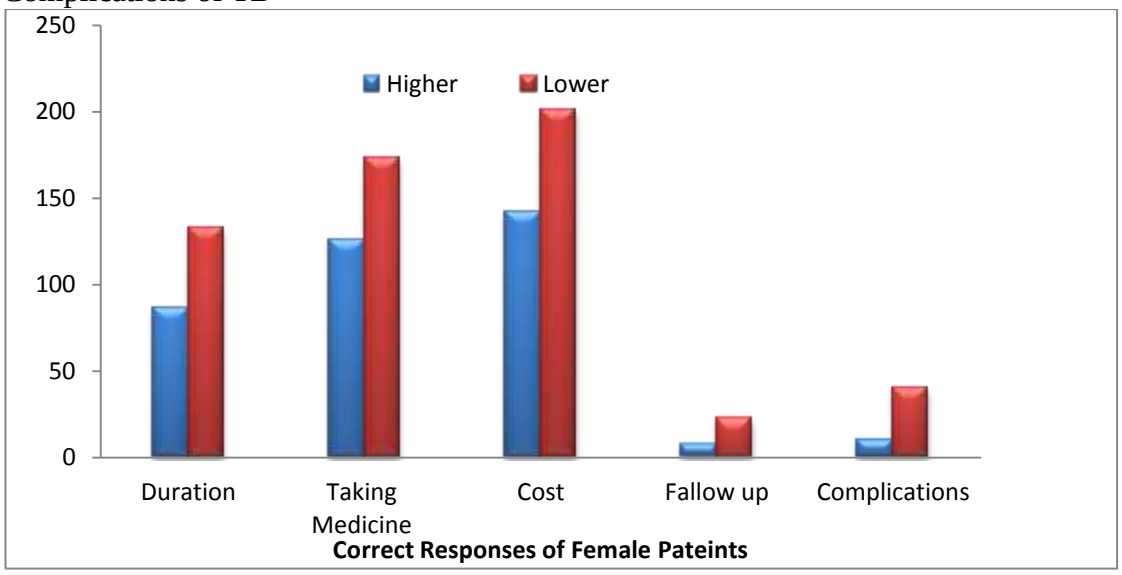


Figure 21 shows the summary of correct responses of female patients in higher and lower notifications districts about the treatment, cost, fallow up and complications of TB. It again graphically demonstrates that women in higher notification districts had lower knowledge than women in low notification districts.

8.10 Summary

Chapter 8 describes the results of questions regarding knowledge of TB patients in the province of Khyber Pakhtunkhwa. The data show that female patients in higher notification districts were less knowledgeable than females in the lower notification districts. Knowledge may be one of the factors in explaining gender differences between high and low notification districts.

CHAPTER 9: RESULTS - PHYSICIANS' KNOWLEDGE

9.1 Introduction

This chapter describes the results related to the level of knowledge of general practitioners working in selected TB diagnostic and treatment centres of KPK. These are the doctors who are responsible for the diagnosis, treatment and follow up of TB patients and assessing their knowledge is an important component of understanding why some areas may have higher notification rates

9.2 Demographic Distribution of Physicians

A total of fifty physicians were interviewed. Twenty five were selected from each of the higher and lower notification districts. All the participants included in the study were male. The mean age of the participants was 44.22 years, ranging from 32 to 55 years. There was no significant difference in between the mean ages of doctors working in higher (41.28 years) and lower districts (43.83 years) When categorized by those below 45 years and those above 45 years, there was no significant difference.(Table 44) (*Chi-Square=0.080, p= 0.785*) [Table 47].

Table 47: Age Distribution of Physicians in Higher and Lower Notification Districts

Age	Higher (n=25)		Lower (n=25)		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Younger (<45)	12	48.00%	11	44.00%	23	46.00%
Older(≥45)	13	52.00%	14	56.00%	27	54.00%

Chi-Square=0.080, p= 0.785

9.3 Qualification and Service of Physicians

All the physicians were medical graduates but only 16.00% (8) had a post-graduate qualification [Table 48]. The year of graduation of doctors included in the study was ranged from 1980 to 2006.

Table 48: Distribution of Physicians by Qualification

Qualification	Frequency	Percent
MBBS	41	82.00%
MBBS and Post Graduation	7	14.00%
MD	1	2.00%
MD and Post Graduation	1	2.00%
TOTAL	**50**	**100.00%**

More than half (54.00%) of the participants had less than ten years of service experience. There was no statistically significance reported between higher and lower districts and service experience (*Chi-Square=0.080, p= 0.785*) [Table 49].

Table 49: Distribution of Physicians by Service and District of Notification

Service	Higher		Lower		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
< 10 Years	14	56.00%	13	52.00%	27	54.00%
≥ 10 Years	11	44.00%	12	48.00%	23	46.00%
TOTAL	**25**	**100.00%**	**25**	**100.00%**	**50**	**100.00%**

Chi-Square=0.080, p= 0.785

9.4 Knowledge about the Causes, Spread and Diagnosis of TB

Only 58.00% (29) of general practitioners replied correctly that a cough of more than three weeks duration was the most common symptom of TB. Forty two per cent (21) correctly identified that cough of more than 2 weeks or combination of weight loss, fever, cough and anorexia were major signs and symptoms of TB. Nearly two-thirds of the physicians responded that sputum smear microscopy was the recommend

test for the diagnosis of TB. The remaining 40.00% (20) advised that sputum smear, microscopy with combination of x-ray chest, ESR (erythrocytes sedimentation rate) and biopsy. These results suggest that all the participants had satisfactory knowledge of causes, symptoms, spread and diagnosis of TB [Table 50].

9.5 Knowledge about Treatment of TB Patients

When asked the question "what is the minimum duration of TB treatment?" over three-quarters (38) of the physicians replied correctly describing the recommended duration of treatment specified by the NTCP and WHO. When asked "how will you treat a pregnant woman with TB?", only 14.00% (7) of the physicians gave the correct answer with 30% replying that they would treat a pregnant woman with TB in the same way as a non-pregnant female patient. Thirty per cent of the physicians failed to answer this question, leaving a blank response, suggesting that knowledge in relation to this question was limited. Nearly two-thirds (62.00%) of the respondents incorrectly identified the correct answer when asked about the recommended dosage of anti-TB drugs. Forty four per cent of these of these incorrect responses described drug dosage levels below the recommend guidelines. So although knowledge of the causes and symptoms of TB was good, nearly two-thirds of the doctors were less knowledgeable about the treatment and management of TB [Table 50].

9.6 Knowledge about Follow-up and Complications of TB

More than half (54.00%) of the physicians were aware about the DOTS programme. However, 60.00% (30) of the physicians were unaware about the guidelines regarding the correct follow-up of TB patients. When we asked "which TB drugs are contraindicated in Hepatitis?", only 24 (48%) of the doctors replied correctly. Most alarmingly, 88% (44) of the participants were ignorant about how to treat multi-drug

resistant (MDR) TB. So knowledge in relation to the follow-up and complications of TB was poor [Table 50].

Table 50: Summary of Questions Asked for Assessing Physicians' Knowledge about the Diagnosis, Treatment and Complications of TB.

Questions	Correct response		Incorrect responses	
	Frequency	Percent	Frequency	Percent
Knowledge about cause, spread and diagnosis of TB				
What germs cause TB? (Mycobacterium)	50	100.00	0	0.00
Do you know the most common symptom of TB?(Cough more than 3 weeks)	29	58.00	21	42.00
How you will diagnose TB?(Sputum for AFB)	50	100.00	0	0.00
Do you think TB is a communicable disease? (Yes)	50	100.00	0	0.00
Do you know how TB is spread? (Infectious Droplet)	50	100.00	0	0.00
Knowledge about treatment of TB patients				
What is the minimum duration of TB treatment? (Cat-I=6months, Cat-II =8 Months)	38	76.00	12	24.00
How you will plan TB treatment? (Initial Phase and Continuation phase)	20	40.00	30	60.00
How you will treat a pregnant woman with TB? (Avoiding Streptomycin and careful monitoring)	7	14.00	43	86.00
How you will treat a 15 year child with TB?	21	42.00	29	58.00
What are the recommended dosages of anti TB drugs?	19	38.00	31	62.00
Knowledge about follow up and complications of TB				
What is DOTS?	27	54.00	23	46.00
How you will follow up the TB patient?	20	40.00	30	60.00
Which TB drugs are contraindicated in Hepatitis?	24	48.00	26	52.00
What is MDR? (multi-drug resistance)	32	64.00	18	36.00
How you will treat MDR TB?	6	12.00	44	88.00

9.7 Overall Knowledge of Physicians

A total of 15 questions were asked to assess the level of knowledge of physicians regarding the causes, symptoms, diagnosis, treatment and special cases of TB. In order to obtain an overall score related to knowledge, all the correct observations were marked one and incorrect answers given a zero score. The overall knowledge score was achieved by calculating the addition of all the correct responses. A mean score for

knowledge was derived (9.58) and physicians scoring below this mean were classified as having poor knowledge. Those with a score above this mean value were classified as having satisfactory knowledge. Overall, 54.00% (27) of the physicians were classified as having poor knowledge [Table 51].

Table 51: Knowledge of Physicians in Relation to Causes, Management and Complications and Summary of Overall Knowledge.

Knowledge about Complications of TB	**Frequency (n=50)**	**Percent**
Knowledge regarding the causes, symptom and spread of TB.		
Unsatisfactory	0	0.00%
Satisfactory	50	100.00%
Knowledge about the management of TB		
Unsatisfactory	30	60.00%
Satisfactory	20	40.00%
Knowledge about Complications and follow up of TB		
Unsatisfactory	32	45.45%
Satisfactory	18	54.55%
Over all knowledge of Physicians		
Unsatisfactory	27	64.00%
Satisfactory	23	36.00%

When classified by higher and lower notification districts, there was no significant difference in overall knowledge of physicians (*Chi-Square=0.08, p= 0.388*). These data suggest that it was not knowledge amongst physicians that accounted for differences in notifications between districts. An interesting finding in this study was that physicians trained by the National TB Control programme (NTCP) were significantly more knowledgeable than those who were not trained by the NTCP (*Chi-Square=15.52, p= <0.001*) [Table 52].

Table 52: Summary of Overall Knowledge of Physicians by Age, Years of Service, Experience, Training and Qualifications.

Variables	Knowledge		OR	Chi-Square	P-value
	Poor	Satisfactory			
Age					
Younger (<45)	16(69.57)	7(30.43)	0.30	4.15	0.0486
Older (≥45)	11(40.74)	16(59.26)			
Service					
< 10 Years	8(34.78)	15(65.22)	4.45	6.33	**0.014**
≥ 10 Years	19(70.37)	8(29.63)			
TB experience					
Yes	23(53.49)	20(46.51)	0.86	0.033	0.8742
No	4(57.14)	3(42.86)			
Training					
Yes	10(32.26)	21(67.74)	17.85	15.52	**0.00007**
No	17(89.47)	2(10.53)			
Qualification					
MBBS, MD	27(64.29)	15(35.71)	12.64	7.31	**0.003**
Post Graduate	1(12.50)	7(87.50)			
Districts					
Higher	14(56.00)	11(44.00)	1.17	0.08	0.388
Lower	13(52.00)	12(48.00)			

9.8 Summary

Chapter 9 has described the results of knowledge of physicians working in the selected TB diagnostic and treatment centres and comparing the knowledge between those working in higher and lower notification districts of Khyber Pakhtunkhwa. Although there were no significant differences in the overall knowledge between those working in high and low notification districts, the overall level of knowledge was generally poor re-enforcing the importance of training as a means of maintaining knowledge.

CHAPTER 10: DISCUSSION

10.1 Introduction

The aim of this research was to explore the risk factors associated with higher notification of TB in the province of Khyber Pakhtunkhwa (KPK), Pakistan. I was trying to identify why more women were presenting with TB in certain districts in KPK with a view to understanding how we can improve the associated morbidity and mortality of this condition.

Tuberculosis (TB) remains one of the most important causes of morbidity and mortality for young women in KPK. The literature review in Chapter 3 identified the fact that that globally, TB notifications are higher in men (compared to women). However we have also established in Chapter 5, that within KPK women were at much greater risk of developing TB when compared to men. This is an unusual pattern which has not been previously documented and could have significant implications for women's health in the region (49)(112-114) and on the management of TB control programmes. There is an issue that needs to be considered in relation to the whether the data are an artefact – for example is the higher notification rate in the higher prevalence districts due to a deficiency in male cases or is there a true excess of female cases? A plausible explanation could be that a reduced male rate results from the fact that males work away from home and present in another district. They could of course be better nourished and hence less susceptible.

I have argued that the structure of the health system in Pakistan encourages use of the health centres where TB is diagnosed – the fact that diagnosis and treatment are free presents fewer barriers for accessing treatment. There is a consistent approach to the diagnosis and treatment of TB in these health centres and the trends in increasing notifications over the 10 year period suggest that patients are seeking out this service,

especially since the trend of notification is also plateauing. My own experience of working in this area suggests that there is not a migratory effect which can account for the under-reporting of males. However, I do believe that the fact that women are more under nourished as exemplified by being more underweight and having a higher incidence of anaemia suggests that socio-economic factors are probably responsible for some of the higher notification of women.

Data collected by the National TB program follows guidelines developed by the WHO and whilst these have not been independently verified, it is my view that the data are robust and comprehensive. I was previously employed by the organisation and can vouch for the completeness of data collection. It is unlikely that the higher notification rate for females is from under-reporting of males. The data in KPK in terms of gender notifications are distinctly different from the rest of Pakistan.

Although the higher notification of TB in women in KPK has been previously described (6)(92)(115), I believe that this is the first time that anyone has tried to establish the risk factors associated with this higher notification rate. It is through this understanding of the risk factors that services will be able to develop interventions aimed at mitigating the impact of TB in this group of patients. In addition, by exploring the knowledge of both patients and doctors we can consider the value of public health campaigns and training strategies to improve public understanding of the disease amongst this group of patients and on the training of doctors. , The reality remains that at present there are no specific interventions aimed at women. It is my contention that if the current stakeholders of the MOH, NTCP, and the WHO, who sponsor the TB control programmes, are to reduce the spread of TB then they have to consider the specific epidemiology of the disease in this area which has a much greater impact on women.

Before the discussion and comparison of the results of the field work with other published studies, it is important to discuss the methodology, study limitations and problems associated with this field work.

10.2 Discussions of Methodology and Limitations

The present study was carried out from 1st July 2012 to 30th September 2012 in 10 districts of Khyber Pakhtunkhwa (KPK), Pakistan. Districts were grouped into higher and lower on the basis of male to female notifications of TB that were identified from the National TB Control Programme (NTCP) data between 2002 and 2010. My plan was to randomly select five TB diagnostic and treatment centres (TBDCs) from each district. Initially, my research team (I include the technicians conducting the interviews and collecting the data here as well as my supervisory team) proposed the random selection of five Basic Health Units (BHUs) from each district, but after meeting with National TB Control Programme Officials, I was informed that diagnostic and treatment services for TB were not available in all BHUs and only designated BHUs were providing those services. These were now designated as TBDC's.

The first key issue faced in relation to the selection of the districts was that there were only four (TBDCs) in Kohistan district. After meeting with the district TB Control Officer in Kohistan, I agreed that referred patients from the Rural Health Centre (RHC) would be registered as TBD-RHC and that these patients would be treated as though they were from the fifth centre in the district. For the registration of patients, a trained medical technician was provided in much the same way as existed in the other four health centres. Data collected from TBD-RHC was further verified by the area supervisor who worked with the TB register of NTCP. The data related to the patients from TBD-RHC were matched with the TB register of NTCP.

In order to explore the risk factors for higher notification of TB in adult females in the province of KPK, I initially proposed to conduct research in districts with higher female notification against districts with higher male notification. However, in a descriptive analysis of NTCP data from 2002 to 2010, it was noted that all districts in KPK reported higher female notification of women compared to men [Table 22]. Based on local knowledge, the research team suggested that we selected five districts (Kohistan, Battagram, Chitral, Buner and Upper Dir) with the highest female notification and compared these with five districts (Karak, Kohat, Mardan, Nawshera and Malakand) with the lowest female notification when compared to males [Figure 17]. This could introduce a bias because the women with higher notification may have characteristics predisposing them to TB. I therefore re-read the data relating to this; however the baseline characteristics of both men and women in these districts suggest that there were no particular features that may make them more predisposed to TB, nor were there any features in the Health centres which might have resulted in increased notification of cases. In reality the control group became women in low notification districts and the logistic regression compared the features between the low and high notification districts in essentially the same geographic area of Pakistan. Some studies in the literature review described the importance of using appropriate control group as means of exploring risk factors for TB. In our view the comparison of patients in low and high notification areas was an appropriate comparator group. The use of newly diagnosed patients allowed us to identify a distinct group of patients who we could compare.

One of the issues with data collection was consent taking. Due to high level of illiteracy, written consent was a problematic issue and as agreed with the ethics committee, verbal consent was taken from all patients included in the Study. In many respects prior to carrying out the fieldwork I deliberated long and hard about this

process. I knew for instance that tape recordings would help with accuracy and transcribing (116). However I also know the region and the culture. Indeed, Hafkin & Huryer found rural illiterate women in the region were often suspicious and reluctant to use technology (computers, tape recorders etc) (117). Also, Zakar *et al* cautioned on its use due to cultural belief. Video recording was not a viable option not only because of the aforementioned, but also because in some of the locations electricity was unpredictable (118). Therefore, medical technicians and LHWs were trained and informed to read the provided consent statement to all patients before starting interview for verbal consent. The training included communication skills and all aspects of sensitivity.

The exclusion criteria that we developed required us to exclude patients below the age of 15. In general, the date of birth and exact age awareness was very limited amongst rural populations where there is a high rate of illiteracy Therefore in order to ensure that we excluded people under 15 years of age we attempted to verify their age by cross referencing patients' names on the TB register with NTCP. Similarly, many ages may be inaccurate with many patients reporting their approximate age. However I do not believe that this would have biased the overall results since the practice of using approximate ages is widespread and does broadly compare to peoples' chronological ages.

Some researchers argue that the use of focus group discussion is a gold standard for assessing knowledge (119). However, due to cultural restrictions, geographical locations, and problems in transportation, time and accessibility to all patients, I used a cross-sectional survey for assessing the individual knowledge of participants.

In relation to knowledge assessment we know that patients with a previous history of TB or with a positive family history for TB are likely to be more

knowledgeable when compared to those without a family history or previous exposure. These patients were not excluded when assessing such knowledge and this might have artificially raised the knowledge level of participants in the districts. However, the proportion of patients with such conditions was 9.01% (n=71), which we believe is not large enough to alter the knowledge level of the sample.

Because of social conventions regarding the role of women in KPK, female patients are not normally allowed to be interviewed by male interviewers or without being accompanied a family member. In this study, the National TB Control Programme had to collect data and registration details of all newly diagnosed TB patients as part of the requirements of the National TB Programme. In such situations, women are unlikely to agree to give accurate information to the mainly male technicians working in these centres. To avoid this problem, I recruited lady health workers for both higher and lower notification districts to collect data from female patients, who refused to be interviewed by male medical technicians. Of the total 785 women, no one was reported as having declined an interview with a male medical technician.

Another limitation of my study design was my use of medical technicians already working in the TDBCs for data collection. Their presence possibly has led to professional bias in interviewing patients because they know the results will be published internationally and any refusal for interview or having very low knowledge will be reported to NTCP. However, in the training sessions in each district, all medical technicians were encouraged to be honest and accurate with the patient responses for data collection.

10.3 Discussions of Descriptive Epidemiology (2002-2010)

The objective of this part of the study was to confirm that female patients in Khyber Pakhtunkhwa were at a higher risk of TB when compared to males. Using NTCP data from 2002 to 2010, a preliminary quantitative analysis of the existing National MoH data of confirmed TB admission records was performed to identify trends in TB notifications according to age, gender and location, Descriptive analysis of this data was critical in identifying the epidemiological characteristics of patients and planning for the data collection phase relevant for objectives two, three and four.

The data showed that a total of 222,051 TB patients were reported in KPK and a large number of cases were reported from Peshawar (5763, 16.81%) followed by Mardan (3060, 8.93%) and Nawshera (2117, 6.18%). The lowest number of TB cases were reported in Tank (471, 1.37%) fallowed by Upper Dir (679, 1.98%). The difference in the registration of patients was more likely due to the population difference of people living within the districts [Table 7].

Of the total notifications in this data set, 43.78% were male and 56.22 % were female patients. A higher number of female patients were registered when compared to males throughout the reported period. None of the twenty-five districts had higher notifications of men. The differences in gender distribution were statistically significant (Chi-Square=29.74, p= <0.0001). These gender differences were noted in research conducted by the National TB Control Programme in Pakistan, whose findings were similar to our results (6). These gender differences were also described by Sabawoon and Sato in Afghanistan, (6)(19)(49)(61)(120). The geographical proximity of these regions suggests that this gender difference is specific to this part of the world and could be linked to a range of factors including poverty, educational levels, and other factors

that relate to the highly gendered nature of the society where women's status is very subservient to men.

10.4 Discussions of Results Risk Factors

10.4.1 Sample of Patients

Figures in Table 23 showed differences in the registration of patients between the selected districts. The difference in the percentages of patient registration was possibly due to the difference in the population of the districts and reflects population density [Table 7]. The majority (101) of patients were reported from Mardan Districts and sample size represents the figures reported in descriptive epidemiology of TB in KPK, which validates our results [Figure 9]. This higher patient registration was probably due to the higher population of Mardan as compared to other districts.

The significant gender differences that were identified in our study (58% females compared to 41% males) contradicts the general pattern of TB notifications where there is a higher registration of men compared to women (72)(95)(112)(121).

10.4.2 Age Distribution of Patients

Studies in the literature review suggested that a large number of TB patients were in the reproductive age group (19)(72)(96)(114)(122). Our findings confirmed that over three-quarters (76.94%) of the participants were in a younger age group [Table 24]. This is a concern because those between the ages of 15 to 45 are considered to be the most economically active age group in the population, and morbidity due to TB in this group is a substantial economic burden for both the state and individuals. In a local study in Swat districts of KPK, researchers also found that younger female patients were more likely to be registered with TB when compared to males (120).

10.4.3 **Educational Status of Patients**

Our results suggest that the level of education of female patients could be related to the higher notification. Nearly eighty per cent (79.30%) of females were illiterate in higher notification districts compared to 38.00% illiteracy in lower notification districts (*Chi-Square=70.34, p= <0.001*) [Table 25]. Gender differences were striking - out of the total sample of illiterate patients (n=400), 68.50 % were female compared to 31.50% male. Possible causes for significant illiteracy in higher notification districts are geographical location of the area, low socio-economic status and lack of educational institutions in the area.

The logistic regression confirmed an association between being female and education with less educated women being around 6 times more likely to be in a higher notification area. These are highly significant and plausible results.

Literacy rates in general in Pakistan are higher in males than females (98). Several studies in our literature review reported that TB occurrence is associated with education. Shah *et al* reported that more than half (n=239, 59.1%) of patients with TB in a juvenile prison were uneducated (112). Similar findings were reported by Hussain *et al*, where just over half (57.0%) of their study subjects were uneducated with a further third (34.0%) only receiving primary education. Similar results were reported by Akhter *et al* in a study of 170 patients where the majority (n=277, 71.9%) of participants were uneducated (68). Several other studies also reported the higher rates of illiteracy in females (54)(95)(79).

Mushtaq *et al* reported that the majority (25.5%) of patients from rural areas were illiterate. This study also suggested that patients living in urban areas were more educated than those living in rural areas (75). This is because of the availability of schools, better transportation system and socio-economic status of the people living in

urban areas. Our study was primarily based in rural areas, which again may explain the high illiteracy rates that we found

10.4.4 **Socio-economic Status of Patients**

Our results suggested that more than half (50.76%) of the patients were living in overcrowded houses with 7-12 family members. Shockingly, 24.45% of the participants were reported living with 13 to 40 family members in a single house.

Our results were not different from other studies that we identified in our literature review, which have suggested that overcrowding was a major risk factor for Tuberculosis (54)(71)(75). The majority of patients living in higher notification districts were poor and living in a joint family system, which leads to overcrowding and limited space for living. Similarly, the income status is directly related to poverty and TB. Soomro and Qazi, reported that nearly three quarters (71.2%) of the patients with TB belonged to low income groups (54). Similar findings were found by other researchers, where the majority of TB sufferers were classified as having low income (75)(77).

Our results therefore replicated what others have found where nearly two thirds (63.18%) of the participants were living below the poverty level, earning less than $100 a month compared to the national average of $255 monthly (123-125). The monthly income of female patients in higher notification districts was significantly different from the monthly income of female participants in a lower group (*Male versus Female: Chi square = 23.77, p=<0.001; Higher Versus Lower: Chi square = 27.54, p=<0.001)* [Table 27, Table 28]. Female participants in lower notification districts were twice as likely to be educated when compared to female patients in higher notification districts. Similarly, female participants in lower notification districts were more likely to be employed than women in higher notification districts. Education and employment were therefore the two main reasons for the significant differences in income. The logistic regression confirmed the interaction between gender and education and gender and employment.

We also found a significant difference between the participants living in different types of houses in higher and lower notification districts (*chi-square=30.26, p=<0.001*) [Table 31].This difference is probably related to income and rurality of the districts. Due to financial limitations and transportation, people living in rural areas can't afford bricks and blocks, preferring mud and stones for construction (122)

Several studies have identified smoking as a major risk factor for Tuberculosis (54)(72)(95). However in our study, out of the 462 notified cases, only 3 female participants reported smoking. Therefore, we didn't find any association of cigarette smoking with higher notification of TB in females of Khyber Pakhtunkhwa. However, (80.38%) of the participants were using firewood as a main source of fuel for cooking. In higher notification districts 95.00% (342) of the patients were using firewood compared to 68.00% (631) in lower notification districts *(Chi-Square=81.14, p=<0.001)* [Table 30]. Indoor smoke from firewood has higher toxic poisons which could have increased the risk of TB infection in females in higher notification districts (122)(126).

10.4.5 **Malnourishment and Social Empowerment of Women**

Findings in this study showed that the majority (68.10%) of female patients were anaemic. Similarly, 74.90% of female participants were underweight. Poverty and male dominant culture, where males have a higher priority than females, is common practice in Pakhtun's families who are prevalent in this geographical area. For example males are served food earlier than females who would also tend to get smaller portions of food. This inevitably contributes to malnutrition, which is one of the risk factor for Tuberculosis (51).

Similarly, a significant difference was reported between male and female patients and the duration of time they spent out of the home (*Chi-Square=133.1,*

p=<0.001). Nearly fifty per cent (48%) (234) of female participants replied that they were only going out of the home for less than 1 hour per day. These figures suggest that females were not exposed to the same amount of sunlight as male participants, suggesting women may have lower levels of Vitamin D. In a study conducted in Pakistan on 129 patients (male= 42.00%, female= 58.00%), 89.00% female participants were highly susceptible for TB infection due to vitamin D deficiency (127). Furthermore, these figures also throw some light on the status of women. Female patients in lower notification districts were spending four times more time outside the home when compared to female patients in higher notification districts. One interpretation of the data could be that women in lower notification districts were more empowered in their social life when compared to female patients in higher notification districts. Agboatwalla *et al* also reported that females living in the rural areas were not allowed to go out of home freely (79). There is clearly a significant coalescence of educational level, income, empowerment and nutritional status and their association with TB.

10.4.6 Analysis of Logistics Regressions

A logistic regression was used to identify associations between gender difference in higher notification of TB and statistically significant variables reported in the univariate analysis. All significant variables (gender, education, income, etc) were included in the logistic regression model.

Table 36 shows that female patients in lower notification districts were six times (1/0.16) less likely to be educated when compared to females in high notification districts (*OR= 0.16, p=<0.001)*. Similarly, women in lower notification districts were four times (1/0.23) less likely to be employed as compared to women in higher notification districts (*OR= 0.23, p=<0.05*). Female participants in lower notification

districts were almost 2.5 times less likely (1/0.42) to have high income as compared to female patients in higher notification districts (*OR= 0.42, p=<0.05*). Similarly, older female patients (≥ 45 years) were 2.8 times (1/0.35) less likely to be in lower notification districts than females in higher notification districts (*OR= 0.35, p=<0.05*) Therefore the results in our study confirm that socio-economic factors were most likely risk factors associated with the higher notification of TB in female patients of KPK, Pakistan. Education was the most important risk factor directly related to knowledge, employment, income and women's empowerment, which were responsible for the higher notification of TB in KPK Province. Several studies in our literature review descried that socio-economic characteristics of an individual were the main risk factors for TB occurrence (68)(75)(77)(79)(128) so in that respect our findings confirm the important role of socio-economic factors as a risk factor for TB. One of the conclusions that we can draw from this data is that the increased notification rate for women could be because they are more susceptible – through malnutrition, anaemia, lack of Vitamin D and overcrowding. Illiteracy is almost certainly a proxy for poverty. All these factors will contribute to a higher notification rate but in the absence of robust population level data I can't conclusively state that women are at greater risk for contracting TB.

10.5 Patients' Knowledge of TB

I believe that we have carried out the first study that has evaluated the knowledge of TB patients regarding TB in the province of KPK. The results of our study suggested that female patients in lower notification districts were six times more knowledgeable as female patients in higher districts. It is likely that the socio-economic factors identified above played a significant role on the level of knowledge of adult TB patients.

A significant gender difference was reported between the knowledge of patients in lower and higher notification districts about the causes, symptoms and spread of TB (*Chi-Square= 13.20, p= <0.001*). This means that male patients were more informed than females. However, female patients living in lower notification districts were more knowledgeable than female patients in higher notification districts about the causes and transmission of TB. Mushtaq *et al* also explored the knowledge and behaviour patterns about TB in urban and rural communities of Punjab province and reported that urban patients were more knowledgeable as compared to rural patients (75).

Almost half of the participants in this study replied correctly that germs, bacteria or mycobacterium causes TB. However, the knowledge of 42 % of male and 57% of female participants was still poor (*Chi-Square= 21.40, p= <0.001)* [Table 39]. Nearly two-thirds of the participant's knowledge about the spread of TB was poor and the gender difference was statistically significant (*Chi-Square= 27.58, p= <0.001*). Ali *et al* reported that more than four out of five participants (n=166, 82.0%) were aware that TB was a communicable disease and that just over half (n=110, 54.0%) said that it was spread through respiratory droplets (78).

However, some false perceptions were also noted about the signs and symptoms of TB. For example, 13.31% of male and 15.58% of female participants still believed that fever was the most common symptom of TB. In a cross-sectional study of 170 patients, Khan *et al* also reported fever as a main symptom of TB in 57.70% of patients (77). Worryingly, 27% of male and 29% of female patients believed that sharing of food causes spread of TB. This is an alarming situation particularly for females living in rural areas, where they are already facing rejection from the community due to these false perceptions. This can only exacerbate the gender differences that we identified.

Even though treatment by directly observed treatment short course (DOTS) is free in Pakistan 79.83% (95) patients in higher notification districts were unaware that TB treatment is free (Chi-Square=53.23, 95% CI= 3.41-9.21, p= <0.001). Knowledge of TB patients was extremely deficient regarding treatment and follow up. Possible reasons for this higher ignorance of TB treatment may be due to poor implementation of Community Health Worker (CHW) programme in higher notification districts. Several studies reported that DOTS and the role of CHW is essential in proper TB management (121)(129-131).

Varmund *et al* reported that the number of MDR cases increasing in Pakistan is due to lack of community participation (19). Similarly, Javaid *et al* found that incomplete and inappropriate TB treatment may lead to increase in MDR TB in Pakistan (77). So the lack of knowledge that we identified may be a factor in the gender differences we noted.

Results showed in this study that knowledge of female patients in higher notification was poor as compared to female patients in lower notification districts (Chi-Square=62.87, 95% CI= 3.41-7.96, p= <0.001). There are several possible reasons for this poor knowledge of female patients in higher notification districts. Firstly, the

majority of female patients in higher notification districts were illiterate, unemployed and poor. Mondal *et al* reported that socio-economic indicators play an important role in the knowledge of TB patients (113). Therefore, due to low socio-economic status, the female patients' knowledge is limited in higher notification districts. Secondly, despite 100% DOTS coverage in KPK, the programme is still inefficient in higher notification districts due to lack of proper monitoring and training of CHWs. Finally, geographical and culture issues are the main barriers for women's access to education and knowledge in higher notification districts.

10.6 Physicians' Knowledge of TB

Overall, 54.00% (n= 27) of the general practitioners were reported with poor knowledge regarding causes, management and complications of TB

There was no significant difference reported between higher and lower notification districts and TB knowledge (Chi-*Square=0.08, 95% CI= 0.39-3.58, p= 0.388*). Results in this study showed that doctors who received training in TB were significantly more knowledgeable (*Chi-Square=15.52, 95% CI= 3.44-29.69, p= <0.001*) [Table 52]. Several studies in our literature review reported similar results. (80)(84)(132).

Ahmed *et al* in their study of 170 patients found that 68.0% of respondents correctly identified that a cough for ≥ 3 weeks was the main symptom of TB, with 32.0% saying that cough, together with haemoptysis and weight loss was one of the main features of TB (80). In another study in Pakistan, Khan *et al* reported that nearly all participants (95.0%, n=114) knew that cough was a major symptom of TB, whilst 86.7 % (n= 104) also said that fever and weight loss (74.2 %, n= 89) were features of the disease (84). Similarly, 40.00% of the participants recommend sputum smear microscopy with combination of x-ray chest, ESR (erythrocytes sedimentation rate) and biopsy for the diagnosis of TB. Whereas, World Health Organization and National TB Control Programme recommend sputum smear microscopy alone for the diagnosis of TB, our study findings are similar to other studies conducted locally and regionally on the same topic (80-81)(86)

Almost, two-thirds of the doctor's knowledge was poor regarding the treatment and management of TB. Over three quarters of the participants reported the correct duration for TB treatment. However, only 14.00% (n= 7) of the participants were aware of how to treat pregnant women who were diagnosed with TB. The majority (62.00%)

of the general practitioners were ignorant about the recommended dosage of anti TB drugs and 56.00% prescribed above the recommended dosage. A similar percentage was unaware of knowledge regarding follow up and complications of TB. Similarly, two thirds of the participants were ignorant about the follow up of TB patients. Several studies in our literature review also reported findings similar to our results (80-81)(84). Since 1993, when TB was declared as a global emergency, DOTS has been recommended for treatment of TB. Follow up of TB patients is the most important component of TB DOTS for monitoring and treatment outcome. Ahmed *et al* found that 50.0% of the private practitioners who reported treating TB patients were not following DOTS strategy. Furthermore, few knew how to follow up TB patients (80). Shah *et al* also reported similar findings in a research project to assess the level of knowledge and practices of PPs in two major cities of Punjab. Out of 245 PPs, nobody advised treatment under DOTS (83). Surprisingly, 88.00% (44) of the doctors were unaware about the management of multi drug resistant (MDR) TB. According to WHO and other studies, the prevalence of MDR TB increased in Pakistan (133-134) and this could be a factor. Varmund *et al* and Javaid *et al* found that incomplete and inappropriate TB treatment may lead to increase in MDR TB in Pakistan (19)(77). Therefore, knowledge of doctors regarding MDR TB is very important and needs to be assessed further.

CHAPTER 11: IMPLICATIONS, CONCLUSIONS AND RECOMMENDATIONS

This study is the largest study carried out to date to investigate the risk factors associated with higher notification of TB in Khyber Pakhtunkhwa (KPK), Pakistan. To investigate the issue, we used national data sources, field work and surveys of the knowledge of patients and physicians.

The objective of the first phase of the research project was to confirm the higher notification of TB in female patients in the province of KPK. Retrospective data from National TB Control Programme (NTCP) was collected for all registered TB patients between 2002 and 2010. Through descriptive analysis, we confirmed that there was a higher notification of female patients in Khyber Pakhtunkhwa.

The descriptive analysis showed that these gender differences were reported from 2002 to 2010 annually. Unfortunately, these findings have not been published and this has resulted in no action being taken to reduce the gender disparities. Therefore, it is recommended that annual TB data of the provincial TB Control Programme should be published scientifically for research purposes to monitor trends in the notification of TB cases and the gender differences.

Objective two of the research has explored different risk factors associated with the higher notification of TB in adult female patients of Khyber Pakhtunkhwa. Results found in objective two showed that the majority of female patients in higher notification districts were illiterate, unemployed, poor and living with low socio-economic status. Furthermore, through logistic regression, education was identified as one of the main risk factors for the higher notification of female patients in KPK. The results are important because optimal TB control will only be possible if we have a better understanding of the gender-associated risk factors for TB.

Literacy level of females is much lower in Kohistan, Battagram and Upper Dir. The Government of Pakistan should take necessary steps for increasing girls' enrolment in education in higher notification districts of KPK. It is very encouraging that on the basis of our preliminary results, which were discussed with the Minster of Health Khyber Pakhtunkhwa in 2012, the government started a financial support project (PKRs.200/month) for girl students attending schools in Upper Dir, Battagram, Hango, etc. Because of the success of this program, a special increase in the financial support (PKRs.1500-2000/month) was announced for girl students in Kohistan district (135).

In objective three, we investigated the knowledge of TB patients in the province of Khyber Pakhtunkhwa. We identified that female patients in higher notification districts were less knowledgeable than females in the lower notification districts.

It is recommended that special focus should be given to DOTS and Community Health Workers (CHW) programmes. Both should be strengthened and integrated to provide health education to TB patients in KPK. Moreover, the Government of Pakistan, National TB Control Programme and International donors should construct a media policy for public awareness about TB.

Finally, knowledge of general practitioners working in the selected TB diagnostic and treatment centres of higher and lower notification districts of KPK was assessed in objective four. This study suggested that Physicians' knowledge about the treatment, follow up and complications of TB was poor and there needs to be regular training as per WHO and NTCP guidelines for appropriate TB management.

The findings of this study reported that Physicians' knowledge regarding multi drug resistant (MDR) TB was extremely poor. It is more likely that due to incomplete and inappropriate treatment, TB will continue to become more complex in the future in

the form of MDR in Pakistan and particularly in KPK province. Therefore, it is highly recommended that special attention should be given to the causes, diagnosis and treatment of MDR TB.

CHAPTER 12: FUTURE RESEARCH

Recent descriptive research conducted by NTCP in four provinces of Pakistan reported that female patients in KPK and Balochistan are at higher risk for TB than those in Punjab and Sindh provinces (6)(115). Therefore, on the basis of the results of this study, it is recommended that the same study should be carried out in higher (KPK and Balochistan) versus lower (Punjab and Sindh) notification provinces. This will help identify risk factors for higher notification of females; if the results replicate those that I found then I would suggest that the case for a Pakistan wide initiative for increasing the educational level of women as a means of reducing the incidence of TB would be compelling.

The knowledge of doctors is vital for the diagnosis and treatment of TB. There is only one study available on the knowledge, practice and treatment behaviour of general practitioners in KPK (81). However, that study was carried out on private practitioners and had very limited information with a low sample size (n= 88). Similarly, the sample size (n= 50) of our study was also small and was further limited to male general practitioners only. It is therefore recommended to thoroughly evaluate the knowledge of those physicians (male and female) who are responsible for the management of TB patients in KPK working in either Basic Health Units or as private practitioners.

CHAPTER 13: REFERENCES

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CHAPTER 14: APPENDIX

14.1 Ethical Approval (The University of Manchester)

MANCHESTER 1824

The University of Manchester

Secretary to Research Ethics Committees
Room 2.004 John Owens Building

Tel: 0161 275 2206/2046
Fax: 0161 275 5697
Email: timothy.stibbs@manchester.ac.uk

Compliance and Risk Office
University of Manchester
Oxford Road
Manchester, M13 9PL

ref: ethics/11341

Professor Aneez Esmail,
Professor of General Practice
Williamson Building 5th floor.

5th March 2012

Dear Aneez,

Research Ethics Committee 2
Aziz: Exploring factors associated with the higher incidence of TB in adult females in the provinces of Khyber, Pakhtunkhwa, Pakistan (ref 11341)

I write to thank you for attending the meeting on 16th January on behalf of Muhammad Aziz and to confirm that the amended information sheet and additional documents set out in your email of 16th February satisfy the concerns of the Committee and that the project has been given a favourable ethical opinion.

This approval is effective for a period of five years and if the project continues beyond that period it must be submitted for review. It is the Committee's practice to warn investigators that they should not depart from the agreed protocol without seeking the approval of the Committee, as any significant deviation could invalidate the insurance arrangements and constitute research misconduct. We also ask that any information sheet should carry a University logo or other indication of where it came from, and that, in accordance with University policy, any data carrying personal identifiers must be encrypted when not held on a university computer or kept as a hard copy in a location which is accessible only to those involved with the research.

Finally, I would be grateful if you could complete and return the attached form at the end of the project or by January 2013.

Yours sincerely

Timothy Stibbs

Dr T P C Stibbs
Secretary to the University Research Ethics Committee

Enclosed: Report form

14.2 National TB Control Programme Ethical Approval Letter

DIRECTORATE GENERAL HEALTH SERVICES
KHYBER PAKHTUNKHWA PESHAWAR

Communication should be addressed to the Director General Health Services Peshawar and not to any official by name.

Office Ph 091- 9210269 Exchange 091 – 9210187, 091- 9210196 Fax 091-9210230

No: 1686 /TB

Dated: 13 / 07 / 11

Dr. Muhammad Aziz

PhD student, TB Research Project (Pakistan)

University of Manchester (UK)

Subject: Literature Review of TB Control Programme Khyber Pakhtunkhwa Pakistan

I have gone through the document under review and appreciate your efforts in preparing and compiling the report. A good endeavour is being undertaken by you in collaboration with TB Control Programme Khyber Pakhtunkhwa and it is hoped that this project will go a long way in resolving important queries pertaining to gender issues in TB control Khyber Pakhtunkhwa in comparison with other provinces of the country. It is hoped that by the completion of the project, we will have better options and solutions to address long standing unanswered questions. This will also help the TB Control Programme to devise new strategy and better planning on the issue keeping in view the results of the study.

PTP (TB Control Programme) assures you full support and cooperation during the next step that is data collection and suggests sharing all the necessary details with the Programme before proceeding with the next step.

Thanks and Best regards

Dr.Ubaid Hussain

Project Director,

TB Control Programme

Khyber Pakhtunkhwa, Peshawar.

TB CONTROL PROGRAMME
KHYBER PAKHTUNKHWA.

No. 1392-1401 / TB.
Dated. 14 / 06 / 2012.

To:

The Executive District Officers (Health)
Buner, Malakand, Mardan, Nowshera, Kohat, Karak,
Chitral, Dir Upper, Battagram and Kohistan.

SUBJECT: **RESEARCH ON HIGHER INCIDNENCE OF TB IN FEMALE.**

Sir,

We are conducting TB research with the collaboration of University of Manchester and Islamic Development Bank to identify the causes of higher incidence of TB in females in Khyber Pakhtunkhwa. In the regard Dr. Muhammad Aziz Principal Investigator TB Research Project will visit to discuss and start the data collection from selected districts and will meet with EDOs(Health) and District TB Control Officers on the below dates.

S.No.	District	Dated
1	Buner	18th June2012
2	Malakand	19th June 2012
3	Malakand ano Nowhsera	20th June 2012
4	Kohat	21st June 2012
5	Karak	22nd June 2012
6	Chitral	25th June 2012
7	Dir Upper	26th June 2012
8	Battagram	28th June 2012
9	Kohistan	29th June 2012

Your cooperation will be highly appreciated in this regard.

Project Director,
TB Control Programme
Khyber Pakhtunkhwa.

Project Director
TB Control Programme

35 (Jun) i

GOVT OF KHYBER PAKHTUNKHWA
HEALTH DEPARTMENT PESHAWAR
No. 2995 **/MF Dated:** 23/12/**2014**

To

Visa Officer
Pakistan Consulate
Manchester, UK

SUBJECT: **INVITATION LETTER FOR DR MUHAMMAD AZIZ**

Dear Sir/Madam

Tuberculosis Research Project (TRP) is a joint research project of the University of Manchester, Islamic Development Bank and Health Department of Khyber Pakhtunkhwa. The Objective of the research is to identify the causes of higher occurrence of TB in females of KPK.

Data collected by medical technicians of 50 Basic Health Units from 10 Districts in KPK, analyzed and presented by Dr Aziz in the 44th and 45th International Conferences, on Tuberculosis, organised by the International Union against Tuberculosis and lung diseases in Paris France (November 2013) and Barcelona Spain (November 2014) respectively.

We therefore would like to invite Dr Aziz to visit and share the results and recommendations of the research work with us. This will help the health department for appropriate intervention to minimise the problem and guide us for future research.

On this visit he will be required to stay in Pakistan from 27th December 2014 to 7th Feb 2015, therefore you are kindly requested to issue visa clearance for the proposed trip.

Your Sincerely,

23/12/14

Secretary
Khyber Pakhtunkhwa Medical Faculty
Peshawar.

Cc to. Dr Muhammad Aziz University of Manchester UK.

BUNGALOW NO. 86/D-5 SCHOOL ROAD UNIVERSITY TOWN PESHAWAR
PHONE # 091-9216008 FAX #.091-9218630Email: info@kpmf.edu.pk Website: www.kpmf.edu.pk

14.3 Training of Medical Technicians for Data Collection Project

List of Medical Technicians Trained for data collection

Name	Treatment Centre	District
Ghazi Khan	TBC Daso	Kohistan
Fazal-u- Rehman	TBC Daso	-do-
Khair Muhammad	RHC Pattan	-do-
Umar Sadiq	RHC Ranolai	-do-
Abdul Rashid	RHC Shatyal	-do-
Muhammad Amir	BHU Shamlai	Battagram
Nasir Muhammad	RHC Thakot	-do-
Muhammad Ayub	THQ Bama	-do-
Hafeez Ullah	RHC Koza Banda	-do-
Shakeel Ahmed	TB Centre Battagram	-do-
Ijaz Ahmed Khan	DHQ/ Town/ RHC Kauzi	Chitral
Zakir Hussain	Teh Torkoh/ Mulkoh	-do-
Muzfar Ahmed	Chitral Rural	-do-
Subeiman ul Mulk	Mastoch Sub Division	-do-
Altaf Ahmed	Drosh	-do-
Amir Murad	THQ Booni	-do-
Abdul Haq	DHQ Hospital Darrar	Buner
Bahram Shah	THQ Hospital Pocho Kali	-do-
Mushtaq Ahmed	Rural Health Centre Johar	-do-
Zafar Ali	CH Totalai	-do-
Sher Rasool	RHC Nagrai	-do-
Sher Zaman	CH Chamla	-do-
Safi ullah Khan	DHQ Dir Upper	Upper Dir
Saiful Haq	Cat D Hospital Patrak	-do-
Dr Wazir Zada	RHC Bibyaware	-do-
Ghulam Hazarat	Cat D Hospital Wari	-do-
Sadiqullah	Cat D Hospital Barawal	-do-
Noor Janan	WCH Karak	Karak
Luqman uddin	RHC Sabir Abad	-do-
Khalid Usman	RHC Latamber	-do-
Muhammad Nasir	Type Chospital Takht e Nasrati	-do-
Muhammad Iqbal	DHQ Karak	-do-
Aziz ur Rehman	RHC Ahmad Abad	-do-
List Continue....		
Mir Nawab Khan	DHQ Kohat	Kohat
Muhammad Yasin	Liaqat MH Kohat	-do-

Faisal Anwar	RHC Lachi	-do-
Ghulam Haider	RHC Chor laki	-do-
Muhammad Basheer	RHC Ustarzai	-do-
Nazik Muhammad	RHC Billitang	-do-
Gul Sher Khan	DHQ/DTO office	Mardan
Muhammad Ayub	CH Lond Khwar	-do-
Muhammad Ali	Type D Hospital Katlung	-do-
Aziz ur Rehman	Mardan Medical Complex	-do-
Syed Sabir Shah	CH Rustam	-do-
Muhammad Ali	RHC Sheer Ghar	-do-
Nasir Khan	RHC Khair Abad	Nawshehra
Younas Khan	CH Akora Khattak	-do-
Khiasta Rehman	RHC Kheweshqi	-do-
Sharif Gul	RHC Nizam Pur	-do-
Syed Sajjad Ali Shah	CH Kaka Sahib	-do-
Majid Ali	DHQ Naw Shehra	-do-
Muhammad Ismail	DHQ Batkhela	Malakand Agency
Muhammad Naeem	Ch Thana	-do-
Mian Akbar ullah	Ch Thota Kan	-do-
Ghour Ayub	RHC Dhery Jolagram	-do-
Amar Nat	DLS Malakand	-do-
Izat Begum	RHC Skhakot	-do-

Photographic presentation of Training Sessions of Medical Technicians







14.4 Data Collection Instruments

The University of Manchester

MANCHESTER 1824

Islamic Development Bank
Saudi Arabia

National TB Control Programme,
Khyber Pakhtunkhwa

Tuberculosis Research Project

Khyber Pakhtunkhwa (Pakistan)

Questionnaires

To Explore the Risk Factors for Tuberculosis in Adult TB Patients of Khyber Pakhtunkhwa and to Assess the Knowledge of TB Patients about TB.

By Dr Muhammad Aziz

Consent Statement

Informed consent for Tuberculosis research project in Khyber Pakhtunkhwa, Pakistan

Instruction to the interviewer: read this consent form in a loud and clear to the respondent

Good Morning/good afternoon. My name is [**Name of the interviewer**]. I am representing National Tuberculosis Control Programme and Ministry of Health Khyber Pakhtunkhwa who is carrying out some research in this Area, The University of Manchester, England, Islamic Development Bank and National Tuberculosis Control Programme are carrying out research on tuberculosis to improve the treatment and prevention of Tuberculosis in Khyber Pakhtunkhwa. Research indicates that female patients are more likely than males to have been diagnosed with TB in last 10 years in this province. The University of Manchester and the National Tuberculosis Control Programme would like to know what is happening in the general population in order to explore factors associated with this higher occurrence of tuberculosis in females. We will be doing this by asking you some questions and if you agree I will do this shortly. Some of these questions will be about your personal life. I am aware that some of the questions are sensitive, but all the information you give me will be kept strictly confidential. Participation in the survey is voluntary. You can refuse to answer all or some of the questions, but National Tuberculosis Control Programme and the University of Manchester would appreciate your help in answering all the questions. It is important to know that your participation will not affect your ability to use health facilities or free treatment. We are hoping that you will participate since your views are highly valued and important. Do you want to ask me anything about the survey? May I begin asking you question now?

[Instruction to the interviewer: Wait for the answer and make sure you do not rush the respondent into answering. If the respondent is not answering, gently ask the question again until you get an answer]

I understand the details of the survey have informed me about the requirements and hereby agree to participate in the survey.

The respondent has been informed about this survey and understands its purpose and objectives

Signature of the interviewer _____

* Modified consent form, form the Guidelines for measuring National HIV prevalence in population based surveys, 2005.

Tuberculosis Research Questionnaire

A. Baseline Data

1. Name _____ 2.Gender[1] Male[2]Female
2. 3. Age____ Years
4. Citizenship [1] Pakistani [2] Foreign Specify _____ 5.Weight__Kg 6.Height___Cm
7. BCG [1] No scar [2] Scar Seen [3] Dubious 8.HBLevel_____gm/dl
9. BHU / Treatment Centre_____ 10.District _____
11. Contact No _____ 12.Type of TB?[1] Pul [2] Ex Pul

13. Date of Entry _____ **14.Form No _____**

B. Interview

I. Demographic Information

1. Educational Status

[1] Illiterate [2] Primary [3] High School [4] Secondary [5] Graduate [6] Post Graduation [7] Madrassa [8] Other Specify _____

2. Occupation

[1] None [2] House Wife [4] Teacher [3] Business [4] Driver [5] Labourer
[6] Other Specify_____

3. What is your average monthly income?

[1] ≤ 5000 [2] ≤10000 [3] ≤20000 [4] ≥30000 [5] Not sure [6] Refused to Answer

4. What is your marital status at time of Diagnosis of TB?

[1] Never married [2] Married [3] Divorced [4] Widowed [5] Refused to Answer

5. For men only, how many wives do you have?

[1] 1 [2] 2 [3] 3 [4] 4

6. How many Children do you have?

[1] None [2] _____ [3] Refused to Answer

7. Age of the youngest child?

[1] 1-3 months [2] 6 months [3] 12 months [4] > 1 year

8. Family Type [1] Joint [2] Separated

9. Family Size [1]_____Total family members sharing the same roof.

10.How many rooms do you have? [1] 1 [2] 2 [3] 3 [4] 4 [5] ≥5

11.How many people living per room? [1] 1 [2] 2 [3] 3 [4] 4 [5] ≥5

12.Cooking Mode [1] indoor [2] outdoor

13.Type of fuel [1] Firewood [2] Kerosene [3] Gas [4] Electricity

14.How many times you eat meat in a week?

[1] 1 [2] 2 [3] 3 [4] other _____

15.Place of residence [1] village [2] Township/ Town [3] Do not know

16.How many hours you stay out from home daily?

[1] 0-1 [2] 2-5 [3] 6-8 [2] >9

17.Type of House

[1] Mud House [2] Block / Bricks House [4] other Specify _____

18.Do you have toilet? [1] Yes [2] No

19.Placement of Toilet [1] Attached to Room [2] inside home [3] outside home

II. Past Medical History (Risk Factors)

20.Do you have any previous history of TB?

[1] Yes [2] No [3] Refused to Answer

21. Does anyone in your family have history of TB?

[1] Yes [2] No [3] Do not know

22. If yes who are affected?

[1] Spouse [2] Parents (one or Both) [3] Brother/ Sisters
[4] Children [5] Other Specify _____

23. Do you have any associated disease?

[1] Blood Pressure [2] Diabetes [3] other Specify _____

24.Do you smoking? [1] Never [2] Past [3] Current

25.How many cigarettes per day?

[1] 1-10 [2] 11-20 [2] >20

26.Do you snuffing? [1] Yes [2] No

III. Knowledge and Understanding of Tuberculosis

27. What Germ Cause TB?

[1] Germ/ Bacillus [2] Hard Work [3] Hereditary TB
[4] Do not know [5] Other _____

28. Do you know the most common symptom/sign of TB?

[1] Fever [2] Cough more than 3 weeks
[3] Chest pain [4] Do not Know [5] other Specify____

29. Do you think TB is curable disease?

[1] Yes [2] No [3] Do not Know

30. Do you think TB is transmittable diseases?

[1] Yes [2] No [3] Do not Know

31. How TB is spread?

[1] Infectious droplet Spread [2] Sharing food

[3] Smoking

32. What is the minimum duration of TB treatment?

[1] 2 months [2] 6 Months [3] 8 Months

[4] 2 years [5] Do not know

33. How you will take TB medicines?

[1] once/day [2] Twice/day [3] Other

34. Do you know TB treatment is free?

[1] Yes [2] No [3] Do not know

35. When is the follow-up performed?

[1] At the end of 2nd, 4th and 6th Month

[2] At the end of 2nd, 5th and 8th Month

[3]After completion [4] Do not know

36. What is the main complication of incomplete or inappropriate TB treatment?

[1] Prolong disease [2] Death [3] Drug Resistance TB

[4] Do not know

The University of Manchester

MANCHESTER 1824

Islamic Development Ban
Saudi Arabia

National TB Control Programme,
Khyber Pakhtunkhwa

Tuberculosis Research Project

Khyber Pakhtunkhwa (Pakistan)

Questionnaire

Knowledge of General Practitioners Regarding the Signs, Symptoms, Diagnosis and Treatment of TB Patients

By Dr Muhammad Aziz

Consent Statement

Informed consent for Tuberculosis research project in Khyber Pakhtunkhwa, Pakistan

Instruction to the interviewer: read this consent form in a loud and clear to the respondent

Good Morning/good afternoon. My name is [**Name of the interviewer**]. I am representing **The University of Manchester United Kingdom.** National Tuberculosis Control programme is working for the treatment and prevention of Tuberculosis in Khyber Pakhtunkhwa Research indicates that female patients are more likely to suffer from TB compared to males in last 10 years in this province.

The University of Manchester would like to know what is happening in the general population in order to explore factors associated with this higher occurrence of tuberculosis in females. We hope to gain this information by asking you some questions.

If you agree, I will ask you some questions. Some of these questions will be about your personal life. I am aware that some of the questions are sensitive, but all the information you give me will be kept strictly confidential. Participation in the survey is voluntary. You can refuse to answer all or some of the questions, but **The University of Manchester** would appreciate your help in answering all the questions. It is important to know that your participation will not affect your ability to use health facilities or free treatment. We are hoping that you will participate since your views are highly valued and important.

Do you have any questions about what I am asking you to do?

May I begin asking you question now?

[Instruction to the interviewer: Wait for the answer and make sure you do not rush the respondent to answer. If the respondent is not answering, gently ask the question again until you get an answer. If you feel that he/she is not willing to take part, don't pursue this]

He/She understands the details of the survey have informed about the requirements and here by agree to participate in the survey.

ID Number _____ Date_____

The respondent has been informed about this survey and understands its purpose and objectives

Signature the respondent _____

Signature of the interviewer _____

* Modified consent form, form the Guidelines for measuring National TB/HIV prevalence in population based surveys, 2005. WHO/UNAIDS.

Physician's Knowledge Questionnaire

A. Baseline Data

1. Name _____
2. Gender [1] Male [2] Female
3. Age_____Years
4. BHU_____ 5.District _____
6. Contact No _____ 7.Date of Entry _____

B. Interview

I. Demographic Information

1. Medical School attended

[1] Government [2] Private [3] Foreign

2. Qualification

[1] MBBS [2] MD [3] MBBS + Post Graduation
[4] MD + Post Graduation

3. Year of Graduation _____

4. Do you have any Experience in Pulmonology?

[1] Yes [2] No

5. What Experience and for how long?

_____

_____

6. Duration of Service _____ years

7. Did you receive any training on TB?

[1] Yes [2] No

8. Do you need Training on TB?

[1] Yes [2] No

II Knowledge and Understanding of Tuberculosis (TB)

1. **What Germs Causes TB?**

_____ _____

_____ _____

What is the Most Common Symptom of TB?

_____

_____

2. **How you will diagnose TB?**

_____

_____

3. **Do you think TB is Communicable Disease?**

[1] Yes [2] No [3] Don't Know

4. **Do you know how TB Spread?**

_____

_____

5. **What is the minimum duration of TB Treatment?**

_____

_____

6. **How you will plan TB treatment?**

[1] _____

[2] _____

7. **How you will treat a pregnant woman with TB?**

_____

_____

8. **How you will treat a 15 years (25 Kg) child with TB?**

_____

_____

9. **Do you know the recommended doses of TB drugs?**

[1] Rifampacin _____ [2] Isoniazid _____

[3] Ethambutal _____ [4] Pyrazinamide _____

[5] Streptomycin _____

10. **What is TB DOTS?**

_____

_____

11. **How you will do follow up of TB patients?**

_____

_____

12. **Which TB drugs are contraindicated in Hepatitis?**

_____

_____

13. **What is MDR-TB?**

_____

_____

14. **How you will treat MDR-TB?**

_____

_____

14.5 Conference Presentations

International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

Dr Muhammad Aziz
The University of Manchester
PhD Scholar
2 Batty Street
M80RQ Manchester
United Kingdom, Lanchashire

Passport number: OA 133866
Date of birth: 01/04/1976

July 16, 2013

44th Union World Conference on Lung Health
30 October to 3 November 2013 - Paris, France

Dear Colleague,

We thank you in advance for your valuable participation at the 44th World Conference on Lung Health organised by the International Union Against Tuberculosis and Lung Disease (The Union). This conference, which will be held at the Palais des Congrès in Paris from 30 October to 3 November 2013, will focus on the theme "*Shared air, safe air?*"

The conference sessions will emphasise the growing concerns about the need to improve or preserve the quality of the air we breathe for both healthy and vulnerable persons alike. For five days, conference delegates from more than 120 countries will be able to discuss, debate and network with colleagues, strengthening anew their commitment to global efforts to improve lung health and find health solutions for the poor and underserved.

As The Union is a nonprofit organisation working primarily in low- and middle-income countries, our funds are very limited, and we regret that we will not to be able to assume financial responsibility for your conference participation. However, we hope you will be able to secure funds covering the expenses related to your participation from another source.

Meanwhile, should you need an entry visa for France, please initiate your application early with the local French embassy to make sure that you will obtain it in due time before the conference.

For further information on the conference, please visit the website www.worldlunghealth.org

We look forward to greeting you in Paris.

Yours sincerely,

José Luis Castro

Jose Luis CASTRO
Interim Executive Director

PS: This letter can be used for your administrative and visa purposes

Union Internationale Contre la Tuberculose et les Maladies Respiratoires
Unión Internacional Contra la Tuberculosis y Enfermedades Respiratorias
Association reconnue d'utilité publique. Fondée en 1920.
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www.theunion.org

Abstract

Do you know women are at a higher risk of Tuberculosis (TB) than male in Khyber Pakhtunkhwa (KPK), Pakistan?

M Aziz, D Baxter, A Esmail,

[1]Primary Care Research, School of Medicine, University of Manchester UK

Introduction: A descriptive epidemiological study of Tuberculosis in the province of KPK, Pakistan between 2002 and 2010. Research provides important data regarding the diseases burden and to confirm that women are at a higher risk for TB in the region.

Methods: We retrospectively collected data for all registered TB patients between 2002 and 2010 in KPK using National TB Control Programme (NTP) database. Access to database was provided by the NTP Information technology (IT) department with valid user name and password. The data were analysed through Microsoft Excel 2007 and tabulated in aggregated style to show the distribution of TB by age, gender, type of disease, geographical location and treatment outcome. Central tendency and variability parameters included mean, median and standard deviation obtained using SPSS 17. Qualitative data reported in absolute rate percentages.

Results: Total of 69,387 new TB patients were reported, with 57% female and 42% male. Majority of cases registered in Peshawar District 11836 (56.41% female, 43.59% Male). The lowest no of cases reported from Hungu District 646 (59.24% Female, 40.87% Male). Kohistan District showed the greatest gender difference with female constituting 78.80% and 22% male. Another five districts Battagram, Chitral, Buner, Upper Dir and Swabi reported that women accounted for more than 60% of the total TB cases.

Discussion: We confirmed that women of Khyber Pakhtunkhwa are at higher risk of TB than male. Further research is in progress to explore the causes of this higher incidence as a PhD project in the University of Manchester, UK.

Funding: We thanks to The University of Manchester United Kingdom, Islamic Development Bank Jeddah Saudi Arabia and National Tuberculosis Control programme Khyber Pakhtunkhwa for funding and providing technical support for the study.

Competing Interests: It has been declared that no competing interests exist by the authors for this study.

International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

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University of Manchester
Community Medicine
2 Batty Street
M80RQ Manchester
United Kingdom

Passport number: OA133866
Date of birth: 01/04/1976

October 01, 2014

45th Union World Conference on Lung Health
28 October to 1 November 2014 - Barcelona, Spain

Dear Colleague,

We thank you in advance for your valuable participation at the 45th World Conference on Lung Health organised by by the International Union Against Tuberculosis and Lung Disease (The Union).
This conference will be held at the Centre de Convencions Internacional de Barcelona (CCIB) in Barcelona, Spain from 28 October to 1 November 2014.

The conference theme is "Community-driven solutions for the next generation", which reflects the need to find solutions to the lung health challenges we face by involving all stakeholders form health care professional and policy-makers to the people and communities they serve. For five days, conference delegates from more than 120 countries will be able to discuss, debate and network with **colleagues, strengthening anew their commitment to global efforts to improve lung health and find** health solutions for the poor and underserved.

As The Union is a nonprofit organisation working primarily in low- and middle-income countries, our funds are very limited, and we regret that we will not to be able to assume financial responsibility for your conference participation. However, we hope you will be able to secure funds covering the expenses related to your participation from another source.

Meanwhile, should you need an entry visa for Spain, please initiate your application early with the local Spanish embassy to ensure that you will obtain it in due time before the conference.

For further information on the conference, please visit the website www.worldlunghealth.org.
Thank you again for your contribution to the conference, the success of which depends on the creativity and research excellence of presenters like yourself.
We look forward to greeting you in Barcelona.

Yours sincerely,

José Luis Castro

Jose Luis CASTRO
Executive Director

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PS: This letter can be used for your administrative and visa purposes

Dr. AZIZ will be accompanied by his wife and two children named as follows: Farida AZIZ, Sahil AZIZ, and Uzma AZIZ.

Article ID: GIC1552102

Global Research & Development Services

www.grdsweb.org

Participation Certificate

This certificate is awarded to

Dr Muhammad Aziz

of, School of Medicine, University of Manchester, England, United Kingdom.

for paper title

Tuberculosis in Adult Women: A systematic Review of Gender Differences in Tuberculosis Notification in the province of Khyber Pakhtunkhwa, Pakistan

as

PRESENTER

In technical presentation and research contribution to

6th International Conference on Healthcare and Life Science Research (ICHLSR), held at Imperial College London, Exhibition Road, London SW7 2AZ

GRDS Conference Secretariat

September 18-19, 2015

Abstract

Tuberculosis in Adult Women: A systematic Review of Gender Differences in Tuberculosis Notification in the province of Khyber Pakhtunkhwa, Pakistan.

[1]M Aziz, [2]M Ali, [1]A Esmail,

[1]Primary Care Research, School of Medicine, University of Manchester UK

[2]National Tuberculosis Control Programme Khyber Pakhtunkhwa, Pakistan.

Background:

Mycobacterium Tuberculosis (TB) is a serious public health threat globally and particularly in developing countries. Among the 22 high burden countries, Pakistan ranks 5th with a diagnosis of about 420,000 new cases every year. Globally, TB case notification is high in male as compared to female but in Khyber Pakhtunkhwa (PK) female patients are at a higher risk of TB than male. Similar data reported from Afghanistan, where 68.50% new sputum positive patients were female.

Aims and Objectives:

The purpose of this systematic review of published studies was to explore the causes of gender differences in the notification of Tuberculosis in KPK. The review formulates a theoretical base for my research identifying key areas for data collection (Social and Epidemiological Risk factors, Patients knowledge and Physicians Knowledge).

Methodology:

A relevant literature was identified through covering key theoretical papers and review articles on risk factors for Tuberculosis and gender issues. Databases accessed were MEDLINE, EMBASE and GLOBAL HEALTH and searches were conducted focusing on literature published between January 2000 and February 2015. The websites of specific journals, including the Journal of Infectious Diseases and American Journal of Public Health (AJPH) were used to locate references cited in articles (mostly review articles). Additionally, the websites of the World Health Organisation (WHO), the National Tuberculosis Control Programme (NTCP) and the Department of Health, Pakistan, were used to find related reports. Data were extracted from selected 85 research articles for tabulation, comparison and synthesis.

Results:

A total of 85 research articles were selected from 4,630 screen citations. Evidence extracted from these articles was used for metasynthesis of hypothetical base. Different main themes were noted reviewing the literature; age and gender; educational status of TB patients; economic status; nutritional status; overcrowding and household status; fuel consumption; rural and urban residence; knowledge of patients regarding TB and knowledge of general practitioners about diagnosis, treatment and fallow up. Our systematic analysis of the literature explained how socioeconomic issues interrelate to influence TB management. Results of our review are limited due to personal selection and quality of articles.

Conclusions:

The results of our literature review showed that very limited literature available on gender differences in TB. Gender and TB is a complex and neglected area of research in high burden countries. In spite of higher female notification of TB in KPK since 2000, no study has been carried out to address this issue. The results of this study will help National TB Control Programme to initiate a gender specific research in KPK.

14.6 University Positions for Students

MANCHESTER 1824

The University of Manchester

MHS/net Secure

Welcome **Mohammad Aziz** | Logout |

Back to the page you visited this site from

- Faculty of Medical and Human Sciences
- Secure

Graduate office

- Milestones
- Personal Development Programme
- Handbooks
- Supervisor's guide
- Peer mentoring

Medicine Peer Mentors

- **Biomedicine**
- **Cancer and Enabling Sciences**
- **Community Based Medicine**
- **Translational Medicine**

School of Biomedicine

Name: Chris Fisher, School of Biomedicine

Specialist areas: City life; Campus facilities

I moved to Manchester in 2007 and worked for the University before starting my PhD. Finding your feet isn't always straight forward but talking to people who have gone through similar experiences can really help. I really enjoy living here – it's a great city and there's always something going on. I try to see live music and go the cinema when I can. There's always plenty to see and there's something to suit all tastes.

Email: Christal.Fisher@postgrad.manchester.ac.uk

Name: Amanda Patist

Specialist areas: City life; Laboratory based studies; Coping as a student again; Studying full-time

I moved to Manchester from the Netherlands six years ago to start my undergraduate degree. Manchester appealed to me (and continues to do so) because of the high quality research as well as the city life. Living in Manchester for four years made settling into my PhD much easier as did the support from my supervisor and the postgraduate training team. My hobbies include mainly music (gigs and festivals) and occasionally I like to play badminton.

Email: Amanda.Patist@postgrad.manchester.ac.uk

Name: Louise Walkin

Specialist areas: Accommodation; City life; Laboratory based studies; Work/life balance

Manchester is my home town and I like the fact that it is a big city. The University has a good reputation and I settled into my PhD really well. My previous qualifications include a BSc and an MRes degree. I enjoy reading, swimming and travelling.

Email: louise.walkin-2@postgrad.manchester.ac.uk

School of Cancer and Enabling Sciences

Name: Emily Holmes

Specialist areas: Laboratory based studies; Studying full-time

I moved to Manchester two years ago to begin studying for my PhD at the Paterson Institute after gaining my BSc in Genetics from the University of Leeds. I have enjoyed my time in Manchester as there is always something going on in the city which provides a welcome break from studying. I enjoy keeping fit either at the gym, running or swimming, and also enjoy going to the cinema and cooking.

Email: Emily.Holmes@postgrad.manchester.ac.uk

Name: Katherine Holliday

Specialist areas: Accommodation; City Life; Campus Facilities; Studying full-time; Work/life balance

I have lived in Manchester for six years as an undergraduate and postgraduate student. I found that studying for a PhD is a lot different to a degree and there is lot to pick-up quickly. The city has something for everyone: sport, culture and social activities. I enjoy ice hockey and mountain biking.

Email: katherine.holliday@postgrad.manchester.ac.uk

School of Community Based Medicine

Name: Dr Muhammad Aziz

Specialist areas: Accommodation; Studying as an international student; Studying full-time

I moved to Manchester in September 2010 to pursue my PhD under the Islamic Development Bank Scholarship Program. I like Manchester due to its vibrant and multicultural environment. I am also really enjoying the research facilities and support provided by the University. I have 3 years teaching experience as an Assistant Professor at NIMS, College of Medicine in Pakistan and two years experience as a Medical Doctor with UNHCR in Pakistan. My hobbies include reading, volunteering, visiting historical places, sports and socialising.

Email: muhammad.aziz.dr@postgrad.manchester.ac.uk

Name: Sandra Flynn

Specialist areas: Studying part-time; Copying as a student again; Work/life balance

I am originally from Manchester and returned following the completion of my undergraduate degree. Manchester is a diverse city; there is a place for everyone and opportunities to follow your interests and hobbies. I enjoy photography and cycling.

Email: Sandra.M.Flynn@manchester.ac.uk

Name: Kathryn Oliver

Specialist areas: Coping as a student again; Studying full-time; Work/life balance

I moved from London to start a PhD here in 2009. There's lots of support available through the University and through research groups as well. I was worried about whether I would be able to do a good quality PhD and if my supervisor was going to be any good. The University has a lot of structures and support in place to deal with problems like this though, so as long as you know how to access then, and feel ok about doing so, it's fine. My hobbies include music, climbing, sailing, camping and reading.

Email: Kathryn.Oliver@postgrad.manchester.ac.uk

Name: Nicola Small

Specialist areas: Accommodation; City life; Campus Facilities; Work/life balance

I have lived in Manchester all my life and think it is a great city. I have worked at the University for 4 years. I worked for a year as a Research Assistant and then embarked on a PhD. I also have an MSc in Health Psychology. My hobbies include meeting people, music and art.

Email: Nicola.Small@manchester.ac.uk

School of Translational Medicine

Name: Charlotte Bryant

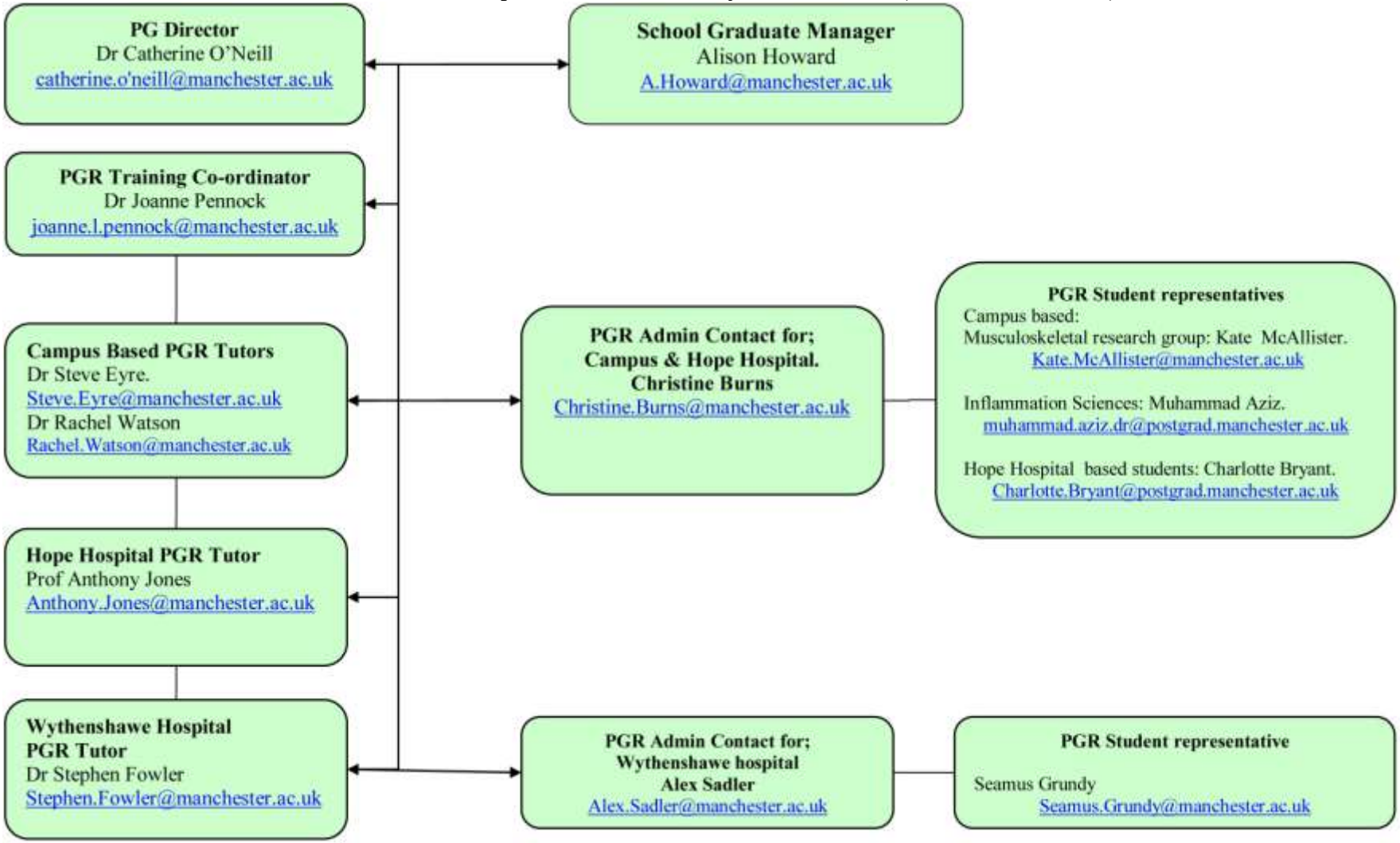
Specialist areas: City life; Coping as a student again; Studying full-time; Work/life balance

Manchester is a fantastic city to live and study in. There is always something for everyone. I moved to Manchester in 2009 to start my PhD. It is always daunting moving to a new city but my goal was to throw myself into everything and anything both socially and academically. I really wanted to make the most of being in such a fantastic city.

Email: Charlotte.Bryant@postgrad.manchester.ac.uk

Name: Seamus Grundy

PGR Student Representaives University of Manchester (School of Medicine)



14.7 National TB Control Programme Data Collection and Reporting Instruments

TB01 FRONT SIDE

National Tuberculosis Control Program — TB01

Tuberculosis Treatment Card

Name of diagnostic centre (BMU)

CNIC #:

Name of Patient _____ (S/o; D/o; W/o)

Father / G Father Name _____

Sex ☐ M ☐ F Age _____ Date of registration _____

Address of patient _____

Name/address of contact person _____

Phone No. _____

Name of treatment center _____

Address _____

Name/Type of treatment supporter with phone No. _____

Patient Identifier Code: _____

Disease site (tick one)

☐ Pulmonary

☐ Extra pulmonary specify _____

Confirmatory evidence Yes/No

If yes (tick) Histopathology/Bacteriology

Type of patient (check one)

☐ New ☐ Treatment after default

☐ Relapse ☐ Treatment after failure

☐ Transfer in ☐ other _____

I. INITIAL PHASE

CAT (I,II) ☐

Number of tablets (per doze) and Dosage of S

Referral by

☐ Self-referral

☐ Community member

☐ Public facility

☐ Private facility/provider

☐ LHW

☐ other .....

Sputum smear microscopy				Weight (kg)	CXR
Month	Date	Lab No.	Result		

ADULT

RHZE (150/75/400/275)	S	RHZ (60/30/150)

CHILD

RH (60/30)	S

Tick appropriate box after the drugs have been administered

Daily supply: enter √ Periodic supply: enter X on day when drugs are collected and draw a horizontal line (——) through the number of days supplied. O = drugs not taken

Day / Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

TB01 BACK SIDE

National Tuberculosis Control Program — TB01

II. CONTINUATION PHASE

	ADULT		CHILD
	RH (150/75)	RHE (150/75/275)	RH (60/30)
Number of tablets per dose			

Daily supply: enter √ Periodic supply: enter X on day when drugs are collected and draw a horizontal line (——) through the number of days supplied. O = drugs not taken

Day / Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

(Household) CONTACTS*

Name of contact	Age	Sex	Method of screening			Date & result of screening			Remark
			Tub	X-ray	DSM	Tub	X-ray	DSM	

Treatment outcome

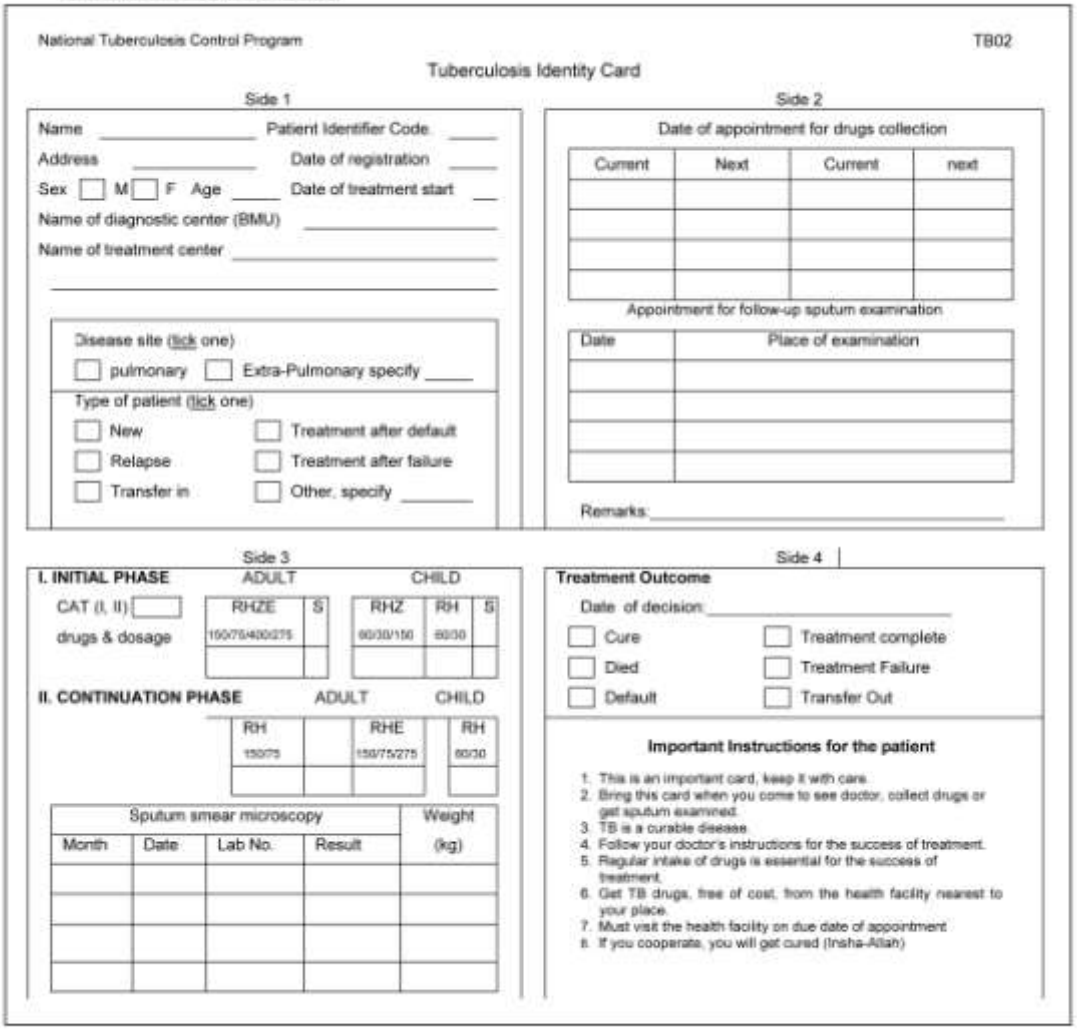
Date of decision _____

- ☐ Cure
- ☐ Treatment complete
- ☐ Died
- ☐ Treatment failure
- ☐ Default
- ☐ Transfer out

Comments

*Joint International Review mission (July 2008) recommended screening of all Sputum Smear Positive (SS+) contacts.

TB PATIENT CARD (TB02)



National Tuberculosis Control Program — TB02

Tuberculosis Identity Card

Side 1

Name _____ Patient Identifier Code _____

Address _____ Date of registration _____

Sex ☐ M ☐ F Age _____ Date of treatment start ___

Name of diagnostic center (BMU) _____

Name of treatment center _____

Disease site (tick one)

☐ pulmonary ☐ Extra-Pulmonary specify _____

Type of patient (tick one)

☐ New ☐ Treatment after default

☐ Relapse ☐ Treatment after failure

☐ Transfer in ☐ Other, specify _____

Side 2

Date of appointment for drugs collection

Current	Next	Current	next

Appointment for follow-up sputum examination

Date	Place of examination

Remarks: _____

Side 3

I. INITIAL PHASE

CAT (I, II) ☐

drugs & dosage

ADULT		CHILD		
RHZE	S	RHZ	RH	S
150/75/400/275		60/30/150	60/30	

II. CONTINUATION PHASE

ADULT		CHILD	
RH		RHE	RH
150/75		150/75/275	60/30

Sputum smear microscopy				Weight
Month	Date	Lab No.	Result	(kg)

Side 4

Treatment Outcome

Date of decision: _____

☐ Cure ☐ Treatment complete

☐ Died ☐ Treatment Failure

☐ Default ☐ Transfer Out

Important Instructions for the patient

1. This is an important card, keep it with care.
2. Bring this card when you come to see doctor, collect drugs or get sputum examined.
3. TB is a curable disease.
4. Follow your doctor's instructions for the success of treatment.
5. Regular intake of drugs is essential for the success of treatment.
6. Get TB drugs, free of cost, from the health facility nearest to your place.
7. Must visit the health facility on due date of appointment.
8. If you cooperate, you will get cured (Insha-Allah).

TUBERCULOSIS REGISTER (TB03)

National Tuberculosis Control Program

TB03

Year: _____

Date of registration	Patient Identifier Code	Name (S/o; D/o; W/o) & CNIC #	Father & G.Father Name 4 F=Father G=Grand Father (encircle relevant information F/G)	Sex M/F	Age	Complete Address	Name of Treatment Center	Date treatment started	Treatment category	Cat-I ,Cat-II	Site **P/EP**	**Type of Patient****						Results of sputum smear microscopy								Date Treatment Stopped***						No of TB cases detected through contacts screening		Remarks
												N	R	F	D	T	O	Sputum Smear Microscopy Before treatment		FOLLOW UP SPUTUM EXAMINATIONS 2-3 months		5th month		6th /8th month 3		(record the date in relevant column)								
																		ear Microscop	Lab. No	ear Microscop	La b. No	ear Microscop	La b. No	ear Microscop	La b. No	Cured	Treatment	Died	Treatment	Defaulted	Transferre	contacts	confirmed	
			F/G																													
			F/G																													
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			F/G																																			
			F/G																																			
			F/G																																			

(*, **, *** definitions/ elaboration given at end of the register)

1. First follow up at the end of 2nd month for NSS+ cases and at the end of 3 month for those NSS+ not converted at 2 month and for CAT 2 patients.
2. Mention the result as NEG.1- 9, 1+, 2+, 3+. ND for smear not done.
3. Last follow-up at the end of 6th month for CAT-1 cases and for CAT-II at the end of 8th month will be recorded in the same column accordingly.
4. Write Father and G.father name in case of male and female unmarried & fathers and husband name in case of married female

TB LABORATORY REGISTER (TB04)

Lab. Serial No.	Date Specimen received	Name (S/O;D/O;W/O) & CNIC#	Sex (M/F)	Age	Complete address with Cell Number(Patients for Diagnosis)	Name of referring facility[1]	Reason for Sputum smear microscopy examination		Results of sputum smear microscopy examinations[2]			Patient Identifier code (after registration)	Remarks	Signature
							Diagnosis (Tick)	Follow-up (Write Month with Registration No.)	1	2	3			

National Tuberculosis Control Program **TB07**

QUARTERLY REPORT ON TB CASE REGISTRATION

INDIVIDUAL/CONSOLIDATED REPORT (tick one) In case of consolidated report: Functional _____ Reporting _____ centres _____

Name of district _____ Name of BMU (Diagnostic Center)_____ _____

Name of TB Coordinator _____ Signature _____

Patients registered during _____ Quarter of year _____

Date of completion of this from _____

Block 1: All TB cases registered [2]

Sex1	Pulmonary sputum smear microscopy positive 2					New pulmonary sputum smear microscopy negative			New pulmonary sputum smear not done 4			New extra pulmonary 5			Others 6 previously treated (SS Neg. & EP)	Total 7 all cases (Col. 2-6)
	New cases	Previously treated				0-4 yrs	5-14 yrs	>15 yrs	0-4 yrs	5-14 yrs	≥ 15 yrs	0-4 yrs	5-14 yrs	≥ 15 yrs		
		Relapses	After failure	After default	Others (SS+)											
Male																
Female																
Total																

Block 2: New pulmonary sputum smear microscopy positive cases – Age group

Sex	0-4	5-14	15-24	25-34	35-44	45-54	55-64	≥ 65	Total
M									
F									

Block 3: Laboratory active – sputum smear microscopy [4]

No. of TB suspects examined for diagnosis by sputum smear microscopy	No. of TB suspects with positive sputum smear microscopy result	Total OPD

Block 4: Contacts screening

Total No. of contacts screened out through different screening tools	No. of confirmed TB cases detected through contacts screening

TB-08

QUARTERLY REPORT ON THE SPUTUM CONVERSION AFTER 2 AND/ OR 3 MONTHS TREATMENTS OF PULMONARY TUBERCULOSIS SMEAR-POSITIVE PATIENTS REGISTERED 3 TO 6 MONTHS EARLIER

INDIVIDUAL/CONSOLIDATED REPORT (tick one). In case of Consolidated report: Functional____ Reporting ____centre

Name of District: _____ HMIS District No: _____ Name of BMU(Diagnostic Center):_____ Tehsil:_____	Patients registered during ____ Quarter of 20	Date of completion of this form: _____20 ____ Signature:

Patients Registered(1)			Type of Patient (2)	Smear Negative 3	Smear Positive 4	**Died 5**	Defaulted (6)	Transferred Out 7)	Total Patients Evaluated (8)
New Cases									
M	F	T**	**1**. New Cases: **1.1 Smear Positive**						
			1.2 Smear Negative	X					
			1.3 Extra-Pulmonary						
			1.4 Smear Not Done						
Re-treatments									
M	F	T**	2. **Re-treatments** 2.1 Relapses						
			2.2 Treatment After Failure						
			2.3 Treatment After Default						
			2.4 Others SS +ve Previously Treated						
			2.5 Others SS-ve Previously Treated						
			Total						

* From the quarterly Report on New, Relapses and Treatment after Failure and Treatment after Default Cases (TB07)

** Of the New Cases _____ (number) were excluded from evaluation of chemotherapy ~~because:~~_____

*** Of the Re-treatments _____ (number) were excluded from evaluation of chemotherapy ~~because:~~_____

14.8 PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Tuberculosis in Adult Women: A systematic Review of Gender Differences in Tuberculosis Notification in the province of Khyber Pakhtunkhwa, Pakistan.	53
ABSTRACT			
Structured summary	2	The results of our literature review showed that very limited literature available on gender differences in MTb. Gender and MTb is a complex and neglected area of research in high burden countries. In spite of higher female notification of MTb in KPK since 2000, no study has been carried out to address this issue. The results of this study will help National TB Control Program to initiate a gender specific research in KPK	59
INTRODUCTION			
Rationale	3	Mycobacterium Tuberculosis (MTb) is a serious public health threat globally and particularly in developing countries. Among the 22 high burden countries, Pakistan ranks 5th with a diagnosis of about 420,000 new cases every year. Globally, MTb case notification is high in male as compared to female but in Khyber Pakhtunkhwa (KPK) female TB notification is higher as compared to male. Similar data reported from Afghanistan, where 68.50% new sputum positive patients were female.	53
Objectives	4	The purpose of this systematic review of published studies was to explore the causes of gender differences in the notification of Tuberculosis in KPK. The review formulates a theoretical base for my research identifying key areas for data collection (Social and Epidemiological Risk factors, Patients knowledge and Physicians Knowledge), using PRISMA-P	53
METHODS			
Protocol and registration	5	PRISMA-P	59

Eligibility criteria	6	Empirical research or a systematic review relevant to the epidemiology and risk factors for TB. Articles published in English Knowledge, Attitude, Awareness and Treatment seeking behaviour in TB patients-related papers. Assessment of learning, approach and management of TB amongst family physicians-related papers.	58
Information sources	7	Databases: MEDLINE, EMBASE and GLOBAL HEALTH Journals: The Journal of Infectious Diseases and American Journal of Public Health (AJPH) Websites: Health Organisation (WHO), the National Tuberculosis Control Programme (NTCP) and the Department of Health, Pakistan.	54
Search	8	The search strategy sought material evaluating epidemiology and gender differences, risk factors, patient knowledge and general practitioners knowledge of TB in Pakistan and Khyber Pakhtunkhwa. Key words "Tuberculosis or TB", "risk factors", "adult female or females", "Pakistan" and "Khyber Pakhtunkhwa or NWFP" were used to search at the national level. I also used key words "China", "India", "Iran", "Afghanistan" for available studies to compare the situation of the disease at the regional level as well.	55-58
Study selection	9	The systematic review identified 4,630 screen citations using multiple approach search strategy. Of the total, 2530 studies yielded by MEDLINE search, EMBASE search yielded 1155 and GOLBAL HEALTH 730 articles only. Additionally, from the websites of WHO, NTCP, MOH and online journals (JID, AJPH) further 250 articles were identified. The preliminary search reviewed, 3067 articles were excluded as not relevant to the research area. Further reviewing the findings by titles and abstracts, 749 more research articles were removed. After reading full text articles, 154 studies were considered eligible on the basis of our inclusion criteria. Finally, after removing the duplicate articles 85 studies were remained for literature review	59
Data collection process	10	A piloted questionnaire was made on the basis of variables reported on literature and data collected for most important variables such as age, gender, educational and economic status etc. The piloted questionnaire was updated after literature review as advised by the supervisory team.	207-14

Data items	11	List of variables	72-91
Summary measures	12	Summary tabulated as tables 12,13,14,15	72-80
RESULTS			
Results	13	A total of 85 studies were selected for details please see a flow diagram. Summary tabulated as tables 12,13,15 and 15	59 61-69
DISCUSSION			
Summary of evidence	14	The literature on patient's knowledge about Tuberculosis is very limited. In Khyber Pakhtunkhwa, I could not identify any research on the knowledge of TB patients. However, there were several studies carried out on patient's knowledge in Pakistan. It is evident from the results of studies included in the literature review that patient's knowledge regarding TB is very limited, especially in rural communities. Since nearly 75 % of KPK population live in rural areas, it is a reasonable assumption that patients from rural districts of KPK have poor knowledge of TB and should be investigated for the association between knowledge and higher notification of TB in females	72-92
Limitations	15	Literature regarding gender and tuberculosis is very limited especially in KPK	76-77
Conclusions	16	Data from National TB control program and research done in KPK suggested that female notification of TB is higher than male and further research should be carried out to explore the reasons behind this variation.	77
FUNDING			
Funding	17	Islamic Development Bank Jeddah Saudi Arabia (IDB)	