CHAPTER 1

GENERAL INTRODUCTION

1.1 Overview of the History of Tuberculosis

Kumar and colleagues define Tuberculosis (TB) as an infectious disease caused by various strains of mycobacteria, usually Mycobacterium tuberculosis.[1] It has also been indicated that there are two main types of TB: pulmonary tuberculosis (PTB), which usually affects the lungs, and extra-pulmonary tuberculosis (EPTB), which can affect almost any part of the body.[2]

It is well known that tuberculosis has affected humans since ancient times. However, it was only in 1882 that Robert Koch discovered that TB was caused by Mycobacterium tuberculosis.[3] In this regard, an investigation conducted by Zink et al, when applying spoligotyping to the skeletal remains of ancient Egyptians, found the presence of particular subtypes of the Mycobacterium tuberculosis complex among these prehistoric humans from as long ago as 4000 BC.[4]

A report indicates that tuberculosis was introduced to South Africa by the European colonisers and by the late nineteenth century there were already several tuberculosis sanatoria established in specific areas of the country to care for sufferers. TB sufferers from European countries settled in areas of the Western Cape in search of a suitable climate for curing the disease. On the other hand, based on the belief that fresh air and rest could cure tuberculosis, an increasing number of tuberculosis sufferers from Europe journeyed to South Africa in the hope that the climate would cure them. Subsequently, Europeans infected with TB transmitted the disease to contacts across the country.[5]

Although many lives have been saved through the use of DOTS and the Stop TB Strategy recommended by WHO,[6] and despite all the achievements through chemotherapy and efforts carried out to decrease the impact of this disease, TB control and management remains a huge medical and social challenge.

1.1.1 The Burden of Tuberculosis Globally

Based on a recent published TB report, tuberculosis is considered a leading cause of adult mortality in low and middle-income countries (LMIC). These authors indicate that after the

human immunodeficiency virus (HIV) it ranks as the second leading cause of death from an infectious disease worldwide and it is among the top three causes of death for women aged 15 to 44.[6] Additionally, it was declared a global public health emergency by the World Health Organization (WHO) in 1993.[7]

According to the WHO, nearly 2 billion people (one–third of the world's population) are infected with Mycobacterium tuberculosis. Worldwide, there are approximately nine million new cases of TB — and close to two million deaths — annually caused by TB.[8] Previous reports from the WHO have indicated that in Southern Africa, the TB epidemic has escalated to be one of the worst in the world. Of the 44 million people estimated to be living with HIV/AIDS, 12 million are co-infected with TB and over 66% of these live in sub-Saharan Africa.[9]

A subsequent WHO study, addressing the co-epidemic of TB and HIV (2011), estimates that Africa — with just 11% of the world's population — accounts for about a quarter of the world's TB burden, with an estimated 2.4 million cases and 500,000 deaths in the region every year. Globally in 2010, it is estimated that 0.35 million HIV sufferers died from TB. As a consequence, WHO, UNAIDS and the Stop TB Partnership have set a target for 2015 to reduce TB mortality rates among people who are HIV-positive by 50% from the number in 2004 — the year in which TB mortality among HIV-positive individuals is estimated to have peaked.[10]

According to WHO Global Tuberculosis Report (2007) tuberculosis presents a major public health problem in South Africa. The incidence rate of TB is well over 200/100 000; an incidence of this figure is classified by the WHO as a serious epidemic. A study on global tuberculosis control (2011) has indicated that the country is burdened by one of the worst tuberculosis epidemics in the world.[11]

A recent international report on tuberculosis country profiles (2012) indicated that the disease rate in the country is estimated at more than double those observed in other developing countries and up to 60 times higher than those currently seen in the USA or Western Europe.[12] According to Fourie and Weyer, this tuberculosis problem in South Africa can be seen largely as a result of historical neglect and poor management systems, compounded by the legacy of fragmented health services.[13]

1.2 Risk factors for PTB; evidence of association

1.2.1 TB and HIV

The sixteen global reports on Tuberculosis published by WHO (2011) indicated that with HIV/AIDS and TB, the world has faced two global epidemics that are significantly interlinked and the relationship between the two has long been recognised. In this report, the authors suggest that it is evident that the HIV epidemic fuelled the TB epidemic in populations through the overlap of those infected with HIV and those infected with Mycobacterium tuberculosis. This expert opinion that HIV infection is the most influential factor increasing the risk of TB is supported by statistical data, which indicates that the lifetime risk of an HIV-negative person developing TB is 5 – 10%, while the probability for HIV-infected persons is 50%.[8]

The same report, details 8.8 million new cases of TB in 2010, of which 1.1 (13%) million were HIV positive individuals. Of the 1.1 million new TB cases among people living with HIV, 910,000 (76 %) were concentrated in the African region and 180,000 (14%) in the South East Asian region.[8]

The results of one 2007 study shows that the relative risk of an HIV-positive individual developing TB was estimated at 20.6 times (95% CI 15.4–27.5) in countries with a serious HIV epidemic (i.e. countries where the prevalence of HIV is above 1% in the general population). In contrast, the relative risk was estimated at 26.7 times (95% CI 20.4–34.9) in countries where the prevalence of HIV in the general population is between 0.1% and 1%, and 36.7 times (95% CI 11.6–116) in countries where the prevalence of HIV in the general population is less than 0.1%.[14]

Even though according to Dye, HIV infection has clearly had a profound effect on TB epidemiology, other potentially important risk factors have not been extensively investigated.[15]

1.2.2 TB and Age

Worldwide studies on TB have indicated that all age groups are at risk of developing TB but it is primarily a disease that affects young adults in their most productive years.[16] However, according to Zevallos and Justman, the elderly remain one of the most vulnerable groups. These authors suggest that the increased risk of developing TB for those who are immune compromised by age is well-known.[17]

In contrast, some studies have reported that the incidence of TB infection varies with age. Whereas in Africa, TB primarily affects adolescents and young adults,[18] in countries where TB has gone from high to low incidences (as in the United States), TB is mainly a disease of older people.[19] In addition, another study illustrates that in the United States, with exception of HIV-infected persons, the incidence of TB is higher in elderly persons than in any other segment of the population.[20]

Wu et al, also support the theory that aging is a risk factor for TB and may be attributed to a weakened immunologic system.[21]

1.2.3 TB and Gender

According to a WHO report (2010) on TB studies, worldwide more men are diagnosed and die from TB than women. Nevertheless, as can be seen from the statistics, TB is still a leading infectious cause of women's deaths – annually, about 700, 000 women die of TB, and over three million contract the disease. These startling figures clearly show that TB has become a major women's health issue, with particularly serious implications for women living with HIV. Some studies show that TB affects women differently from the way it affects men. In particular, TB progresses more quickly in women of reproductive age than in men in the same age group.[22] Based on WHO TB and Woman report (2005), it has been suggested that tuberculosis has implications for women's reproductive health, including risks with infertility, prematurity and low birth weight, and obstetric morbidity.[23]

Current studies on the impact of gender dynamics on TB detection and treatment indicates that although this area has not been studied extensively, there are some clear links. To begin with, gender-related barriers can impact women's access to TB information and services, which contribute to missed case detection in women. These studies have indicated that some evidence suggests that where women do not control family resources, they often delay seeking medical care for themselves. If women are not allowed to leave the home without permission, and are fearful of being seen going to a TB clinic, they often miss health promotion programmes and remain unaware of the symptoms of TB. Where women may suffer stigma and discrimination related to their HIV or TB status, they may not seek treatment because of this.[24]

1.2.4 TB and Overcrowding

A study carried out by Tekkel et al, reported that prisoners are particularly vulnerable to infectious diseases such as HIV/AIDS and TB. These authors suggest that imprisonment facilities provide conditions that allow TB to spread rapidly due to overcrowding, poor nutrition, and the lack of health services.[25]

According to Lienhardt et al, there are a number of factors that could explain the role of crowding as a risk factor for PTB. One of the main reasons these researchers identify crowding as a PTB issue is because it is an air-borne disease; the risk of becoming infected is strongly associated with contact with an infectious PTB case, as well as with the intimacy/proximity of that contact — shared airspace increases exposure to Mycobacterium tuberculosis. However, the researchers argue that rather than the number of people in contact with a PTB case in a limited environment, it is the increased occurrence of contact and the proximity of contact with the case that are determinant in the transmission of infection. In addition to the degree of exposure, it has been also indicated that the risk of TB infection depends on the infectivity of the source case.[26]

In Canada, the National Occupancy Standards fixed bedroom requirements to prevent household crowding: for adequate housing, there needs to be a bedroom for each adult couple; un-attached household member 18 years or older; same sex pair of children under 18; one boy or girl and two opposite sex siblings under the age of five.[27]

1.2.5 TB and Smoking Status

Some worldwide studies on Tuberculosis and Tobacco indicate that in 2009 approximately 1.3 billion people were reported to smoke cigarettes or use other tobacco products, with nearly 70% of them living in low-and middle-income countries. According to these studies, tobacco use is the leading preventable cause of death. In addition, it has been indicated that more than 5 million people die per year from tobacco use and, if unchecked, the epidemic will kill more than 8 million people a year by 2030.[28]

Global research into TB and tobacco control have pointed out that the high prevalence of tobacco use has been noted in TB risk studies since 1918. However, the association between TB and tobacco use has been widely considered up to the present day by TB experts to perhaps be a chance association. Recently, the predominant experts' view was that existing studies were not in-depth enough to provide confirmation of any link between

TB and tobacco use. However, the researchers have indicated that more recent studies and some recent reviews of existing studies have seemed to provide a better-evidenced link between active and passive tobacco smoking and a range of TB outcomes, including infection, response to treatment, relapse rates and mortality (WHO, 2007).[29]

Lin et al, conducted a systematic review and meta-analysis of observational studies. They reported that there is consistent evidence that tobacco smoking is associated with an increased risk of TB. It was identified that passive smoking and biomass fuel combustion also increase the risk of contracting TB and should be substantiated by further studies in the future. In addition, the findings show that smoking — along with causing an increased risk of TB infection — is associated with death from TB. Tobacco smoking is increasing in many countries where TB is already a problem. These results therefore suggest that it is important for health policy makers to further develop strategies for controlling tobacco use in order to reduce the impact of TB worldwide.[30]

Bates et al, carried out a systematic review and meta-analysis of epidemiologic data to quantify the relationship between active tobacco smoking and TB infection, pulmonary disease, and mortality. The researchers reported that the meta-analysis produced evidence that smoking is a risk factor for both TB infection and TB disease. However, these authors suggested that it is not clear that smoking causes an additional mortality risk for persons who already have active TB.[31]

To sum up, given the association between tobacco smoking and TB, increasing rate of smoking in the developing world poses a severe risk to the health of this population.[32]

1.2.6 TB and Alcohol Consumption

According to Lönnroth et al, there has been evidence to support a strong association between alcohol use and the risk of contracting TB. However, according to these authors, early studies did not allow for the confounding issues of other factors such as smoking, malnutrition and other aspects of poverty such as overcrowded conditions — all of which are also associated with TB. With regard to this issue, these researchers in a systematic literature review identified 3 cohort and 18 case control studies to determine the available evidence on the association between alcohol use and the risk of contracting TB. The study showed that the risk of active TB is substantially elevated in people who drink more than 40g of alcohol per day, and/or have an alcohol use disorder.[33]

Based on the results from meta-analyses studies that have been published since 2008, it has been noted that while there is considerable epidemiological evidence of an association between alcohol and TB, according to this report the presence of multiple confounders complicates the relationship. For instance, the Lönnroth et al, analysis noted that there were inadequate controls across studies, specifically, virtually no control regarding the TB risk factors to assess the influence of malnutrition, diabetes and indoor air pollution.[33]

On the other hand, Fok et al, conducted research into risk factors for the clustering of TB cases in a systematic review of population-based molecular epidemiology studies. The meta-analyses yielded significant estimates of odds ratios (ORs) for several risk factors across both levels of TB incidence. Alcohol abuse, injected drug habits and homelessness — all characteristics of marginalized populations — were found to be consistently significant in populations of low TB incidence.[34]

A systematic review conducted by Rehm et al, concluded that epidemiological and other evidence indicates that heavy alcohol and alcohol use disorders (AUD) constitute a risk factor for incidence and re-infection with TB. In addition, the course of the disease is worsened by alcohol use and by AUD.[35]

1.2.7 TB and Silicosis

According to Rosenman and Hall, epidemiological and case studies have shown that workers exposed to silica dust have increased morbidity and mortality from Pulmonary TB.[36] A study carried out by Hnizdo and Murray on the risk of South African gold miners contracting TB revealed that the silica dust which they accumulate in their lungs during exposure is a lifelong risk for the development of PTB, even if silicosis is not present in the lungs. According to these authors, this is because even after their exposure to dust ends, ex-miners continue to be at risk of developing silicosis and its development places them at even greater risk of developing PTB.[37] One study reported that PTB is currently epidemic in South African goldmines, being associated with both silicosis and HIV infection.[38] Given that silicosis greatly increases the risk of TB, more research into the effect of various indoor or outdoor air pollutants on the disease is necessary.

1.3 Rationale

The extensive literature review revealed the consensus in the scientific community regarding the major risk factor for the onset of tuberculosis is HIV infection, along with an

acknowledgement that a number of other important risk factors make people susceptible to developing TB infections.

The purpose of this study is to assess the risk factors that are contributing to the increased development of PTB among adult HIV-positive patients attending the Themba Hospital Wellness Clinic. Because no previous research of this kind has been conducted in this hospital, it is hoped that this study would allow identification and greater understanding of the risk factors that are unique to the hospital's specific context.

This study could offer a basis for the generation of hypotheses for further studies, and from an epidemiological point of view, this data will make a modest contribution to the scope of medical knowledge.

This research assesses some of the most relevant risk factors for the development of TB in line with previous research studies and includes: demographics; socioeconomics; behavioural and lifestyle aspects; medical history; and environmental conditions. Finally, a comparison of the presence (or prevalence) of these risk factors among HIV positive patients with tuberculosis and without tuberculosis is presented.

An awareness of the risk factors for tuberculosis is important for targeted interventions for both TB screening and prophylaxis. This is particularly important when resources available to public health agencies are limited and disease control activities must be prioritized.

1.4 Aim

The overall aim of the research was to assess contributory risk factors for Pulmonary Tuberculosis among adult patients suffering from Human Immunodeficiency Virus attending the Wellness Clinic at Themba Hospital.

1.5 Objectives

1. To describe the socio-demographic characteristics of the study participants.
2. To determine the prevalence of PTB among HIV positive patients.
3. To compare HIV positive patients with and without pulmonary tuberculosis in order to identify the potential additional individual risk factors for the development of PTB
4. To model PTB outcomes against potential risk factors in a multivariable analysis.

CHAPTER 2

LITERATURE REVIEW

2.1 The Purpose of the Literature Review:

This literature review provides an overview of studies of Pulmonary TB risk factors to:

- Define the scope of the literature review and explain the search criteria used.
- Gain a global perspective of the risks factors associated with TB among adult patients with HIV in other parts of the world, as well as defining the current situation in South Africa.
- Obtain an idea about additional risk factors for PTB among HIV patients related to their socioeconomic status, habits, medical history, and living environment in other parts of the world and in South Africa in terms of demographic characteristics and other relevant information.

2.2 Search criteria and search engines used:

This literature review analyses findings from previous risk factors for Pulmonary TB related research. The internet, medical journals and text books, and relevant articles and information leaflets were all used. In terms of the internet, different search engines were used, which included Pub Med central, Google, Google scholar and direct searches within on-line World Health Organization (WHO), and the Centre for Disease Control and Prevention (CDC).

A number of relevant medical journals were reviewed, including: The International Journal of Tuberculosis and Lung Disease; The Journal Global Epidemiology of Tuberculosis; The Journal of Infection Disease Clinical of North America; The Journal of Acquired Immune Deficiency Syndromes(JAIDS); The Southern African Journal of Epidemiology and Infection; The International Journal of Epidemiology; Archives of Internal Medicine; The South African Journal of Family Practice (SAJFP) ; and The African Journal of Primary Health Care and Family Medicine (PHCFM).

On the Pub Med website, the key words used for the search were “Risk Factors for PTB” “TB and HIV”,“TB and age”, “TB and gender”, “TB and smoking”, “TB and alcohol”, “TB and the environment” ...and other isolated terms which related to “Risk Factors for PTB among HIV patients”, further refinement led to: “Risk factors for PTB and HIV and adults”. The criteria for

the selection of articles included: free full-text articles related to the risk factors for TB, especially within the HIV positive population. Articles detailing African studies were also prioritised.

The limits for the search were publications in journals and reviews and the time limit for publications was ten years (including 2013). Exceptions were allowed if the study was within the scope of the topic, and the methodology and results were relevant to the current review.

2.3 Review of the Literature

This literature review provides an overview of studies on the common PTB risk factors. For instance (socioeconomic, behavioural, medical, and environmental) locally and internationally are, in the main, already well documented but despite this, there are factors which are unique and specific for each context and world region.

According to Lienhardt, factors reported to influence the risk of mycobacterial infection include age, sex, crowding, socioeconomic conditions, urbanization, racial/ethnic group, and human immunodeficiency virus (HIV) infection. The author argues that in patients infected with Mycobacterium tuberculosis, the disease can develop at any time through the re-activation of a previously acquired (latent) infection or through exogenous re-infection. On the other hand, the study suggest that any condition modifying the balance established in the body between the tubercle bacilli and the host's immune defences can have an impact on the risk of developing the disease.[39]

Lienhardt et al*,* in a subsequent study (2005), indicated that tuberculosis is considered a multifactorial disorder in which the environment interacts with host-related factors. These authors see its development in humans as a two-stage process, in which a susceptible person exposed to an infectious case first becomes infected and second, after an interval of years or decades, may later develop the disease, depending on a variety of factors.[40]

Lönnroth and Raviglione have pointed out that the importance of any risk factor in public health is determined by both the strength of the association and the prevalence of the risk factors across the population.[41]

2.3.1 Studies Research on Risk factors for PTB in an International Perspective

2.3.1.1 Overview of studies of risk factors for PTB in Europe

A vast amount of the medical literature indicates that most studies investigating factors associated with TB have been conducted in developed countries, for instance a Swiss HIV cohort study of risk factors for PTB among HIV-infected patients in Switzerland showed that in countries of low prevalence of Mycobacterium tuberculosis infection originating in a country with a high prevalence of TB infection and to have advanced immunodeficiency are significant risk factors for the development of TB.[42]

On the other hand, a case-control study carried out by Tekkle et al, to determine factors contributing to TB in Estonia, reported that the pattern of risk factors there were somewhat different from that in Western European countries; a large percentage of the patients were men, but were not elderly, and immigration and drug abuse did not increase the risk. The major risk factors were related to poverty and low socio-economic status.[25] A cohort study by Story et al, was conducted on all patients with TB in Greater London during July 2003. The results indicated that homelessness, imprisonment and problematic drug use were independent risk factors for the onset of TB.[43]

As a different research approach, a contact investigation study with drug addicts and the homeless was carried out in Rotterdam, The Netherlands. Special tests, using DNA analysis fingerprinting of the Mycobacterium Tuberculosis isolates, showed that a specific cluster had developed in Rotterdam with a substantial number of the patients being drug addicted or homeless. The study found an increase of TB cases among drug addicts or the homeless from 8.8% of total cases in Rotterdam in 1999 to 12.6% of total cases in 2000.[44]

A study in Stockholm, Sweden, into risk factors associated with TB concluded that smoking, diabetes and anti-tumour necrosis alpha factor (anti-TNFα) drugs, and new immunosuppressive treatments represent important common risk factors for TB.[45]

Coker et al, in an a study into the risk factors in Russia found that the main ones were low accumulated wealth, financial insecurity, the consumption of unpasteurised milk, diabetes, living with a relative with TB, being unemployed, living in overcrowded conditions, illicit drug use, and a history of incarceration.[46]

2.3.1.2 Overview of studies of risk factors for PTB in North America

An early case-control study was conducted into TB risk factors in adults in King County, Washington, from 1988 to 1990. The research reported that HIV status, being of non-white race/ethnicity, and being born in a foreign country were each associated with a six-fold or greater increase in risk of developing TB. Each of the following was associated with at least a doubled risk: history of selected underlying medical conditions; low weight for height; low socioeconomic status; and being aged 70 years or older. Men had 1.9 times the risk of women, smokers of 20 years or more duration had 2.6 times the risk of non-smokers, and heavy alcohol consumers had 2.0 times the risk of non-drinkers.[47]

In a differently designed research project, a descriptive epidemiological analysis of foreign-born persons in the United States diagnosed with TB was carried out between 2001 and 2006; the study reports that immigrants accounted for 57% of all TB cases in the United States in 2006.[48] In contrast, a cross-sectional analysis was performed on data on US TB cases in patients 15 years or older to analyse the relationship between TB and substance abuse in the United States between 1997 and 2006. The study reports that substance abuse (the use of illicit drugs or alcohol) was the most prevalent behavioural risk factor among patients with TB in the United States.[49]

A study in Alberta, Canada, identified that immigrants accounted for 56.3% of all TB cases between 1989 to 1998, and by far the highest rates were seen in immigrants to Canada from Asia, in particular Vietnam, the Philippines, China, Hong Kong and India.[50]

2.3.1.3 Overview of studies of risk factors for PTB in other parts of the world:

At the Tuberculosis Research Centre in India, a community-based cross-sectional survey was conducted; results show that risk factors such as age, sex, smoking and alcoholism were all independently associated with Pulmonary TB and concluded that risk factors of age and sex showed a stronger association than smoking and alcoholism.[51] Another study conducted in South India — a matched case-control as epidemiological evaluation of risk factors for TB — reported that TB was associated with low education levels, kitchen types and diabetes in the region, but high income, cooking with biomass fuels, a history of smoking and alcohol consumption were not associated with TB.[52]

In a southeast Brazilian city, a case study of TB risks and socio-economic levels reported lower socioeconomic status as a significant risk factor for TB.[53] A population-based case-

control study into social and economic behaviour and the environment associated with the risk of TB carried out in China revealed that a poor environment and exposure to dust and chemical fumes at work, smoking and alcohol consumption were combined risk factors for adult PTB in this area.[54]

2.3.1.4 Overview of studies of risk factors for PTB in Africa

According to Lönnroth and Raviglione, the TB epidemic in Africa is on the rise, even in low-HIV prevalence settings. They argue that host-related and environment-related factors have been shown to play a role in the development of TB, but few studies have been carried out to identify their respective roles in resource-poor countries.[41] As indicated by some studies, risk factors associated with TB in sub-Saharan Africa show their own peculiarities, for example, a case-control study conducted at the Medical Research Council Outpatients' Clinic in The Gambia, reported that household crowding and past household exposure to a known TB case were the outstanding risk factors for TB development.[55]

On the other hand, in a prospective community study in Bissau, increasing age, male sex, ethnicity, adult crowding, family structure, and poor housing conditions were identified as independent risk factors for TB.[56] Across the region, other research has focused on HIV as a risk factor for TB, for instance, in the Mwanza Region of Tanzania a case-control population-based study was conducted to investigate the relative and population related risks of HIV infection for developing active TB. The study reported that HIV infection was associated with an eight-fold increase in the risk of developing active TB. The study further showed that 29% of the total TB cases were attributable to HIV infection.[57] Another study with the same aim but using different methodology design took place in Karonga District, in the north of Malawi. This research showed an increase of new smear-positive TB cases attributable to HIV increased from 17% in (1988-1990) to 57% in (2000-2001).[58]

Studies investigating other factors associated with TB in sub-Saharan Africa were limited to countries with low HIV prevalence and low TB incidence, especially in West Africa. In this regard, Lienhardt et al, conducted a multi-centre study in low HIV prevalence West African countries, Guinée, Guinea Bissau, and the Gambia. Their aim was to investigate the combined effect of both host and environmental related factors on TB. They found that TB was associated with the male sex, HIV infection, a history of asthma, a family history of TB, marital status, adult crowding, smoking (with a dose-effect relationship) and rented housing.[40]

2.3.1.5 Overview of Studies into the Risk Factors for PTB in South Africa

The literature reviewed shows that despite earlier research activities on the topic, there is limited conclusive information related to PTB risk factors in South Africa. A population-based case-control study carried out to determine whether crowding and alcohol were risk factors for TB in the Mamre population found an association between alcohol abuse and TB but no association between crowding and TB.[59] Another study conducted in an urban community of South Africa to determine the relationship between socio-economic factors and Pulmonary TB no found association between these and the risk of developing TB.[60]

Similarly, the multi-level analysis of self-reported TB disease based on the 1998 Demographic and Health Survey (DHS) found alcohol abuse, cigarette smoking and low body mass index (BMI) were each independent risk factors for TB in South Africa.[61] Other studies on miners' health have revealed the most contributing risk factors include age, mining occupation, silicosis status, and HIV infection.[62] HIV infection and silica exposure have been reported as major risk factors for TB in other studies conducted on South African gold mining populations.[63, 38]

Therefore, there is need for more in-depth research studies in the South African context to allow a better understanding of the risk factors for PTB across the country and within the communities. There are movements in this direction in the form of recently published studies on this topic in the deferent Medical Research Centres (MRCs), Public Health and Family Medicine Departments around the country.

2.4 Summary

From an international research perspective on risk factors for Pulmonary TB, it was noticed that there is a great diversity and variation of the important contributing factors for PTB globally. This statement is supported by evidence of the results of multiple studies, conducted across different countries and geographical areas (urban and rural) worldwide on the topic. On the other hand, it was significant that most of these studies have been conducted in industrialized societies while few studies have been carried out in Low to-Middle Income Countries (LMICs), particularly in high TB burdened nations. In addition, the studies in developed nations, for example, in Europe and North America, showed that the risk factors for TB also varies across countries and within.

From the studies that have been conducted in developing nations — for instance, in sub-Saharan Africa — these were limited to countries with low HIV prevalence and low TB incidence, especially in West Africa and most of this research had methodology designs limitations and their analysis approach for risk factors for TB were usually investigated separately. As reported by many researchers, the critical TB epidemic in Africa is attributable to multiple factors, where HIV infection has been recognized as the most important.

In South Africa, as evidenced by the reviewed literature, the data about risk factors for PTB are limited, and the situation looks to be similar to other countries in the region but also shows its own peculiarities, for instance, some early studies have shown a conflicting association between host and environmental factors and active TB disease. In addition, the design of previous studies also had their own methodology design limitations. Additionally, in South Africa a considerable number of studies on the topic have focused mainly on miner populations. There is, therefore, a great need for further rigorously designed investigations to discover the respective roles of each risk factor in this area.

Finally, a significant number of reports indicated that some of the risk factors for PTB were unique to some countries and population groups. Therefore, as suggested by experts in the field, a better understanding of TB risk factors could help to find out why TB risk varies across countries, within countries, and within communities. It is hoped that future research could provide new scientific information which will be of benefit to governments and health authorities in order to adjust and adapt TB control policies to contribute to the reduction of TB epidemics globally.

CHAPTER 3

METHODOLOGY

3.1 Study design:

A cross-sectional descriptive design was employed in this study.

3.2 Site of the Study

This study took place at the Wellness Clinic of Themba Hospital, situated in Kabokweni Township, Ehlanzeni District, Mpumalanga Province in South Africa. Themba Hospital serves a diverse population of approximately 350,000 people, while the Wellness Clinic provides a range of health services to a significant number of HIV/AIDS patients on weekdays, Monday to Friday.

3.3 Study Population

The study population consisted of adult patients (age≥18 years) registered at the Wellness clinic at Themba Hospital. People who attended consultations between January 2009 and March 2009, the period research was conducted, formed the study population.

3.4 Sample Size

The sample size was based on the objective to determine the prevalence of PTB among HIV patients. An accuracy of within 5% was required. It was then determined that a sample size of 303 patients would estimate the expected prevalence of 27% to an accuracy of 5% with 95% confidence (nQuery Advisor 7 Software). Furthermore, by convention, 10 – 15 subjects needed to be included into the study when determining the risk factors in a multivariable analysis (logistic regression). No more than 10 risk factors are expected to pursue in a multivariable analysis and hence the planned sample size was deemed adequate. This sample size calculation was done with help of a statistician in the Biostatistics Unit of the South African Medical Research Council (MRC) in Pretoria.

In this study, the researcher managed to collect data from a total of 300 participants which was thought to be adequate to carry out this project.

3.4.1 Sampling Method

The researcher used a systematic sample and the study took into consideration the average number of patients received monthly by the Wellness Clinic (850 per month), and the number was divided by the sample size of 300. The systematic sample included every third patient in the queue. The first participant was selected using a random number generator, after which every third patient who met the research criteria was invited to participate. If the patient declined the invitation to participate, the researcher selected the next patient in the queue.

3.4.2 Selection or Recruitment of subjects

This process was done voluntarily after the investigator had educated the subjects about the purpose of the research. An informed consent form was read and explained to the patients to enable them to make an informed decision on whether to participate in the research. All patients who wished to participate in the study were given a consent form to sign and were assured of anonymity and project confidentiality. Those who agreed to participate were considered part of the study sample. After the patients had given their written consent to participate, the researcher stored the consent form to protect their identity as well as to ensure the confidentiality of the research process.The content of the information leaflet and the consent form are provided: Appendix A and Appendix B respectively.

3.4.3 Inclusion criteria

All patients HIV positive attending the wellness Clinic at Themba Hospital, who were 18 years old or older at the time of the interview and willing to participate in the study.

3.4.4 Exclusion criteria

Patients below 18 years. Patients HIV negative status. Patients with extra-pulmonary tuberculosis. Patients, who were very ill confused, or mentally impaired (as they were not able to respond to questionnaire objectively); or who were reluctant or who refused to be part of the study.

3.5 Measuring tool or instrument

The investigator used a structured questionnaire to interview participants and measurement was achieved by means of closed questions (Appendix C). The questionnaire assessed

several of the known important risks factors associated with pulmonary tuberculosis, i.e. demographic variables, socio-economic status, habits, medical history, and environmental factors. The source data were questionnaire information, patients' medical files, the results of laboratory screening tests for Pulmonary Tuberculosis (Sputum for Acid Fast Bacilli (AFB) and TB cultures) and Chest X-rays.

3.6 Data collection

A total number of 300 participants were interviewed one-to-one in this study and questionnaires were used to collect data from participants. Then data collected were transferred into the pre-built data sheet in the Epi Info programme version 3.5.3 for further statistical analysis. To maintain the confidentiality of study participants, every questionnaire was allocated a code and this code linked the data entered into Epi Info.

The data collection took place during the working week, Monday to Friday between 8am and 4pm, ran over two months until the target sample size was obtained and took place between 9 January 2009 to 18 March 2009. No data collection took place on public holidays.

To ensure each subject was giving their informed consent, a staff nurse at the reception desk informed the patients about the ongoing study after registering the patient's personal details. After this stage, the interviewer personally introduced himself to the patients and briefly explained the background of the interviews, explaining that the study was voluntary and declining to participate would not involve any penalty or result in them being treated differently from other patients. The participants could refuse to take part in the study or refuse to answer any questions and were free to withdraw from the interview at any time.

After the staff nurse on duty had assessed the patients, their vital signs were taken and their number in the queue recorded. The interviewer proceeded to select every third patient in the queue, and the patient selected was considered as an eligible candidate to participate in the research. If this patient declined to participate, they received a verbal acknowledgement for their time and the next patient in the queue was asked if they would like to be included in the study.

The researcher was allocated a private room at the Wellness Clinic to guarantee privacy. All patients who wished to participate in the study were given the consent form to sign and participants were assured of their anonymity and the confidentiality of the research.

The content of the information leaflet and the consent form are shown in Appendix A and Appendix B respectively.

After the patients had given their written consent to participate, the researcher stored the consent form to protect the identity of participants and ensure confidentiality. The researcher was able to overcome any language barriers by providing training to two nurse assistants. The nurses were able to enhance clarity and accuracy of the interview process by communicating with patients in languages such as Zulu, and siSwati. The pilot study was also used to translate the response of patients into English.

The data collection process consisted of two parts

First, the researcher interviewed each participant to collect responses to the questionnaire. In order to determine the pulmonary tuberculosis status of the participants such as PTB positive (+) or PTB negative (-), the researcher collected information from the patients' medical files and then asked questions about their PTB symptoms, which included: chronic coughs; night sweats; blood stained sputum; loss of weight, etc. For those patients with the signs and symptoms of PTB, without diagnosis of pulmonary tuberculosis available in the medical file, the next stage was to request TB screening tests following the National Tuberculosis Management Guidelines 2009, still in force and based on the algorithm of TB diagnosis in a new case: HIV positive (Appendix H and I).

The researcher explained the need for pulmonary tuberculosis screening tests and obtained their verbal consent. The participants who agreed to the TB screening tests were informed about the importance of sputum specimen collection and the correct procedure to use. The nurse assistants also offered advice at this point to guarantee the quality of sputum collected. Thereafter, the patients with coughs with expectoration were taken to a designated area, and were asked to provide cough specimens. The procedure was to collect sputa for acid-fast bacilli (AFB) into a re-capable bottle. The researcher collected two specimens on two consecutive days for TB microscopy. The first specimen was collected on the day of the interview with the patient and the second specimen was collected in the early morning of the second day; the results of the tests were made available within 48 hours.

The researcher made a follow-up appointment with patients suspected of having PTB, explaining that the sputum results were confidential and anonymous and to ensure confidentiality, the researcher used a unique Barcode system to collect and store the laboratory test results. When a chest X-ray (CXR) was necessary, to protect the patients'

identity, names, files or x-ray film numbers were not used. Therefore, patients were categorized in this study as PTB positive or negative.

3.6.1 Data capturing

The data was entered from the questionnaire forms into the Epi Info programme version 3.5.3 where it was stored for further statistical analysis.

3.6.2 Pilot Study

A pilot study was conducted between 6 January 2009 and 8 January 2009 in the Wellness clinic, at Themba Hospital to test the measuring tool and the sampling methods. This process was done before the data collection was carried out for the study and involved 10 patients who were not part of the original research sample and a similar questionnaire was used.

This assessment helped the researcher to identify the strengths and weaknesses of the interview questions, to modify the content of some of the questions to make the process easier to understand, and to estimate the average interview duration.

The pilot served as a useful tool to train the two nurse assistants who volunteered to help with translation and it also provided ground to test the interviewer's ability to accurately use the questionnaire before the final data collection exercise. After the data collection, the data was input into the Epi Info programme and a minimized data analysis was carried out to serve as a framework for the analysis of the original research.

3.6.3 The questionnaire content

The researcher designed the questionnaire using the input of the supervisor, colleagues, and information gathered from previous studies. The questionnaire contained the most relevant known risks factors for pulmonary tuberculosis, which include: demographic characteristics; socioeconomic status; habits and lifestyle; medical history; and environmental factors.

The first part of the questionnaire was designed to determine demographic details of participants and this included age and sex. Other questions explored were designed to determine the risk factors and socio-economic status of patients and these included: level of education, marital status, and employment status. Other questions considered for the risk

factors are those related to patients' habits, which included level of alcohol consumption and smoking.

The last part of the questionnaire related to patients' medical history, which included any family history of PTB and previous history of PTB or treatment. Finally, the research also used patients' environmental factors, for example, living outdoors or in crowded conditions.

3.6.4 Sources of bias

Sampling bias

Sampling bias is unlikely in this study, due to the systematic selection of participants throughout the day every day of the week.

Information bias

Patients' memory, the presence of the interviewer and the environment of the consultation room could all have influenced information bias. To minimize bias in the study, a pilot study was conducted to test and adjust the measuring tool.

A structured questionnaire, coupled with closed questions and simple language was used in all of the questions. To overcome bias when the researcher examined the CXR of patients, the researcher requested a second opinion from a colleague, a senior TB expert, to ratify the radiological findings with the clinical picture of the cases and to establish an accurate diagnosis of PTB.

3.6.5 Ethic

Identification Issues

An anonymous questionnaire was used in this research and no participant names or file numbers were entered into the data programme. A sequence number was assigned to access the information in the Epi Info and the researcher only used a unique Barcode system to gather the information of sputum results from the laboratory and an order number was allocated for the chest X-ray results. The questionnaire form and the data in the Epi Info were protected in a safe place and retained as confidential material.

Benefits to the Institution

This research could be used to generate hypotheses for further studies. From the epidemiological point of view, the research hopes to make a modest contribution to medical fields which will be of benefit for healthcare professionals. No previous research of this kind has been conducted in this institution and therefore it is hoped that the results will enhance the greater understanding of risk factors for PTB in the locality.

Justice and fair process

This research is based on scientific evidence and has applied the principles of fairness and equality for inclusion and exclusion of criteria as defined in the criteria detailed in the previous section.

Benefits to the participants:

This study did not provide any financial remuneration or reward to the individuals included in the investigation. The contribution of participants was acknowledged and appreciated and if they required, will receive full feedback on the research.

Risks

This study did not include any risky procedures. The patients' physical, social and psychological welfare were protected at all times. Patients who were found to be confused or very ill were referred to casualty for appropriate medical attention.

Respect for participants

Patients were informed about the objectives of the research. They were told that the study was voluntary and declining to participate any time did not involve penalties or result in them being treated differently from other patients. The participants were free to refuse take part in the study, or to answer questions or withdraw from the interview at any time. Informed consent was required and patients were assured of their anonymity, privacy and study confidentiality. Participants were asked at the end of the session if they would like to know the results of the study and if they wished, a visit was arranged before the research was due to be completed so that the results could be revealed and explained.

Conflict of interest

The only conflict of interest that could be identified within the research was that of the researcher with the aim of completing master level degree studies in Family Medicine. There are no other conflicts of interest identified in this study.

Approval by the Research Ethics Committee

Approval by the Human Research Ethical Committee (HREC) (Medical) at Witwatersrand University was requested and a clearance certificate was obtained. Ethics clearance Number: M080416 (Appendix F and Appendix G).

Other approval or consent

Written consent and approval was obtained from the Chief Executive Officer, (Appendix D) as well as written consent and approval from The Clinical Manager of the Wellness Clinic of Themba Hospital (Appendix E).

3.7 Outcome Variable

The outcome variable for this study was PTB, i.e. a patient is undergoing treatment for pulmonary tuberculosis (Mycobacterium tuberculosis positive in bacteriological studies) and was diagnosed by laboratory examination or on clinical-radiological grounds (Appendix H and Appendix I).The source of the outcome variable was patients' clinical files and the results of TB screening tests (e.g. Sputum for Acid Fast Bacilli, TB cultures and Chest X-ray). In the absence of such information for patients' with signs and symptoms of PTB, the researcher performed screening tests (Appendix H).

3.8 Explanatory Variables

Explanatory variables in this study were as follows:

Age, gender, educational level, marital status, employment status, crowding ,smoking habits, level of alcohol consumption, previous medical history of PTB or treatment ,family history of PTB, living environment and conditions. Appendix J details for variables and definitions.

The influential factors/explanatory variables were extracted from the questionnaires data stored in the Epi Info database.

3.9 Data Analysis

Data were entered using the Epi-Info programme version 3.5.3 which generated an Excel sheet that was transferred to Stata Release 11 software for analysis. Frequencies, including rates and proportions were carried out on all of the categorical variables (sex, age group, marital status, etc.). A Pearson Chi-square (χ^2) test was applied to test for an association between risk factors for PTB and demographics variables among HIV positive patients, at Themba Hospital.

The subjects' under investigation were presented by the set of 11 variables mentioned above in section 3.8. This list of variables is presented in Appendix J.

Univariate and multivariable logistic regression models were used to investigate factors associated with PTB. Estimated Odds ratios were reported with 95% confidence intervals, and in all the analyses, a p-value of <0.05 was taken to be significant.

This data analysis was carried out with the help of a statistician in the Biostatistics Unit of the South African Medical Research Council (MRC) in Pretoria.

CHAPTER 4

RESULTS

4.1 Introduction

This chapter describes the overall findings of the study; the discussion follows the sequence of the objectives and the presentation of results categorized as follows:

- Socio-demographic information of the participants.
- Behavioural factors of the participants such as smoking and alcohol consumption.
- Medical history of the participants, which includes previous medical history of PTB or treatment, and family history of PTB.
- PTB prevalence of the participants.
- Comparison of risk factors among HIV patients (PTB-) and (PTB+) which includes socio-demographic characteristics, behavioural factors, and medical history.
- Risk factors for pulmonary tuberculosis among HIV patients.
- Logistic regression analysis.

4.1.1 Socio-demographic Information on the Participants

Table 4.1 presents the demographic characteristics of the study sample. The study comprised n=300 participants. The mean age of patients was 38.2 years with standard deviation (SD=10.9 years) and ranged from 18 to 86 years of age. Forty per cent of the participants were aged 31-40 years, with (63.6%) of the subjects aged under 41 years. More than half (67.0%) of the study's participants were females. In terms of educational level, this study found that more than two thirds of the participants (69.3%) were of low level educational backgrounds, including primary and secondary education. With regard to marital status, this study identified that more than half (65.7%) of the participants reported being single. The majority of participants (59.7%) were unemployed. A large proportion of the patients (63.3%) reported living in a non-overcrowded environment. Finally, the majority of the study participants (64.7%) reported living in dusty outdoor conditions.

Table 4.1: Socio-demographic information of the participants

Variables	Frequency (%)
Age group in years	
18-30	70(23.3%)
31-40	121(40.3%)
41-50	64(21.3%)
>50	45(15.1%)
Sex	
Female	201(67.0%)
Male	99(33.0%)
Level of education	
High School/ University Degree	68(22.7%)
Primary/ Secondary	208(69.3%)
Illiterate/No Formal Education	24 (8.0%)
Marital Status	
Married/ Cohabitation	72(24.0%)
Widowed/ Divorced	31(10.3%)
Single	197(65.7%)
Employment Status	
Presently Employed	93(31.0%)
Pensioner	28(9.3%)
Unemployed	179(59.7%)
Household class	
Normal	190(63.3%)
Overcrowded	110(36.7%)
Outdoor Environment	
Clear	106(35.3%)
Dusty	194(64.7%)

4.1.2 Participants' Behavioural Habits

Table 4.2 shows the smoking habits and different levels of alcohol consumption among the participants. The result indicates that the majority of the patients (75.0%) were non-smokers and that most of the participants (89.7%) were non-drinkers.

Table 4.2: Participants' Behavioural Habits

Variables	Total n=300(%)
Smoking	
No	225(75%)
Yes	75(25%)
Drinking habit	
Non-Drinker/ Light Drinker	269(89.7%)
Moderate Drinker/ Heavy Drinker	31(10.3%)

4.1.3 Medical history of the participants

The data shows that approximately half of the patients (52.7%) reported not to have previous medical history of PTB or treatment. And more than half (65.0%) of the participants reported not to have a family history of PTB (Table 4.3).

Table 4.3: Medical history of the participants

Variables	Total n=300(%)
Previous medical history/treatment of PTB	
Yes	142(47.3%)
No	158(52.7%)
Family history of PTB	
Yes	105(35.0%)
No	195(65.0%)

4.1.4 PTB prevalence among the participants

More than half (67.3%) of the participants were PTB-, whilst 32.7% individuals were PTB+ (Figure 4.1). In this study research from the total of 98 PTB+ subjects in 72 patients the confirmation of the PTB + status was obtained from the information available in the patient's medical files, whilst for the remaining 26 cases, the researcher carried out screening tests for PTB.

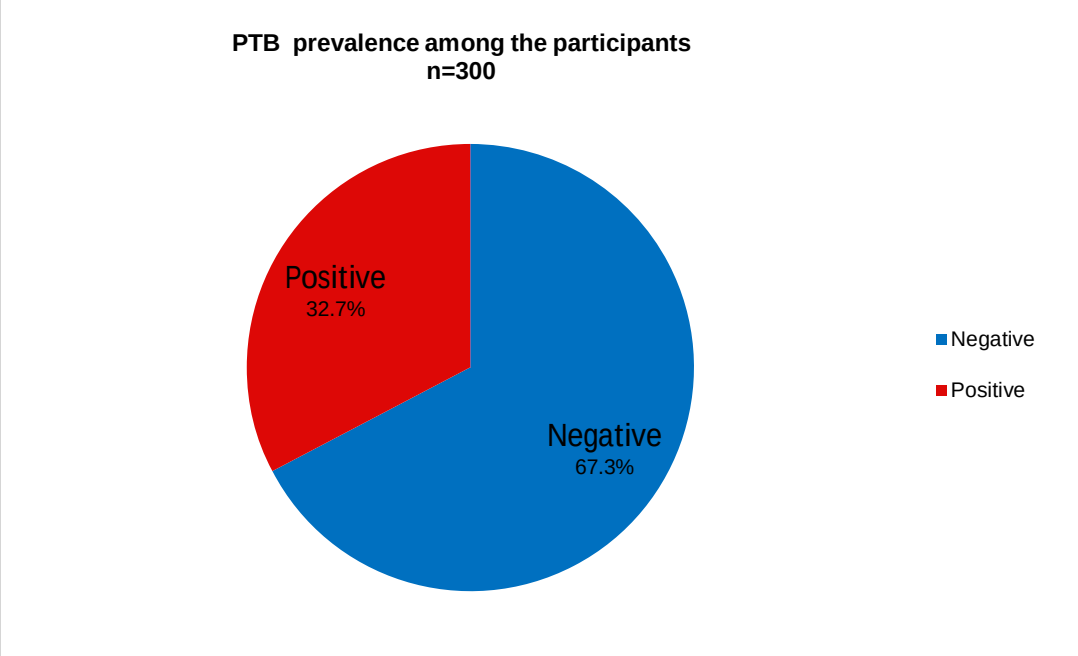


Figure 4.1: PTB prevalence among the participants

4.2 Comparison of risk factors among HIV patients PTB- and PTB+

4.2.1 Socio-demographic characteristics among HIV patients PTB- and PTB+

The socio-demographic characteristics of HIV patients are presented in Table 4.4. It was apparent that in the age group 31- 40, the highest number of participants (62.0%) belonged to the PTB- group while the PTB+ group contained only 38%. This study also identified a greater number of female participants in both the PTB- (69.6%) and in the PTB+ group (30.4%), compared with their male counterparts. In terms of educational level, this study found that the majority of participants who had completed primary and secondary education (68.3%) were in the PTB- group, while the PTB+ group consisted of 31.7%. With regard to marital status, a higher number of patients who reported being single (62.9%) were in the PTB- group compared with 37.1% singles in the PTB+ group. Furthermore, there were more unemployed participants in the PTB- group (65.9%) than in the PTB+ group (34.1%). The majority of patients (69%) who reported that they did not live in overcrowded households belonged to the PTB- group, compared with 31.0% in the PTB+ group. Finally, a larger number of participants who reported living in a dusty outdoor environment (61.9%) were also identified in the PTB- group compared with 38.1% in the PTB+ group.

Table 4.4: Socio-demographic characteristics among HIV patients PTB- and PTB+

Variable &category	PTB- n=202(%)	PTB + n=98(%)	Total n=300	χ^2	P-value
Age group in yrs.					
18-30	53(75.1%)	17(24.9%)	70	4.85	0.183
31-40	75(62.0%)	46(38.0%)	121		
41-50	41(64.0%)	23(36.0%)	64		
>50	33(73.3%)	12(26.7%)	45		
Sex					
Female	140(69.6%)	61(30.4%)	201		
Male	62(62.6%)	37(37.4%)	99	1.48	0.222
Level of education					
High School/ University Degree	43(63.2%)	25(36.8%)	68	0.77	0.692
Primary/ Secondary	142(68.3%)	66(31.7%)	208		
Illiterate/No Formal Education	17(70.8%)	7(29.2%)	24		
Marital Status					
Married/ Cohabitation	56(77.8%)	16(22.2%)	72	5.48	0.064
Widowed/ Divorced	22(71.0%)	9(29.0%)	31		
Single	124(62.9%)	73(37.1%)	197		
Employment status					
Presently Employed	64(68.8%)	29(31.2%)	93	0.46	0.791
Pensioner	20(71.4%)	8(28.6%)	28		
Unemployed	118(65.9%)	61(34.1%)	179		
Household class					
Normal	131(69.0%)	59(31.0%)	190	0.61	0.433
Overcrowded	71(64.6%)	39(35.4%)	110		
Outdoor Environment					
Clear	82(77.4%)	24(22.6%)	106	7.48	0.006*
Dusty	120(61.9%)	74(38.1%)	194		

*p<0.05

4.2.2 Behavioural factors of HIV patients PTB- and PTB+

The data in Table 4.5 indicate that a large proportion of participants who reported being smokers (64%) were in the PTB- group compared with the number of smokers (36%) in the PTB+ group.

It was apparent that there was a difference in proportion between the PTB+ and PTB- groups. For instance, in the categories of moderate or heavy drinker, the proportion was higher in the PTB+ group (58.1%), compared to the same drinking categories (41.9%) in the PTB- group (Table 4.5).

Table 4.5: Behavioural factors of HIV patients PTB- and PTB+

Variables	PTB- n=202(%)	PTB + n=98(%)	Total n=300	χ^2	P-value
Smoking					
No	154(68 .4%)	71(31.6%)	225	0.50	0.477
Yes	48(64.0%)	27(36.0%)	75		
Drinking category					
Non-Drinker/ Light Drinker	189(70.3%)	80(29.7%)	269	10.1	0.001*
Moderate Drinker/ Heavy Drinker	13(41.9%)	18(58.1%)	31		

*p<0.05

4.2.3 Medical history of HIV patients PTB- and PTB+

The PTB- group had a greater number of participants who had no previous medical history of PTB or treatment (70.9%) compared with 29.1% in the PTB+ group. Moreover, in the PTB- group there were more individuals who did not report a family history of PTB (67.2%) compared to only 32.8% in the PTB+ group (Table 4.6).

Table 4.6: Medical History of HIV patients PTB- and PTB+

Variables	PTB n=202(%)	PTB+ n=98(%)	Total n =300	χ^2	P- value
Previous medical history/treatment of PTB					
No	112(70.9%)	46(29.1%)	158	1.91	0.166
Yes	90(63.4%)	52(36.6%)	142		
Family history of PTB					
No	131(67.2%)	64(32.8%)	195	0.006	0.938
Yes	71(67.6%)	34(32.4%)	105		

*p<0.05

4.3 Risk factors for pulmonary tuberculosis

There was a statistically significant association between PTB status and living in a dusty outdoor environment (p=0.006) (Table 4.4). PTB categories differed significantly with respect to the reporting of being a moderate drinker/heavy drinker (p=0.001) (Table 4.5).

4.4 Logistic regression analysis

4.4.1 Univariable logistic regression model for risk of pulmonary tuberculosis

The univariable analysis was conducted to identify significant risk factors associated with PTB in order to inform the multivariable model (Table 4.7).

In summary, compared with individuals who self-reported as being non-drinkers or light drinkers, moderate and heavy drinkers had increased odds of pulmonary tuberculosis (OR=3.27; 95% CI=1.51-7.09). When compared with being married or cohabiting, being widowed or divorced, single marital status increased the odds of PTB (OR= 2.06; 95% CI=1.09-3.88).The odds of PTB were also higher for individuals living in a dusty outdoor environment (OR= 2.11; 95% CI=1.22-3.64) (Table 4.7).

Table 4.7: Logistic regression analysis for risk factors of pulmonary tuberculosis

Variable & category	Univariate OR (95% CI)	P-value (p<0.05)*	Multivariate OR (95% CI)	P-value (p<0.05)*
Age group in years				
18-30	1	-		
31-40	1.91(0.98;3.72)	0.052		
41-50	1.75(0.82;373)	0.142		
>50	0.13(0.48;2.68)	0.775		
Marital Status				
Married/ Cohabitation	1	-	-	-
Widowed/ Divorced	1.43(0.55;3.74)	0.462	1.48 (0.54;403)	0.445
Single	2.06(1.09;3.88)	0.022*	1.96 (1.01;3.79)	0.047*
Drinking category				
Non-Drinker/ Light Drinker	1	-	-	-
Moderate Drinker/ Heavy Drinker	3.27(1.51;7.09)	0.001*	3.46(1.56;7.69)	0.002*
Outdoor Environment				
Clear	1	-	-	-
Dusty	2.11(1.22;3.64)	0.006*	2.05(1.16;3.61)	0.013*

Note. CI= confidence interval: OR=odds ratio: *significant at p<0.05

4.4.2 Multivariable logistic regression model for risk of pulmonary tuberculosis

In multivariable logistic regression models, an analysis of the variables was assessed. In the final multivariable model, all factors were assessed together. Only factors found to be significantly associated with PTB (p<0.05) were retained in the final model. Single marital status was significantly associated with PTB (p=0.047) (OR=1.96; 95% CI=1.01-3.79). Being a moderate or heavy drinker remained strongly associated with pulmonary tuberculosis (p=0.002) (OR=3.46; 95%CI=1.56-7.69). Living in a dusty outdoor environment was also significantly associated with pulmonary tuberculosis (p=0.013) (OR=2.05; 95% CI=1.16-3.61) (Table 4.7).

CHAPTER 5

DISCUSSION

5.1 Introduction

The main objective of this study was to assess the risk factors for PTB among adult HIV patients attending the wellness clinic at Themba Hospital. A sample of 300 patients was used and data was collected over a two-month period.

The most interesting findings to emerge from this study were that single marital status, a dusty outdoor environment, and being a moderate to heavy drinker were identified as risk factors significantly associated with PTB among adult HIV positive patients at this hospital. However, contrary to expectations, age, gender, educational attainment, employment status, crowding, smoking, previous medical history of PTB or treatment, and a family history of PTB showed not to be associated with pulmonary tuberculosis.

5.1.1 Marital Status

More than half of the participants reported being single, meaning that this investigation was able to demonstrate that being single increases the risk of PTB.

According to Lienhardt et al, marital status has long been associated with the risk of developing TB in Africa. The authors suggest that the most plausible mechanism of this association is that family structure seems to play a role, since it determines the risk of exposure and reflects the socio-economic status of individuals.[40] On the other hand, it has been indicated that marital status affects the risk of TB, with single men having a greater risk of TB than married men. [40, 56]

Similar findings to this investigation were reported in a study conducted in Guinea-Bissau which illustrated that being single and living alone was an independent risk factor for contracting TB.[56] A multi-centre study conducted in three Western African countries showed that single marital status was a risk factor for TB.[40] Moreover, Wang et al, in a case control study conducted in Henan, China, reported that being single was a risk factor of PTB.[64]

On the other hand, a recently published study, conducted in South Africa found that cohabiting was statistically associated with PTB,[65] while a study conducted in Estonia

reported that any marital status other than being married was the main risk factor for contracting tuberculosis.[25]

Cain et al, suggested that being single implies a lack of family support,[48] according to these researchers, vulnerability to TB could increase at times of psychosocial stress. However, according to Pang et al, marital status is also closely associated with other socio-economic characteristics, and they suggest that it would be extremely difficult to distinguish its effect from the many possibly confounding variables in a simple study.[66]

Therefore, based on this study results, further studies exploring the direct effect of family structure at the individual level are needed to accurately determine the mechanism underlying this perceived association.

5.1.2 Outdoor Environment / Dusty Environment

The data reveal that living in dusty outdoor conditions increases the risk of pulmonary tuberculosis. After an extensive review of the literature on dusty outdoor environments as a contributory risk factor for pulmonary tuberculosis, there is surprisingly scanty information available on this topic in South Africa. The majority of published studies in the country were mainly related to occupational health environments and the mining industry.[67] Therefore, this is a clear indication that further research is required in this particular field.

A study in the country indicated that dust control management is an important component when attempting to decrease the impact of the PTB epidemic in South African gold mines.[67] Another study reported that older in-service gold miners in South Africa have a high prevalence of PTB, which is significantly associated with dust and silica exposure, even in the absence of silicosis.[37] A population-based case-control study conducted in China revealed that a poor environment and exposure to dust were risk factors for adult PTB in that region.[54]

It is also well recognized that better atmospheric conditions lead to a better quality of life, which could enhance the immunological function of patients who suffer from PTB. It follows that better environments and/or working conditions may reduce the risk of individuals developing pulmonary tuberculosis.

5.1.3 Drinking Habits; Moderate and Heavy Drinkers

As revealed by the analysis and the statistically significant result, adult HIV patients who are moderate and heavy drinkers were found to be more at risk for contracting pulmonary tuberculosis.

Moreover, the present finding seems to be consistent with other studies, which have reported alcohol use as a recognised risk factor for tuberculosis. In particular, a study conducted by Lönnroth et al, attributed the risk of active tuberculosis to be substantially elevated in people who drink more than forty grams of alcohol per day, and/or have an alcohol use disorder. The researchers indicate that this may be due to both increased risk of infection related to specific social interaction patterns associated with alcohol use as well as alcohol's influence on the immune system and alcohol related conditions.[33]

It has been suggested in the same report that these specific social interaction patterns may increase the risk of exposure to people with infectious TB disease in settings such as bars, shelters for homeless, prisons and social institutions.[33] A study in a high incidence area of Western Cape Province, South Africa, conducted between1993 – 1996, reported that most PTB transmission took place outside of households, and that 58% of the identified contacts outside the home occurred whilst drinking in social groups.[68]

The present study's finding is consistent with those which have reported alcohol use as a strong risk factor for TB in South Africa. An early study carried out on the Mamre population showed that alcohol use was strongly associated with TB.[59] More recently, Harling et al*,* reported alcohol use as an independent risk factor for TB in South Africa.[61]

Furthermore, studies from different parts of the world have also reported that alcohol use is a risk factor for tuberculosis. A case-control study carried out in Estonia found that alcohol consumption was a risk factor for tuberculosis.[25] A systematic review conducted by Rehm et al, reported that heavy alcohol consumption and alcohol use disorders (AUD) constitute a risk factor for the incidence of and re-infection with TB.[35]

Contrary to the finding of the present study, there are other studies which have indicated no association between alcohol and tuberculosis. A recently published study in South Africa reported that alcohol use was not in fact associated with TB.[65] In West Africa, Lienhardt et al*,* reported that alcohol intake was not associated with TB after adjusting for other factors.[40] The Gambian study showed evidence that alcohol use was not a strong predictor of TB.[55]

A study conducted in India showed no effect of alcohol consumption on TB; these authors suggested that the weak association between alcohol and tuberculosis could be attributed to the fact that alcohol use is associated with smoking.[52]

It is the researcher's opinion that there is growing evidence from within and outside the country that supports the association between alcohol and tuberculosis, and supports the variety of widely known harmful effects of alcohol.

5.2 Study limitations

This was a cross sectional descriptive study and could only measure an event at one specific point in time. On the other hand, it could not provide information about cause and effect or sequence of events. In view of the findings, and the method and design employed in this research, it is important to acknowledge some limitations, which this kind of study might impose. Such limitations could have influenced the data collected and the conclusions reached.

One limitation of the study could be related to the accuracy of participant feedback during interviews. As this interview data relied on what the patients said, participants' answers could have been influenced by different factors, including ability to accurately recall experiences, or embarrassment, leading to inaccurate information being given.

The researcher could still infer the role of other factors such as patient honesty, educational level, fear to disclose personal issues, time restraints, reluctance to report embarrassing or socially undesirable behaviours (e.g. smoking and alcohol abuse) etc.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The assessment of risk factors for pulmonary tuberculosis is an important component to obtain a better understanding of the epidemiology of tuberculosis. The purpose of the current study was to examine risk factors for Pulmonary Tuberculosis in adult patients suffering from Human Immunodeficiency Virus (HIV) attending the Wellness Clinic at Themba Hospital. The results of this investigation showed that being of single marital status, living in a dusty outdoor environment and being a moderate or heavy drinker were all strongly associated with an increased risk of PTB for the study participants.

Our findings have obvious important implications for TB control strategies both in the region and nationally, particularly in areas of the country where a high proportion of pulmonary tuberculosis can be attributed to alcohol use, a dusty outdoor environment and single marital status. The main implication of these findings is that interventions and strategies to minimize the impact of these risk factors for TB should be considered as a matter of priority by health and government authorities.

6.2 Recommendations

1. There is a need to develop specific programmes for screening and detecting alcohol use disorders (AUD) in patients being treated for PTB at the Wellness Clinic in Themba Hospital. This could also be applied to other TB health institutions across the country.

2. The findings presented in this study suggest that government authorities should continue to address and assist the critical social problems of the poor and disadvantaged populations within South Africa. There is a need to prevent or reduce dust emissions mainly from the unpaved roads of rural areas, which could improve the outdoor air quality and subsequently, the population's health.

3. Across the country, health policy makers need to further develop strategies and interventions to limit the impact of the risk factors for developing pulmonary tuberculosis.

4. To that end, further research on these risk factors for TB may be beneficial to extend the scope of this study and enable more positive health interventions and a local and national level.

APPENDICES

APPENDIX A

INFORMATION ABOUT THE PURPOSES OF THE RESEARCH

Date of the research: January to February 2009

Title of the research: An assessment of risk factors for PTB among HIV adult patients attending the wellness clinic at Themba hospital.

Dear patient

My name is Dr. Félix Alberto Herrera Rodriguez.

I am a student in the Family Department at the Witwatersrand Medical School. As part of the requirement for my masters in Family Medicine, I have to conduct a research. I have selected to carry out a study about of risk factors for PTB among HIV adult patients attending the wellness clinic at Themba Hospital.

Over a period of one month, all patients18 years old or older attending wellness clinic will be requested for an interview. Participation in the research is voluntary and you are therefore free to consent to the interview or not. There will not be any penalty or reward for participation or non-participation.

Herewith I am inviting you to participate in my research project. I would like you to assist me by answering a questionnaire. In this study, I will ask some questions to obtain information from you and other patients, about the risks factors for PTB in our clinic. The Hospital Manager and the Family Medicine Department at University of Witwatersrand in Johannesburg have approved this research.

I will appreciate your participation and your support during the interview answering the questionnaire herewith included. All the responses that you give will remain confidential and will be accessible only to me as the researcher. Your name will not be recorded and there will not be any mark on the questionnaire to reveal your identity.

The results of the research will be presented to the University of Witwatersrand, and to the Hospital Manager. Should you want to know more about the study you are welcome to contact me on the numbers and other contact details supplied herewith.

The time you will spend in answering this question will be approximately 10 minutes or less, and this will be in a private room where the interview process will take place, you will have all the assistance or clarification in the content of the questions. You right not to answer any of the asked will be respected at all times.

If you are willing to partake in the study, please do so now. If you do not want to participate, feel free to do so.

Thank you for your understanding and cooperation.

_____

Dr. Félix Alberto Herrera Rodriguez. (Student)

The Researcher

Family Medicine Department

University of the Witwatersrand

Cell: 072 532 6160/ e-mail alifelix@lantic.net

APPENDIX B

CONSENT FORM

Consent Form

I _____

Patient attending the Wellness Clinic at Themba Hospital, herewith Consent/ do not consent

to take part in the research title: An assessment of risk factors for Pulmonary Tuberculosis among adult patients suffering from Human Immunodeficiency Virus attending the wellness clinic at Themba Hospital.

Conducted by Dr. Félix Alberto Herrera Rodriguez.

_____ (Signature) or thumbprint.

Date: _____

APPENDIX C

QUESTIONNAIRE

(This is an anonymous document) **Date:** _____

Questionnaire Number _____ (for official use only)

1. **Age……** Years.
2. **Sex:** Male / Female.
3. **Level of education.**

- Primary ☐
- Secondary ☐
- High School ☐
- University Degree. ☐
- Other ----------(specify)
- No formal education ☐
- Illiterate ☐

4. **Employment status?**

- Present Employment ---------- (Occupation)
- Unemployed ☐
- Pensioner ☐

5. **Marital Status?**

a. Married ☐
b. Single ☐
c. Divorced ☐
d. Cohabitating ☐
e. Widowed ☐

6. **Do you drink alcohol? Yes/No**

- If yes, what do you normally drink? ---------- (Specify name of alcohol group beer, wine, whisky, etc)
- How often do you drink? ---------- (Times per day/week/month etc)
- How much do you drink? ---------- (Specify quantity in glass, pint, tot, bottles, etc)

7. **Do you smoke? Yes/No**

If yes, How many cigarettes per day? Sticks or pipes or snuff?

0 – 10 ☐

11- 20 ☐

> 20 ☐

8. **No. of persons in Household** ☐
9. **No. of bedrooms in the house** ☐
10. **Family history of TB Yes/No**
11. **Past history of TB or treatment Yes/No**
12. **TB test result Positive/ Negative**
13. **Reported tuberculosis symptoms or signs**

in last 3 months Yes/No

If yes, which of these of the following:

Symptoms or signs of PTB	**Yes**	**No**
Cough		
Coughing blood		
Low of Weight		
Night Sweating		
Fever		
Tiredness		

14. Living outdoor environment

Outdoor living environment	Yes	No
Dusty		
Clear		

APPENDIX D

LETTER OF APPROVAL FORM HOSPITAL CEO

MPUMALANGA PROVINCIAL GOVERNMENT

1213 Kabokweni Main Road
Kabokweni
1245
South Africa

Private Bag X 1002
Kabokweni 1245
Tel.: (013) 796 9400
Fax: (013) 796 0339
Fax: (013) 796 1276

Department of Health and Social Services
THEMBA HOSPITAL

Litiko Letemphilo
Nemisebenti Yenhlalakahle

Umnyango WezePilo
neZehlalakuhle

Departement van Gesondheid
en Maatskaplike Dienste

Enq.: MJ SHABANGU **25 March 2008**

Dear Dr Felix A Herrera Rodriguez

RE: PERMISSION TO CONDUCT RESEARCH AT WELLNESS CLINIC OF THEMBA HOSPITAL

Study Title: An assessment of risk factors for PTB among adult patients with HIV attending the wellness clinic at Themba Hospital.

Principal investigator: Dr Felix A Herrera Rodriguez
Contact Details: Tel: 013 976 9400 Fax: 013 796 0339 Cell: 0725326160

With reference to the above study we are pleased to inform you that Dr Felix A Herrera Rodriguez has been granted permission to conduct research at the wellness clinic at the Themba Hospital.

I understand that the study will involve interviews patients attending wellness clinic at the hospital.

We would also like the study to follow all protocols as outlined in your study proposal and should there be any changes, Mr MJ Shabangu should be informed immediately.

At the end the study Dr Felix A Herrera Rodriguez will be expected to share his search findings with Themba Hospital Management.

Thank you

M.J. SHABANGU
ACTING CEO

APPENDIX E

LETTER OF APPROVAL FORM WELLNESS CLINIC HEAD OF UNIT

MPUMALANGA PROVINCIAL GOVERNMENT

1213 Kabokweni Main Road
Kabokweni
1245
South Africa

Private Bag X 1002
Kabokweni 1245
Tel.: (013) 796 9400
Fax: (013) 796 0339
Fax: (013) 796 1276

Department of Health and Social Services
THEMBA HOSPITAL

Litiko Letemphilo
Nemisebenti Yenhlalakahle

Umnyango WezePilo
neZehlalakuhle

Departement van Gesondheid
en Maatskaplike Dienste

Enq.: R. Ntambi **25 March 2008**

Dear Dr Felix A Herrera Rodriguez

RE: PERMISSION TO CONDUCT RESEARCH AT WELLNESS CLINIC OF THEMBA HOSPITAL

Study Title: An assessment of risk factors for PTB among adult patients with HIV attending the wellness clinic at Themba Hospital.

Principal investigator: Dr Felix A Herrera Rodriguez
Contact Details: Tel: 013 976 9400 Fax: 013 796 0339 Cell: 0725326160

With reference to the above study we are pleased to inform you that Dr Felix A Herrera Rodriguez has been granted permission to conduct research at the wellness clinic at the Themba Hospital.

I understand that the study will involve interviews patients attending wellness clinic at the hospital.

We would also like the study to follow all protocols as outlined in your study proposal and should there be any changes, Dr Ntambi should be informed immediately.

At the end the study Dr Felix A Herrera Rodriguez will be expected to share his search findings with Themba Hospital Management.

Thank you

DR R. NTAMBI
HEAD OF THE WELNESS CLINIC

APPENDIX F

LETTER OF APPROVAL FROM THE ETHICS COMMITTEE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Rodriguez

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M080416**
PROJECT	An assessment of risk factors for pulmonary tuberculosis among adult patients with HIV attending the wellness clinic at Themba Hospital
INVESTIGATORS	Dr FAH Rodriguez
DEPARTMENT	Family Medicine
DATE CONSIDERED	08.04.25
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 08.05.07 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr S Onojaagbo

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX G

LETTER OF APPROVAL FROM THE FACULTY

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2745

Reference: Ms Tania Van Leeve
E-mail: tania.vanleeve@wits.ac.za
11 August 2008
Person No: 0616892M
PAG

Dr FA Herrera Rodriguez
P O Box 4320
WHITE RIVER
1240
South Africa

Dear Dr Herrera Rodriguez

Master of Family Medicine: Approval of Title

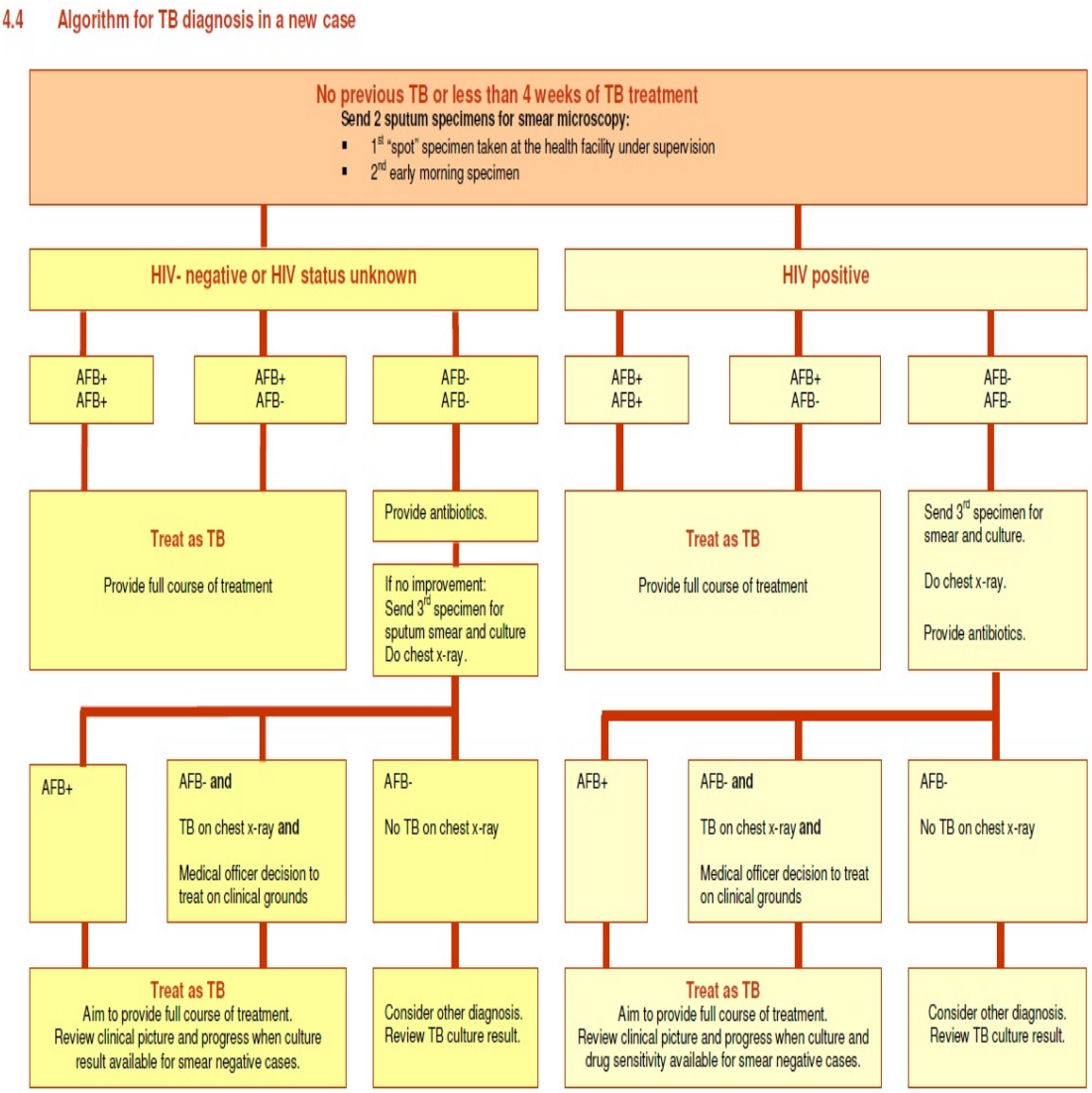
We have pleasure in advising that your proposal entitled "*An assessment of risk factors for pulmonary tuberculosis among adult patients suffering from hum immunodeficiency virus attending the wellness clinic in Themba hospital*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX H

ALGORITHM FOR TB DIAGNOSIS IN A NEW CASE



Algorithm for TB diagnosis in a new case (source: Department of Health. National Tuberculosis Management Guidelines; 2009.p. 25)

APPENDIX I

DEFINITION OF CATEGORIES

PTB positive (PTB+) Status: All patients undergoing treatment for pulmonary tuberculosis (Mycobacterium tuberculosis positive in bacteriological studies) diagnosed by laboratory examination or on clinical-radiological grounds.

PTB negative (PTB-) Status: All patients without diagnosed of pulmonary tuberculosis (No Mycobacterium tuberculosis detected in bacteriological studies) no clinical or radiological evidence of PTB.

Drinking Categories of the participants:

Based on Dawson and colleagues (1995) definitions, where one drink is equivalent to 0.5 fluid ounces (fl oz) alcohol. Patients were classified in this study as follows:

1. Light drinker: drinks 0.01 to 0.21fl oz alcohol per day (i.e., 1 to 13 drinks per month)
2. Moderate drinker: drinks 0.22 to 1.00 fl oz alcohol per day (i.e., 4 to 14 drinks per week)
3. Heavy drinker: drinks more than 1.00 fl oz alcohol per day (i.e., more than 2 drinks per day).

Definition of housing overcrowding among of the participants:

Crowding in households relates to situations where the number of people residing in a household exceeds the capacity of the household to provide adequate shelter and services to its members. There is not universally accepted definition of what constitutes an overcrowded household, this study utilises the Canadian National Occupancy Standard (CNOS) based on overcrowding housing number of persons/bedroom.

The CNOS assesses the bedroom requirements of a household by specifying that:

- There should be no more than two persons per bedroom
- Children less than 5 years of age of different sexes may reasonably share a bedroom
- Children less than 18 years of age and of the same sex may reasonably share a bedroom
- Single household members aged 18 years and over should have a separate bedroom, as should parents or couples
- Alone person household may reasonably occupy a bed sitter.

APPENDIX J

VARIABLES OF INTEREST AND THEIR DEFINITIONS

Variables	Categories	Definition
General socio-demographic		
Age group in years	0=18-30 1=31-40 2=41-50 3=>50	Age group
Sex	0= Female 1= Male	Sex
Level of education	0=High School/ University Degree 1=Primary/ Secondary 2=Illiterate/No Formal Education	Level of education
Marital Status	0=Married/ Cohabitation 1=Widowed/ Divorced 2=Single	Marital Status
Employment Status	0=Presently Employed 1=Pensioner 2=Unemployed	Employment Status
Household class	0=Normal 1=Overcrowded	Household class
Outdoor Environment	0=Clear 1=Dusty	Outdoor Environment
Behavioural factors		
Smoking	0=No 1=Yes	Smoking
Drinking habit	0=Non-Drinker/ Light Drinker 1=Moderate Drinker/ Heavy Drinker	Drinking habit
Medical history		
Previous medical history/treatment of PTB	0=No 1=yes	Previous medical history/treatment of PTB
Family history of PTB	0=No 1=yes	Family history of PTB

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