RISK FACTORS FOR PULMONARY TUBERCULOSIS AND THE EFFECT OF CHEMOTHERAPY ON THE QUALITY OF LIFE OF INFECTED PATIENTS IN NAIROBI CITY COUNTY, KENYA

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DEDICATION

This work is dedicated to my late parents; Jenaro Karimi and Ruth Wangeci. It is their sacrifice and guidance that greatly contributed to my success.

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CONTENTS

ABBREVIATIONS

ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
ALP	Alkaline Phosphatase
AOR	Adjusted Odds Ratio
AST	Aspartate Aminotransferase
BMI	Body Mass Index
CDC	Centre for Disease Control
CHS	Centre for Health Solutions
CI	Confidence Interval
COR	Crudes Odds Ratio
DOTS	Directly Observed Therapy, Short-course
DI	Dimension index
DLM	Delaminid
DKP	Dimension of Knowledge for Prevention
DKSS	Dimension of Knowledge on Sign and Symptoms
DKT	Dimension of Knowledge on Transmission
DKTr	Dimension of Knowledge on Treatment
EMB	Ethambutol
EN	Environment
ENT	Ear/Nose/Throat
GIT	Gastrointestinal Tract
HB	Haemoglobin
HIV	Human Immunodeficiency Virus
HRQoL	Health-Related Quality of Life
INH	Isoniazid
LFTs	Liver Function Tests
LTBI	Latent TB Infection
MDR-TB	Multidrug -Resistant Tuberculosis
MSS	Musculoskeletal System

MTB	*Mycobacterium tuberculosis*
MCS	Mental Component Summary
MH	Mental Health
NS	Nervous System
OKI	Overall Knowledge Index
OKL	Overall Knowledge Level
OQOL	Overall Quality of Life
OQoLBT	Overall Quality of Life before treatment
OQoLDT	Overall Quality of Life during treatment
PF	Physical Functioning
PH	Physical Health
PS	Psychological Health
PZA	Pyrazinamide
RBC	Red Blood Cells
RIF	Rifampicin
RP	Role Play
RS	Respiratory System
SD	Standard Deviation
SF-36	Short-Form 36
SES	Social Economic Status
SR	Social Relationships
STATA	Statistics and Data Software
TB	Tuberculosis
UEC	Urea, Electrolytes, Creatinine
UNDP	United Nations Development Program
VT	Vitality
WHO	World Health Organization
WHOQOL- BREF	World Health Organization Quality of Life- brief
WBC	White Blood Cells
XDR-TB	Extensively Drug-resistant Tuberculosis
ZN	Zeel Neelsen

DEFINITION OF TERMS

Adherence	The extent to which the patient's behavior in medication taking corresponds to the recommendation of a healthcare provider. It involves use of drugs at the right dose, frequency, and duration.
Cases	Participants with a confirmed diagnosis of pulmonary tuberculosis.
Continuation Phase	The second phase of tuberculosis treatment. For participants on firstline TB therapy, it was four months but for those on MDR-TB treatment, it was twelve months.
Controls	Participants who were not suffering from tuberculosis.
Cross-Resistance	Resistance occurring between drugs that are chemically related and/or have a similar target within the mycobacterium cell.
Environment	Aspects that influence the ability to interact with the surrounding effectively. The components are the availability of financial resources, freedom, physical safety and security, health and social care: accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in opportunities for recreation/leisure activities, physical environment (pollution/noise / traffic/climate) and mode of transport. The score was expressed as a percentage.
Hepatotoxicity	Damage or injury to the liver. It is characterized by elevated levels of serum liver enzymes. In this study, elevated alanine aminotransferase above 40 IU/L was a marker for hepatotoxicity.
Health-Related Quality of Life	A multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning. It focuses on the impact health status has on quality of life. The score was expressed as a percentage.

Hypothyroidism	Hypofunction of the thyroid gland. Thyroid stimulating hormone level above 4.2 mU/L was used as the marker of hypothyroidism.
Hyperthyroidism	Defined as hyperfunction of the thyroid gland. Thyroid stimulating hormone level below 0.27 mU/L was used as the marker for hyperthyroidism.
Hyperkalemia	Elevated level of serum potassium beyond the normal values. In this study potassium level above 5.1, mmol/L was recognized as hyperkalemia.
Hypokalemia	Low serum potassium level. In this study, potassium serum concentration below 3.5mmol/L was recognized as hypokalemia.
Intensive Phase	The first phase of tuberculosis treatment. For participants on first-line TB therapy, it was two months but for those on MDR-TB treatment, it was eight months.
MDR-Tuberculosis	Tuberculosis caused by *Mycobacterium tuberculosis* that is resistant to rifampicin and isoniazid.
Newly diagnosed participants	Participants without a history of active Tuberculosis infection.
Nephrotoxicity	Damage or injury to the kidneys. It is characterized by elevated serum creatinine. Concentration above 106 µmol/L was interpreted as nephrotoxicity.
Physical Health	A state of well-being when all internal and external body parts, organs, tissues, and cells can function properly as they are supposed to function. The components of physical health investigated were; activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility, pain, and discomfort, sleep and rest and work capacity. The score was expressed as a percentage.

Psychological Health	Emotional, behavioral, and social maturity of a person. The components of psychological health investigated were; bodily image and appearance, feelings, self -esteem, spirituality, and ability to think, learn, memorize and concentrate on different activities. The score was expressed as a percentage.
Quality of Life	The general well-being of individuals and societies, outlining negative and positive features of life. It measures life satisfaction, including physical health, family, education, employment, wealth, religious beliefs, finance and the environment.
Smoking	Use of cigarettes before or during treatment for tuberculosis.
Social Relationships	Ability of an individual to effectively interact with others. In this study the indicators considered were the quality of personal relationships, availability of social support and satisfaction derived from the sexual activity. The score was expressed as a percentage.
Primary Resistance	The development of active TB after infection with resistant strains.
Relapsed Cases	Patients who had a previous TB infection that was treated but recurred after remission.

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ABSTRACT

BACKGROUND

According to World Health Organization, there were 10.4 million cases of tuberculosis worldwide in 2015 and eighty-seven percent of the victims were in Asia and Africa. Kenya is among the countries with high burden of tuberculosis in Africa. The risk factors and the increase in the incidence of drug-resistant strains of *Mycobacterium tuberculosis* coupled with HIV infection poses a big challenge in the control of the disease. The anti-tuberculosis drugs have adverse effects which affects quality of life. Health-related quality of life has not been considered as an important factor during treatment of pulmonary tuberculosis. Lack of attention to the quality of life of patients causes poor treatments outcomes since some of the adverse reactions are debilitating and interfere with their daily activities.

OBJECTIVE

To determine the risk factors for pulmonary tuberculosis and the effects of chemotherapy on the quality of life of patients in Nairobi City County.

METHODS

Study design: Three different designs were used to achieve the objectives of the study. A case-control design was used to determine the risk factors for tuberculosis and the level of knowledge of the disease among the participants. A cross-sectionalalal design was adopted to investigate the impact of adverse drug reactions of first line anti-tuberculosis drugs on adherence and quality of life of patients. Finally, a longitudinal design was adopted to determine the incidence of adverse drug reactions and quality of life of patients on therapy for resistant tuberculosis.

Setting: The study was carried out in Nairobi City County health facilities. These included health centers and hospitals where patients with tuberculosis access care.

Target and study population: All patients attending health facilities in Nairobi were eligible. Three different groups of participants were used in the study. They included patients with pulmonary tuberculosis and on first line anti-tuberculosis drugs and those on drugs for resistant disease.The controls were tuberculosis free.

Sampling: Three different samples were used. For the case-control study, 92 participants were recruited where 46 participants with pulmonary tuberculosis (cases) were compared with an equal number without the disease (controls). The selection was done using simple random sampling. The cross-sectionalalal study involved 190 participants with pulmonary tuberculosis and on first-line treatment who were selected through simple random sampling. A total of 23 participants on treatment for drug-resistant tuberculosis were involved in the longitudinal study.

Inclusion criteria: All participants above 18 years of age who were able to communicate effectively were considered depending on the requirement of each design. All the participants consented.

Data collection: A researcher administered questionnaire was used to collect the data. Participants were interviewed and their medical records examined for additional data.

Ethical and logistical considerations: Approval to conduct the study was obtained from Kenyatta National Hospital- University of Nairobi Ethical Research Committee and managers of all the

study sites. All the study participants gave written informed consent. The data collected was stored in a password protected data base and the hard copies stored in a locked cabinet which was only accessible to the researcher and the assistants.

Data analysis: The data were entered into an Excel sheet and exported to STATA version 13 software. Descriptive analysis was done. The inferential analysis utilized Fischer's exact test and t-test determine association between variables. Regression models were used to determine the strength of association between the predictor and outcome variables.

RESULTS

Case control study

In the case control study, there were more females than males. Among the risk factors for pulmonary tuberculosis identified were; male sex ($p<0.001$), age below 30 years ($p=0.004$), HIV infection ($p=0.03$), use of alcohol ($p<00001$), smoking ($p=0.021$) and previous contact with a patient suffering from tuberculosis ($p=0.005$). The independent predictors for tuberculosis infection were male sex (AOR=23.88, 95%= 3.89-146.5, $p=0.001$), increased number of risk factors (AOR=7.1, 95%CI=1.74-29.1)) and age (AOR=0.025, 95%CI=0.001-0.74, $p=0.033$).

Majority of the participants identified cough as the common symptom of pulmonary tuberculosis and they were also aware of the availability of treatment of the disease. The independent predictors of knowledge were sex, level of education, TB infection and HIV infection. The cases had significantly more knowledge of signs and symptoms, (AOR=359.8, 95% CI=17-7627, $P<0.001$**)** than the controls. Those who had HIV coinfection were less knowledgeable (AOR=0.26, 95% CI= 0.001-0.59, $p=0.022$) compared to those who had TB alone. The cases were significantly more

knowledgeable (AOR=5.2, 95%CI= 0.88-30.9) on the mode of transmission of tuberculosis compared to the controls. A similar trend was observed among those who were HIV co-infected (AOR=23.54, 95%CI=1.6-341, p=0.07) compared to those who were not. The knowledge of treatment was significantly higher in cases (AOR=69.49, 95%CI=1.8-2638, p=0.022) than controls. The males had significantly more knowledge on prevention (AOR=13.5, 95%CI=1.7-109.1) than females. On the overall knowledge of the different dimensions assessed, the cases were significantly more knowledgeable (AOR=13.5, 95%CI= 1.7-109.1, p=0.015) than the controls. The participants who had attained secondary level of education and above were more informed (AOR=4.58, 95%CI= 1-20.5, p=0.046) than those with primary education.

Cross sectional study

The most common adverse drug reactions to first-line anti-tuberculosis drugs were; loss of appetite (58, 30.5%), Nausea and vomiting (59, 31.1%), clumsiness and unsteadiness (70, 38.2%), numbness (70, 36.8%), tingling sensation (61, 32.1%), skin rash (58, 30.5%), arthralgia (69, 36.3%), and blurred vision (38, 20%). Majority of the participants adhered to treatment. Mental depression was significantly associated with enhanced adherence (p=0.026). Use of alcohol (p=0.02) and prolonged duration of therapy (p=0.05) decreased adherence.

The mean scores of the domains of health-related quality of life as percentages were; physical health (57.3), psychological health (58.9), social relationships (61.2), environment (54.8) and overall quality of life (57). Increase in body weight enhanced quality of life and the adverse drug reactions decreased it.

Physical health scores improved significantly with increase in body mass index (p=0.014), duration of treatment (p<0.001) and level of education (p=0.003). The adverse drug reactions that

depressed it were arthralgia (p=0.002) and clumsiness/ unsteadiness (p=0.009). A similar trend was observed with psychological health. Among the variables that improved social relationships were increased BMI (p<0.001) and level of education (p<0.001). Participants who were not married had significantly reduced social relationship (p<0.001). The environment score was enhanced significantly with increase in BMI (p=0.012), and level of education (p<0.001). It was however depressed in those participants with impaired vision (p<0.001) and psychosis (p<0.001). A similar trend was noticed between the overall quality of life and the sociodemographic characteristics.

Longitudinal study

Among the patients who were on therapy for drug-resistant tuberculosis, the main adverse drug reactions involved disturbances of the nervous (91.3%), gastrointestinal (87%), musculoskeletal (73.9%), cardiovascular (43.5%) and endocrine (43.5%) systems. The other less common but serious adverse drug reactions were nephrotoxicity (6, 21.6%), hepatotoxicity (5, 21.7%) and rash (5, 21.6%). All the participants suffered from many adverse drug reactions and 12(52.2%) had experienced ten and below while 11(47.8%) had more than ten adverse reactions. The mean percentage scores for the respective domains of health-related quality of life were; social relationships (48.5), environmental health (48), psychological health (45.8), physical health and the overall quality of life (40.5). Malnutrition, hepatotoxicity, neuropathy, and depression decreased the scores of various domains of health-related quality of life.

CONCLUSIONS

The risk factors for tuberculosis identified were; male sex,use of alcohol, smoking, contact with an infected person and HIV infection. Knowledge of pulmonary tuberculosis was inadequate,

especially among the noninfected participants. The level of adherence to first-line TB drugs was satisfactory and the majority of the participants were categorized as high or medium adherers.Majority of patients on TB therapy suffered from several side effects affecting most of the body systems. The quality of life of TB patients on therapy was generally low but improved in the course of treatment.

THESIS PRESENTATION AND LAYOUT

This thesis is organized in chapters which have sections and subsections. **Chapter one** contains the the background, statement of the problem, justication, research questions, objectives and significance of the study. **Chapter two** is entirely literature review. It highlights the epidemiology and risk factors of tuberculosis. In addition, the factors that affect adherence resistance anti tuberculosis drugs are described. **Chapter three** describes the methodology of the research. It outlines the design, study area, target and study population, sampling, ethical considerations, data collection and analysis. The subsequent chapters outlines the results obtained and consists of an introduction, hypotheses, objectives, results, discussion , conclusion, reommendations and references . In **Chapter four**, the risk factors of tuberculosis are outlined while **chapter** five deals with the factors that influence knowledge of the disease. The aspects of adverse drug reactions and adherence to first line anti-tuberculosis drugs are described in **chapter six**. The quality of life and associated factors are demonstrated in **chapter seven.** Adverse drug reactions and quality of life of partcipants on therapy for drug resistant tuberculosis are described in **chapter eight**. All the findings of the study are summarized in **chapter nine .** The appendices contains the consent form, questionnaires used to collect the data, letters of approval from ethics and research committee as well from Nairobi City County health department.

CHAPTER ONE: INTRODUCTION

1.1 Background

Quality of life (QOL) encompasses the subjective assessment of both negative and positive aspects of life which are influenced by both genetic and environmental factors (CDC, 2016). The domains of Health-Related Quality of Life (HRQoL) includes those aspects of overall quality of life that affect the physical or mental health of an individual. (Selim et al., 2009). HRQoL is used to evaluate both individual and public health. At a personal level, it is used to assess physical and mental status and associated factors such as social support, health risks and conditions, functional status and social economic status. HRQoL tools have been used in public health surveillance during the assessment of the unmet needs and intervention outcomes. Self-assessed health status is a powerful predictor compared to several measures of health used to evaluate morbidity and mortality. By using measures of HRQoL it is possible to show scientifically the effect of health on the quality of life in addition to physical findings during patient assessment.

Health-related quality of life has not been given priority as an important clinical indicator of effective therapy during clinical care of patients. This is more critical for patients on prolonged treatment for chronic and debilitating diseases such as TB, HIV, and diabetes mellitus among others. Management of such diseases is aggressive using a combination of drugs that at times cause severe adverse reactions. Lack of attention to the quality of life of patients causes poor treatments outcomes since some of the adverse reactions are debilitating and interfere with their daily activities. A holistic approach to management of chronic diseases is desirable in order to optimize therapy

Tuberculosis is one of the diseases that has ravaged mankind for many years. Evidence dating back to 5000 BC has been found of the infection in human bones (Medical heritage library, 2017). Deformities consistent with TB disease have been elucidated in Egyptian mummies and the disease has been described in Biblical scripture. The disease has also been mentioned in Chinese literature that was written around 4000 BC, and in Indian religious books dating back to 2000 BC. The Greek philosopher, Hippocrates described TB, and Aristotle talked about the disease. The "Great White Plague" in Europe was tuberculosis. Throughout history, TB has been accorded several descriptions such as; a wasting away disease (Phthisis) and swelling of neck lymph nodes (scrofula). The organism that causes TB was discovered by Robert Koch in 1882 and called it tubercle bacillus because it appeared as small rounded bodies in diseased tissues (Medical heritage, 2017).

Despite the discovery of the drugs, TB has remained a public health problem during the past 40 years. *Mycobacterium tuberculosis* can be found in about one-third of the world's population which is approximately 2 billion people (WHO, 2016). The disease causes high morbidity and mortality especially in developing countries partly due to serious adverse reactions induced by anti-TB drugs. Current statistics show that the disease manifests in about 8 million people each year worldwide. Among those who become sick, 2 million die.

Concurrent infection of Tuberculosis and HIV is problematic especially in sub-Saharan Africa which has a high prevalence of the two diseases (Alimuddin et al., 2013). The HIV epidemic has worsened the existing TB control programs which are already strained. These programs have many constraints and innovative home-grown solutions which are appropriate need to be formulated. These constraints include unspecific signs and symptoms leading to an untimely diagnosis of the

disease especially in the face of paucibacillary pulmonary infection. The diagnosis is also delayed due to atypical presentations in patients with HIV/AIDS. Other challenges are inadequate clinical expertise, overworked healthcare workers, inadequate drug supplies, delayed diagnosis of MDR-TB, limited laboratory facilities, lack of environmental and personal protection especially in resistant cases and poor contact tracing (Nema, 2012). Lack of adequate follow up during and after treatment to document and address issues that affect the quality of life of the patients contributes to the increased morbidity and mortality.

Without treatment, active Tuberculosi kills about two-thirds of the infected people. Among those who are treated the mortality rate is less than 5% (Adeeb et al., 2013). The current first-line treatment for non-resistant tuberculosis in Kenya involves the use of rifampicin, isoniazid, ethambutol, and pyrazinamide for two months, followed by rifampicin and isoniazid for an additional four months. The treatment period takes six months and the patient is declared cured if all the signs and symptoms disappear at the end of this period. Drug-resistant tuberculosis is treated with several drugs and for a longer period. The six categories of drugs used include; fluoroquinolones, cycloserine, thioamides, polypeptides, p-aminosalicylic acid and aminoglycosides. Occasionally, rifabutin and macrolides are used as alternatives (Saleem & Azher, 2013).

The fight against Tuberculosis is facing serious challenge arising from the emergence of resistance which develops due to patients not adhering to drugs. Approximately 20% of TB cases globally are estimated to be resistant to at least one of the first- or second-line anti-TB drugs, and 5% are resistant to rifampicin and isoniazid which are the cornerstone of first-line TB therapy (Centre for Infectious Disease Research and Policy, 2017). While TB is curable when patients adhere to the

treatment regimen, MDR- and XDR-TB are more problematic. Treatment options are limited, expensive, and often toxic, and drug therapy can last up to 2 years. Drugs used to treat this form of TB are; kanamycin, capreomycin, cycloserine, levofloxacin, prothionamide, pyrazinamide, moxifloxacin, ciprofloxacin, and DLM. The treatment is divided into intensive phase and continuation phase and to optimize therapy daily observed therapy (DOT) approach is used.

Currently, much attention during tuberculosis treatment in Nairobi focuses on a microbiological cure. The influence of the disease on health-related quality of life (HRQoL) is either disregarded or rarely considered. The aim of this study was to evaluate the risk factors and the impact of TB treatment on HRQoL of patients with pulmonary tuberculosis. The study also investigated whether the selected socio-demographic and clinical variables were predictive of variability in the HRQoL scores over time.

1.2. Statement of the problem

Tuberculosis is a major cause of morbidity and mortality and the number of cases is increasing in Nairobi. The problem is compounded by the rising number of drug-resistant cases which are expensive to treat and carry high morbidity. The insidious onset of TB disease is associated with nonspecific constitutional symptoms that often lead to progressive deterioration of health. Loss of body mass and fatigue are common clinical manifestations which cause stigmatization because of the association with HIV. Psychological disturbances often arise due to the disease among the victims. Dissemination of information regarding the disease to the public is inadequate in Nairobi which may contribute to the progressively high number of cases over time. Treatment of tuberculosis takes a long time and therefore adverse drug reactions are common. They usually involve several body systems and can cause permanent disabilities and are occasionally fatal.

The overriding goal for managing tuberculosis is to enhance the patients' quality of life which lead to a feeling of well-being and increased productivity. The adverse drug reactions, inadequate knowledge and risk factors for tuberculosis affect the physical health, psychological health, environment and social relationships of a patient. All these dimensions of health determine the overall quality of life.

The prevalence of adverse drug reactions due to anti-tuberculosis drugs is unknown because there is no regular monitoring. Level of knowledge regarding signs and symptoms, transmission, treatment and prevention of the disease is unknown. The effect of the disease and drugs used on the quality of life has not been evaluated in Nairobi and emphasis has always been on completing treatment. These observations need to be investigated and appropriate recommendations given to improve the quality of care.

1.3. Study Justification

The overriding goal of the treatment of tuberculosis is to improve the quality of life of patients and reduce residual disability. Health education to the community is important to reduce the stigma as well as improve treatment adherence and the quality of life. The effective management of tuberculosis requires a multifaceted approach that encompasses treatment, monitoring, prevention and health education. This can be achieved if the stakeholders are empowered with knowledge regarding the disease and especially the effect of drugs used in the treatment. The health workers, patients, and the community should be well informed about risk factors, transmission, diagnosis, treatment and prevention in order to decrease the incidence, morbidity and mortality associated with treatment and enhance good prognosis. Adequate monitoring of patients on treatment for

tuberculosis is a prerequisite for effective management since the adverse effects can be detected early and appropriate measures instituted to mitigate the undesirable consequences.

No study has been documented that determined the strength of association between sociodemographic characteristics, adverse drug reactions and the quality of life of patients with pulmonary tuberculosis. Lack of this information denies the health worker and the patient crucial leads on what to prioritize when mitigating the effects of TB treatment. The increase in the incidence of drug-resistant tuberculosis is worrisome and default to treatment has caused serious concerns despite that patients are counseled. It was prudent therefore to conduct research to identify the risk factors, knowledge and adverse drug reactions and their effect on the quality of life. The findings of this study may influence therapeutic approaches and give more insight to some of the problems facing TB treatment practices in Kenya and also contribute to policy change.

1.4. Research questions

1. What are the risk factors for pulmonary TB?
2. How does the level of knowledge for tuberculosis compare between the infected and non-patients?
3. What is the prevalence and types of adverse drug reactions in patients on first-line and those on drug resistant TB therapy?
4. What is the health-related quality of life of patients on various TB therapies?

1.5 Objectives

1.5.1 General Objective

To investigate the risk factors for pulmonary tuberculosis and the effect of chemotherapy on the quality of life of patients in Nairobi.

1.5.2 Specific Objectives

1. To identify the risk factors for pulmonary tuberculosis in Nairobi.

2. To compare the level of knowledge for tuberculosis among patients with the disease and those without it in Nairobi.

3. To determine the prevalence and types of adverse drug reactions in patients on first-line and those on drug resistant TB therapy.

4. To determine the health-related quality of life of patients on treatment for tuberculosis.

1.6. Significance of the study

Among the beneciaries of the study includes the Nairobi City County health department which is charged with the responsibility of taking care of patients suffering from tuberculosis. The department will be able to use these results to come up with other strategies to enhance the quality of life of patients by closely monitoring the treatment. These measures may include retraining the staff on how to handle patients and outreach programs to educate the population about tuberculosis thereby minimizing the burden of the disease. The findings will form part of their reference materials that will facilitate the further improvement of the TB program within the County and Kenya in general.

The academic institutions concerned with the training of healthcare personnel will use the findings of the study in training their students and staff to enhance their skills and competencies in the management and follow up of TB patients focusing on the overall quality of life. This will give them a holistic view of the management of tuberculosis thereby improving the outcome of treatment. The findings will also be resource materials for future reference in their research undertakings.

Patients suffering from tuberculosis and the general public will benefit from the study in various ways. The society will be empowered to recognize the symptoms and signs of TB early and seek assistance from the health facilities. They will also be educated on the rational use of drugs especially the importance of adherence to therapy, recognizing and responding to adverse effects. This may reduce the stigma associated with the disease. Risk factors for pulmonary TB will be identified and the public notified in order to enhance prevention.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of tuberculosis

In 2015, the incident cases of TB were about 10.4 million worldwide (WHO, 2016). Asia had the highest number of cases followed by Africa, Eastern Mediterranean region, Europe and the Americas. An estimated 87% of the incident cases globally were in 30 countries. The six countries with the highest number were India, Indonesia, China, Nigeria, Pakistan and South Africa. These countries contributed 60% of the world total. People with HIV coinfection accounted for an estimated 11%.

The proportion of TB cases co-infected with HIV was more in Africa and was beyond 50% in some parts of southern Africa. Most patients with TB in Africa have documented HIV test results. Over 90% of known HIV-positive TB patients in India, Kenya, Malawi, Mozambique, Namibia, and Swaziland were on ART. The success rate for TB treatment was highest among new cases followed by MDR-TB and finally extensively drug-resistant TB.

In Kenya, a survey conducted to provide an estimate of Kenya's TB burden, despite challenges in TB testing and treatment was done (CHS, 2017).The report showed that there are more TB cases than previously estimated. Men between 25-34 years and living in urban centers were more affected than women. Most of the patients were HIV negative which suggests that a holistic approach to controlling TB is required.

2.2 Risk factors for tuberculosis

The possibility of progression of latent TB to active disease is dependent on both exogenous and endogenous factors and occurs in two stages (Padmanesan et al., 2013). The bacterial load in the sputum and the proximity of an individual to an infected case are important factors in the transmission of the disease. The status of the body immune system is a critical endogenous factor that determines whether an exposed person develops the disease or not. The factors that affect immunity includes infection with human immunodeficiency virus, malnutrition, extremes of age, diabetes mellitus, alcohol, smoke, and use of immunosuppressive drugs among others. Low socioeconomic status which is associated with overcrowding and certain behavioral characteristics is also a risk factor. Healthcare workers are predisposed to the disease due to frequent contacts with infected patients.

The immune system in most infected persons is able to contain the bacteria by prreactionsing its spread leading to the formation of caseous granulomas or tubercles (Padmanesan et al., 2013). Within two years, however, a small proportion of latent cases develop the active disease after the initial infection. Approximately 10% of people with a latent infection will develop active disease. Half of them will reactivate within the first year and the remainder of their lifetime. This occurs mostly by reactivation of the dormant bacteria in the body (WHO, 2017). Approximately 10–15% of people with the latent disease will develop the active form in their lifetime especially if the immunity is depressed (Wolters, 2015).

The development of symptomatic tuberculosis after exposure to the causative agent is mainly dependent on external factors. It relies on an inherent combination of the intensity and virulence

of the bacteria from the source, closeness to the contact, and social and behavioral predisposing factors such as alcohol, smoking, and air pollution. In overcrowded settings the rate of transmission is high (Padmanesan et al, 2013). Other factors that affect the spread of the disease include prolonged exposure to an infectious patient occasionally due to delayed diagnosis. Factors that increase the progression of infection to disease are primarily endogenous and usually depress the body immune system.

Patients who shed the bacteria in the sputum are more infectious than those who do not (Padmanesan et al., 2013). Approximately 10 individuals annually can get infected by the Mycobacteria from one person (Madhukar et al, 2016). Patients who are smear negative have reduced the number of bacteria than smear positive ones despite that they can also transmit the disease through exhaling (Patricia et al., 2010). Close contacts facilitate spread of the bacteria and they are usually caregivers and health workers (Joshi, 2006). These people are at a higher risk of becoming infected with *Mycobacterium tuberculosis* and developing primary active tuberculosis.

2.2.1. Immunosupression as a risk factor for tuberculosis

The most potent immunosuppressive factor in developing countries is HIV coinfection which is a risk for developing active TB disease (Yonge et al., 2016). HIV coinfection tend to worsen the severity of TB disease. On the other hand, TB accelerates HIV replication in affected organs including the pleura and lungs (Walker et al., 2013). The main defense mechanism against *Mycobacterium tuberculosis* is cell-mediated immunity. HIV infection weakens this defense mechanism thereby allowing the bacteria to reactivate and cause the disease (Majeed et al., 2015). HIV coinfection increases the mortality and progression of the disease among patients (Takarinda et al., 2017).

Immunosuppressive drugs increase the risk of TB (Bruce et al., 2015). Tumor Necrosis Factor-alpha (TNF-α) is an important player in the body's inflammatory responses. The randomized clinical trial revealed that infliximab which is a TNF-α blocker leads to a fourfold increase in the risk of TB infection.

The immune response is depressed in patients with malnutrition and they are at risk of developing tuberculosis. Decreased appetite and derangement in metabolic processes occur in patients with TB disease leading to malnourishment (Abba et al., 2008). Patients with low body mass index have 2- to 3-fold risk increase in developing active TB than the general population (Kirenga et al., 2015).

The risk of contracting tuberculosis is higher in children. Among those exposed to the smear-positive patient over two-thirds become infected compared to about a third who are exposed to those who are smear negative (Karen, 2017). Household source case is the primary source of infection among most children below 2 years of age but older ones contract the disease from the community (Marais, 2017). Within the first year following primary infection, most of the children develop the disease. Children above 10 and those below 2 years are at increased risk for tuberculosis.

Studies have shown that diabetes mellitus increases the risk of active tuberculosis disease (Lawson et al., 2017). Diabetes impairs humoral and cell-mediated immunity responses thereby enhancing the multiplication of the *Mycobacterium tuberculosis*. Reduction in the production of cytokines

including IFN-γ depresses T-cell mediated immunity and neutrophil chemotaxis in patients with diabetes mellitus and this is presumed to contribute in developing active TB (Knapp, 2013). TB, on the other hand, induces glucose intolerance leading to poor glycemic control in diabetics (Gyan, 2013).

2.2.2 Socioeconomic and behavioral Factors

Low socioeconomic status between and within countries increases the risk of developing active TB (Lönnroth et al., 2014). Poverty exposes people to several risk factors suchuse of alcohol, indoor air pollution due to use of fuel that produces smoke and malnutrition arising from lack of a balanced diet. Poor housing that is poorly ventilated and crowded with limited safe cooking facilities also contributes to TB burden among the poor. Although the rate of smoking is higher among the poor, HIV, diabetes mellitus, anduse of alcohol do not have a correlation with lower socioeconomic status (Lönnroth et al., 2014).

Several systemic reviews have been carried out to find out the association between TB and smoking (Moustafa, 2013). Smokers have a higher relative risk than nonsmokers of developing TB. Biological explanations includes reduced mucosal secretion clearance (Dubaissi et al., 2014), decreased ability of the alveolar macrophages to engulf bacteria (Vlahos & Bozinovski, 2014) and diminished response of the immune system induced by the negative effect of nicotine in cigarettes on the CD4 - T cells (Green et al., 2016).

Among the strong risk factors for TB disease isuse of alcohol (Imtiaz et al., 2017), which have been found to influence clustering of *Mycobacterium tuberculosis* in high and low-incidence countries (Pareek et al.,2016). Alcohol changes the working of the immune system especially the production of cytokines due to alteration of the signaling molecule (Szabo et al., 2015).

The use of solid fuels for cooking is high in developing countries (Amegah et al., 2014). The smoke arising from the burning of firewood and biomass damages the respiratory tract and is an independent risk factor for tuberculosis (Smith & Sagar, 2014). Data on how smoke from biomass causes chronic pulmonary disease is limited (Hansel et al., 2016) but impairment of macrophages phagocytic actions and surface adherence have been shown to be caused by wood smoke (Guarnieri et al.,2014). The smoke also reduces bacterial clearance thereby promoting TB infection (Dwivedi et al., 2017). Compounds such as formaldehyde and polyaromatic hydrocarbons, carbon monoxide and nitrogen oxide arise from biomass combustion. When deposited in the alveoli, these substances cause considerable damage thereby promoting the entry and spread of the *Mycobacterium tuberculosis* (Narasimhan et al., 2013).

A study done in Kampala found that the magnitude of TB risk factors in decreasing order was overcrowding, alcohol consumption, HIV infection, poverty, smoking, family history, close contact, and diabetes mellitus (Kirenga.et al., 2015).Overcrowding increased smear positive rate but all the other risk factors studied did not affect clinical, radiological,mycobacteriological and radiological characteristics of study participants. Dhanaraj et al. (2015) observed higher odds ratios for positive PTB among individuals aged thirty-five years and above, relapsed cases and slum dwellers. Other risk factors included lower body mass index,use of alcohol, smokers, and those exposed to cooking fuel producing smoke. The prevalence of smear-positive cases with positive cultures increased with the quantity of alcohol consumed, age, and the number of cigarettes smoked per day according to a study done in India (Dhanaraj et al., 2015).

Tuberculosis infection is significantly associated with use of alcohol, married individuals, asthma, smoking, contact with infected persons and diabetes mellitus (Khaliq et al., 2015). The environmental and socioeconomic factors associated with the disease include overcrowding, increased family size, poor ventilation and use of biofuels, illiteracy, unawareness of the disease, migration, and presence of animals in the house. Males are more predisposed than females due to weak immunity, more frequent external contacts, and differences in health-seeking behavior (Stevens et al., 2014).

2.3 Risk factors for MDR-TB

Tuberculosis that does not respond to treatment with rifampicin and isoniazid is said to be a Multidrug-resistant disease (CDC, 2016)). Some types of MDR-TB are resistant to fluoroquinolones and at least one of three injectable second-line drugs which are amikacin, kanamycin, and capreomycin. This type of disease is referred to as extensively drug-resistant TB (XDR-TB) which is rare. The treatment options available for XDR- TB are less effective since the disease is resistant to the most potent TB drugs. People infected with HIV or suffering from other immunodeficiency disorders have a higher risk of death if they have concurrent XDR TB.

Resistance to rifampicin and isoniazid at the molecular level has been elucidated. Mutations in either inhA or Kat genes causes resistance to isoniazid (Jaksuwan et al., 2017). Rifampicin resistance occurs due to point mutations in the rpo gene in the beta subunit of DNA-dependent RNA polymerase (Ullah et al., 2016). Since there is no direct connection between these mutations, different changes are required for the Mycobacteria to change from being susceptible isolate to MDR-TB. Diagnosis of MDR-TB requires culture and drug susceptibility pattern of the sputum.

However, the advent of GeneEpert technology genetic probes has eased the diagnostic process and can detect resistance to rifampicin with >95% accuracy. Resistance to rifampicin is suggestive of MDR-TB and is used as a marker for MDR-TB in >90% of cases (Saugat et al., 2015). Due to increasing resistance to drugs, MDR-TB is now subdivided into 'basic' MDR-TB, with resistance only to rifampicin and isoniazid only, and XDR-TB which is resistant to isoniazid, rifampicin additional second-line drugs.

The prevalence of drug-resistant tuberculosis is higher in relapsed cases of TB than new ones. A study by Abdella et al., 2015, found that 48.3% of new and 85.3% of retreatment cases had positive cultures for *Mycobacterium tuberculosis* resistant to at least one first-line anti-tuberculosis drugs. The MDR-TB prevalence was 28.1% and was almost five times more in retreatment cases compared to newly diagnosed participants. The risk factors for MDR-TB were; female gender, being a retreatment case and history of injection drug use.

In countries with high prevalence of HIV, MDR-TB presents a serious threat to the people (Saidi et al., 2017). In a study carried out is South Africa, 15.3% of new case-participants and 49.5% of relapsed cases had drug-resistant strains. MDR-TB was almost five time more prevalent in previously treated cases compared to new case-participants. HIV infection and past TB treatment were independently associated with MDR TB.

According to Boum et al. (2014), the prevalence among the previously treated patients is almost five times that of newly diagnosed cases. Factors that are independently associated with MDR are a prior history of incomplete treatment and female gender. In addition, delay in initiating TB treatment and age are predisposing factors (Sagwa et al., 2012). Side effects of TB treatment, financial burden, poor knowledge, lack of coordination of services, unsatisfactory supervision of

treatment and infection control jeopardizes the management of MDR-TB. Other risk factors are Low income, previous history of TB treatment and family history (Workichoet al., 2017). Treatment failure, alcohol consumption, young age, lung cavitations on chest x-ray and contact with MDR-TB patients are more likely to promote the spread of TB (Zhang et al., 2016). Male gender is an independent risk factor (Tadesse, 2015).

2.4 Factors that contribute to drug resistance

Since microbial resistance to anti–TB therapy develops fast, nonadherence or inadequate treatment often causes the development of drug-resistant disease. The drug-resistant strains are subsequently transmitted to other people. This may be the result of several overlapping programmatic factors, including the none establishment of recommended regimens, poor medical management of treatment and lack of supervised treatment. Others include limited or interrupted drug supply, poor quality drugs with inferior bioavailability, poorly managed and supported national TB control programmes and widespread availability of anti-TB drugs without a prescription (Bate et al., 2013).use of alcohol, lack of a home sewer system, irregular treatment and number of relapses, smoking, and a number of previous treatments, and lung cavities are also risk factors for developing resistance (Lui et al., 2013). Major causes for XDR-TB emergence in developing countries include poor quality drugs, nonadherence to treatment, poor infection control, incorrect prescription of drug regimens, and erratic drug supply (Jimmy & Jose, 2011).

Smokers are at high risk of developing MDR-TB compared to non-smokers (Rifat et al., 2014). MDR-TB is more prevalent in secondary tuberculosis, extrapulmonary tuberculosis, and participants taking drugs irregularly. Others risk factors include previous treatment, hepatic cirrhosis, and age (Kirenga et al., 2015).

2.5 Risk factors of non-adherence

The duration of TB treatment and the high number of drugs that must be taken makes it hard for participants to complete the full course of therapy (Leibert et al., 2010). Non-adherence to treatment is usually due to relieve of symptoms, large doses and a long course regimen, adverse reactions to anti-tuberculosis drugs, worry about dangers of drugs, financial burden, medical expenditures and other concurrent disorders. It is instructive that over a quarter of non-adherent participants abandon their treatment because they believe they have been cured.

Other risk factors for defaulting treatment include inadequate family support, distance from the hospital, side effects , not being on the first course of TB medications, lack of repeated smears, poor knowledge about the management of the disease, being more than 25 years old, and use of public transport (Tola et al.,2015). In a study carried out in India, most participants were found to be adherent to TB therapy (Kulkarni et al., 2013). Risk factors for nonadherence among the newly-diagnosed group wereuse of alcohol, smoking, and lack of drugs.

2.6 Adverse Drug Reactions

More than fifty percent of patients develop at least one adverse drug reaction to anti-TB drugs (Shamna et al., 2014). Most of the ADRs affect the gastrointestinal system, Liver, and biliary systems. Hepatitis is the most serious adverse reaction and a third of patients shows raised liver transaminases but only a small proportion develops increased enzymes level more than three times of the baseline. Increase in plasma uric acid occurs in a few participants due to Pyrazinamide which leads to arthritis. ADRs occur after about thirty days following initiation of treatment. Isoniazid causes peripheral neuropathy and constipation, while rifampicin is the major cause of rash, headache, pruritus, and diarrhea. The majority of adverse reactions are detected in the first ten days

of drug therapy. The frequency of adverse reactions increases with time and those that cause hospitalization mainly occur between twenty-one and thirty days of therapy (Ibrahim et al., 2017).

2.7 Effect of anti-tuberculosis treatment on HRQoL

A prospective study measured the active TB participants' health-related quality of life (HRQoL) from initiation to the end of treatment (Louw, 2016). After the anti-TB treatment, significant improvement was observed in all physical health subscales of the Short Form-36 (SF-36); two health subscales improved significantly, but mental health (MH) and vitality (VT) did not improve. In the course of treatment, VT, MH, and role- physical (RP), VT scores decreased after the initial 2 months but showed overall improvement at the end of the treatment. All the other subscales increased gradually over the treatment period. There was a gradual improvement in active TB participants over the course of the treatment. Overall, a more marked improvement occurred in symptom scores than that in exercise adaptation and socio-psychological scores.

Although HRQoL improves during anti-TB treatment, the patients have poorer overall HRQoL compared to the general population especially in psychological well-being and social functioning at the end of treatment. After the 6 months of treatment, active TB patients scored significantly lower at SF-36 physical component summary (PCS) and mental component summary (MCS) scores compared to people with latent TB infection (LTBI). Muniyandi et al. (2007) evaluated the HRQOL among participant who had successfully completed TB treatment. Forty percent of these people reported persistent symptoms, such as a cough, occasional fever, breathlessness, and chest pain. The scores were determined for social, mental and physical well-being. No gender difference was observed on physical well-being score but females scored much lower at mental and social

well-being scores. Older participants had significantly lower mental well-being and physical scores compared to younger ones. The reverse occurred with the social scores.

CHAPTER THREE: MATERIALS AND METHODS

3.1 Introduction

The study objectives were achieved using different designs . These were; case-control, longitudinal and cross- sectional designs. Each approach had a specific design, target and study population, sample size, sampling technique, inclusion/exclusion criteria, and variables. The study area, ethical and logistic considerations were similar. This chapter describes the three approaches separately. What was common is discussed together. The study was conducted from September 2015 to February 2017.

3.2 Study area

The study was carried out in Nairobi City County. Nairobi is the capital and largest city of Kenya and covers 694.9 km^2. At 1,795 meters above sea level, evenings may be cool, especially in the June/July season, when the temperature can drop to 9 °C (48 °F). The sunniest and warmest part of the year is from December to March when temperatures average the mid-twenties during the day. The mean maximum temperature for this period is 24 °C (75 °F). The city has a well-established healthcare system comprising of 2 National hospitals, 3 District hospitals, 67 health centers and 9 dispensaries. Administratively, these health facilities are located in 8 districts. These districts are; Embakasi, Makadara, Kasarani, Kamukunji, Njiru, Starehe, Dagoreti, and Westlands. The identity of the health facilities and their location is shown in **appendix 5.** The research was carried out in selected health facilities. The choice of the health facilities was guided by the availability of the eligible participants.

3.3 Case-control study for determining risk factors and knowledge of TB

3.3.1 Study design

A case-control study design was used. Cases comprised of participants with pulmonary tuberculosis confirmed through ZN staining of the sputum. Controls were patients selected within the study area but were not suffering from tuberculosis.

3.3.2 Target and study population

All adult patients attending health facilities in Nairobi City County were targeted. However, it was not feasible to include all patients and therefore the study population comprised of patients who visited; Kayole I, Kayole II, Umoja, Dandora I, Dandora II, Ruai, Njiru, Kariobangi South and Kariobangi North health centers. These health centres were selected because they were accessible and had large number of patients suffering from tuberculosis. Only those who satisfied the inclusion criteria were enlisted into the study.

3.3.3 Inclusion and exclusion criteria

Participants that were included as cases were;

a. Eighteen years of age and above.

b. Patients confirmed with pulmonary tuberculosis.

c. On first line anti-tuberculosis drugs.

d. Those who consented to participate in the study.

e. Able to communicate effectively in either Kiswahili or English.

Participants who selected as the controls;

a. Were at least 18 years of age.

b. Did not have pulmonary tuberculosis but were suffering from other illnesses.

c. Consented to participate in the study.

d. Were able to communicate effectively

All those who did not meet the above criteria were excluded.

3.3.4 Sampling considerations

3.3.4.1 Sample size

The sample size was determined using the following formula for calculating sample sizes for two independent groups (Marlies et al., 2010).

Equation 1: Formula for computation of sample size for the case-contol study

$$n = \frac{[\,(a+b)^2\,(p_1q_1 + p_2q_2)\,]}{x^2}$$

Where

n = case sample size = control sample size.

Smoking was used as a risk factor from a previous study done in Zambia where 30.8% of cases and 7.8% of controls were smokers (Stephen et al., 2016). Smoking was used because it is a known risk factor for TB.

Therefore from the above equation;

p_1 = proportion of subjects who smoked and had pulmonary tuberculosis.

q_1 = proportion of subjects who did not smoke and had pulmonary tuberculosis which is equal to $(1- p_1)$

p_2 = proportion of subjects who smoked and did not have pulmonary tuberculosis.

q_2 = proportion of subjects who were non- smokers and did not have pulmonary tuberculosis. equal to $(1- p_2)$.

x = the difference between the two proportions.

a = conventional multiplier for alpha and in this case the level of significance was 0.05. Therefore a = 1.96.

b = conventional multiplier for power. In this study, the power was 80% which is adequate to give reliable results. The value of b= 0.842.

Using the study done in Zambia; X = 0.308-0.078 = 0.23

$$N = \frac{(1.96 + 0.842)^2 \, (0.308 \times 0.692 + 0.078 \times 0.912)}{0.23^2} = 42$$

The calculated sample size was adjusted by 10% to carter for inadequate responses. Therefore each arm had 46 participants and the total number was 92.

3.3.5 Sampling technique and participant recruitment

The cases were selected from the TB clinics after collecting the anti-TB drugs and were informed about the study. They were then requested to volunteer to participate and those who agreed were taken through the next step of selection whereby a coin was flipped. The cases who scored the head of the coin were recruited after consenting **(Appendix 1)**. This procedure was repeated until the desired sample was achieved. Controls were recruited and selected in a similar way as the

Table 3.1. Participants for the Case- Control study (N=92)

Health facility	**Number of participants**	
	Cases	Controls
Kayole I	6	6
Kayole II	7	7
Umoja	5	5
Dandora I	6	6
Dandora II	6	6
Njiru	6	6
Ruai	5	5
Kariobangi South	5	5
Total	**46**	**46**

cases from among the patients who visited the health facilities but were not suffering from tuberculosis. At the end of the exercise, 92 participants were recruited, with each arm having 46 participants. These participants were selected from the health facilities listed in **table 3.1**.

3.3.6 Data collection

Data was collected using a questionnaire by the researcher or his assistants **(Appendix 2).** The participants after voluntary consenting were invited individually for a face to face interview and assisted to complete the questionnaire. This was done in a place within the health facility where only the researcher and participant were present to ensure privacy. Some of the data that could not be obtained directly from the participants were abstracted from the clinic records and entered into the questionnaire. Permission to access the patients' records was given by the administrators of the respective health facilities after production of a letter of ethical approval of the study.The questionnaire had two main sections, namely; sociodemographic characteristics and dimensions of knowledge that were assessed.

3.3.7 Variables

The tuberculosis status was the dependent variable and the independent variables were sociodemographic characteristics and adequacy of knowledge of the disease. The sociodemographic characteristics investigated were; sex, age, marital status, education level, HIV infection, previous TB infection, malnutrition, diabetes mellitus,use of alcohol, smoking, previous contact with TB patient, overcrowding, hospitalization, and a number of occupants in the house. Dimensions of knowledge on TB explored included; signs and symptoms (DKSS), transmission (DKT), treatment (DKTr) and prevention (DKP).

3.3.7 Data analysis

3.3.8.1 Analysis of the risk factors

The collected data were entered into an MS Excel sheet and imported to STATA version 13 software. Both descriptive and inferential statistics were conducted. The results for categorical variables were presented as frequencies and percentages. inferential analysis was carried out using Fischer's exact test on all categorical variables to determine the relationship between TB status and sociodemographic characteristics. Bivariable and Multivariable logistic regression analysis was used to determine the strength of the relationship between TB and sociodemographic characteristics. Risk factors were identified as those variables with an odds ratio greater than one and P value less than 0.05.

3.3.8.2 Analysis of the level of Knowledge

The knowledge score was calculated in using the dimension index formula as presented in Equation 2 (UNDP, 2011);

Equation 2: Formula for computing knowledge level of tuberculosis

$$\text{Dimension Index (DI)} = \frac{\text{Actual value - Minimum value}}{\text{Maximum value - Minimum value}}$$

For example, based on above equation, dimension scores for prevention (DKP) were computed as follows;

$$\text{DKP} = \frac{\text{Actual value of prevention- minimum value of prevention}}{\text{Maximum value of prevention- minimum value of prevention}}$$

Each correct response was scored as 1 mark and a wrong answer as zero. Actual value was obtained by adding all correct responses in each dimension and the minimum correct value was 1 mark in all cases. The maximum actual values of DKSS, DKT, DKTr and DKP were 6, 4, 3 and 4 respectively.

Overall knowledge index (OKI) was the average of the respective index in each dimension as calculated using Equation 3.

Equation 3. Formula for computing overall knowledge level of tuberculosis

$$OKI = \frac{DKSS + DKT + DKTr + DKP}{4}$$

A score of 50% and above was regarded as adequate knowledge and designated a value of one. A score less than 0.5 was considered as inadequate knowledge and designated a value of zero. The scores index were entered in the Excel sheet as absolute and binary value.

The average was determined for each dimension while Bivariable and Multivariable analysis were computed to find the distributions of different dimensions of knowledge items and some selected sociodemographic characteristics across the arms. Any association that yielded odds ratio greater than one accompanied with a P value less than 0.05 was considered a statistically significant.

3.4 Cross-sectional study for determining adverse drug reactions and HRQoL

This study was used to assess the adverse drug reactions, level of adherence to treatment and quality of life of patients on first-line TB regimens. The impact of adverse drug reactions and sociodemographic characteristics on adherence to treatment and quality of life was determined.

3.4.1. Study design

A cross-sectional design was used which involved an exit interview with participants in the health facilities.

3.4.2 Identification of target and study population

All patients suffering from tuberculosis in Nairobi City County were targeted. The study population comprised of those patients attending Kayole I, Kayole II, Umoja, Dandora I, Dandora II, Ruai, Njiru, Kariobangi South and Kariobangi North health centers. The participants were on first-line TB drugs.

3.4.3 Inclusion and exclusion criteria

Participants enlisted in the study had the following characteristics;

a. They were at least 18 years of age.
b. They were on first-line TB drugs for at least one month.
c. Were able to communicate effectively in English or Kiswahili.
d. Consented to participate in the study.

Patients who did not meet any of the inclusion criteria were excluded.

3.4.4 Sampling

3.4.4.1 Sample size calculation

The sample size was calculated using the following single population proportion formula (Charan & Biswas, 2013) as presented in equation 4.

Equation 4. Formula for computing sample size for the cross-sectional study

$$n = \frac{Z_{\frac{\alpha}{2}}^{2} P (1 - P)}{d^{2}}$$

Where

- $Z_{\alpha/2}$ is the critical value at 95% confidence interval (= 1.96 from Z- table).
- n is the minimum sample size required for very large population (≥10,000).
- P is the prevalence of adverse reactions among patients on first-line TB therapy.
- d is the margin of erro**r** (5%).

A study carried out in Nigeria revealed that 70.3% of patients on first-line TB therapy experienced adverse drug reactions (Michael et al., 2016).

Hence, estimated minimum sample size (n) = $\frac{1.96x1.96x\ 0.703x\ 0.297}{0.5x0.5}$ = 321

However, since study population was less than 10, 000 the sample size was determined using equation 5.

Equation 5. Formula for computing corrected sample size

$$\text{Corrected sample size} = \frac{n*N}{n+N}$$

Where N= source population and n= estimated sample size for the N≥10,000 population.

According to the Nairobi county health records department, 373 cases were reported in 2015 from the study area.

$$\text{Corrected sample size} = \frac{321*\ 373}{321+373} = 173$$

Hence, the corrected sample size with additional 10% contingency for non-responses yielded a sample of 190 patients.

3.4.4.2 Sampling technique and participant recruitment

The researcher visited the TB clinics in the selected health facilities where patients were being attended. After the researcher introduced himself and explained the purpose of research to the personnel working in the clinics, permission was sought and given to select the participants by the management. Sampling of patients was done by simple randomization. As the patients streamed in, the researcher flipped the coin and the patient who scored the head was approached and requested to participate in the study. Those who agreed were taken through the voluntary consenting process as guided in **Appendix 1**. The consenting process and subsequently the interview was done in a secluded room to maintain privacy. Only those who consented were selected to participate in the study. This procedure was repeated until 190 participants were enlisted. The distribution of participants according to health facility is shown in **table 3.2.**

Table 3.2 Disribution of participants for Cross-sectional study (N=92)

Health Center	**Number of participants**
Kayole I	25
Kayole II	32
Umoja	18
Dandora I	20
Dandora II	25
Ruai	22
Kariobangi South	22
Njiru	18
Total	**190**

3.4.5 Data collection

Data was collected using a questionnaire which was administered by the researcher or his assistants **(Appendix 3).** The questionnaire had four main sections, namely; sociodemographic characteristics, adverse drug reactions, adherence to drug therapy and quality of life. The approach used to collect the data was the same as 3.3.5.

The data for the quality of life was grouped into five domains, namely; physical health, psychological health, environment, social relationships and overall quality of life. Each domain had specific responses which were obtained from participants self-reporting.The interview was done in a secluded room to ensure privacy and confidentiality.

The data concerning adverse drug reactions were obtained from patient self-reporting and the medical records. The level of adherence to drugs was determined using Morisky eight-point scale **(Appendix 3).** Each correct response had a score of one and the sum was calculated for the appropriate responses for each individual. A score below six was labeled mild adherence while scores of 6 and 7 weremoderate adherence. A score of eight was consideredgood adherence.

3.4.6 Variables

The quality of life and level of adherence were the dependent variables and the independent variables were sociodemographic characteristics and adverse drug reactions. Quality of life domains investigated were; physical health, psychological health, social relationships, and environment. The facets incorporated into physical health were; activities of daily living, dependence on medicinal substances and medical aids, energy, and fatigue, mobility, pain and discomfort, sleep, rest and work capacity. Psychological health encompassed; bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality/religion / personal beliefs, thinking, learning, memory, and concentration. The aspects evaluated in Social relationships include; personal relationships, social support, and sexual activity. The environment was assessed

using the following variables; financial resources, freedom, physical safety and security, Health and social care: accessibility and quality, home environment, opportunities for acquiring new information and skills, participation and opportunities for recreation / leisure activities, physical environment (pollution / noise / traffic / climate) and transport.

Sociodemographic characteristics that were assessed included; sex, age, marital status, education level, HIV infection, previous TB infection, malnutrition, diabetes mellitus,use of alcohol, tobacco smoking, previous contact with TB patient, overcrowding, hospitalization, duration of treatment, and a number of occupants in the house.

Assessment of adverse drug reactions was done according to the body systems and involved; gastrointestinal, cardiovascular, neurological, liver, renal, skin, musculoskeletal, eyes, and ears. Specific signs and symptoms are shown in in the questionnaire.

Level of adherence to therapy involved use of Morisky eight-point scale. Computation of the scores was done which involved summation of the correct responses regarding how the anti TB drugs were used. Three variables were generated from the results obtained following summation. These were; low (1-5), moderate (6-7) and good (8) adherence.

3.4.7 Data analysis for the cross-sectional study

3.4.7.1 Computation of the quality of life scores for each domain of HRQoL

All the 26 items in the WHOQOL-BREF were assessed for completion and the respective score noted **(Appendix 3).** The calculation of the respective domain score was determined by considering the relevant questions according to the tool. The Overall quality of Life and general health was computed from questions 1 and 2. Physical health score was obtained from questions;

10,15, 16, 17, 18 and a reversal score of Q3 and Q4. Psychological health was calculated from questions; 5, 6, 7, 11, 19 and a reversal of Q26. Social relationships score was derived from questions 20, 21, and 22. Finally, environment health score was determined from questions; 8, 9, 12, 13, 14, 23, 24 and 25. The raw score was computed by a simple algebraic sum of each item in each of the four domains. Transformation of each raw scale score was done using equation 6.

Equation 6. Formula or computing quality of life scores

$$\text{Transformed score} = \frac{[\text{actual raw score} - \text{lowest possible score}] \times 100}{\text{Possible raw score}}$$

Where "actual raw score "is the value achieved through summation, "lowest possible raw score" is the possible value that could occur through summation, and "possible score range "is the difference between the maximum and minimum possible raw scores. The maximum possible raw scores for each domain were as follows: Physical Health=28, Psychological health=24, Social relationships=12, Environment=32 and the overall quality of life= 8. The transformed scores were presented as percentages.

Measures of central tendency (mean) and dispersion (range, standard deviation) were computed. Linear regression analysis with robust estimation was conducted to investigate the association between both sociodemographic characteristics and adverse drug reactions with the various domains of the quality of life. The strength of association between the dependent and independent variables was determined by the value of the beta coefficient. A P value equal or less than 0.05 was considered statistically significant. Multivariable linear regression analysis was conducted to adjust for confounding.

3.4.8.2 Data analysis for adverse drug reactions due to first-line TB treatment

The frequency of each adverse reactions was computed and tabulated as absolute number and percentage. Fischer's exact test was conducted to compare the prevalence of adverse drug reactions across socio-demographic characteristics, and phase of therapy.

3.4.8.3 Data analysis for level of adherence to TB treatment

The level of adherence was assessed using Morisky eight-point scale**.** Each correct response was awarded one score and the total was determined for each participant. The level of adherence was presented as bar charts and Fischer's exact test was used to compare levels of adherence across sociodemographic characteristics. The level of significance was set at 0.05.

3.5 Longitudinal study on adverse drug reactions and HRQoL in patients with MDR-TB therapy

3.5.1 Study design and population

An ambidirectional descriptive longitudinal study design was used to identify the adverse drug reactions and measure quality of life of patients on treatment for drug-resistant TB. All the participants suffering from drug-resistant tuberculosis and attending the target health facilities in Nairobi City County were eligible to participate in the study.

3.5.2 Inclusion and exclusion criteria

Participants enlisted in the study had the following characteristics

a. Aged 18 years and above
b. They were on treatment for MDR-TB for at least one month
c. Were able to communicate effectively in English or Kiswahili

d. Consented to participate in the study

All the patients who did not meet any one of the above criteria were exclude from the study.

3.5.3 Sampling and participant recruitment

Universal sampling was used because there were very few cases with MDR-TB. A list of all patients with MDR-TB was officially requested for and obtained from the Nairobi City County Health Office. The patients were contacted with the the assistance of the nurse in charge of the TB clinics in the respective health facilities. The patients were invited to participate in the study during their daily refill of their medicines. Twenty-three patients out of thirty- three were avilable to participate in the study. The patients were individually informed about the study and requested to participate. Those who agreed were enlisted after being taken through the consenting process.

3.5.4 Data collection

Data was collected using researcher administered questionnaire **(Appendix 4).** The participants were individually invited for a face to face interview and responses entered into a structured questionnaire with coded responses. This was done in a place within the health facility where only the researcher and participant were present to ensure privacy. Some of the data that could not be obtained directly from the participant were abstracted from the clinic records and entered into the questionnaire. Permission to access the patients' records was given by the administrators of the respective health facilities upon presentation of a letter of ethical approval.

The questionnaire had three sections, namely; sociodemographic characteristics, adverse reactions, and quality of life.

The haematological and biochemical results were abstracted from the patients' records and entered into the questionnaire. They included the serum levels of potassium, creatinine,

hemoglobin, liver enzymes and thyroid hormones. All the samples had been analyzed by one deignated internationally certified laboratory called Lancet Laboratories in Kenya.

3.5.6 Interpretation of laboratory results

The biochemical and haematological data were interpreted according to the reference ranges provided by Lancet Laboratories . The interpretation of the various parameters is summarized in table 3.3. The readings were interpreted depending on whether they were below, within or above the reference range.

Table 3.3. Guide for interpretation of laboratory results

Parameter	**Normal reference range**	**Interpretation of results**	
Haemoglobin			
Male	13.0-18.0 g/dl	< 13.0 g/dl **Anemia**	
Female	11.5-16.5 g/dl	< 11.5g/dl Anaemia	
Potassium	3.5- 5.1 mmol/L	< 3.5 mmol/L **Hypokalemia**	>5.1 mmol/L **Hyperkalemia**
Liver function tests			
Alanine aminotransferase	10-40 IU/L	>40 IU/L **Hepatotoxicity**	
Renal function test			
Serum Creatinine	62-106 µmol/L	>106 µmol/L **Nephrotoxicity**	
Thyroid function test			
Thyroid stimulating hormone	0.27-4.2 mU/L	>4.2 mU/L **Hypothyroidism**	< 0.27 mU/L **Hyperthyroidism**

3.5.6 Interpretation of hearing acuity

The results of hearing acuity were abstracted from the patient records. The assessment of hearing acuity is routinely done for patients with MDR-TB every month. However this assessment is not

conducted for patients on first line medications. The hearing acuity was assessed using an audiometer during clinic visits.The hearing was categorized as presented in **table 3.4.**

Table 3.4. Guide for interpretation of audiometry results

Lowest hearing range in decibels	Interpretation
0-20	Normal hearing
21-40	Mild hearing loss
41- 70	Moderate hearing loss
71-90	Severe hearing loss
91 and above	Profound hearing loss

Those participants who had any degree of hearing loss were considered to hearing impaired.

3.5.7 Variables

The variables were similar to those described in section 3.4.7. However, the level of adherence was not explored because these patients relied on DOT which was administered in the respective health facilities.

3.5.8 Data analysis

Analysis of the quality of life and adverse drug reactions was carried out according to the procedure described in section 3.4.7. Comparison of the means of overall quality of life before and during treatment was carried out using a paired t-test.

3.6 Quality Assurance for all the studies

To ensure data quality for all the studies, the questionnaire was first pre-tested using a sample of ten participants in the case-control and cross-sectionalalal study designs but five were used for the longitudinal study using the researcher administered questionnaires. The responses were evaluated to find out whether the questions were understood by the participants. Any ambiguity was addressed and the questionnaires properly edited. The participants that were used during pretesting were excluded from the final samples.

3.7 Data management

Data were entered the same day after collection into an Excel spreadsheet for each design. Double data entry was done and discrepancies compared. The database was backed up daily and the copies stored away from the site of the study. Data security was enhanced by keeping the filled questionnaires under lock and key as well as having a computer password only known to the researcher. Data cleaning was done by checking for inconsistencies, missing and unrealistic values. It was verified by checking source documents or patient files. Any changes made to the database was noted.

3.8 Ethical Considerations

Prior to the study, ethical clearance was granted by the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee. After receiving the ethical approval number KNH-ERC/A/146, further permission was sought from the head of health services in Nairobi City County and research authorization number CHS/PH/109/24 granted. Comprehensive study information was provided to the prospective participants who thereafter voluntarily consented to participate in the study. The participants were assured of confidentiality in all aspects by

concealing their identity and an assurance that the research data will be stored in safe custody under lock and key and accessed only by authorized persons. The detailed consenting process is explained in **appendix 1.**

CHAPTER FOUR: THE IMPACT OF GENDER AND LIFESTYLE ON THE PREVALENCE OF TUBERCULOSIS IN NAIROBI CITY COUNTY

4.1 Introduction

Kenya is among the countries in the world with high TB burden. The disease is the 4th leading cause of death among infections in the country (Centre for Health Solutions, 2017). The high proportion of people of low socioeconomic status are vulnerable to TB, thereby contributing to the burden of the disease. This social class is associated with poor housing, alcohol and substance abuse, overcrowding in homes and workplaces. They also have poor nutrition and access to health care services. In 2015, ten counties in Kenya had higher TB case notification accounting for 48% of the total TB burden and Nairobi was leading with 12,425 cases (Tibu, 2016). The disease causes severe ill health and associated enormous economic burden in most low income countries (Perpetual et al., 2013).

Several medical conditions and lifestyle behavior are risk factors for TB (Lönnroth et al., 2014). Poor treatment results and the disease itself can complicate the course of other ailments. Knowledge of these risk factors can facilitate early diagnosis and improve management of the disease. When risk factors are highly prevalent in the general population, they can be important contributors to the TB burden. Consequently, reducing the prevalence of these risks can prreactions its spread.

A case-control study was carried out in selected health care centers in Nairobi and the methods are described in chapter 3, section 3.3. The main objective was to determine the impact of lifestyle habits and gender on the prevalence of tuberculosis in Nairobi.

4.2. Hypotheses

In order to evaluate the impact of sex and selected lifestyle habits on tuberculosis, two hypotheses were formulated. These were;

1.

H_0: There is no association between tuberculosis and sex of patients in Nairobi.

H_1: There is an association between tuberculosis and sex of patients in Nairobi.

2.

H_0: Use of alcohol and smoking is not associated with tuberculosis in Nairobi.

H_1: Use of alcohol and smoking is associated with tuberculosis in Nairobi.

3.

H_0: TheAssociation between alcohol use and TB is confounded by gender in Nairobi.

H_1: The Association between alcohol use and TB is not confounded by gender in Nairobi.

4.3 Objectives of the case control study to identify risk factors for tuberculosis

The main objective was to determine the impact of lifestyle habits and gender on the prevalence of tuberculosis in Nairobi. The specific objectives were to:

i. determine if gender is associated with tuberculosis
ii. measure the association between alcohol and smoking
iii. to determine if gender confounds the association between smoking, alcohol conumptions and tuberculosis

4.4. Results

4.4.1 Sociodemographic characteristics of the participants

Of the 92 participants, 46 (50%) had pulmonary tuberculosis and there were 29(31.5%) the difference was statistically significant ($p< 0.001$); but among those who had tuberculosis, the males were the majority (29, 31.5%). Forty-nine (53.2%) participants were between 18 and 30 years of

age while 55(59.8%) were not married. Fifty-seven (62%) participants had attained at least secondary school education. Twenty-one (22.8%) tested positive for HIV which was males and 17(18.5%) females **(Table 4.1)**.

Table 4.1. Sociodemographic characteristics (N=92)

Variable	Cases n (%) (n=46)	Controls n (%) (n=46)	P value
Sex			
Male	29 (31.5)	6 (6.5)	**<0.001***
Female	17 (18.5)	40 (43.5)	
Age [years]			
18-30	20 (21.7)	29 (31.5)	0.094
31 and above	26 (28.3)	17 (18.5)	
Marital status			
Married	24 (26.1)	13 (14.1)	0.085
Single	22(23.9)	33(35.9)	
Education level			
Primary	16 (17.4)	19 (20.7)	0.522
Secondary and above	30 (32.6)	27 (29.3)	
Number of occupants in the house			
Two and below	27 (29.3)	11 (12)	**0.001***
3 and above	19 (20.7)	35 (38)	
HIV infection	15 (16.3)	6 (6.5)	**0.045***
Previous TB infection	3 (3.3)	1 (1.1)	0.617
Malnutrition	4 (4.3)	0 (0)	0.117
Diabetes mellitus	1 (1.1)	1(1.1)	1
Use of alcohol	25 (27.2)	7 (7.6)	**<0.001***
Smoking	13 (14.1)	4 (4.3)	**0.03***
Previous contact with TB patient	17 (18.5)	5 (5.4)	0.06
Overcrowding	5 (5.4)	2 (2.2)	0.434
Hospitalization	4 (4.3)	0 (0)	0.117

*- Statistically significant p-value

Overall, females were more (57, 62%) than males and this difference was significant (P<0.001); associated with TB infection (p=0.04) and 4 (4.3%) had previous tuberculosis infection. Thirty-two (34.8%) participants used alcohol and 17 (18.5%) were smokers prior to initiation of therapy and both characteristics showed a statistically significant relationship with TB (p=0.03). Twenty-

two (23.9%) participants had a history of the previous contact with a person infected with tuberculosis and 38 (41.3%) were residing in houses with at least three occupants

4.4.2 Predictors for pulmonary tuberculosis infection in Nairobi City County

Bivariable and multivariable logistic regression analysis was done to establish the risk factors for tuberculosis using the TB status as the dependent variable and the results are summarized in **table 4.2.** Among the characteristics that were found to be predictors of the disease in the bivariable model were; sex (COR= 0.088, 95% CI= 0.029-0.237; p<0.001) where females were 0.088 times likely to have the disease compared to males. The disease was more prevalent among those participants below 30 years of age (COR= 1.078; 95% CI=1.028-1.137, p=0.004). HIV was a strong predictor (COR= 3.226; 95% CI: 1.166-9.942, p=0.03) where those infected were about 3 times likely to develop TB compared to uninfected ones. Alcohol consumption (COR= 6.63; 95% CI= 2.566-19.032, p<0.001) was a strong predictor and the victims were 6.63 times more likely to get have TB. Smoking (COR= 4.136; 95% CI= 1.325-15.766, p=0.021) and previous contact with a patient suffering from tuberculosis (COR= 4.807; 95% CI= 1.688-15.982, p=0.005) increased the likelihood of having TB by four times. However, diabetes mellitus, overcrowding, and previous tuberculosis infection were not significantly associated with the disease. Multivariable logistic regression revealed that only three characteristics were statistically significant as predictors of tuberculosis. Males had about 23 times (AOR=23.88 95%CI=3.89-146.5, p=0.001) the odds of

Table 4.2. Logistic regression analysis of predictors for tuberculosis *(*N=92)

Variable	Bivariable analysis		Multivariable analysis	
	COR (95% CI)	**P value**	**AOR (95% CI)**	**P value**
Sex	11.37 (3.994,32.378)	**<0.001***	23.88 (3.89, 146.5)	**0.001***
Age	1.078 (1.028, 1.137)	**0.004***	0.025 (0.001, 0.737**)**	**0.033***
Marital status	0.43(0.181, 1.02)	0.055	0.308(0.05, 1.91)	0.206
Education	0.923 (0.527, 1.616)	0.779	1.23(0.413,3.658)	0.711
No of occupants in the house	0.221 (0.087, 0.530)	**0.001***	0.899(0.149, 5.43)	0.908
HIV infection	3.226 (1.166 ,9.942)	**0.03***	1.396 (0.183, 10.66)	0.748
Alcohol consumption	6.633 (2.566, 19.032)	**<0.001***	1.5 (0.193, 11.676)	0.693
Tobacco smoking	4.136 (1.325,15.766)	**0.021***	0.064 (0.003,1.504)	0.088
Diabetes mellitus	1 (0.0387, 25.810)	1	0.173 (0.002,16.37)	0.449
Previous contact with TB patient	4.807(1.688, 15.982)	**0.005***	1.95 (0.183, 20.709)	0.580
Number of risk factors	2.429 (1.631, 3.857)	**<0.001***	7.1 (1.738, 29.014)	**0.006***
Overcrowding	2.68 (0.545, 19.46)	0.254	0.823 (0.0386, 17.56)	0.901
Previous infection with TB	3.14 (0.385, 54.81)	0.33	0.034 (0.001, 2.261)	0.115
Marital status	0.385 (0.145,1.004)	0.31	0.308 (0.05, 1.91)	0.206

*- Statistically significant relationship

developing tuberculosis compared to females. People above 30 years of age (AOR=0.025, 95%CI=0.001- 0.737, p=0.033) were less predisposed; and the odds were about seven times

(AOR=7.1, 95%CI=1.738- 29.014, p=0.006) with every additional risk factor of developing the disease.

4.4.3 Effect of the number of risk factors on tuberculosis

The score test for trend of odds showed a statistically significant dose-effect relationship as shown in **table 4.3.** As the number of known risk factors an individual had increased the odds of having TB increased. The effects of a total number of risk factors that a patient had were positively confounded by gender. Patients who had two or more risks factors had about eleven times the odds of contracting TB (adjusted OR) than those who did not have any known risk factor. Those with only one known risk factor had much lower odds.

Table 4.3. Effect of number of risk factors for tuberculosis (N=92)

No of risk factors	OR (adjusted for gender)	95%CI	P-values
0	1		
1	4.764	0.977,23.215	
2	11.333	1.952, 65.802	**<0.001***
3	11.426	1.700, 76.797	**0.002***

*-Statistically significant relationship

4.4.4 Link between smoking, alcohol consumption, sex, and tuberculosis

HIV was more prevalent in females (52.4%) while males dominated in alcohol use (71.9%), smoking (88.2%), and previous TB infection (75%). There was a strong negative association between female sex and the social habits of smoking and alcohol consumption **(Table 4.4).** Therefore, gender was expected to confound the association between TB and these two habits. Similarly, there was a very strong positive association between alcohol consumption and smoking. Therefore, smoking was expected to confound the effects of alcohol consumption and vice versa. The variable sex, smoking, and alcohol were each positively associated with TB. From the results

above sex was found to be strongly associated with tuberculosis in both bivariable and Multivariable logistic regression analyses since in both instances the p-value was less than

Table 4.4. Comparison of prevalence of risk factors for TB across gender (N=46)

	Percentage of males and females with the risk factor			
Variable	**Male**	**Female**	**COR (95%CI)**	**P-value**
HIV infection (n=21)	47.62	52.38	0.598 (0.223, 1.601)	0.306
Previous TB (n=4)	75	25	0.073(0.019, 1.908)	0.158
Malnutrition (n=4)	50	50	0.600 (0.081 4.464)	0.618
Use of alcohol (n=32)	71.88	28.13	0.098 (0.036, 0.265)	<**0.001***
Smoking (n=17)	88.24	11.76	0.048 (0.010, 6 .231)	<**0.001***
Prior contact (n=22)	50	50	0.522 (0.198, 1.377)	0.189
Overcrowding (n=7)	28.57	71.43	1.587 (0.291, 8.627)	0.594
Hospitalization (n=4)	50	50	0.600 (0.081, 4.464)	0.618

*- statistically significant relationship

0.05 and odds ratio greater than one. Therefore sex is a strong predictor of tuberculosis infection. Males are more predisposed than females to the disease. Bothuse of alcohol and smoking were found to be associated with tuberculosis in the bivariable logistic regression and the odds ratios were greater than one while the p values were less than 0.05.

4.5 Discussion

This case-control study demonstrated that predictors for TB are multifaceted. Males were found to be at higher risk compared to females and the results were similar to a study done in Uganda where males were twice as likely to be diagnosed with culture-positive TB compared to females

(Yap et al., 2014). In Pakistan, the majority of TB patients across all age groups were females, and in Peru, a higher prevalence of TB was found in women of reproductive age compared to males in the same age range. These countries are an exception. However in Africa and Eastern Europe males represent the majority of adult patients with TB. Several reasons may explain this scenario. Men tend to be more outgoing than women. They are more exposed to persons with TB due to their socialization which often involves drinking alcohol and smoking as well as activities associated with pollution such as construction and motor vehicle repair. Moreover, specific biological factors may render men even more susceptible to pulmonary TB than women due to the sex hormones and sex-specific metabolic features which depresses immunity (Sharma & Eghbali, 2014).

Smoking was found to be positively associated with tuberculosis. This is consistent with many studies done in different parts of the world (Prasad et al., 2009; Hassmiller, 2006; Yap et al., 2014). However, after controlling for gender, the association dissipated. A possible explanation is that smoking in Nairobi is mainly a behavior of men and therefore it is difficult to dissociate the two variables. The exact mechanism that correlates smoking with TB is not fully understood, but there is a lot of evidence of declining respiratory tract defence that enhance susceptibility to TB infection in smokers (Lasmaria, 2013). Trachea, bronchi, and bronchioles that supply air to the lungs provide the first line of defense by prreactionsing TB bacteria from reaching the alveoli. Smoking has been proven to interfere with mucociliary clearance. Pulmonary alveolar macrophages function decline as well as the phagocytic prowess and in killing germs among individuals who smoke. Smoking has been found to be associated with decreased levels of proinflammatory cytokines which are essential for early responses of local defence to bacterial infection including TB.

There was a positive association between alcohol intake and TB which was consistent with other studies (Vendhan & Richard, 2009: Kuznetsova et al., 2013). This may be due to both increased risk of infection related to specific social mixing patterns associated with alcohol use, as well as weakened immune system leading to higher predisposition. The latter may be through direct toxic effects of alcohol on the immune system (Massey et al., 2015) or indirectly through micronutrient deficiency or other alcohol-related conditions such as malignancy and depression (Simet & Sisson, 2015). Despite this observation, the association was absent after controlling for confounding by sex. Habitual alcohol intake is often associated with males in Nairobi which may explain this finding.

HIV infection was identified a risk factor for tuberculosis and about 16% of the participants tested positive for the virus. The virus depresses the body immune system thereby promoting the proliferation of the Mycobacterium in the body. HIV is the most important known risk factor that promotes progression to active tuberculosis in people with latent *Mycobacterium tuberculosis* infection (Sudha, 2015).

Age was found to be associated with tuberculosis where those below thirty years were more susceptible which is consistent with findings from other studies (Kirenga et al., 2015). Possible explanations is that they have robust social interactions which exposes them to infected people. This group also is more predisposed to HIV infection in Kenya.

Marital status was not significantly associated with TB despite the fact that majority of the participants had spouses. Spouses are likely to infect each other and a cohort study is the most suitable design to determine likely association (Crampin et al., 2015) since the incubation period

is long. This finding contradicts a Nigerian study where an association was observed (Aghol et al., 2014)

History of the previous contact with TB patient was significantly associated with the disease and 18.5% of the cases had prior contact with an infected person. TB is an infectious disease and the more close and intense contact with a sufferer is, the greater the intensity of the organisms that can be inhaled with the subsequent manifestation of the clinical disease. Gounder et al., (2015) demonstrated this narrative in a retrospective cohort study carried out in New York City.

No association existed between the level of education and development of tuberculosis which was contrary to a Nigerian study (Ogboi et al., 2010). Education is important since it enhances the knowledge of the disease transmission, clinical manifestations, diagnosis, and treatment. All the participants in this study had at least primary level of education and majority had attained a secondary level and above which was sufficient. Since the study was carried out in a densely populated area within an urban center, level of education may not have been very crucial because the organisms are transmitted by air and everyone was predisposed.

A new finding in this study is that the odds of tuberculosis infection increased with the number of risk factors. It appears that risk factors have additive effects on each other probably due to the different postulated mechanisms of action discussed above. This is an important observation which should be considered during the management of the disease so that patients can be educated appropriately.

4.6 Conclusion

Male sex was the most important predictor for tuberculosis in Nairobi which has not been emphasized in previous studies. This an important finding and suggests that although smoking, HIV and previous contact with TB patient are associated with TB, their contribution is largely

dependent on sex. As the number of risk factors increased, the chance of contracting the disease was enhanced.

4.7 Recommendations

4.7.1 Recommendations for policy and practice

Health promotion should be introduced in Nairobi where information regarding tuberculosis will be disseminated to the public. The message should contain among others the behaviors that predispose people to the disease. Smoking anduse of alcohol should be discouraged. The ban of smoking in public places should be vigorously enforced including the drinking places. Sensitization of the public regarding the association between the TB and thses habits should be done. Men should be targeted due their vulnerability arising both genetic and behaviours. People should be encouraged to undergo HIV testing so as to know their status and preferably put on antiretroviral drugs before the immune system is destroyed to a great extent which in turn will facilitate the bacteria that causes tuberculosis to proliferate.

4.7.2 Recommendations for research

Research should be conducted to find out the reasons why men smoke and drink more than women. The findings may assist to reduce these habits and thereby decrease the number of TB cases especially among men who are naturally predisposed.

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CHAPTER FIVE: COMPARATISON OF KNOWLEDGE OF TUBERCULOSIS AMONG PATIENTS WITH AND WITHOUT THE DISEASE

5.1 Introduction

Management of tuberculosis is enhanced if the level of knowledge regarding the disease is increased. Several international studies have reported poor knowledge, attitudes, and practices towards TB (Wang et al., 2012). Lack of knowledge and stigmatization cause underutilization of health services, delay in seeking diagnosis, and poor adherence to treatment (WHO, 2006). This has led to victims hiding vital information from even close family members thereby enhancing the spread of the disease. The onset of signs and symptoms is often insidious and diagnosis may be realized after considerable damage has occurred. Signs and symptoms subside markedly following the initiation of therapy and some of the patients stop taking the drugs prematurely due to a false perception of cure. The long duration of treatment, difficulty in accessing a health facility and adverse effects also contribute to poor adherence. The results of this behavior are detrimental and include treatment failure, increased incidence of MDR-TB and death.

Researchers have mainly focused on knowledge among TB patients and healthcare workers (Nabil et al., 2012) thereby leaving out many people who should be assessed in order to contain the disease more effectively. The objective of this study was to compare the knowledge level of TB and its determinants among participants receiving first-line TB therapy (Cases) and those who were not (Controls) among residents of Nairobi City county. The detailed methods of this study are described in **chapter 3 section 3.3**. The Knowledge level was categorized into four dimensions, namely; signs and symptoms, transmission, treatment and prevention of tuberculosis.

5.2 Hypotheses

Hypotheses were developed to investigate whether there was a relationship between knowledge level and TB status. Each dimension was therefore subjected to test using logistic regression analysis. An association that yielded an odds ratio greater than one and a p-value equal or less than 0.05 was considered statistically significant. The hypotheses formulated were as follows;

Hypothesis 1

H0: There was no difference in the level of knowledge of signs and symptoms of tuberculosis between participants on first-line treatment and those who were not on treatment for TB.

H1: There was a difference in the level of knowledge of tuberculosis of signs and symptoms between participants on first-line treatment and those who were not on treatment for TB.

Hypothesis 2

H0: There was no difference in the level of knowledge of modes of transmission of tuberculosis between participants on first-line treatment and those who were not on treatment for TB .

H1: There was a difference in the level of knowledge of modes of transmission of tuberculosis between participants on first-line treatment and those who are not on treatment for TB .

Hypothesis 3

H0: There was no difference in the level of knowledge of the treatment of tuberculosis between participants on first-line treatment and those who are not on treatment for TB .

H1: There was a difference in the level of knowledge of the treatment of tuberculosis between participants on first-line treatment and those who are not on treatment for TB .

Hypothesis 4

H0: There was no difference in the level of knowledge of prevention of tuberculosis among participants on first-line treatment and those who are not on treatment for TB .

H1: There was a difference in the level of knowledge of prevention among participants on first-line treatment and those who are not on treatment for TB .

Hypothesis 5

H0: There was no difference in the overall level of knowledge of tuberculosis among participants on first-line treatment and those who are not on treatment for TB .

H1: There was a difference in the overall level of knowledge of tuberculosis among participants on first-line treatment and those who are not on treatment for TB .

5.3 Objectives of the case control study to identify risk factors for tuberculosis

The main objective was to determine the level of knowledge of tuberculosis in Nairobi. The specific objectives were to:

iv. determine the overall level of knowledge of tuberculosis
v. measure the level of knowledge on signs and symptoms, transmission, treatment and prevention of tuberculosis.
vi. to investigate the factors that influence the level of knowledge of tuberculosis.

5.4 Results

5.4.1 Comparison of knowledge of tuberculosis between cases and controls

The sociodemographic characteristics of the study participants are as described in **chapter four.**

Table 5.1. Comparison of Knowledge of tuberculosis between cases and controls (N=92)

Variable	Cases (N=46) n (%)	Controls, (N=46) n (%)	P value
DKSS			
Coughing with or without blood for at least three weeks	40 (87)	39 (84.8)	0.500
Chest pain	30 (65.2)	8 (17.4)	< **0.001***
Shortness of breath	30 (65.2)	10 (21.7)	<**0.001***
Loss of appetite	36 (78.2)	8 (17.4)	<**0.001***
Weight loss	40 (87)	12 (26)	<**0.001***
Fever with night sweats	35 (76)	20(43.4)	**0.003***
DKT			
TB is communicable	41 (89.1)	6 (13)	**0.001***
TB can be communicated through sneezing	38 (82.6)	20 (43.5)	<**0.001***
TB can be communicated through coughing	39 (84.8)	27 (58.7)	**0.010***
TB can be communicated through using clothing and utensils of affected people.	22 (47.8)	14 (30.4)	0.134
DKTr			
Treatment for TB is available	45 (97.8)	43(93.5)	0.617
Regular intake of TB medicine cure patients	44 (95.7)	40 (87)	0.267
Irregular intake of medicine causes death and drug resistance	40 (87)	35 (76.1)	0.283
DKP			
Vaccine against TB is available	23 (50)	22 (47.8)	1.0
Keeping far away from affected people when sneezing should be observed	16 (34.8)	10 (21.7)	0.247
One should avoid sharing clothing and utensils with infected people	20 (43.5)	32 (69.6)	**0.02***
Cleanliness protects against TB	34 (73.9)	38 (82.6)	0.449

*- Statistically significant p-value

The dimensions of knowledge that were assessed are summarized in **table 5.1**. Generally, the cases were more informed of the signs and symptoms of TB than the controls. Assessment of

knowledge on transmission revealed that cases were more informed than the controls. Coughing was recognized as a cardinal symptom of tuberculosis by both cases and controls. Forty (87%) cases and 39 (84.8%) controls were aware that a cough is a characteristic of TB and the difference was not statistically significant (p=0.5). There were statistically significant differences between the two

groups in identification of other clinical manifestations including chest pain (p<0.001), shortness of breath (p<0.001), loss of weight (p<0.001) and fever with night sweats (p=0.003). Forty-one (89.1%) cases and 6 (13%) controls knew that TB is a communicable disease and the difference was statistically significant across arms (p=0.01). In addition, 38 (82.6%) cases and 20 (43.5%) controls knew that spread of TB can occur through sneezing (p<0.001). The exception was whether tuberculosis can be transmitted through sharing of items such as utensils where the difference was not statistically significant (p= 0.134). Majority of the cases intimated that TB can be spread through sharing of utensils which was contrary to the opinion of the controls but the difference was not statistically significant. The assessment of knowledge on treatment showed that there was no statistically significant difference between cases and controls among most variables. Forty five (97.8%) cases and 43 (93.5%) controls knew that TB is curable.

Majority of the participants were aware that regular intake of medicines cures patients and non-adherence can lead to death or development of MDR-TB. Majority of the participants were aware of the different prreactionsive approaches used to halt the spread of the disease. Twenty three (50%) cases and 22(47.8%) controls were aware of the existence of a vaccine. Sixteen (34.8%) cases and 10(21.7%) controls believed that a healthy person should keep away from infected people during sneezing. For both variables, however, the difference was not statistically significant.

5.4.2. Level of knowledge of tuberculosis

The score for each dimension of knowledge was determined using the procedure described in

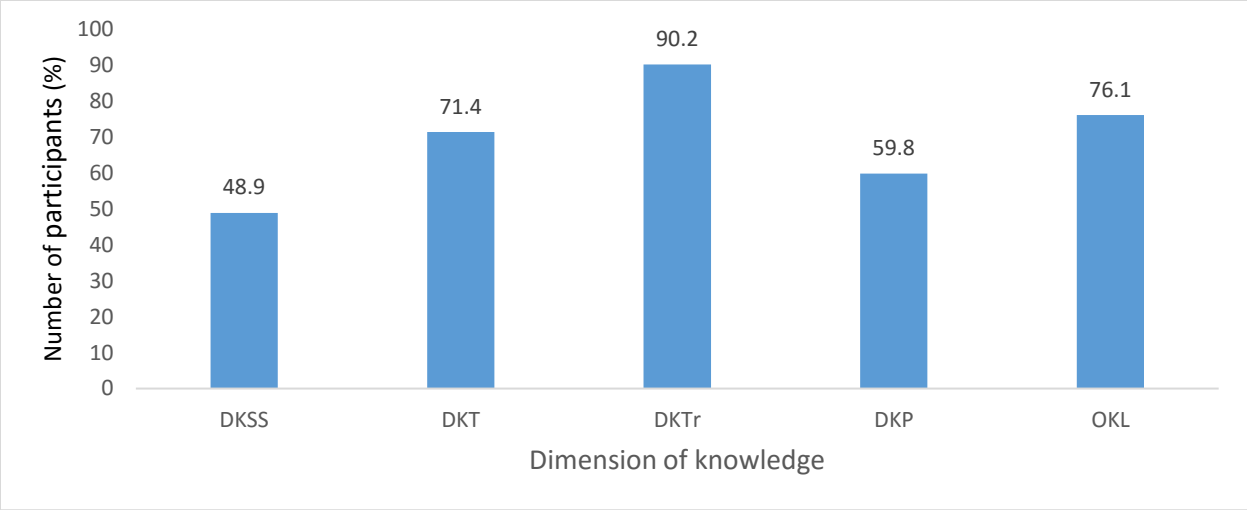

Fig 5.1 Adequacy of knowledge of tuberculosis (N=92)

chapter 3 page 24 and categorized as either adequate or inadequate. The results for all the dimensions are shown in **figure 5.1**. The majority (83, 90.2%) of the participants had adequate knowledge about treatment followed by transmission and prevention. Knowledge of signs and symptoms was generally inadequate (45, 48.9%). Most (70, 76.1%) participants had adequate knowledge of TB.

Additional analysis was conducted to compare the adequacy of knowledge between the cases and controls and the results are shown in **table 5. 2**. Generally, the cases scored highly in all dimensions of knowledge explored except prevention (DKP) where the controls were better. The differences in knowledge level were statistically significant except for DKP.

Table 5.2. Comparison of adequacy of level of knowledge (N=92)

Dimension of Knowledge	Cases (n, %)	Controls (n, %)	P-value
DKSS	40(87)	5(10.9)	**<0.001***
DKT	38 (82.6)	28(60.9)	**0.036***
DKTr	45(97.8)	38 (82.6)	**0.03***
DKP	25 (54.3)	30 (65.2)	0.395
OKL	42 (91.3)	28 (60.9)	**0.001***

*-Statistically significant p-value

5.3.3. Predictors of knowledge for tuberculosis

Bivariable and multivariable logistic regression analyses were conducted to determine which sociodemographic characteristics were associated with the different dimensions of knowledge. Dimensions of knowledge were the dependent variables and sociodemographic characteristics were the independent variables. The results of the bivariable logistic regression analysis are summarized in **table 5.3**.

Table 5.3. Bivariable logistic regression for predictors of knowledge of tuberculosis (N=92)

Variable	DKSS COR (95% CI)	DKT COR (95%CI)	DKTr COR (95%CI)	DKP COR(95%CI)	OKL COR (95% CI)
TB infection	54.7(15.4,193.5) **P <0.001***	3.05(1.16,8.02) **P=0.023***	9.47 (1.1,79.18) **P=0.038***	0.63(0.27,1.47) P=0.289	6.75(2.06,22.06) **P=0.002***
Sex	9.4(3.45,25.69) **P< 0.001***	11.56(0.59,4.1) P=0.369	1.25(0.29,5.37) P=0.76	1.83(0.76, 4.42) P=0.180	2.55(0.85,7.69) P= 0.096
Age	2.65(1.15,6.15) **P=0.024***	1.01(0.97,1.06) P=0.537	1.05(0.97,1.13) P= 0.202	1.01(0.97,1.06) P=0.502	1.02(0.96,1.06) P=0.664
Marital status	0.59(0.25,1.37) P=0.218	0.81(0.32,2.1) P=0.671	3.58(0.7,18.28) P=0.125	2.12(0.9,5.01) P=0.088	0.7(0.25,1.93) P=0.492
Education level	0.94 (0.54,1.63) P=0.814	1.85(0.77,4.49) P=0.170	0.83(0.37,1.77) P=0.629	0.89(0.51,1.55) 0.677	2.26(0.86,5.91) P=0.096
Number of occupants in the house	0.31(0.13,0.73) **P=0.008***	0.53(0.2,1.39) P=0.201	0.69(0.16,2.93) P=0.611	1.38(0.59,3.20) P=0.459	0.58(0.21,1.62) P=0.303
HIV infection	1.98(0.73,5.37) 0.179	4.85(1.04,226) **P=0.044***	2.53(0.3,21.56) P=0.393	0.68(0.25,1.8) P=0.432	2.19(0.58,8.3) P=0.248
Previous TB infection	3.28(0.33,32.82) P=0.311	1.19(0.12,12) P=0.882	1	0.21(0.02,2.1) P=0.184	0.94(0.09,9.5) P=0.958
Use of alcohol	9.35(3.3,26.5) **P<0.001***	2.91(0.98,8.67) P=0.055	4.76(0.57,39.9) P=0.15	0.97(0.41,2.33) P=0.954	4.48(1.21,16.56) **P=0.025***
Previous contact with TB patient	3.42(1.19,9.84) **P=0.023***	2.06(0.54,7.88) P=0.289	2.54(0.3,21.6) P= 0.393	0.68(0.25,1.8) P=0.432	3.72(0.79,17.48) P=0.095
Smoking	11.25(2.4,52.8) **P=0.002***	2.06(0.54,7.88) P=0.289	1	1.79 (0.57,5.58) P=0.318	1.58(0.41,6.11) P=0.505

*Statistically significant p-value

Foot note

Adequate knowledge of signs and symptoms of tuberculosis was found to be strongly associated with sex where males were 9.4 (p<0.001) times more informed compared to females. Participants who were infected with tuberculosis were 54.7 (p<0.001) times more informed compared to uninfected ones. In addition, those with a history of taking alcohol were 9.35 (p<0.001) times more knowledgeable compared to non-alcoholics. Smokers were 11.25 (p=0.002) times more

informed than non-smokers. Those who had previous contact with a patient suffering from tuberculosis were 3.4 (p=0.023) times more knowledgeable of the signs and symptoms than those who did not. Participants older than 30 years were 2.65 (p=0.024) times more informed compared to younger ones. Participants residing in houses with three or more occupants were 0.3 (p=0.008) times more likely to know about signs and symptoms of pulmonary tuberculosis. The characteristics that were not significantly associated with knowledge of signs and symptoms were; marital status (p=0.218), HIV infection (p=0.179), previous TB infection (p=0.311) and level of education (p=0.814). Adequate knowledge on transmission of tuberculosis was significantly associated with only two sociodemographic characteristics. Participants with HIV infection were 4.85 times (p=0.044) more knowledgeable compared to those without the disease. Those with tuberculosis had 3.05 fold (p=0.023) times more knowledge compared to uninfected ones. The other characteristics, namely; sex, age, marital status, education level, number of occupants in the house, previous TB infection,use of alcohol, smoking and previous contact with patients infected with TB did not have a significant association with the knowledge of how the disease is transmitted.

No sociodemographic characteristic was found to be significantly associated with adequate knowledge of treatment and prevention. For the overall level of knowledge, alcoholics were 4.48 (p=0.025) more knowledgeable compared to non- alcoholics. Participants with tuberculosis were 6.75(p=0.002) more informed than those without the disease.

Table 5.4. Multivariable logistic regression analysis of determinants of knowledge of TB

Variable	DKSS AOR (95% CI)	DKT AOR (95%CI)	DKTr AOR (95% CI)	DKP AOR (95% CI)	OKL AOR (95%CI)
TB infection	359.8 (17,7627) **P<0.001***	5.2 (0.88,30.9) P=0.07	69.49 (1.8,2638) **P=0.022***	0.304(0.06,1.4) P=0.128	13.5(1.7,109.1) **P=0.015***
Sex	1.37 (0.13, 14.07) P=0.792	0.33(0.07,1.65) P=0.177	0.11(0.01,1.71) P=0.114	13.5(1.7,109.1) **P=0.015***	0.313(0.04,2.5) P=0.271
Age	0.84(0.88,1.11) P=0.142	0.99(0.88,1.11) P=0.804	0.95 (0.73,1.22) P=0.673	0.97(0.88,1.11) P=0.818	1.12(0.95,1.13) P=0.162
Marital status	1.01(0.11,9.15) P=0.99	1.86(0.45,7.73) P=0.393	1.24(0.12,12.83) P=0.855	2.51(0.72,8.83) P=0.149	1.09(0.22,5.46) P=0.916
Education level	0.56 (0.86, 3.6) P=0.54	3.47 (1, 12.07) P=0.051	0.178(0.017, 1.84) P=0.148	1.1 (0.44,2.78) P= 0.838	4.58(1, 20.5) **P=0.046***
Number of occupants in the house	1.33 (0.14, 13) P=0.81	0.44 (0.1, 1.98) P=0.287	1.34(0.149, 12.07) P=0.794	1.2(0.19,7.82) P=0.825	2.4(0.3, 21.95) P=0.437
HIV infection	0.26 (0.001,0.59) **P=0.022***	23.54(1.6,341) **P=0.021***	0.16 (0.003, 7.28) P=0.343	1.2 (0.19, 7.82) P=0.825	2.4(0.3, 21.95) P=0.437
Previous TB infection	0.5 (0.002, 110.7) P=0.803	1.5 (0.1, 341.3) P=0.805	1	0.25 (0.01,5.03) P=0.364	(0.003,5.85) P=0.3
Use of alcohol	0.4(0.02, 7.24) P=0.536	4.72(0.5, 46.6) P=0.184	0.53(0.02,16.15) P=0.718	1.04(0.16, 6.87) P=0.962	39.4(1.1,1385) **P=0.043***
Previous contact with TB patient	0.62(0.03, 13) P=0.761	0.4(0.06, 2.59) P=0.061	0.9 (0.04, 21.44) P=0.943	0.52 (0.09, 281) P=0.445	2.23(0.3, 20.1) P=0.475
Smoking	10.2(0.2, 663.4) P=0.761	1.71(0.1, 21.5) P=0.676	1	1	1

*- Statistically significant relationship

Additional analysis was carried out to determine the sociodemographic characteristics that were associated with the various dimensions of knowledge of tuberculosis using Multivariable logistic regression model and the results are shown in **table 5.4.** Participants with TB were about 13 (p=0.015) times more overall knowledgeable compared to those without the diseases. Those with a history of taking alcohol were 39 (p=0.043) times more knowledgeable compared to the ones

without. The overall level of knowledge increased with level of education and those who had attained a secondary level and above were 4.58 (p=0.046) times better than those who had not. Participants with tuberculosis had about 360 odds of knowing about the signs and symptoms than those without the disease. Males were 13.5 (p=0.015) more knowledgeable about different prreactionsive methods used to reduce the spread of tuberculosis than females and participants with tuberculosis were 69.5 (p=0.022) more cognizant of the availability of treatment. HIV infected participants were 23.5 (p= 0.021) more informed about the transmission of tuberculosis but on the other hand, they were less aware of the signs and symptoms (AOR=0.26, 95%CI= 0.001-0.59, p=0.022).

The cases were generally more informed than controls on all aspects of tuberculosis that were investigated**.** There was a difference in the level of knowledge of signs and symptoms of tuberculosis between participants on first-line TB therapy (cases) and those who were not (controls). This difference remains significant even after adjusting for confounding.

There was a difference in the level of knowledge of transmission of tuberculosis between participants on first-line TB therapy (Cases) and those who were not (Controls). The P values from Fischer's exact test was 0.036 and the one from logistic regression analysis was 0.023. The cases had more knowledge than the controls because the odds ratio was 3.05.

There was no difference in the level of knowledge of the treatment of tuberculosis between participants on first-line TB therapy (Cases) and those who were not (Controls). The P values from Fischer's exact test was 0.395 and the one from logistic regression analysis was 0.289.

There was a difference in the overall level of knowledge of tuberculosis between participants on first-line TB therapy (Cases) and those who were not (Controls). The P values from Fischer's exact test was 0.001 and the one from logistic regression analysis was 0.002. The cases had more knowledge than the controls because the odds ratio was 6.75.

5.5 Discussion

This study showed that TB patients had better knowledge of the disease than non-TB patients. A cough for more than three weeks was mentioned by both groups of participants as a common symptom of the disease which was comparable to findings of a study done in China (Zhiping et al., 2016).

For cases, 87% knew that coughing is a symptom of TB which was superior to the findings in Ethiopia (Bati et al., 2013) . This may be attributed to counseling offered in the clinics. The majority (84.8.1%) of the cases knew that the disease could be transmitted through coughing which was higher than findings of a study conducted in Dhaka city (Esmael et al., 2013). Among the non-TB patients, 84.8.7% were aware that coughing is a symptom of TB which was higher than findings from an Ethiopian study (Tolossa et al., 2014). Non-TB patients showed extremely poor knowledge that chest pain, shortness of breath, poor appetite and weight loss are clinical manifestations of TB. The majority (69.6%) of the Non-TB participants believed that sharing clothes and utensils are modes of transmitting the disease which was less than what was observed in Brazil (de Freitas et al., 2015). The basic knowledge about the clinical manifestations and modes of transmission of TB are important components of TB control program in the current study area, because it could reduce patient and health system delays in the diagnosis and treatment (Makwakwa et al., 2014)], as well as the transmission of the disease (Marais et al., 2010).

A notable finding in this study was that majority of cases (97.8%) and controls (93.5%) knew that TB is curable, which was higher than what was observed in China, South Africa (Naidoo et al., 2013) and Iran (Benhaz et al., 2014). This suggests that the counseling done in the health facilities during treatment was effective.

The knowledge of signs and symptoms and prevention of tuberculosis was adequate for 48.9% and 59.8% of all the study participants respectively. This was a worrying observation since a significant proportion of the participants might not have been able to suspect potential cases thus enhancing the spread of the disease and associated morbidity. This finding might have been caused by lack of adequate public awareness arising from insufficient health education.

The characteristics that were independent predictors of overall knowledge for tuberculosis were use of alcohol, education level, sex, age, previous contact with TB patient and tuberculosis infection. Participants who were above 30 years of age and those who had attained the secondary level of education and above were more likely to have adequate knowledge probably due to maturity and formal education that enables them to treat the disease with seriousness required. This observation was similar to findings of a study conducted in Bangladesh (Mondal et al., 2014). Males were more knowledgeable about tuberculosis than females. It is probable that males had attained higher levels of formal education and this contributed to better knowledge about TB. In addition e males were more affected and therefore the chances of encountering another victim were high during socialization. Males tend to be outgoing and take more alcohol compared to females in Nairobi. The possibility of coming into contact with a person with tuberculosis was comparatively high. This finding concurred with an observation from a study carried out in Ethiopia (Sifrash, 2016).

5.6 Conclusion

The level of knowledge on signs and symptoms of tuberculosis among the participants was low. Most participants knew about prevention, transmission, and treatment of the disease. Sociodemographic characteristics that were predictors of the knowledge about pulmonary tuberculosis were male gender, use of alcohol, education level, HIV infection, age and previous contact with a person with pulmonary tuberculosis.

5.7. Recommendations for policy and practice

Health promotion should be introduced in Nairobi regarding signs and symptoms, transmission, treatment and prevention of tuberculosis where the public will be engaged. This approach will reduce the spread of the disease and reduce social stigma associated with it. In addition, the people will be empowered and encouraged to seek treatment early to reduce morbidity and mortality.

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CHAPTER SIX: PREVALENCE OF ADVERSE DRUG REACTIONS AND THEIR IMPACT ON ADHERENCE AMONG PATIENTS ON TREATMENT FOR TUBERCULOSIS

6.1 Introduction

The willingness of a patient to comply with prescribed regimens is the mainstay of tuberculosis treatment (Michael et al., 2016). Several factors influence patients' compliance with treatment. Adverse drug reactions play an important role and these reactions are common when drugs are taken frequently, in combination and over prolonged periods. There is a high level of under-reporting of actual and suspected ADRs but there are significant factors in the treatment of chronic conditions like tuberculosis (Oshikoya & Awobusuyi, 2009). Adverse drug reactions can cause considerable morbidity and mortality (Athira et al., 2015). These reactions may lead to substantial additional costs because of added outpatient visits, tests, and hospitalizations. The frequency, severity, and the nature of TB therapy induced ADRs have always been a concern to patients and health workers (Alasghar et al., 2014). The overall incidence of ADRs caused by anti-TB therapy ranges from 5.1 to 83.5% (Maciel et al., 2010). In Nairobi City County, the incidence of adverse drug reactions has not been adequately explored. There is no protocol for regular monitoring of adverse drug reactions due to tuberculosis chemotherapy and patients present in the health facilities occasionally with severe signs and symptoms. The specific objectives of this study were to determine the prevalence of adverse drug reactions and level of adherence to first- line TB drugs in Nairobi. The methodology used to accomplish these objectives involved a cross sectional study where 190 participants were selected using simple sampling as described in chapter 3 section 3.4.

6.2. Results

6.2.1 Sociodemographic characteristics of participants on first-line TB therapy

The majority (115, 60.5%) of the participants were males and 103(54.2%) had spouses **(Table 6.1).** Fifty-six (29.5%) participants had a body mass index below 18.5 and therefore underweight.

Table 6.1. Sociodemographic characteristics of participants on first-line TB therapy(N=190)

Variable	Frequency	Percent
Sex		
Male	115	60.5
Female	75	39.5
Marital status		
Married	103	54.2
Single	87	45.8
Age category		
18-30	84	44.2
31-40	69	36.3
Above 40	37	19.5
BMI		
Below 18.5	56	29.5
18.6- 25	116	61.1
Above 26	18	9.5
Highest education level		
No formal education	2	1.1
Primary	64	33.7
Secondary	88	46.3
Tertiary	36	19
HIV Co-infected	48	25.3
Relapsed TB infection	16	8.4
Diabetes mellitus	5	2.6
Use of alcohol	102	53.7
Tobacco smoking	67	35.3

Thirty-seven (19.5%) participants were above forty years of age and 36(18.9%) had a tertiary level of education. Forty-eight (25.3%) participants were infected with HIV while 16 (8.4%) had been treated for tuberculosis before. Sixty-seven (35.3%) and 102(53.7 %) participants used to smoke and take alcohol respectively before diagnosis and initiation of tuberculosis therapy. The participants were at different stages of treatment as shown in **figure 6.1** below. Sreactionsy-three

(38.4%) were in the first two months intensive phase of therapy where four drugs (isoniazid, rifampicin, ethambutol, and pyrazinamide) were used. The continuation phase where two drugs (isoniazid and rifampicin) were administered commenced from the third month of treatment and 117(61.6%) participants were involved.

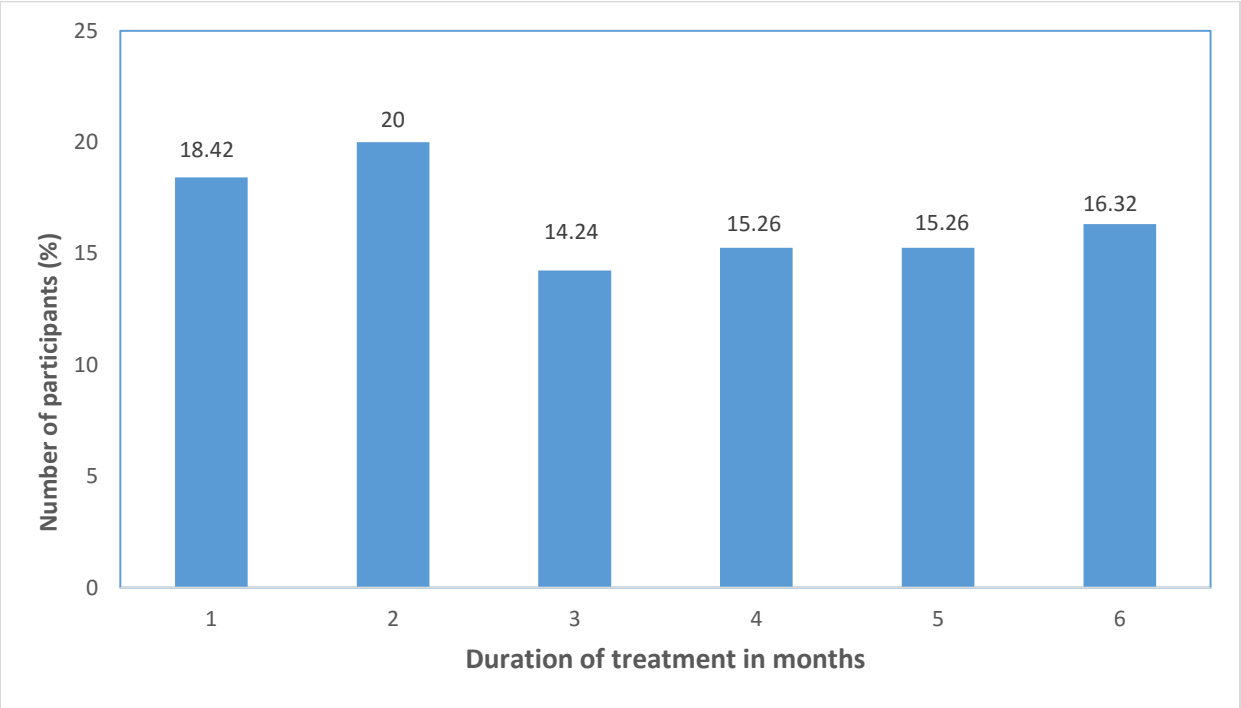

Fig 6.1. Distribution of participants according to duration of treatment (N=190)

6.2.2 Prevalence of adverse drug reactions in participants on first-line TB therapy

The most common adverse drug reactions were neurological, immunological and gastrointestinal disturbances **(Table 6.2)**. Ninety-nine (52.1%) participants complained of tiredness, 70(36.8%) experienced numbness of the extremities, 61(32.1%) had tingling sensations, and 14 (7.4%) were depressed. The most prevalent gastrointestinal disturbances were nausea and vomiting (59, 31.1%) and anorexia. The prevalence of skin rash and arthralgia were 58(30.5%) and 69(36.3%) respectively. Blurred vision occurred among 38 (20%) participants.

Table 6.2. Prevalence of adverse drug reactions of first-line TB therapy (N=190)

Adverse drug reactions	Frequency	Percent
Gastrointestinal disturbances		
Loss of appetite	58	30.5
Nausea and vomiting	59	31.1
Neuropsychiatric disturbances		
Clumsiness/unsteadiness	38	20
Numbness	70	36.8
Tingling sensation	61	32.1
Burning or pain in the hands and feet	32	16.8
Mental depression	14	7.4
Psychosis	3	1.6
Seizures	2	1.1
Hematological disturbances		
Sore throat	14	7.4
Unusual bleeding and bruising	3	1.6
Musculoskeletal disturbances		
Arthralgia	69	36.3
Muscle twitching	3	1.6
Pain in the joints	17	9
Dermatological reactions		
Skin rash	58	30.5
Visual disturbances		
Blurred vision	38	20
Loss of vision	2	1.1
Inability to distinguish green and yellow	3	1.6
Eye pain	17	9
Others		
Tiredness/ weakness	99	52.1
Decreased or increased urine	48	25.3
Increased thirst	36	19

6.2.3. Comparison of adverse drug reactions between HIV and non-HIV co-infected

All the 48 participants who were HIV co-infected were on anti-retroviral drugs concurrently with the TB regimens. The concurrent administration of the drugs predisposed the participants to adverse drug reactions and therefore it was prudent to compare the two groups as shown in **table 6.3**. Gastrointestinal disturbances were common for both groups where 16 (33.3%) and 42(29.6%)

Table 6.3 Adverse drug reactions between HIV and non- HIV infected participants (N= 190)

Types of adverse drug reactions	Frequency (n, %)		P- value
	HIV positive (n=48)	HIV negative (n=142)	
Gastrointestinal disturbances			
Loss of appetite	16 (33.3)	42 (29.6)	0.717
Nausea and vomiting	19 (39.6)	40 (28.2)	0.152
Neuropsychiatric disturbances			
Clumsiness/unsteadiness	12 (25)	26 (18.3)	0.404
Numbness	18 (37.5)	52 (36.6)	1
Tingling sensation	14 (29.2)	47 (33.1)	0.721
Burning sensation or pain in the hands and feet	6 (12.5)	26 (18.3)	0.503
Mental depression	5 (10.4)	9 (6.3)	0.349
Psychosis	0 (0)	3 (2.1)	0.573
Musculoskeletal disturbances			
Arthralgia	16 (33.3)	53 (37.3)	0.729
Muscle twitching	1 (2.1)	2 (1.4)	1.0
Pain in the joints	7 (14.6)	10 (7)	0.143
Visual disturbances			
Blurred vision	10 (21)	28 (19.7)	0.838
Eye pain	4 (8.3)	13 (9.2)	1.0
Others			
Tiredness/ weakness	26 (54.2)	73 (51.4)	0.867
Skin rash	30 (62.5)	40 (28.2)	0.277
Decreased or increased urine	13 (27.1)	35 (18.2)	0.848
Increased thirst	6 (12.5)	30 (21.1)	0.209

experienced loss of appetite among HIV and non-HIV infected participants respectively. Nausea and vomiting were also frequent and 19(39.6%) and 40(28.2%) participants were victims respectively. Neuropsychiatric disturbances were common across both groups. Majority of the participants experienced tiredness and weakness at 26(54.2%) and 73(51.4%) for HIV and non-HIV infected respectively. Other adverse drug reactions involving the nervous system were; clumsiness and unsteadiness, numbness, tingling sensation, burning sensation and mental depression. Musculoskeletal disturbances were common which manifested as arthralgia, muscle twitching and pain in the joints. Thirty (62.5%) HIV and 40 (28.2%) non-HIV infected participants suffered from hypersensitivity reaction that presented as skin rash. The blurring of vision occurred among 10 (21%) and 35 (18.2%) HIV and non-HIV infected participants respectively. The volume of urine excreted varied depending on the amount of fluid intake.

Despite the fact that HIV infected participants were on anti-retroviral drugs , the prevalence of adverse reactions was not statistically different from non-HIV infected ones. However it was notable that they had a higher frequency of side effects. It was notable that in HIV positive patients the prevalence of skin rash was 62.5% compared to only 28.2% amongst patients who were HIV negative.

6.2.4 Level of adherence to first-line TB therapy

The level of adherence to tuberculosis treatment was determined using the Morisky eight-point scale and the results are summarized in **fig 6.2**.Good adherence to treatment was reported among 98(51.6%) participants and 89 (46.8%) of them had moderate adherence. Only 3(1.6%) participants had poor adherence.

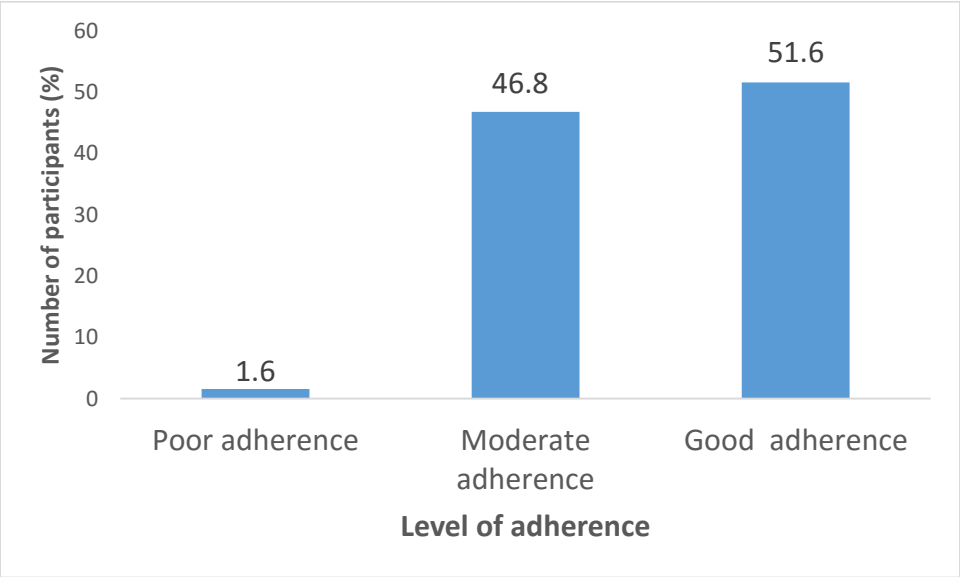

Fig 6.2. Level of adherence to anti-tuberculosis drugs (N=190)

6.2.4. Impact of sociodemographic characteristics on level of adherence

Using Fisher's exact test the relationship between sociodemographic characteristics and level of adherence to TB drugs was explored and the results are summarized in **table 6.4**. Fifty-seven (49.6%) males and 32(42.7%) females exhibitedmoderate adherence compared to 57(49.6%) and 41(54.7%) who hadgood adherence respectively but the difference was statistically insignificant (p=0.459). Participants across all age groups showed medium andgood adherence to therapy with no significant difference (p=0.572). Employment status (p=0.468), level of education (p=0.788) and marital status (p=0.159) did not have a significant effect on adherence. Other attributes that had no statistically significant relationship were; HIV infection (p=0.249), previous TB infection (p=1), malnutrition (p=0.859), diabetes mellitus (p=0.420) and smoking (p= 0.443). A statistically significant association existed between duration of therapy and level of adherence to treatment

(p=0.05). The level of adherence generally decreased in the third month, then went up towards the end of treatment. Use of alcohol was significantly associated with poor adherence

Table 6.4 Comparative analysis between sociodemographic characteristics and level of adherence (N=190)

Characteristic	Level of adherence			P value
	Low (n, %)	Medium (n, %)	High (n, %)	
Sex				
Male	1(0.9)	57(49.6)	57 (49.6)	0.459
Female	2(2.7)	32(42.7)	41 (54.7)	
Age in years				
18-30	2 (1.1)	37 (19.5)	45 (23.7)	0.572
31-40	1 (0.5)	37 (19.5)	31 (16.3)	
Above 40	0 (0)	15 (7.9)	22 (11.6)	
Marital status				
Married	2 (1.1)	42 (22.1)	49 (25.8)	0.159
Single	1 (0.5)	47 (24.7)	39 (20.5)	
Education level				
Primary	1 (0.5)	32 (16.8)	33 (17.4)	
Secondary	1 (0.5)	40(21.1)	47 (24.7)	0.788
Tertiary	1 (0.53)	17 (9)	18 (9.5)	
Employment status				
Formal	0 (0)	21 (11.05)	17 (8.9)	0.468
Non formal	3 (1.6)	68 (35.8)	80 (42.1)	
Duration of treatment in months				
1	0 (0)	12 (6.3)	23 (12.1)	
2	0 (0)	18 (9.5)	20 (10.5)	
3	1(0.5)	16 (8.4)	11 (5.8)	**0.05***
4	2 (1.1)	18 (9.4)	9 (4.7)	
5	0 (0)	10 (5.3)	19 (10)	
6	0 (0)	15 (7.9)	16 (8.4)	
HIV infection	2 (4.17)	21(43.6)	25 (52.1)	0.249
Previous TB infection	0 (0)	8 (50)	8 (50)	1
Malnutrition	0 (0)	8 (44.5)	10 (55.6)	0.859
Diabetes mellitus	0 (0)	1(0.3)	4 (0.8)	0.420
Use of alcohol	0(0)	58 (56.9)	44 (43.1)	**0.002***
Tobacco smoking	0(0)	34 (50.8)	33 (49.3)	0.443

***- S**tatistically significant p-value

to therapy (p=0.002). Fifty-eight (56.86%) reported moderate adherence compared to 44(43.14%) with good adherence.

6.2.4. Impact of adverse drug reactions on level of adherence to therapy

The impact of adverse drug reactions on adherence to anti-tuberculosis drugs is shown in **table 6.5.**

Table 6.5 Comparative analysis between adverse drug reactions and adherence (N=190)

Adverse reactions	Adherence level			
	Poor (n, %)	**Moderate (n, %)**	**Good (n, %)**	**P value**
Gastrointestinal disturbances				
Loss of appetite	1(1.72)	29 (50)	28 (48.28)	0.837
Nausea and vomiting	1 (1.69)	30 (50.85)	28 (47.46)	0.789
Neuropsychiatric disturbances				
Tiredness and weakness	2(2)	52 (52.53)	45 (45.45)	0.184
Clumsiness and unsteadiness	1 (2.63)	20 (52.63)	17 (44.74)	0.385
Numbness	1 (1.43)	38 (54.29)	31 (44.29)	0.221
Tingling sensation	1(1.64)	32 (52.45)	28 (45.9)	0.532
Burning sensation or pain in the hands	0 (0)	16 (50)	16 (50)	0.912
Mental depression	1(7.14)	10 (71.4)	3(21.43)	**0.026***
Psychosis	0 (0)	2(66.7)	1(33.3)	0.946
Seizures	0	2(100)	0	0.250
Musculoskeletal disturbances				
Skin rash	0 (0)	30 (51.72)	28 (48.28)	0.515
Arthralgia	1 (1.45)	33 (47.83)	35 (50.72)	0.946
Visual disturbances				
Impaired vision	0	19 (47.37)	21(52.63)	1
Eye pain	0	7 (41.18)	10 (58.82)	0.713
Others				
Change in volume and frequency of urination	1(2.08)	22(45.84)	25 (52.08)	1
Increased thirst	1(2.78)	15(41.67)	20(55.56)	0.498

*- Statistically significant p -values

Among those participants who experienced nausea and vomiting, 29(50%) and 28(48.28%) had a medium or high level of adherence respectively and only 1(1.72%) depicted poor adherence. Nausea and vomiting occurred in 30(50.85%) and 28(47.46%) participants with medium and good adherence respectively. Despite that these gastrointestinal disturbances were common there was no statistically significant association as all the p values were greater than 0.05.

Among the participants suffering from tiredness and weakness, 52(52.53%) and 17(45.45%) showed medium andgood adherence respectively and the trend was similar among those who presented with tingling and burning sensation in the limbs but no statistically significant association was observed. Mental depression was significantly associated with the level of adherence (p=0.026) and the majority (10, 71.43%) hadmoderate adherence. Skin rash manifested in 30(51.72%) and 28(48.28%) participants with medium andgood adherence respectively. The same trend was observed among those who had arthralgia and impaired vision. In all the instances, however, the associations were statistically insignificant.

6.2.5 Identication of predictors of adherence by binary logistic regression analysis

Low adherence andmoderate adherence were merged to form nonadherence. This was done to make adherence a dichotomous variable to enable binary logistic regression to be conducted. The results of logistic regression analysis with adherence as the dependent variable and sociodemographic characteristics as independent variables are shown in **table 6.6.** Adherence decreased as the duration of treatment increased (AOR =0.93, 95% C I= 0.76- 1.14, p= 0.107). Females were 1.1 more likely to be adherent than males (AOR=1.10, 95% CI= 0.52- 2.32, p=0.107) and age did not influence adherence since the odds ratio was about one. Participants without spouses were less adherent (AOR= 0.71, 95% CI= 0.38 - 1.34, p= 0.287) compared to

married ones but there was no difference noted at different levels of education. The participants who were not formally employed were 1.43 more likely to adhere to the drugs despite that different levels of income did not have an effect. Those infected with HIV were slightly more likely (AOR=1.1, 95% CI= 0.52- 2.34, p= 0.801) to be adherent while previous infection and malnutrition decreased it. Participants with a history of smoking were 1.23 more likely to adhere to treatment. Despite all these associations

Table 6.6. Logistic regression analysis of sociodemographic predictors of adherence (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	COR (95% CI)	**P value**	**AOR (95% CI)**	**P value**
Duration of therapy	0.94 (0.80, 1.11)	0.497	0.93 (0.76, 1.14)	0.477
Sex	1.23 (0.68, 2.20)	0.492	1.10 (0.52, 2.32)	0.802
Age	1.01 (0.98, 1.04)	0.522	1.01 (0.97, 1.05)	0.544
Marital status	0.61 (0.34, 1.08)	0.088	0.71 (0.38, 1.34)	0.287
Education	0.98 (0.67, 1.44)	0.922	1 (0.64, 1.58)	0.981
Employment	1.39 (0.68, 2.84)	0.365	1.43 (0.62, 3.27)	0.401
Income	0.94 (0.71, 1.25)	0.684	1.09 (0.76, 1.57)	0.633
HIV infection	1.03 (0.53, 1.98)	0.936	1.1 (0.52, 2.34)	0.801
Previous TB infection	0.93 (0.34, 2.60)	0.895	0.91 (0.29, 2.86)	0.877
Malnutrition	1.20 (0.45, 3.17)	0.723	0.92 (0.3, 2.85)	0.822
Alcoholism	0.48 (0.27, 0.85)	**0.013***	0.39 (0.18, 0.85)	0.17
Tobacco smoking	0.87 (0.48, 1.57)	0.636	1.23 (0.54, 2.83)	0.619

*- Statistically significant p-value

described, no statistical significance was observed. use of alcohol was a strong predictor for non-adherence (COR=0.48, 95% CI= 0.27- 0.85, p=0.013) and those with a history of drinking were 0.48 times likely to take the drugs as recommended. In other words, they were less adherent.

Additional logistic regression analysis was carried out to determine the association between adherence and adverse drug reactions and the results are summarized in **table 6.7** .

Table 6.7. Logistic regression analysis of adverse drug reactions as predictors of level of adherence to drug therapy (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	COR (95% CI)	**P value**	**AOR (95% CI)**	**P Value**
Loss of appetite	0.83(0.45, 1.53)	0.546	1.21 (0.55, 2.64)	0.635
Nausea, vomiting	0.79 (0.43, 1.46)	0.446	0.86 (0.4, 1.88)	0.714
Tiredness or weakness	0.6 (0.34, 1.06)	0.079	0.52 (0.25, 1.09)	0.083
Clumsiness or unsteadiness	0.71 (0.35, 1.45)	0.347	0.80 (0.33, 1.91)	0.613
Numbness	0.63 (0.35, 1.14)	0.125	0.66 (0.30, 1.44)	0.300
Tingling sensation	0.72 (0.39, 1.32)	0.282	0.75 (0.31, 1.82)	0.531
Burning pain in the limbs	0.93 (0.43, 1.98)	0.845	1.63 (0.60, 4.45)	0.341
Sore throat	0.68 (0.23, 2.06)	0.500	0.66 (0.16, 2.71)	0.567
Skin rash	0.83 (0.45, 1.53)	0.546	1.07 (0.52, 2.17)	0.859
Arthralgia	0.95 (0.52, 1.7)	0.859	1.16 (0.57, 2.34)	0.680
Mental depression	4.3 (1.16, 15.95)	**0.029***	4.21 (0.93, 19.07)	0.062
Psychosis	0.46 (0.04, 5.2)	0.533	0.25 (0.01, 12.63)	0.492
Muscle twitching	0.46 (0.04, 5.2)	0.533	1.26 (0.01, 144.4)	0.923
Blurred vision	1.05 (0.52, 2.15)	0.885	1.26 (0.49, 3.24)	0.635
Inability to distinguish green and yellow	1.89 (0.17, 21.26)	0.604	3.53 (0.17, 74.48)	0.417
Eye pain	1.38 (0.50, 3.79)	0.532	1.6 (0.48, 5.25)	0.445
Chills	0.94 (0.06, 15.2)	0.964	4.38 (0.07, 278.2)	0.485
Joint pains	0.82 (0.30, 2.22)	0.696	0.73 (0.22, 2.43)	0.612
Decreased or increased urination	1.03 (0.53, 1.98)	0.936	0.90 (0.38, 2.12)	0.814
Increased thirst	1.22 (0.59, 2.52)	0.596	1.6 (0.62, 4.1)	0.323

*****-Statistically significant p-value

Nausea and vomiting decreased adherence (AOR=0.86, 95% CI= 0.4 - 1.88, p=0.714).A similar effect was noted with tiredness and weakness (AOR=0.52, 95% CI= 0.25- 1.09, p=0.079). Among the adverse drug effects involving the peripheral nerves, numbness and tingling sensation were

associated with non- adherence but those who experienced a burning sensation in the extremities were more likely to be compliant to drugs (AOR=1.63, 95% CI= 0.60- 4.45).The participants experiencing loss of appetite were more likely to be adherent (AOR=1.21, 95% CI= 0.55 - 2.64, p=0.635) probably because of the effects of the anti TB drugs.

Mental depression was a strong predictor of the level of adherence to drug therapy (COR= 4.3, 95% CI=1.16- 15.95, p=0.029). Participants with psychosis and joint pains had were less adherent but those with eye involvement such as the inability to distinguish yellow and green were approximately 3.5 times more likely to be adherent.

6.2.6 Association between treatment phase and type of adverse drug reactions

The first line treatment was divided into intensive and continuation phase. In the intensive phase, four drugs (isoniazid, pyrazinamide, ethambutol, and rifampicin) were used for two months followed by continuation phase where two drugs (isoniazid and rifampicin) were used for four months. Logistic regression was done to explore the relationship between the phase of therapy and adverse drug reactions and the results are shown in **table 6.8**. Participants in the intensive phase of therapy were more likely to experience loss of appetite (AOR=1.79, 95% CI = 0.75- 4.25, p= 0.188), nausea and vomiting (AOR=2.03, 95%CI=0.86- 4.81, p= 0.107) compared to those in the continuation phase but the associations were not statistically significant. Tiredness and weakness were associated with the phase of therapy and participants in the intensive phase were about two times more likely (AOR= 2.43 95% CI=1.09 -5.47, p=0.031) to experience these symptoms compared to those in the continuation phase. Neurological adverse drug effects were less likely to manifest in the intensive phase of therapy and some were associated with duration of therapy such as numbness (COR=0.47, 95% CI= 0.26 - 0.85, p=0.013) and burning or pain sensations (COR=

0.43, 95% CI=0.2- 0.94, p=0.035) in the extremities. Other less common adverse reactions in the intensive phase compared to continuation phase including were skin rash (COR=0.62, 95% CI= 0.33- 1.16, p=0.134), eye pain (COR=0.42, 95% CI=0.15- 1.18, p=0.099).Arthralgia was associated with the phase of therapy (COR= 0.49, 95%=0.27- 0.89, p=0.019) and occurred mainly during the intensive phase

Table 6.8. Logistic regression analysis of adverse drug reactions and phase of therapy (N=190)

	Bivariable analysis		**Multivariable analysis**	
Variable	**COR (95% CI)**	**P value**	**AOR (95% CI)**	**P value**
Loss of appetite	1.71 (0.91, 3.22)	0.098	1.79 (0.75, 4.25)	0.188
Nausea, vomiting	1.78 (0.95, 3.36)	0.074	2.03 (0.86, 4.81)	0.107
Tiredness and weakness	1.38 (0.78, 2.45)	0.267	2.43 (1.09, 5.47)	**0.031***
Clumsiness or unsteadiness	0.53 (0.26, 0.85)	0.083	0.53 (0.20, 1.38)	0.190
Numbness	0.47 (0.26, 0.85)	**0.013***	0.43 (0.19, 1.01)	0.054
Burning sensations in the extremities	0.43 (0.2, 0.94)	**0.035***	0.5 (0.17, 1.48)	0.209
Sore throat	0.81 (0.27, 2.42)	0.712	0.88 (0.19, 4.03)	0.870
Skin rash	0.62 (0.33, 1.16)	0.134	0.76 (0.35, 1.62)	0.473
Arthralgia	0.49 (0.27, 0.89)	**0.019***	0.64 (0.29, 1.39)	0.258
Mental depression	1.2 (0.41, 3.65)	0.712	1.04 (0.25, 4.30)	0.953
Eye pain	0.42 (0.15, 1.18)	0.099	0.54 (0.14, 2.03)	0.358

***-** Statistically significant p-value

6.3 Discussion

Gastrointestinal side effects were experienced by about a third of the participants. They included loss of appetite, nausea, and vomiting. The drugs, which were responsible for these side effects, were most likely be pyrazinamide and rifampicin. The prevalence was lower than what was observed in Nepal where it was 48.6% (Koju et al., 2005). The most common neurological adverse reactions were unsteadiness, numbness, tingling sensations, depression and psychosis. Isoniazid

may be the responsible drug for this side effect since it is a competitive inhibitor of pyridoxine which is essential for maintaining the integrity of nerves. Visual disturbances characterized by blurred vision, eye pain and inability to distinguish yellow and green color was probably caused by ethambutol since it damages the retina. Arthralgia occurred in over a third of cases which was likely due to pyrazinamide that causes accumulation of uric acid which gets deposited in the joints leading to inflammation and pain.

Loss of appetite was more common in the intensive phase than continuation phase. This was probably because the participants were very ill and a substantial effect of treatment had not been realized. Neurological adverse effects such as numbness and tingling sensation were more common in the continuation phase of treatment due to the effect of isoniazid which is time-dependent.

Adherence to treatment for tuberculosis was about 51% which was higher than findings of a study done in Uganda (Amuha et al., 2009). Depression was significantly associated with adherence where the odds were about four times in bivariate analysis. The scenario might have been due to adverse effects of the drugs especially isoniazid. The long duration of treatment of diseases with drugs that predisposes to certain adverse effects is likely to trigger the condition.

History of alcohol consumption had a significant association with non- adherence at bivariable but not Multivariable analysis. However other studies have found a significant association between alcohol consumption and non-adherence (McDonnell et al., 2001). Adherence scores have been found significantly higher in patients who indicated no alcohol consumption. People with a history ofuse of alcohol are more likely to be non- adherent probably because of forgetfulness or fear of adverse effects of drugs. Smoking was not found to be associated with adherence which

was contrary to findings of a study carried out in India (Bagchi et al., 2011). Smoking in Kenya is on the decline due to health promotion with a compelling message about the health risks associated with the behavior. Participants in the continuation phase of therapy were less adherent than those in the intensive phase. It is likely that as patients took drugs for a longer period they felt their health status had improved and forgot often to take them as opposed to those who had just started.

Females were found to be more adherent compared to males. This observation was similar to another study where females were twice as more likely to adhere to treatment (Mkopi et al., 2012). Women often talk to their friends and family about health issues and actively seek out answers to their health concerns. Men, in contrast, tend to give their health the silent treatment. For these reasons, females get encouragement to follow treatment more than men.

Marital status was found to be associated with adherence. Participants without spouses were less adherent to treatment. Married people encourage each other and the outcome is usually good. Those who were single probably got discouraged because they fed for themselves and may not have a confidant to share the information with. In addition, most of them were working and revelation of their health status could have jeopardized their employment. Participants with regular income were more adherent to treatment than those without. This was probably because they could afford to manage their responsibilities easily and therefore concentrate on treatment.

HIV coinfection was not significantly associated with adherence which was contrary to findings from a study in Ethiopia (Adane et al., 2013). There were specific clinics that catered for patients with tuberculosis and HIV co-infection. Intense counseling was conducted and follow up was carried out to monitor patients which probably explains this observation. Education level was not significantly associated with adherence which was different from other studies (Fagundez et al.,

2016). All the participants had attained a certain level of education and were counseled adequately about what the disease and treatment entailed.

6.4 Conclusion

Anti-tuberculosis drugs cause several adverse effects and the most common ones involve the gastrointestinal and nervous systems. The level of adherence to treatment was moderate and negatively affected byuse of alcohol and depression was significantly associated with adherence to therapy.

6.5 Recommendations

6.5.1 Recommendations for policy and practice

Adherence to treatment should be closely monitored in all patients and especially those withuse of alcohol who were found to be significantly nonadherent. A protocol should be developed to monitor adverse drug reactions and treat them accordingly. Pyridoxine should be given to all patients throughout the duration of therapy since many patients were suffering from neurological problems which are prreactionsable. Regular eye checkup should be done to detect and prreactions derangement of vision.The biochemical parameters should be analyzed to find out the effects of the drugs on the electrolytes, blood, liver and renal functions. They include serum creatinine, alanine aminotransferase, potassium, uric acid, haemoglobin and blood cell count. The findings will assist in augmenting the content of the monitoring protocol proposed in 6.5.1 above.

6.5.2 Recommendations for research

The causes of nonadherence should be unearthed and addressed in order to enhance optimization of TB therapy.

6.6 References

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CHAPTER 7: EFFECT OF FIRST LINE TUBERCULOSIS CHEMOTHERAPY ON THE HEALTH-RELATED QUALITY OF LIFE OF PATIENTS

7.1 Introduction

Quality of life (QOL) is an individuals' perception of their mental and physical health in their daily lives. QOL is divided into the following domains; psychological, physical, spiritual, economic, and social functioning (Mamani et al., 2014).The assessment of health related quality of life shows the effect of diseases and related factors on activities and functioning of an individual. QOL measurement is important among patients suffering from a chronic disease who's social and spiritual well-being as well as physical health are affected by the disease and its related long-term treatment (Dion et al., 2004).

The resurgence of TB in Kenya and its association with HIV compounded with lack of adequate knowledge and social support affects the quality of life. Besides, the burden of disease and mortality, the long duration of treatment and high pill burden has led to change in life structure in the affected families. The adverse drug reactions also contribute to the suffering and change in the quality of life. Diagnosis of TB alone can lead to anxiety and depression which may be accompanied by frustration, fear, and disappointment. The social perception of the disease makes the situation worse and can contribute to reduced quality of life. Improvement in health-related QOL is an important factor for better response to treatment among TB patients, which may lead to better outcome (Mamani et al., 2014).

The WHOQOL-BREF is a tool used to determine the quality of life of patients and has four domains. These domains are physical health, psychological health, social relationships, and environment. The facets of physical health are; activities of daily living, dependence on medicinal

substances and medical aids, energy, and fatigue, mobility, pain and discomfort, sleep, rest and work capacity. Psychological health encompasses; bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality/religion / personal beliefs, thinking, learning, memory, and concentration. The aspects evaluated in social relationships include; personal relationships, social support, and sexual activity. Environment is assessed using the following variables; financial resources, freedom, physical safety and security, health and social care including; accessibility and quality, home environment, opportunities for acquiring new information and skills, participation and opportunities for recreation / leisure activities, physical environment (pollution / noise / traffic / climate) and transport (Pergamon, 1998).

Despite that TB drugs are associated with several adverse reactions, no study has been carried out to investigate their effects on the quality of life of patients in Nairobi. The effect of these adverse reactions was evaluated using linear regression analysis where the health domains were the dependent variables and sociodemographic characteristics, as well as adverse drug reactions, were the independent variables. The objective of this study was to measure the health-related quality of life of patients on first-line TB therapy and the associated factors. All the domains (physical health, psychological health, social relationships, environment and overall quality of health) were assessed.

A cross section study design was adopted involving 190 participants selected using simple random sampling. The detailed used is described in **chapter 3, section 3.4.**

7.2 Results

7.2.1 Summary measures of the domains of health-related quality of life

Sociodemographic characteristics are described in chapter six. The mean percentage scores are summarized in **fig 7.1**. Physical health score was 57.3 (SD -/+ 16), psychological health, 58.9(SD -/+16.1), social relationship, 61.2 (SD -/+15), environment, 54.8 (SD -/+11.3) and overall quality of life, 57(SD -/+19.5). The mean score for the environment was the lowest.

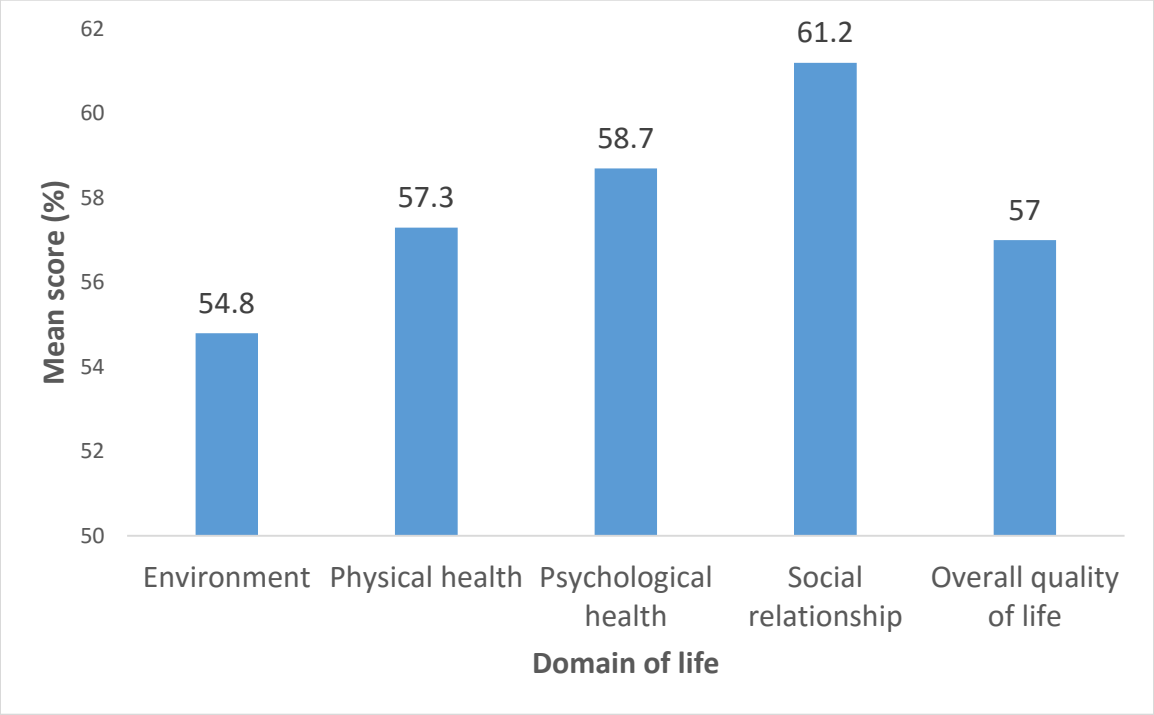

Fig 7.1. Mean scores for the HRQoL during treatment of non- resistant TB (N=190)

7.2.2 Determinants of physical health score

Physical health was computed as a percentage and positive coefficients in a linear regression model indicated a percentage increase in physical health score and vice versa.

The results of the association between physical health (PH) and sociodemographic characteristics are shown in **table 7.1**.

Table 7.1. Association between sociodemographic characteristics and physical health (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	β (95% C I)	**P-value**	**β (95% C I)**	**P-value**
Body Mass Index	7.1 (2.8,11.3)	**0.001***	5.1(1.05, 9.14)	**0.014***
Duration of treatment	3.3 (2.21, 4.4)	**<0.001***	2.9 (1.81, 4.0)	**<0.001***
Sex	0.7 (-3.9, 5.3)	0.765	-3.8 (-8.49, 0.86)	0.109
Age	-4.8 (-7.86, -1.78)	**0.002***	-2.2 (-8.89, 4.59)	0.53
Marital status	-1.8 (-6.41, 2.86)	0.450	-2.2 (-6.6, 2.24)	0.33
Level of education	6.3 (3.05, 9.51)	**<0.001***	4.51(1.53, 7.55)	**0.003***
Employment status	-7.4 (-12.94, -1.81)	**0.01***	-2.9(-7.91, 2.06)	0.248
Monthly income	2.2 (0.05, 4.41)	**0.045***	0.7(-3.21, 1.87)	0.604
HIV infection	-5.2 (-10.32, -0.11)	**0.045***	-1(-6.13, 4.15)	0.704
Relapsed TB	-4.2 (-13.74, 5.45)	0.394	-1.9 (-7.01, 10.76)	0.678
Malnutrition	-10.1(-18.5, -1.7)	**0.018***	-2.3(-10.26, 5.57)	0.559
Diabetes mellitus	-2.4 (-9.24, 14.92)	0.644	-2.4(-13.12, 8.38)	0.664
Alcoholism	-4.3(-8.9, 0.20)	0.061	-0.4(-5.47, 4.72)	0.885
Smoking	-4.8 (-9.83, 0.29)	0.064	-1(-7.44, 5.35)	0.747

*- Statistically significant p-value

An improvement in BMI from low to normal improved physical health by 7.1 (p=0.001) percent in a bivariable model and by 5.1 (p=0.014) percent in a Multivariable model. An improvement in PH score was also noted with an increase in the duration of treatment. An increase by one month was accompanied by an improvement of 3.3 (p< 0.0001) percent in bivariable and 2.9 (p< 0.0001) percent in Multivariable analyses. This is probably because of reduced microbial load thereby facilitating the healing of the body cells enabling them to perform their functions appropriately. An increase in age from below to above 30 years reduced PH score by 4.8 (p=0.002) in a bivariable model and by 2.2 (p=0.53) percent in a multivariable model. Although significance was lost in a Multivariable model the coefficient remained negative. As the participants level of education improved from primary to secondary and above, PH score improved by 6.3 (p<0.001) percent in

bivariable and 4.51 (p=0.003) percent in multivariable models respectively. It implied that participants with primary education had lower PH score than those who attained secondary and tertiary levels respectively. Participants who were engaged in non-formal employment had 7.4 (p=0.01) reduction in PH score in a bivariable and 2.9 (p=0.244) percent in multivariable analyses compared to those in formal employment. It implied that non- formal employment which was characterized by irregular earnings was associated with reduced PH score. This was reinforced by the observation that improvement in PH score 2.2 (p=0.045) percent occurred with an increase in monthly income from a lower category to subsequent higher categories in a bivariable model. Therefore monthly income and employment status were strong predictors of PH.

HIV infected participants had reduced PH score by 5.2 (p=0.045) percent compared to the non-infected ones and although significance was lost in a multivariable analysis, the coefficient was still negative suggesting a negative association. Participants with malnutrition had 10.1 (p=0.018) percent reduction in PH score in a bivariable and 2.3 (p=0.559) percent in a multivariable model compared to those who were not. The other sociodemographic characteristics which reduced PH score wereuse of alcohol and smoking despite that the associations were not statistically significant.

Additional analysis was done to find out the effect of adverse drug reactions on physical health and the results are shown in **table 7.2.** A reduction in PH by 6.9 (p=0.008) percent was noted in a bivariable model and by 4.1(p=0.221) percent in Multivariable analysis in participants who experienced loss of appetite. Nausea and vomiting caused a decrease of 6.3 (p=0.01) percent while those who felt weak and tired had reduced PH by 7.5 (p=0.001) percent .

Table 7.2. Association between adverse drug reactions and physical health (N=190)

Adverse drug reactions	Bivariable analysis		Multivariable analysis	
	β (95% C I)	**p value**	**β (95% C I)**	**P value**
Loss of appetite	-6.9(-11.94, -1.82)	**0.008***	-4.1(10.7,2.5)	0.221
Nausea and vomiting	-6.3(-11.04, -1.52)	**0.01***	-1.9 (-7.38, 3.55)	0.490
Tiredness or weakness	-7.5(11.98, -3.05)	**0.001***	-3.3(-8.68,2.08)	0.228
Clumsiness or unsteadiness	-10.4(-16.31, -4.4)	**0.001***	-9(-15.75, -2.32)	**0.009***
Numbness	-4.2(-8.92, 0.43)	0.075	1.7(-4.06,7.55)	0.554
Tingling sensation	-4.8(-9.63, -0.06)	**0.047***	-2.2(-9.3, 4.81)	0.530
Burning pain in hands or feet	-4.7(-10.44, 1.13)	0.414	2.4(-4.72,9.48)	0.510
Sore throat	1.9(-5.55, 9.42)	0.611	6.3(-0.72, 13.23)	0.078
Unusual bleeding and bruising	1.1(-17.53, 19.55)	0.914	1(-20.72, 22.76)	0.927
Skin rash	-1.1(-5.97, 3.71)	0.645	-0.16(-5.39, 5.08)	0.953
Arthralgia	-8.8(-13.38, -4.26)	**<0.001***	-8.2(-13.28, -3.09)	**0.002***
Seizures	7.0(-13.15, 27.22)	0.493	2.4(-23.36, 28.08)	0.856
Mental depression	8.7(-0.07, 17.52)	0.052	4.9(-5.39,15.29)	0.346
Psychosis	-17.1(-27.58, -6.70)	**0.001***	-15.5(-37.76,6.7)	0.170
Muscle twitching	-12.3(-26.36, 1.76)	0.086	3.3(-21.59, 28.25)	0.792
Impaired vision	-17.1(-27.56, -6.66)	**0.001***	-14.5 (-31.44,2.37)	0.091
Chills	-11.1(-26.23, 4.12)	0.153	3.2(-20.27, 26.67)	0.778
Pain and swelling of joints	-2.1(-9.20, 5.02)	0.563	0.47(-6.58,7.52)	0.895

*- Statistically significant p-value

Participants who suffered from clumsiness and unsteadiness had reduced PH score by 10.4 (p=0.001) and 9 (p=0.009) percent respectively in bivariable and multivariable analyses. All these adverse reactions regarding PH were indicators of lack of energy with consequent negative. Arthralgia (pain in the joints) was noted to be a strong predictor of PH. It reduced PH by 8.8 (p<0.001) and 8.2(p=0.002) percent in bivariable and multivariable models respectively. Pain in the joins reduced mobility thereby interfering with daily activities. Impaired vision and psychosis reduced PH by 17.1 (p=0.001) percent individually in bivariable analysis and despite that

significance was lost in the multivariable model, the coefficient remained negative. Impaired vision probably affected the coordination of daily activities and psychosis was associated with reduced energy and deficient interpersonal skills.

7.2.2 Determinants of psychological health score

Linear regression analysis was carried out with psychological health as the dependent variable and sociodemographic characteristics as the independent variables and the results are summarized in **table 7.3**. Psychological health score improved by 6.5 ($p<0.001$), and 4.9 ($p=0.005$) respectively in bivariable and multivariable linear regression models respectively when BMI was enhanced from low to normal. This was probably because the improvement in BMI usually manifested with an increase in size which enhanced bodily image and appearance. The self- esteem was also elevated and due to increase in energy, the participants were able to concentrate on their daily activities. BMI was a strong predictor of psychological health. Psychological health improved as treatment duration increased. An increase in the duration of treatment by one month enhanced PS score by 2.2 ($p<0.001$) and 1.4 ($p=0.02$) in bivariable and multivariable analyses respectively. As the treatment continued the microbial load decreased thereby allowing the body processes to revert back to normal. The disruptions in the body inflicted by the disease waned with time leading to improved psychological health. PS score improved by 9.23 ($p<0.001$) and 7.1($p<0.001$) with an increase in education level from primary to secondary in bivariable and multivariable models. Education helped to promote and sustain healthy lifestyles and positive choices, supporting and nurturing human relationships and personal, family and community well-being. Increased monthly income increased PS score by 3.3 ($p=0.002$) in bivariable and 1.1($p=0.418$) in multivariable analyses respectively. Availability of financial resources enables people to fulfill their obligations easily since they can cater for them.

The decrease in psychological health was observed with several sociodemographic characteristics. HIV infection decreased PS score by 6.3 (p=0.009) and 2.1(p=0.382) in bivariable and Multivariable analyses respectively. HIV infection is a systemic disease which devastates the body thereby inflicting psychological disturbances partly due to the stigma associated with it.

Table 7.3. Association between sociodemographic characteristics and psychological health (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**P-value**	**β (95% CI)**	**P-value**
Body Mass Index	6.5 (3.02, 10.05)	**<0.001***	4.9(1.53, 8.32)	**0.005***
Duration of treatment	2.2 (0.92, 3.51)	**0.001***	1.4(0.23, 2.61)	**0.020***
Sex	4.0 (-0.67, 8.58)	0.093	0.7 (-3.41, 4.76)	0.747
Age category	-5.7 (-8.58, -2.76)	**<0.001***	-0.8 (-6.84, 5.25)	0.796
Marital status	-2.76 (-7.39, 1.88)	0.243	-.2.2 (-6.5, 2.17)	0.323
Level of education	9.23 (6.43, 12.03)	**<0.001***	7.1 (4.08, 10.04)	**<0.001***
Employment status	-5.8 (-11.96, 0.31)	0.063	-0.5 (-6.04, 4.97)	0.847
Monthly income	3.3 (1.20, 5.47)	**0.002***	1.1 (-1.54, 3.7)	0.418
HIV infection	-6.3 (-10.9, -1.6)	**0.009***	-2.1 (-6.74, 2.59)	0.382
Relapsed TB	-13 (-21.5, -4.4)	**0.003***	-7.2 (-16.78, 2.46)	0.144
Malnutrition	-8.4 (-14.5, -2.2)	**0.008***	1.1 (-5.1, 7.34)	0.720
Diabetes mellitus	5.3 (-10.9, 21.5)	0.520	0.4 (-11.7, 12.48)	0.950
Alcoholism	-4.9 (-9.41, -0.3)	**0.037***	-1 (-5.95, 4.03)	0.705
Smoking	-6.2 (-11.2, -1.2)	**0.015***	0.1 (-6.23, 6.51)	0.996

*- statistically significant p-value

Psychological health score of relapsed cases of TB was 13 (p=0.003) times lower compared to non-relapsed cases. Malnutrition reduced PS score by 8.4 (p=0.008) while use of alcohol and smoking reduced it by 4.9 (p=0.037) and 6.2(p=0.015) respectively in bivariable regression analysis. Malnutrition deprives the brain of essential requirements which are required for proper

functioning.use of alcohol also deprives the body of essential nutrients due to poor feeding habits associated with the victims.

The association between psychological health and adverse drug reactions is shown in **table 7.4.** Simple linear regression analysis showed that statistically significant decrease in psychological

Table 7.4. Association between adverse drug reactions and psychological health (N=190)

Adverse drug reactions	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**p- value**	**β (95% CI)**	**p- value**
Loss of appetite	-1.6(-6.57, 3.31)	0.576	2.8 (-3.47,9.09)	0.379
Nausea, vomiting	-5.4(-10.41, 0.47)	**0.032***	-3.8(-9.6, 2.01)	0.199
Tiredness or weakness	-5.7(-10.26, -1.15)	**0.014***	-2.8 (-8.42,2.79)	0.322
Clumsiness or unsteadiness	-8.3(-14.34, -2.32)	**0.007***	-5.8 (-12, 0.43)	0.068
Numbness	-5.12(-9.71, -0.53)	**0.029***	-0.54 (-5.12, 6.2)	0.851
Tingling sensation	-6.5(-11.37, -1.57)	**0.010***	-2.6(-9.65, 4.5)	0.473
Pain in hands or feet	-6.4(-11.74, -1.03)	**0.020***	-0.32(-7.31, 6.66)	0.927
Sore throat	1.27(-6.75, 9.32)	0.752	4.9 (-2.27,12.17)	0.178
Unusual bleeding and bruising	2.3(-20.42 ,25.02)	0.842	5.6 (-19.48, 30.63)	0.661
Skin rash	1.0(-5.74, 3.74)	0.678	0.75(-4.31,5.81)	0.77
Arthralgia	-8.97(-13.61, -4.33)	**<0.001***	-6.9(-12.17, -1.68)	**0.01***
Seizures	16.2(-13.02, 45.49)	0.275	13.32 (-22.41,49.05)	0.463
Mental depression	5.8(-1.83, 13.44)	0.135	6.1(-2.14,14.31)	0.146
Psychosis	-14.8(-24.82, -4.78)	**0.004***	-23.8 (-53.1, 5.44)	0.11
Muscle twitching	-4.9(-24.54, 14.72)	0.622	22.1(-9.21,53.35)	0.165
Impaired vision	-19.0(-25.39, -12.62)	**<0.001***	-12.7(-29.04, 3.63)	**0.003***
Chills	-9.031(-44.16, 26.10)	0.613	-8.6(-39.01, 21.78)	0.576
Pain and swelling of joints	-2.3(-10.43, 5.82)	0.576	0.98(-6.79, 8.54)	0.822

***-** Statistically significant p-value

health occurred in participants who experienced some side effects. Those who suffered from nausea and vomiting had decreased PS score by 5.4 (p=0.032), while tiredness or weakness reduced it by 5.7 (p=0.014). Neuropsychiatric effects that had deleterious effects on PS were;

clumsiness or unsteadiness (p=0.007), numbness (p=0.029), tingling sensation (p=0.01), pain in the hands or feet (p=0.020), psychosis (p=0.004), arthralgia (p<0.001) and impaired vision (p<0.001). However, multivariable linear regression analysis proved that decrease in psychological health was mainly associated with impaired vision (p=0.003) and arthralgia (p=0.01). The magnitude of the reduction by each adverse drug reactions is indicated in the table as the respective regression coefficient.

7.2.3. Determinants of the score on social relationships

Associations between social relationship and sociodemographic characteristics were investigated where social relationship score was the dependent variable and social demographic characteristics were the independent variables and the results are summarized in **table 7.5.** Statistically significant increase in social relationship (SR) score occurred due to improvement in BMI, duration of treatment, level of education and increase in monthly income. An increase in BMI from low to normal enhanced SR score by 6.7 (p<0.001) in bivariable and 5.5 (p< 0.0001) in Multivariable linear regression analysis. An additional one month in the course of treatment increased SR score by 1.8 (p=0.006). As the education level improved from primary to secondary, SR score increased by 6.3 (p<0.001) and 5.2 (p<0.001) in bivariable and Multivariable regression analyses respectively. An increase in the monthly income by Ksh 10,000 enhanced SR by 2.7 (p<0.009)

Table 7.5. Association between sociodemographic characteristics and social relationships (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**P-value**	**β (95% CI)**	**P-value**
Body Mass Index	6.7(3.93,9.44)	**<0.001***	5.5 (2.67,8.32)	**<0.001***
Duration of treatment	1.8(0.52 1.3)	**0.006***	0.9 (-0.28, 2.05)	0.134
Sex	1.8 (-2.61,6.22)	0.420	-0.7 (-4.78, 3.34)	0.727
Age category	-3.1(-5.98,-0.25)	**0.033***	-1.8 (-7.47, 3.93)	0.541
Marital status	-8.3(-12.53,-4.11)	**<0.001***	-7.9 (-11.78, 3.93)	**<0.001***
Level of education	6.3(3.64,8.90)	**<0.001***	5.2 (2.49, 7.97)	**<0.001***
Employment status	-4.3(-9.22,0.52)	0.080	-1.3 (-6.32, 3.77)	0.618
Monthly income	2.7(0.69,4.77)	**0.009***	-0.1 (-2.63, 2.36)	0.911
HIV infection	-2.2(-9.95,-0.54)	**0.029***	-1.7 (-7.95, 4.4)	0.44
Relapsed TB	-7.2(-14.55,0.19)	0.056	-2.7(-10.03, 4.62)	0.467
Malnutrition	-9.3(-15.03,-3.63)	**0.001***	-1.8(-7.95, 4.4)	0.570
Diabetes mellitus	5.6(-12.04,23.20)	0.553	-0.8 (-15.07,13.46)	0.911
Alcoholism	-3.4(-7.73,0.85)	0.115	-1(-5.67, 3.74)	0.686
Smoking	-3.3(-8.1,1.47)	0.173	1.2 (-4.21, 6.69)	0.654

*- statistically significant p-value

A significant decrease was noted with HIV infection, malnutrition, marital status, age and relapsed TB. Unmarried participants had a reduction of 8.3 ($p<0.001$) in bivariable and 7.9 ($p< 0.0001$) in Multivariable regression analysis in SR than the married ones. Marriage offered a platform for sharing issues with partners and created a wider social network. Malnutrition reduced SR score by 9.3 ($p=0.001$) and those with HIV infection by 7.2 ($p=0.056$). These two characteristics tend to reduce body image which are important components for effective social interactions.

The association between adverse drug reactions and social relationship is summarized in **table 7.6.**

Table 7.6. Association between adverse drug reactions and social relationships

Adverse reactions	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**p- value**	**β (95% CI)**	**p- value**
Loss of appetite	-3.6(-8.08, 0.97)	0.123	-0.9(-7.33,5.58)	0.789
Nausea, vomiting	-5.2(-9.7, -0.74)	**0.023***	-3(-9.01,2.98)	0.322
Tiredness or weakness	-6.1(-10.32, -1.81)	**0.005***	-4.0(-9.15, 1.17)	0.129
Clumsiness or unsteadiness	-3.6(-8.84, 1.57)	0.170	-0.9(-7.21,5.47)	0.788
Numbness	-5.3(-9.56, -1.12)	0.13	-3.0(-8.83,2.76)	0.302
Tingling sensation	-4.3(-8.73, 0.2)	0.061	-2.3(-8.58, 3.89)	0.458
Pain in hands or feet	-1.59(-5.85, 2.67)	0.463	4.0(-2.35,10.26)	0.217
Sore throat	0.71(-7.13, 8.64)	0.859	4.0 (-5.18, 13.22)	0.389
Bleeding and bruising	-5.8(-25.52, 13.96)	0.564	-5.8(-26.4, 14.72)	0.576
Skin rash	-1.3(-5.84, 3.278	0.579	0.9(-4.34, 6.10)	0.741
Arthralgia	-6.3(-10.65, -1.9)	**0.005***	-5.1(-10.23, 0.055)	0.052
Seizures	9.5(-7.93, 26.98)	0.283	7.0 (-16.45,30.4)	0.558
Mental depression	5(-4.09, 14.0)	0.281	5.7 (-4.32, 15.81)	0.261
Psychosis	-5.9(-10.8, -0.097)	**0.019***	-16.3(-38.83,6.18)	0.154
Muscle twitching	2.6(-6.77, 11.94)	0.587	20.1(-5.4,45.5)	0.122
Impaired vision	-8.59(-13.8, -3.61)	**0.001***	-8.8 (-20.51,2.9)	0.142
Chills	-3.2(-27.11, 20.66)	0.790	-4.2(-28.24,19.80)	0.729
Pain and swelling of joints	0.04(-6.824,6.896)	0.992	0.8(-6.85, 8,47)	0.835

*- Statistically significant p-value

Bivariable analysis revealed that decrease in social relationships score occurred among the participants who experienced nausea and vomiting, arthralgia, tiredness or weakness and inability to distinguish green and yellow. Those who suffered from nausea and vomiting, had SR score reduced by 5.2 (p=0.002). The loss of fluids caused body weakness since water and electrolytes are essential components of body systems and metabolism. The loss, therefore, hampered the homeostasis leading to weakness with negative consequences on SR. Participants with arthralgia

had a 6.3 (p=0.005) reduction in the SR score. Painful joints restricted mobility thereby decreasing social interactions and ability to perform physical activities. Impaired vision decreased SR score by 8.59 (p=0.001). However, no statistically significant association was observed on Multivariable analysis for these adverse effects but the regression coefficients remained negative.

7.2.4 Determinants of the environment score

Table 7.7 depicts the association between the environmental and sociodemographic characteristic of the participants.

Table 7.7. Association between sociodemographic characteristics and the environment (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**P-value**	**β (95% CI)**	**P-value**
Body Mass Index	4.4 (1.94 ,6.78)	**<0.001***	3.2 (0.69, 5.61)	**0.012***
Treatment duration	1.1(0.2,1.96)	**0.017***	0.7 (-0.09, 1.49)	0.082
Sex	1.0 (-2.28,4.19)	0.56.	-0.4 (-3.68,2.83)	0.796
Age category	-3.8 (-5.78,-1.74)	**<0.001***	-3.5(-7.76, 0.61)	0.093
Marital status	1.5(-1.79,4.82)	0.367	1.7 (-1.12, 4.45)	0.241
Level of education	7.3 (5.25,9.26)	**<0.001***	6.1(3.96, 8.16)	**<0.001***
Employment status	-4.9 (-9.47,-0.37)	**0.034***	-0.3 (-4.11, 3.42)	0.846
Monthly income	2.9 (1.35,4.35)	**<0.001***	1(-0.82, 2.75)	0.286
HIV infection	-5.3 (-8.65,-1.9)	**0.002***	-2.7 (-5.87, 0.52)	0.10
Relapsed TB	-6.1 (-10.79,-1.43)	**0.011***	-2.2 (-6.75, 2.26)	0.327
Malnutrition	-6.9 (-10.93,-2.77)	**<0.001***	-0.02 (-4.99,4.95)	0.993
Diabetes mellitus	3.3 (-6.46,13.05)	0.506	-0.3 (-6.67, 6.08)	0.927
Alcoholism	-7.7 (-4.92 1.51)	0.296	0.7 (-2.55, 4.01)	0.66
Smoking	-3.8 (-7.3,-3.12)	**0.033***	-1.3 (-5.55, 2.93)	0.544

*- statistically significant p-value

characteristics. Increase in body mass index from low to normal enhanced the environment (EN) score by 4.4 (p<0.001) in a bivariable and 3.2 (p=0.012) in a Multivariable model. Increase in body

mass enables a person to cope up with life challenges and enhances the productivity of an individual. A monthly incremental increase of 1.1 ($p< 0.001$) in EN score occurred in the course of treatment and this could be attributed to the gradual recovery enabling the participants to be proactive in their daily activities. Level of education contributed positively to EN. An increase from primary to secondary and beyond improved EN score by 7.3 ($p<0.001$) in the bivariable and 6.1 ($p<0.001$) in a Multivariable model. Education is a gateway to many opportunities in life including employment which enhances socioeconomic status. Participants who engaged in non-formal employment had EN score reduced by 4.9 ($p=0.034$) compared to those in formal employment. Regular earnings enhanced the standard of living due to the predictability of income which was regular. Improvement in the monthly income by Ksh 10000 increased EN score by 2.9 ($p<0.001$) probably due to the ability to meet financial obligations. HIV infection decreased the score by 5.3 ($p<0.002$) because the disease devastates the body thereby rendering the victim weak and unable to perform adequately. Relapsed TB conferred 6.1($p=0.011$) decrease in EN score. The damage caused by TB in the lungs causes weakness of the tissues which tend to worsen during subsequent infections. Participants with malnutrition had a reduced EN score by 6.9 ($p<0.001$) and those who smoked by 3.8($p<0.033$) percent in a bivariable model.

The association between adverse drug reactions on EN is shown in **table 7.8.** Nausea and vomiting reduced EN score by 3.3 ($p=0.036$). Tiredness and weakness also had a negative effect on EN. Neurological adverse drug reactions reduced EN score significantly. Feeling numb in the limbs reduced EN score by 3.7 ($p=0.023$) while tingling sensations and pain in the limbs reduced it by3.8($p=0.031$) and 3.5($p=0.046$) respectively. Participants who experienced arthralgia had their EN score reduced by 4.3 ($p=0.011$). The impaired vision was a strong predictor of EN since it

reduced it by 14.1 (p=0.001) in bivariable and 18.7 (p<0.001) in Multivariable models respectively.

Table 7.8. Association between adverse drug reactions and the environment (N=190)

Adverse drug reactions	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**p value**	**β (95% CI)**	**p value**
Loss of appetite	-0.6 (-3.47, 3.44)	0.992	2.7(-2.18, 7.56)	0.277
Nausea, vomiting	-3.3 (-6.44, -22.7)	**0.036***	-2.4 (6.26, 1.44)	0.218
Tiredness or weakness	-3.8(-69, 0.06)	**0.022***	-3.2 (-6.95. 0.56)	0.095
Clumsiness or unsteadiness	-1.4 (-5.4, 2.68)	0.508	0.1(-4.49, 4.62)	0.978
Numbness	-3.7 (-6.94, 0.51)	**0.023***	-1.3 (5.57, 3.04)	0.562
Tingling sensation	-3.8 (-7.18, -0.34)	**0.031***	-2.33 (-6.90, 2.32)	0.325
Pain in the hands or feet	-3.5 (-6.9, -0.55)	**0.046***	-1.9 (6.69,2.94)	0.442
Sore throat	2.7 (-3.3, 8.71)	0.375	4.2 (-2.54,10.99)	0.219
Unusual bleeding and bruising	-5.9 (-12.26, 0.42)	0.067	-8.0 (-17.71,1.76)	0.108
Skin rash	-2.2 (-5.46, 1.10)	0.192	-1.3 (-4.86,2.27)	0.474
Arthralgia	-4.3 (-7.53, -1.0)	**0.011***	-2.8 (-6.03, 0.52)	0.099
Seizures	1.38 (-2.39, 25.14)	0.105	11(-8.47,31.42)	0.258
Mental depression	1 (-5.88, 7.85)	0.778	-0.09 (-8.83,8.64)	0.984
Psychosis	0.4 (-13.43, 14.26)	0.06	-13.9 (-20.61,-.23)	**<0.001***
Muscle twitching	5.7 (-4.66, 16.05)	0.279	9.4 (-1.3,20.19)	0.084
Impaired vision	-14.1(-9.4, -18.69)	**<0.001***	-18.7 (8.6,28.87)	**<0.001***
Inability to distinguish green or yellow	2.5 (-9.72, 14.74)	0.686	0.7 (-6.82, 8.18)	0.859
Eye pain	2.1(-3.76, 8.01)	0.478	2.2 (-3.07,7.47)	0.412
Chills	-4.8 (-18.13, 8.44)	0.473	-8.0 (-17.70, 1.68)	0.104
Pain and swelling of joints	-1.6 (-7.9, 4.60)	0.606	-0.5 (-6.62, 5.54)	0.861

*- Statistically significant p-value

7.2.5. Determinants of the overall health-related quality of life score

The sociodemographic predictors of the overall quality of life were determined and the results are summarized in **table 7.9**.

Table 7.9. Sociodemographic characteristics predictors of the overall health-related quality of life (N=190)

Variable	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**P-value**	**β (95% CI)**	**P-value**
Body Mass Index	6.7(2.57,10.89)	**0.002***	6.2 (1.29, 11.01)	**0.013***
Duration of treatment	2.5(0.82,4.15)	**0.004***	1.9 (0.21, 3.55)	**0.028***
Sex	5.6(-0.73,11.31)	0.057	2.5(-3.72, 8.72	0.429
Age category	-6.6(-10.16,-2.97)	**<0.001***	-5.9(-13.8, 2.04)	0.145
Marital status	-1.6(-7.15,4.03)	0.583	-3.7 (-13.12, 8.72)	0.185
Level of education	6.8(2.89,10.70)	**<0.001***	5.5(1.29, 9.75)	**0.011***
Employment status	-6.3(-13.03,0.47)	0.068	-4 (-11.77, 3.77)	0.311
Monthly income	-0.2(-3.342,2.908)	0.891	-2.9(-6.84, 0.98)	0.141
HIV infection	-2.5(-8.17,3.27)	0.399	1.9(-3.89, 7.65)	0.521
Relapsed TB	-9.7(-18.63,-0.75)	**0.034***	-1.7(-11.84, 8.5)	0.746
Malnutrition	-8.0(-16.14,0.05)	0.051	-2.4 (-10.91, 6.03)	0.570
Diabetes mellitus	-7.5(-32.81,17.9)	0.563	-6.7 (-30.01,16.62)	0.571
Alcoholism	-2.8(-8.45,2.83)	0.327	1.6(-4.87, 8.01)	0.631
Smoking	-2.1(-7.1,3.65)	0.476	5.1(-2.02,12.3)	0.159

*- Statistically significant p-value

An increase of the overall health-related quality of life (HRQoL) by 6.7(p=0.002) and 6.2(p=0.018) was realized in bivariable and Multivariable models when the BMI improved from low to normal. Increase in BMI was an indicator that the state of the body systems had improved significantly which positively affected all the domains of the quality of life. BMI was, therefore, a strong

predictor of HRQoL. As the duration of treatment increased by one month HRQoL improved by 2.5(p=0.004) and 1.9 (p=0.028) in bivariable and Multivariable models respectively. Duration of

Table 7.10. Association between adverse drug reactions and the overall quality of life (N=190)

Adverse drug reactions	Bivariable analysis		Multivariable analysis	
	β (95% CI)	**p value**	**β (95% CI)**	**p value**
Loss of appetite	-4.1(-10.57, 2.38)	0.214	-1(-8.81,6.75)	0.794
Nausea, vomiting	-5.05(-10.10, 0.89)	0.095	0.9(-6.79,8.61)	0.816
Tiredness or weakness	-8.1(-13.54, -2.69)	**0.004***	-5.4(-12.01,1.19)	0.107
Clumsiness or unsteadiness	-4.78(-11.68, 2.12)	0.173	-1.5(-9.93, 7.0)	0.733
Numbness	-2.87(-107, 0.96)	0.101	1(-6.45,8.44)	0.792
Tingling sensation	-7.5(-13.84, -1.22)	**0.020***	-3.5(-12.84, 5.84)	0.460
Pain in hands or feet	-5.2(-13.35, 2.98)	0.212	-0.4(-10.58, 9.72)	0.933
Sore throat	0.8(-8.58, 10.15)	0.869	3.7(-5.92,13.32)	0.449
Unusual bleeding and bruising	5.3(-15.16, 25.71)	0.611	6.9(-17.48, 3.19)	0.579
Skin rash	-3.8(-9.61, 3.23)	0.328	-1.4(-8.44, 5.69)	0.701
Arthralgia	-7.8(-13.22, -1.93)	**0.009***	-5.4(-11.60, 0.87)	0.091
Seizures	5.2(-12.51, 23.0)	0.561	0.5 (23.35, 24.31)	0.968
Mental depression	8.9(-1.02, 18.81)	0.078	6.1(-7.11,19.39)	0.361
Psychosis	-7.4(-10.26, -4.59)	**<0.001***	-13.6(-42.2,15.09)	0.351
Muscle twitching	-7.43(-10.26, -4.59)	**<0.001***	4.8(-27.28,36.87)	0.768
Impaired vision	-9.7(-19.35, 0.12)	**0.047***	-16.1(6.13,26.0)	**0.002***
Chills	-20(-37.77, -2.27)	**0.027***	-9.7 (-40.4, 21.1)	0.536
Pain and swelling of joints	-3.5(-13.09, 6.07)	0.471	-2.3(-12.53, 7.96)	0.66

*- Statistically significant p-value

treatment was, therefore, a strong predictor of HRQoL. An enhancement of the level of education from primary to secondary and above improved HRQoL by 6.8(p=0.001) and 5.5 (p=0.011) respectively in bivariable and Multivariable models. Education had a positive impact on the

different domains of HRQoL and therefore a strong predictor. Participants with relapsed TB had their HRQoL score reduced by 9.7 (p=0.034) in the bivariable model but the significance was lost in the Multivariable model despite that the regression coefficient remained negative.

An assessment was also carried out to find the association between adverse drug reactions and overall quality of life and the results are shown in **table 7.10** below. The overall HRQoL score was reduced by 8.1 (p=0.004) among those participants who experienced tiredness and weakness. Neurological damage which manifested as a tingling sensation in the limbs diminished HRQoL score by 7.5(p=0.020). Musculoskeletal adverse effects which manifested as arthralgia and muscle twitching decreased the overall HRQoL score by 7.8 (p=0.009) and 7.4 (p<0.001) respectively. The impaired vision was a strong predictor of HRQoL and the affected participants had a reduction of the score by 9.7 (p=0.047) and 16.1(p=0.002) in bivariable and Multivariable models respectively. The participants who developed psychosis had reduced overall score by 7.4 (p=0.001). Reduced mobility due to neuromuscular and visual disturbances negatively affected the overall HRQoL.

7.3. Discussion

Health-related quality of life mean score was lowest in environment domain followed by physical health, psychological health and social relationships which is similar to findings in a Nigerian study (Sule et al., 2014) where patients had fair grades in all the health domains assessed. Environment and psychological health domains were the worst affected in this study. The association between sociodemographic characteristics and adverse drug reactions with different domains of the quality of life showed similarities and differences. Generally increase in body mass index, level of education, and income improved the quality of life. Domain scores have been found

to be better among younger patients, with higher socioeconomic status (Aggarwal et al., 2013). These characteristics are interrelated since education facilitates employment leading to better earnings which enable people to meet basic necessities of life. There was a positive association between duration of treatment and quality of life. Studies have shown that TB treatment results in a significant improvement in HRQoL, especially in physical and psychological domains (Tanja et al., 2016). The improvement in HRQoL was greatest during the continuous phase of treatment. Increase in age, malnutrition, smoking,use of alcohol and previous TB infection correlated negatively with the quality of life. These factors are associated with decreased immunity which facilitates the organisms to devastate the body. HIV infection was associated with poor psychological health probably due to stigma and fear of the future since it is incurable.

Adverse drug reactions had a negative effect on the quality of life across all domains. Gastrointestinal side effects (nausea and vomiting) decreased the quality of life. The loss of fluids and inadequate intake of food causes systemic disturbances thereby rendering the body weak. Poor physical health characterized by fatigue and weakness has been observed in several studies to have a negative effect and is usually triggered through sleep disturbances, coughing, malnutrition and TB medication (Chang et al., 2014: Hansel et al., 2004). Neurological disturbances (tingling sensation, pain in the hands and feet, psychosis) and arthralgia were associated with poor quality of life. These are known adverse effects of isoniazid. In addition, impaired vision had a negative effect and was caused by ethambutol. All these symptoms portrayed that drug toxicity decreased the quality of life.

7.4 Conclusion

There was a general decline in the quality of life across all domains. The improvement was observed with increasing body mass index, duration of treatment and level of education. Aging, HIV infection and a previous episode of tuberculosis infection were associated with declining quality of life. The adverse drug reactions involving gastrointestinal and nervous system were associated with diminishing quality of life.

7.5 Recommendations

7.5.1 Recommendations for policy and practice

Assessment of quality of life among patients on treatment for tuberculosis should be integrated as part of management. This will enable the service providers to holistically manage the patients with consequent better outcomes. Health education should be enhanced so that the patients can understand the implications of quality of life in their daily activities. This will enhance adherence to treatment and anxiety associated with TB.

7.5.2. Recommendations for research

A prospective cohort study should be carried in order to establish the relationship between health-related quality and time. This can form a basis for developing a protocol mentioned above since it can show the trend of the effects of therapy. The finding may enable healthcare providers to anticipate and intervene in a timely and effective manner.

7.6 References

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CHAPTER 8. IMPACT OF MULTIDRUG RESISTANT TUBERCULOSIS CHEMOTHERAPY ON THE PATIENT'S HEALTH-RELATED QUALITY OF LIFE

8.1 Introduction

Multi-drug resistant is caused by *Mycobacterium tuberculosis* strains that are resistant to at least isoniazid and rifampicin (Raman et al., 2012**)**. Globally, MDR-TB is a threat to the gains made in the control of tuberculosis. According to WHO, there were about 480 000 new cases of multidrug-resistant TB in 2015 (WHO, 2016). Drug resistance surveillance data show that 3.9% of new and 21% of previously treated TB cases had rifampicin-or multidrug-resistant tuberculosis. The incidence of MDR-TB was 4.4% among new cases in 2015 in Kenya (Kerubo et al., 2016).

Drugs used for MDR-TB treatment, are grouped into 5 categories according to efficacy, the experience of use and drug class as shown in **table 8.1.**

Table 8.1 Drugs used in the treatment of MDR-TB

Group	Drugs
1.First line	Pyrazinamide, Ethambutol, Rifabutin, and Isoniazid
2. Injectables	Aminoglycosides - Kanamycin or Amikacin, Capreomycin
3. Fluoroquinolones	Fluoroquinolones-Levofloxacin, Moxifloxacin
4.Oral bacteriostatics	Ethionamide (or protionamide), cycloserine Terizidone
5.Investigative agents	Clofazimine, Linezolid, Amoxicillin/clavulanate, Thiacetazone, Imipenem/cilastatin, high-dose isoniazid, and Clarithromycin

Treatment mainly involves the use of drugs from group 1-4. Occasionally depending on the response, group 5 agent can be added. Group 1 drugs are the most potent and best tolerated. Group 2 which consists of aminoglycosides is the first choice of an injectable agent. Patients who cannot tolerate aminoglycosides are given capreomycin. All patients receive a group 3 medication and a group 4 agents, is often added to the treatment regimen because of effectiveness and low cost. When two agents are needed, cycloserine can be added. Terizidone can be used instead of cycloserine and is assumed to be equally efficacious.

In Kenya, MDR-TB treatment is accomplished in two phases (Ministry of health, 2014). The intensive phase lasts eight months while the continuation phase lasts for 12 months. The drugs used in each phase are shown in **table 8.2.**

Phase of treatment	**Drugs**
Intensive	Kanamycin or capreomycin, Protionamide, levofloxacin, cycloserine, and pyrazinamide
Continuation	levofloxacin, protionamide, cycloserine, and pyrazinamide

Table 8.2 Regimens used in the management of MDR-TB

X-MDR- TB is treated for a longer period. The intensive phase takes 12 months and drugs used are; capreomycin, moxifloxacin, para aminosalicylate, clofazamine, and amoxicillin/ clavulanate. The continuation phase lasts for 18 months and drugs used are moxifloxacin, PAS, clofazimine and amoxicillin/ clavulanate. A shorter treatment regimen is being initiated among newly diagnosed MDR-TB cases which lasts for nine months

Tuberculosis patients, in addition to clinical symptoms, have, to deal with several physiological, financial, and psychological problems (Ahmad, 2016). The symptoms and clinical burden of the

disease often extend beyond the duration of treatment. Also, the treatment itself may cause several side-effects. All these aspects of the disease and its management have a huge impact on the overall well-being of the patient and burden of these factors can equal and even exceed the physical impact of illness. However, at present within the management MDR-TB, much attention is being paid to the traditional microbiological and clinical indicators. Its impact on patients' HRQoL has remained a neglected area and this is what this study has addressed.

This study involved interviewing patients on treatment for MDR-TB and checking their records from the inception of treatment. Hepatotoxicity was diagnosed if the serum level of ALT was elevated. Nephrotoxicity was detected if the serum creatinine was elevated. The methods for this study is described in **chapter 3 section 3.5.** The objective was to evaluate the impact of MDR-TB, and its treatment on patients' HRQoL. This study will help in filling the gaps in patient-reported outcomes, and provide the much-needed data regarding the impact of MDR-TB treatment on patients' HRQoL.

8.2 Results

8.2.1. Sociodemographic characteristics of participants on treatment for MDR-TB

Out of the thirty- six patients who had the disease, twenty-three were recruited into the study and 17 (73.9%) were males **(Table 8.3).** The majority (13, 56.5%) of the participants were married. The mean age was 37.1 (SD ± 11.4) years and the range was 20 to 50 years. Fifteen (65.2%) participants were below forty years of age. Eleven (47.8%) participants had normal body mass index but 9 (39.1%) had lower than required BMI. All the participants were literate; 6 (26.1%) had a primary education while 12 (52.2%) had attained the secondary level of education. Previous lifestyle habits before diagnosis and initiation of treatment of the disease were smoking and use of alcohol which were practiced by 10 (43.5%) participants. Eleven (47.8%) participants had prior

episode of tuberculosis . The comorbidities present were HIV (10, 43.5%), malnutrition (9, 39.1%) and diabetes mellitus (1, 4.4%) respectively.

Table 8.3. Socio demographic characteristics (N=23)

Variable	Frequency	Percent
Sex		
Male	17	73.9
Female	6	26.1
Marital status		
Married	13	56.5
Single	10	43.5
Age category (years)		
18-30	8	34.8
31-40	7	30.4
Above 41	8	34.8
Body mass index		
Below 18.5	9	39.1
18.6-25	11	47.8
25.1-30	2	8.7
Above 30	1	4.4
Level of education		
Primary	6	26.1
Secondary	12	52.2
Tertiary	5	21.7
Comorbidities		
HIV infection	10	43.5
Malnutrition	9	39.1
Diabetes mellitus	1	4.4
Use of alcohol	10	43.5
Tobacco smoking	10	43.5
Previous hospitalization	3	13.0
Previous TB infection	11	47.0

8.2.2 Adverse drug reactions in patients on MDR-TB therapy

Several drugs were used depending on the phase of therapy. Six (26%) participants were in the intensive phase of treatment and th following five drugs were used including; kanamycin or capreomycin, levofloxacin, protionamide, cycloserine, and pyrazinamide **(Fig 8.1)**. Another six (26%) patients were on high dose isoniazid, ethambutol, pyrazinamide, kanamycin, moxifloxacin,

protionamide, and clofazamine. The continuation phase entailed treatment with four drugs; levofloxacin, protionamide, cycloserine, and pyrazinamide.

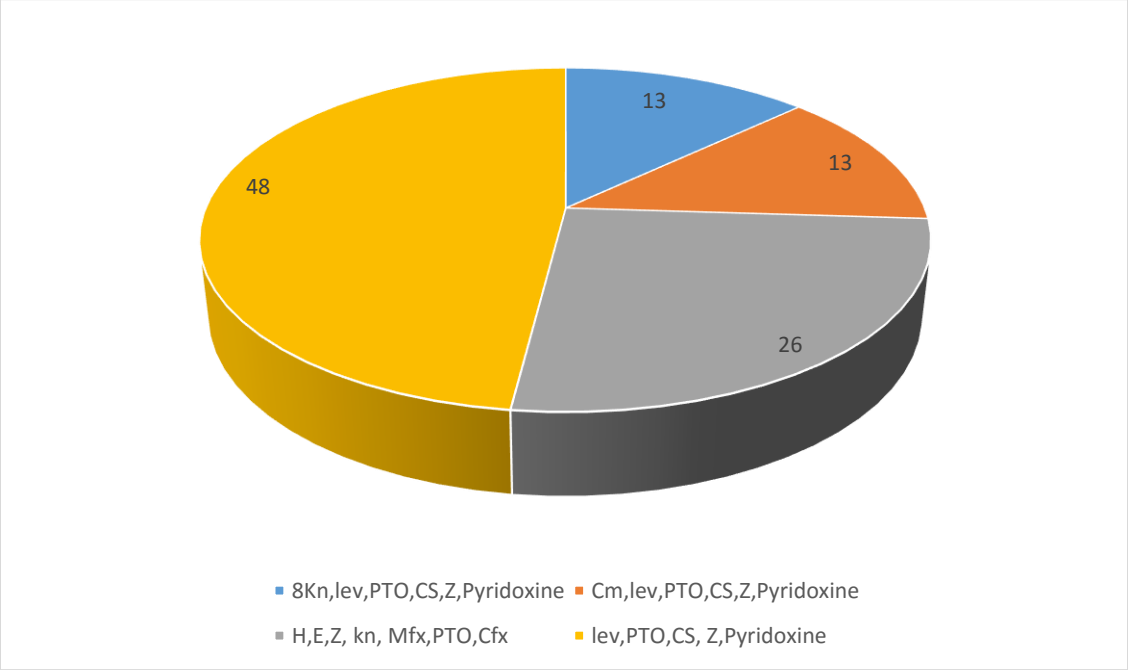


Fig 8.1. Types of drug regimens used by MDR-TB participants (N=23)

The participants experienced several adverse drug reactions as shown in **fig 8.2** and **table 8.4** respectively. Twenty-one (91.3%) participants exhibited nervous system (NS) disturbances which included; drowsiness, tingling sensation, headache, dizziness, insomnia, depression, and nightmares. Gastrointestinal tract (GIT) disturbances were the second most prevalent where 20 (87%) participants were affected and complained of nausea, vomiting, abdominal pain, flatulence, excessive salivation, diarrhea, constipation, abdominal cramps, loss of appetite, black tarry stool, dry mouth and mouth ulcers. Sreactionseen (73.9%) participants suffered from the musculoskeletal system (MSS) adverse effects which included joint pains, backache, muscle spasms and pain in the big toe. The respiratory system was affected in 13 (56.5%) participants who presented with a cough, chest pain and dyspnea.

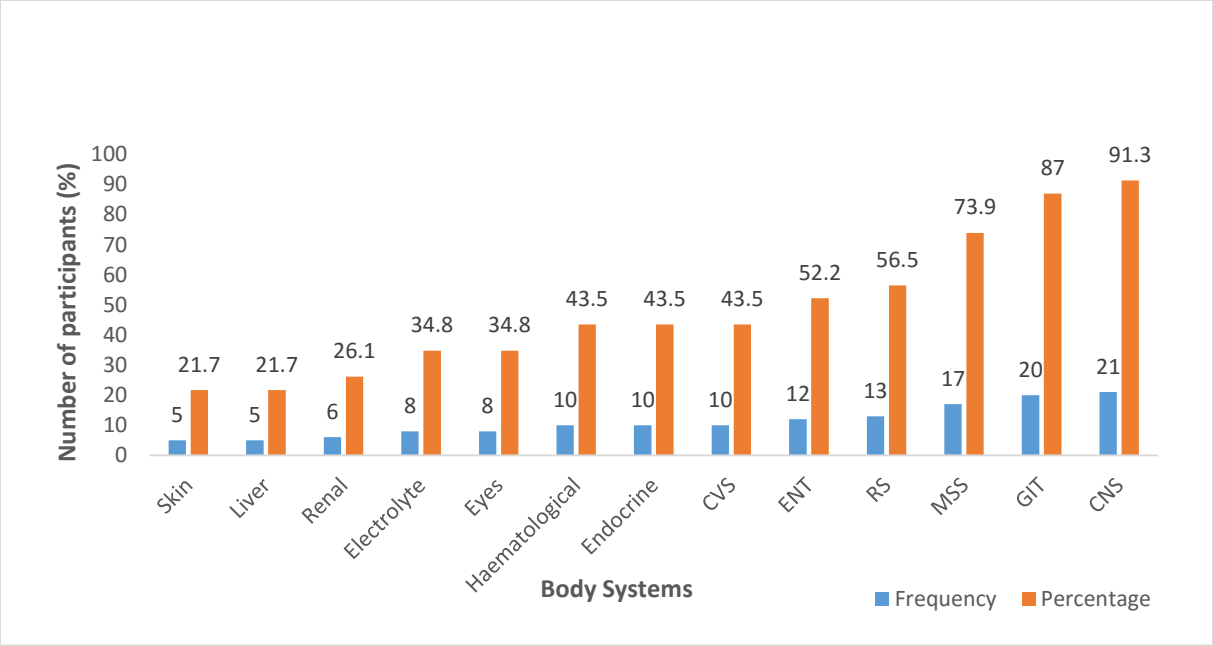


Fig 8.2. Categories of adverse drug reactions due to MDR-TB drugs (N=23)

Twelve (52.2%) participants had ear, nose, and throat (ENT) problems and the most common was a loss of hearing. Cardiovascular system (CVS) was affected in 10 (43.5%) cases who had palpitations. Among the 10 (43.5%) who had endocrine disturbances, 7 (30.4%) had hypothyroidism and 5 (21.7%) experienced sexual dysfunction. Eight (34.8%) participants complained of visual disturbances while 5 (21.7%) and 3 (13%) were victims of hyperkalemia and hypokalemia respectively. Among the 10 (43.4%) participants with hematological problems, anemia was the most common. The other less common but serious adverse drug reactions were nephrotoxicity (6, 21.6%), hepatotoxicity (5, 21.7%) and rash (5, 21.6%). All the participants suffered from multiple adverse reactions and 12(52.2%) had experienced ten and below while 11(47.8%) had more than ten adverse drug reactions.

Table 8.4 Prevalence of adverse drug reactions in patients on MDR-TB therapy (N=23)

Adverse reactions	n	%	Adverse reactions	n	%
Nephrotoxicity	6	26.1	Mental depression	8	34.8
Hypothyroidism	7	30.4	Agitation	6	26.1
Hyperkalemia	5	21.7	Cough	6	26.1
Hypokalemia	3	13	Chest pain	5	21.7
Anemia	9	39.1	Dyspnea	4	17.4
Hepatotoxicity	6	26.1	Painful urination	3	13
Nausea	20	87	Frequent urination	5	21.7
Vomiting	15	65.2	Reduced urine	3	13
Abdominal pain	12	52.2	Joint pains	15	65.2
Flatulence	17	73.9	Backache	9	39.1
Excessive salivation	15	65.2	Pain in the big toe	3	13
Diarrhea	1	4.4	Muscle spasms	3	13
Constipation	3	13	Fullness of the ears	2	8.7
Abdominal cramps	12	52.2	Deafness	10	43.5
Loss of appetite	11	47.8	Vertigo	1	4.4
Black tarry stool	2	8.7	Sore throat	1	4.4
Dry mouth	5	21.7	Sexual dysfunction	5	21.7
Mouth ulcers	1	4.4	Bleeding	2	8.7
Palpitations	7	30.4	Malaise	14	60.9
Headache	9	39.1	Jaundice	1	4.4
Dizziness	9	39.1	Visual impairment	7	30.4
Confusion	4	17.4	Weight gain	3	13
Irritability	8	34.8	Fever	1	4.4
Nightmares	6	26.1	Pale skin	1	4.4
Drowsiness	11	47.8	Tremor	2	8.7
Speech problems	2	8.7	Rash	5	21.7
Suicidal thoughts	5	21.7			
Tingling sensation	10	43.4			
Insomnia	9	39.1			

8.2.2.1 Distribution of ADRs in the different phases of therapy

Types of adverse events experienced in the various phases of therapy and the results are shown in **table 8.5**. The kidney was affected equally in both phases. Endocrine disturbances were more common in the continuation phase than an intensive phase and the difference was statistically significant (p=0.012). Electrolyte abnormalities were present in equal measure but gastrointestinal adverse reactions were more common in the intensive phase. The systems that were affected more in the intensive phase than continuation phase were; nervous, respiratory, musculoskeletal, skin and blood. The eyes, liver, and ear were affected more during the continuation phase but this was not statistically significant.

Table 8.5. Association between adverse drug reactions and phase of therapy (N=23)

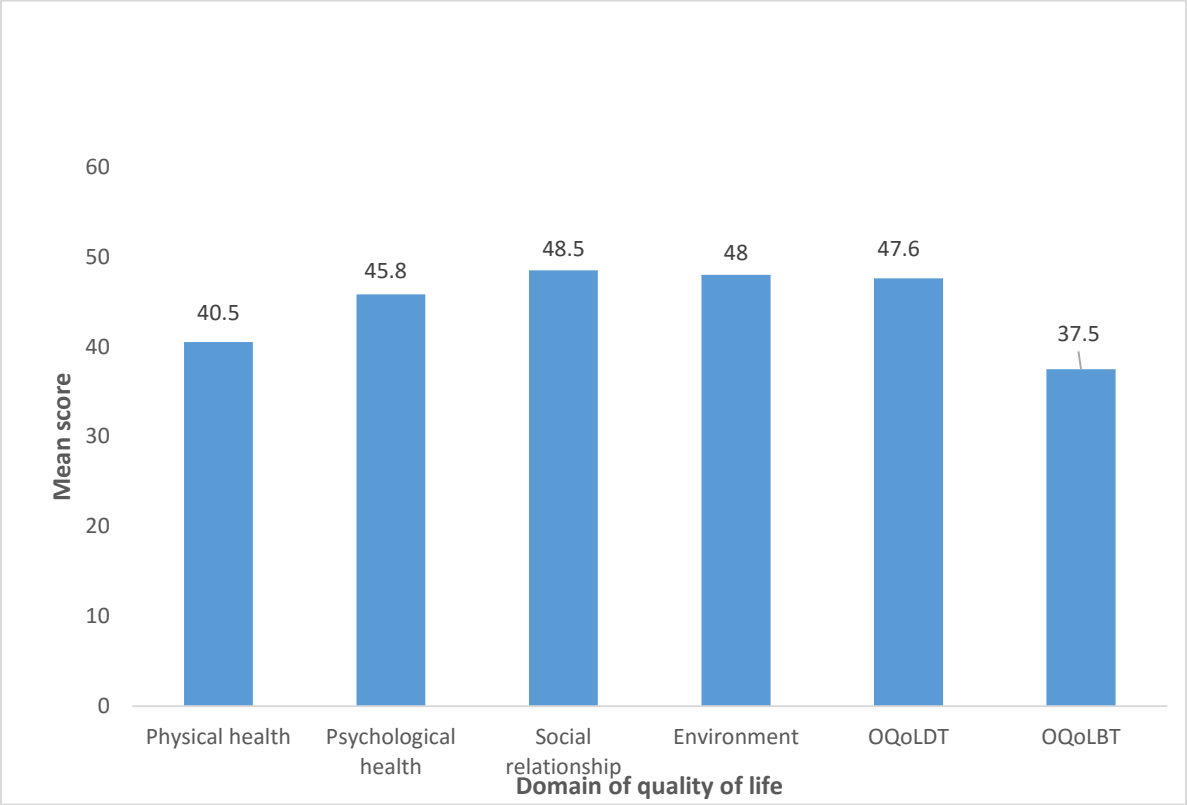
System/ Organ affected	Phase of therapy		P-value
	Intensive phase (n, %)	Continuation phase (n, %)	
Kidney	3 (13)	3 (13)	1
Endocrine	2 (8.7)	8 (34.8)	**0.012***
Electrolytes	4 (17.4)	4 (17.4)	1
Gastrointestinal tract	12 (52.2)	8 (34.8)	0.093
Cardiovascular	4 (17.4)	6 (26.1)	0.414
Nervous	11 (47.8)	10 (43.5)	1
Respiratory	8 (34.8)	5 (21.7)	0.414
Musculoskeletal	9 (39.1)	8 (34.8)	1
Ear	5 (21.7)	7 (30.4)	0.414
Eyes	2 (8.7)	6 (26.1)	0.089
Skin	4 (17.4)	1 (4.3)	0.317
Blood	4 (17.4)	3 (13)	1
Liver	1 (4.3)	4 (17.4)	0.155

***-** Statistically significant p-value

8.2.3 Health-related quality of life of participants on MDR TB therapy

8.2.3.1 Summary of the quality of life measures of participants on MDR-TB therapy

The quality of life was determined during treatment for MDR-TB using WHO–HRQoL Bref questionnaire described in chapter 3 (p 52). The means scores for the respective HRQoL domains are shown in **figure 8.3**. The score on social relationship was highest with a mean of 48.5 (SD± 18.9) and a range of 25-75 followed by followed by the environment.



Key- OQoLDT-Overall quality of life during treatment OQoLBT-Overall quality of life before treatment

Fig 8.3. Mean scores for the HRQoL domains during treatment of MDR-TB

Psychological health followed and the lowest score was for physical health with a mean of 40.5 (SD+/- 15.9), and a range of 21.4 -73.1.

The mean overall scores during and before treatment were 47.6 (SD+/- 20.8) and 37.5(SD+/-17.2) respectively. The difference between the two means was statistically significant (P=0.038). This

meant that the HRQoL among the participants during treatment was better than at the point of diagnosis and initiation of therapy.

8.2.3.2 Determinants of physical health in participant on MDR-TB therapy

Bivariable linear regression analysis with physical health (PH) as the outcome variable and sociodemographic characteristics as the explanatory variables was carried out and the results are summarized in **table 8.6.**

Table 8.6.Linear regression analysis of PH and sociodemographic characteristics (N=23)

Characteristic	β (95% CI)	P value
Body mass index	11 (-0.32,22.3)	0.056
Sex	0.66 (-14.02,15.35)	0.925
Age	0.23 (-0.43, 0.89)	0.468
Duration of treatment	0.99 (-0.47,2.45)	0.168
Marital status	6.78 (-10.01, 23.57)	0.403
Level of education	-7.51 (-17.5,2.46)	0.129
Number of occupants in the house	-2.49 (-21.19, 16.2)	0.780
HIV infection	-1.21 (-18.1, 15.69)	0.881
Previous TB infection	-4.04 (-21.01,12.94)	0.620
Malnutrition	-22.53 (-33.92,-11.12)	**0.001***
Use of alcohol	-10.83 (-27.38, 5.72)	0.184
Smoking	-10.62 (-27.97, 6.73)	0.211
Previous hospitalization	-8.91 (-17.84,0.02)	**0.05***

***-**Statistically significant relationship

As BMI increased from low to normal values, physical health score increased by 11 (p=0.056). An increase in BMI was a sign that the body was regaining its previous health status. Being male

enhanced the PH core by 0.66 (p=0.925) compared to females. An increase in age by one year increased physical health score by 0.23 units (p=0.468) and as the duration of treatment increased by one month PH increased by 0.99 units (p=0.168). Married participants had a higher PH score by 6.78 units (p=0.403) compared to those who were single. As the education level decreased, physical health decreased. HIV infection, previous TB infection, use of alcohol, and smoking and decreased physical health to different extents. Malnutrition decreased PH score by 22.53 units (p=0.001) which was statistically significant. Malnutrition was positively associated with physical weakness, low immunity, and mental ability. Those participants with a history of the previous hospitalization had a lower PH score by 8.91units (p=0.05). They were often very sick prior to the diagnosis of MDR-TB.

The effect of adverse drug reactions on PH was explored and the results are summarized in **table 8.7.** Participants who suffered from hepatotoxicity during treatment had a lower PH score by 16.46 (p=0.001). Hearing impairment decreased physical health score by 6.37 units (p=0.147) but this was not statistically significant. This was attributed to lack of ability to hear which made it difficult to follow or receive instructions and relate with people effectively. Participants who suffered from anemia had lower PH score by 6.76 units (p=0.379) although the association was not statistically significant. Anaemia causes poor oxygenation of body cells which leads to low energy and hence slowdown of body activities which manifests as poor physical health. Participants who suffered from skin rash had a lower PH score by 8.8 (p=0.308) which was not statistically

Table 8.7. Linear regression analysis of physical health and adverse drug reactions (N=23)

Variable	β (95% CI)	P value
Nephrotoxicity	-0.77 (-20, 21.54)	0.938
Hypothyroidism	-1.56 (-17.51,20.64)	0.864
Electrolyte disturbances	-0.93 (-17.84, 15.97)	0.908

Palpitations	-6.38 (-10.53, 23.29)	0.434
Nervous system disturbances	-1.26 (-7.74,10.27)	0.769
Musculoskeletal disturbances	-7.23 (-8.5, 23)	0.343
Deafness	-6.37 (-22.63, 9.88)	0.416
Visual disturbances	-10.16 (-9.9, 30.22)	0.297
Skin rash	-8.8 (-26.55, 8.96)	0.308
malaise	-0.77 (-16.67, 15.14)	0.919
Anemia	-6.76 (-22.62, 9.11)	0.379
Hepatotoxicity	-16.46 (-25.18, -7.73)	**0.001***

*-statistically significant relationship

significant. The rash was often itchy and made the participants uncomfortable. Electrolyte disturbances, which mainly involved deranged serum potassium levels, caused a0.93 units (p=0.908) decrease in PH score. Potassium is an important cation in the body which is involved conduction processes in the muscles and nerves. Deranged levels were likely to impact negatively on PH. Participants who had musculoskeletal disturbances, which manifested as joint pains, backache and muscle spasms, had their PH score reduced by 7.23 units (p=0.343) which was not statistically significant. The physical mobility of these participants was hampered and the associated pain tormented them. Decrease in physical health was positively associated with nephrotoxicity, visual disturbances, hypothyroidism, palpitations and nervous system disturbances but this was not statistically significant.

A Multivariable linear regression analysis was carried out to identify the most important predictor variables among the sociodemographic characteristics and adverse drug reactions. Only malnutrition had a statistically significant negative effect (β= -19.78, 95% CI -30.60, 8.94.) on physical health. Participants who suffered from malnutrition had their PH score decreased by

19.78 compared to those with normal nutrition. Therefore the nutritional status of participants on treatment for MDR-TB is a good indicator of change in physical health.

8.2.3.3. Determinants of psychological health in participants on MDR-TB therapy

The effect of MDR-TB therapy on psychological health (PS) was assessed using linear regression analysis and the results are summarized in **table 8.8.** Improvement of BMI from low to normal increased PS score by 9.51 units (p=0.116) which was not statistically significant. Increase in BMI enhances a feeling of well-being which gave rise to positive emotions. The PS score for males was 4.71 units (p= 0.593) more than that of females but the difference was statistically insignificant. Females are more prone to emotional aberrations due to their intuitive nature than males. An additional month of treatment increased PS by 0.36 units (p=0.667). Progressive treatment had the propensity of decreasing microbial load leading to a feeling of well-being. Married participants had a PS score which was 3.94 units (p=0.66) times more than the single ones. Spouses share and console each other often which promotes positive feelings. HIV infected participants had a PS score which was 6.9 uints (p=0.437) lower compared to those who were HIV negative. The infection causes the destruction of the body immune system predisposing it to opportunistic infections.

Table 8.8.Linear regression analysis of PS against sociodemographic characteristics (N=23)

Characteristic	β (95% CI)	P value
Body mass index	9.51(-2.64, 21.66)	0.116
Sex	4.71 (-13.64, 23.05)	0.593
Age	0.13 (-0.61, 0.86)	0.719
Duration of treatment	0.36 (-1.38, 2.10)	0.667
Marital status	3.94 (-14.74,22.61)	0.660
Level of education	-6.01 (-19.42, 7.39)	0.354
Number of occupants in the house	-4.29 (-23.82,15.24)	0.646
HIV infection	-6.9 (-25.3, 11.5)	0.437
Previous TB infection	-8.85 (-26.97, 9.28)	0.315
Malnutrition	-19.68 (-35.05,-4.3)	**0.016***
Use of al	-7.51 (-24.45, 9.44)	0.366
Smoking	-8.04 (-26.49,10.41)	0.366
Previous hospitalization	-8.86 (-18.78, 1.05)	0.076

*Statistically significant relationship

The disease is associated with social stigma which causes ill feelings among those infected.use of alcohol reduced PS score by 7.51 units (p=0.366). People who drink alcohol have poor feeding habits which affect the functioning of the brain. In addition, alcohol consumption is associated with social stigma since it causes other undesirable social habits. Participants who were smokers before initiation of MDR-TB treatment had a lower PS score by 8.04 units (p=0.336) compared to non-smokers but this was not statistically significant. The toxic components found in the smoke have a deleterious effect on the entire body especially the lungs. Participants who had been hospitalized before had a lower PS score by 8.85 units (p=0.076) probably because they were sick for long which weighed them down emotionally. Malnutrition reduced PS score by 19.68 units (p=0.016) which was statistically significant. The condition is associated with diminished

body functions due to lack of adequate energy which also has negative social ramifications. These factors contributed to the low mood associated with the victims. Analysis was carried out to find out the association between psychological health and adverse drug reactions and the results are

Table 8.9.Linear regression analysis of psychological health and adverse drug reactions (N=23)

Adverse drug reactions	β (95% CI)	P value
Nephrotoxicity	-4.09 (-12.77, 20.96)	0.612
Hypothyroidism	-1.04 (-18.98,21.07)	0.913
Electrolyte disturbances	8.59 (-6.78, 23.96)	0.252
Palpitations	-0.02 (-19.23, 19.19)	0.998
Nervous system disturbances	8.86 (-1.05,18.78)	0.076
Musculoskeletal disturbances	11.79 (-10.72, 34.3)	0.282
Deafness	-8.85 (-26.57, 8.87)	0.304
Visual disturbances	-3.5 (-26.1, 19.07	0.745
Skin rash	-0.002 (-22.15, 22.14)	1
Malaise	-1.35 (-19.12, 16.42)	0.873
Anemia	-11.79 (-29.67, 6.08)	0.180
Hepatotoxicity	8.88 (-1.03, 18.8)	0.076

summarized in **table 8.9.** No statistically significant relationship existed between adverse drug reactions and psychological health in bivariable analysis.

A Multivariable analysis model was constructed involving psychological health as the dependent variable and sociodemographic characteristics as well as adverse drug reactions as the explanatory variables. In the parsimonius model, the independent predictors of psychological health identified were malnutrition, previous hospitalization, and history of hepatotoxicity during therapy. Participants with malnutrition (β= -22.03; 95% CI -39.46, -4.6) had their overall PS score reduced by 22.3 . Participants with a history of hospitalization (β= -17.27; 95% CI -29.7,-4.87) had a

lower PS score compared to those who had not been hospitalized. Participants who experienced hepatotoxicity (β= -21.46; 95% CI 9.24 , 33.67) during treatment had a lower PS score.

8.2.3.4 Determinants of social relationships in participants on MDR-TB therapy

Table 8.10 summarizes the effect of sociodemographic characteristics on social relationships.

Table 8.10. Linear regression analysis of SR and sociodemographic characteristics (N=23)

Characteristic	B (95% CI)	P value
Body mass index	14.74 (5.2,24.29)	**0.005 ***
Sex	-6.84 (-28.01, 14.34)	0.502
Age	0.19 (-0.75, 1.13)	0.669
Duration of treatment	0.71 (-0.78, 2.2)	0.323
Marital status	8.67 (-11.09, 28.43)	0.364
Level of education	-0.98 (-13.89,11.92)	0.873
Number of occupants in the house	-8.68 (-28.21, 10.85)	0.359
HIV infection	-3.11 (-23.31, 17.08)	0.747
Previous TB infection	-8.67 (-28.42, 11.0)	0.364
Malnutrition	-22.8 (-38.52, -7.09)	**0.007***
Diabetes mellitus	28.12 (18.11,31.13)	**<0.001***
Alcoholism	-17.08 (-35.28, 1.12)	0.064
Smoking	-14.47 (-33.61, 4.68)	0.127
Previous hospitalization	48.5 (38.81, 58.26)	**<0.001***

*- statistically significant relationship

SR score increased with improvement in BMI, age, duration of treatment, marital status and previous hospitalization. Participants with normal BMI had a higher SR score 14.74 units (p=0.005) which was statistically significant. Improvement in BMI enabled participants to effectively interact with others and probably enhanced the availability of social support and

satisfaction derived from the sexual activity. An additional month of treatment increased SR score by 0.71 units (p=0.323) which was not statistically significant. As the age increased by one year SR score improved by 0.19 units (p=0.669).

Increase in age is often associated with improved social interaction derived from life experiences. Those participants with spouses had SR score that was 8.67 units (p=0.359) greater than those who did not. Marriage is associated with enhanced social interaction within the family and the society. Unepexpectedly, with a history of hospitalization had SR score increased by 48.5 units compared to those without it. Hospitalization results in social bonding where friends and relatives often meet the patient to console and offer support. This social bonding quite often persists even after leaving the hospital especially if treatment continues.

Decrease in the social relationships was associated with the increased level of education, previous TB infection, alcohol use, smoking, male gender, and increase in the number of occupants in the house. SR score decreased marginally by 0.98 units (p=0.873) among participants with secondary education compared to those who attained primary level and the association was statistically insignificant. Those who resided in a house with more than two occupants had a lower SR score decreased by 8.68 units (p=0.359).

The SR score of participants with HIV infection was 3.11 units (p=0.747) lower than those without the disease. HIV infection carries a social stigma and also weakens the body making it difficult for effective social interactions to be accomplished. SR score diminished by 10.08 units (p=0.064) and 14.47 units (p=0.127) among participants engaged in taking alcohol and smoking. These two habits are repugnant to most members of the society which therefore reduces socialization. The participants who suffered from malnutrition had a lower SR score by 22.8 units (p=0.007) compared to those with normal nutrition and this association was statistically significant.

Malnutrition renders the victims physically and mentally weak thereby reducing their ability to socialize.

Bivariate regression analysis was done to evaluate the association between social relationship and adverse drug reactions and the results are summarized in **table 8.11**. Nephrotoxicity had a negative impact on the SR score though this was not statistically significant. This condition leads to accumulation of waste products in the body which makes the body weak. Hypothyroidism reduced the SR score by 2.03 units (p=0.847). Thyroid hormones are essential for the maintenance of body metabolism and under production will result in reduced body activity due to lack of sufficient energy. Participants who experienced hearing impairment had a lower SR score by 4.73 units (p=0.616). Inability to hear is an impediment to effective verbal communication which is essential for a meaningful social relationship.

Participants who experienced skin rash had lower SR score by 16.77 units (p=0.049) which was statistically significant. This adverse reactions is associated with a change in skin color which does not augur well for the victims because of unsavory remarks made about them. The victims tend to withdraw from other members of the society thereby reducing their social relationships. Participants who experienced hepatotoxicity had SR score reduced by 16.9 units (p=0.005) which was statistically significant. Damage to the liver reduces the rate of metabolism of drugs and toxic macromolecules in the body leading to their accumulation which has a deleterious effect on the body systems. Participants who had anemia scored 14.42 units less in SR than those who were not anemic. Low hemoglobin levels leads to inadequate tissue perfusion making the participants weak.

Table 8.11. Linear regression analysis of SR and adverse drug reactions (N=23)

Variable	β (95% CI)	P value
Nephrotoxicity	-3.54 (-30.36, 23.27)	0.782
Hypothyroidism	-2.03 (-24.16, 20.09)	0.847
Electrolyte disturbances	0.1(-21.32, 21.52)	0.992
Palpitations	4.5 (-16.17, 25.18)	0.649
Nervous system disturbances	-16.08 (- 26.58, -5.58)	**0.005***
Musculoskeletal disturbances	1.54 (-26.39, 29.47)	0.908
Deafness	-4.73 (-24.4,1 14.94)	0.616
Visual disturbances	4.46 (-16.77, 25.03)	0.651
Skin rash	-16.77 (-33.45, -0.09)	**0.049***
Tiredness	0.8 (-24.38, 25.97)	0.947
Anemia	-14.42 (-36.23, 7.4)	0.179
Hepatotoxicity	-16.19 (-26.68, -5.69)	**0.005***

*-statistically significant p-value

Participants with nervous system disturbances had SR scores decreased by 16.08 (p=0.005) which was statistically significant. These participants were unable to interact with other people effectively.

A Multivariable regression analysis was conducted and the most parsimonius model developed to identify the independent predictors of social relationships. The variables that were found to be independent predictors were malnutrition (β -26.8; 95% CI -38.42, -15.21), use of alcohol (β -15.83; 95% CI -26.52, -5.14), previous hospitalization (β -37.9; 95% CI - 45.06, -30.731) and nervous disturbances (β -37.8; 95% CI -44.95, -30.63).

8.2.3.5 Determinants of environment scores in participants on MDR-TB therapy

The effect of sociodemographic characteristics on the environment (EN) is summarized in **table 8.12.** The improvement was noted with an increase in body mass index, level of education and marital status.

Table 8.12. Linear regression analysis of EN and sociodemographic characteristics (N=23)

Characteristic	β (95% CI)	P value
Body mass index	4 (-1.97,10)	0.174
Sex	-0.19(-1.71,12.32)	0.974
Age	-0.09 (-0.7,0.51)	0.751
Duration of treatment	-0.38 (-1.19, 0.43)	0.335
Marital status	0.1(-11.39,11.6)	0.985
Level of education	39 (-5.7, 11.7)	0.474
Number of occupants in the house	4.15 (-6.22,14.51)	0.407
HIV infection	-3.56 (-15.17, 8.06)	0.524
Previous TB infection	-3.81 (-15.31, 7.69)	0.491
Malnutrition	-6.51 (-17.46,4.45)	0.225
Diabetes mellitus	2.14 (-4.05,8.34)	0.472
Alcoholism	-7.34 (-17.94,3.26)	0.161
Smoking	-3.98 (-14.62,6.67)	0.436
Previous hospitalization	-11.14 (-17.15, -5.13)	**0.001***

*- statistically significant relationship

Participants with a normal BMI had an environment score improved by 4 (p=0.174). Increase in BMI confers physical and mental strength which enables the victims to perform better. Those who had attained secondary education had a higher score by 39 units (p=0.474) compared with those with primary education. Participants who lived with more than two people in the same house had a higher score of 4.5 (p=0.407).

Reduction in environment score occurred among participants with HIV infection, malnutrition, advanced age, previous TB infection, smoking, and use of alcohol. Participants with malnutrition had a lower EN score reduced by 6.51units (p=0.225) compared to those with normal nutrition. Smoking decreased the score by 3.98 units (p=0.436) and participants with previous TB infection had a lower EN score reduced by 3.81 units (p=0.491) compared to those who were new cases. Participants who had been hospitalized before or during the course of treatment showed an 11.14 units (p= 0.001).

The results of the association between environment score and adverse drug reactions are summarized in **table 8.13**.

Table 8.13. Linear regression analysis of EN and adverse drug reactions (N=23)

Adverse reactions	**β (95% CI)**	**P value**
Nephrotoxicity	-4.7 (-9.51,18.91)	0.492
Hypothyroidism	-7.34 (-17.94, 3.26)	0.161
Electrolyte disturbances	-5.5 (, 16.33 5.53)	0.294
Palpitations	-1.84(-14.31,10.62)	0.757
Nervous system disturbances	-11.14 (-17.15, -5.13)	**0.001***
Musculoskeletal disturbances	-0.1(-17.49,17.69)	0.990
Deafness	-3.81 (-15.34,7.72)	0.492
Visual disturbances	-5.10 (-14.4, 4.19)	0.260
Skin rash	-0.19 (-10.93,11.32)	0.971
Malaise	-3.68 (-20.3,12.93)	0.643
Anemia	-5.95 (-20.46,8.55)	0.395
Hepatotoxicity	-5.44 (,-11.6, -0.72)	0.079

*Statistically significant relationship

All the adverse events had a negative impact on environment score. The only adverse event with a statistically significant effect was central nervous system disturbances which reduced the score by 11.4 units (95%CI -17.15, -5.13).

The most remarkable reduction on EN score was noted with nervous system disturbances where a reduction of EN score by 11.14 units (p=0.001) occurred which was statistically significant.

A Multivariable regression analysis was conducted to identify the most important independent predictors of the environment score. The most parsimonious model revealed malnutrition (β -22.03; 95%CI -39.46, -4.6) previous hospitalization and hepatotoxicity (β -21.46, 95%CI -33.67, -9.24) were the most important predictors.

8.2.3.5 Determinants of overall health-related quality of life in MDR-TB therapy

The overall score on quality of life was regressed against sociodemographic characteristics

Table8.14. Linear regression analysis of overall HRQoL and sociodemographic characteristics (N=23)

*-statistically significant relationship

Characteristic	β (95% CI)	P value
Body mass index	8.19(0.05,16.33)	**0.049***
Sex	-3.34 (-23.25,16.58)	0.730
Age	-0.4 (-1.07,0.27)	0.228
Duration of treatment	-0.46 (-2.07, 1.15)	0.559
Marital status	-2.16 (-21.51, 17.19)	0.818
Level of education	5.85 (-9.75, 21.45)	0.442
Number of occupants in the house	-8.92 (-28.49, 10.63)	0.351
HIV infection	-5.56 (-24.94,13.83)	0.556
Previous TB infection	-5(-24.29,14.29)	0.594
Malnutrition	-3.84 (-16.32,24.01)	0.694
Alcoholism	-16.35 (-34.02,1.32)	0.068
Smoking	-1.56 (-20.86,17.73)	0.867
Previous hospitalization	-30.26 (-39.93,-20.59)	< **0.001***

and the results are summarized in **table 8.14**. The variables that had a statistically significant effect on HRQoL were BMI and prior hospitalization. A unit increase in BMI increased the score by 8.19

uints (95%CI 0.05,16.33). Prior hospitalization reduced HRQoL by 30.26 units (95%CI -39.93, -20.59). unexpectedly increased duration of treatment reduced HRQoL scores but this was statistically insignificant. The only ADRs that had a statistically significant effect on HRQoL were nervous system disturbances and anemia. These two variables had a negative effect.

Table 8.15. Linear regression analysis of overall HRQoL and adverse drug reactions (N=23)

Adverse reactions	β (95% CI)	P value
Nephrotoxicity	-6.72(-25.6, 12.17)	0.466
Hypothyroidism	-3.85 (-17.87, 25.08)	0.709
Electrolyte disturbances	-3.57 (-14.53, 21.67)	0.684
Palpitations	-4.17 (-16.08, 24.41)	0.671
Nervous system disturbances	-10.41 (-3.21, -46.79)	**0.027***
Musculoskeletal disturbances	-13.28 (36.36, -9.8)	0.243
Deafness	-9.32 (-28.03,9.4)	0.310
Visual disturbances	-9.82 (-31.58, 11.94)	0.357
Skin rash	-6.41 (-10.66,23.48)	0.442
Malaise	-1.79 (-19.68, 23.26)	0.864
Anemia	-22.9 (-40.38, -5.45)	**0.013***
Hepatotoxicity	-8.64 (-36.91, 59.36)	0.530

*-Statistically significant relationship

8.3 Discussion

Most participants with MDR-TB were males and this has been observed in other studies (Mukherjee et al., 2015). Both genetic and behavioral characteristics are predispose males to the infections. Males are known to be more outgoing than women and androgens are known to suppress the immune system of the body. About a third of the participants were undernourished which was lower than that from an Indian study ((Mukherjee et al., 2015). Tuberculosis is a catabolic disease and also cause anorexia leading to loss of body mass. HIV coinfection had a

prevalence of 43.5% which was quite high. The disease destroys the body immune system especially the cell-mediated one which protects the body against intracellular microorganisms. Tobacco smoking and alcohol consumption are also known to be immunosuppressant in different ways. Forty-seven percent of the participants had relapsed tuberculosis suggesting that the resistance was acquired during treatment with first-line drugs. This could have been due to non-adherence or poor quality drugs.

The study set out to investigate the adverse drug reactions and their implications in the health-related quality of life. The most common side effects were central nervous disturbances (91.3%) which are caused by several drugs used especially cycloserine, isoniazid, levofloxacin, and moxifloxacin. The prevalence of these adverse drug reactions was higher than what was reported in a study in South Korea (Yang et al., 2017). The most common symptoms were drowsiness, depression, and insomnia which were more prevalent than what was found in an Ethiopian study (Mohammad et al., 2015). Suicidal ideation which occurred in 21.7% of the cases was mainly due to the effect of cycloserine and prothionamide. Other possible reasons for suicidal thoughts were fear and guilt associated with infection; the socioeconomic and psychological burdens of living with a chronic, life-threatening illness; increased dependence on others; multiple treatment failures; and concomitant poverty (Mehreen et al., 2015). Social stigma, which may produce social isolation, diminished marriage prospects, and limited social support may result in denial of diagnosis and consequent rejection of treatment (Sweetland et al., 2002). Peripheral neuropathy which presented as tingling and burning sensations in the extremities was mainly due to isoniazid, ethambutol, and prothionamide. Isoniazid is a competitive inhibitor of pyridoxine in the nerves. Gastrointestinal disturbances such as nausea, vomiting, and abdominal pain had a prevalence of 87% which was higher than a similar study done in Namibia (Bhardwaj et al., 2012) and drugs that

were are implicated included prothionamide, quinolones, isoniazid and pyrazinamide. Musculoskeletal side effects such as muscle spasms, backache, and joint pains were probably due to the accumulation of uric acid triggered by pyrazinamide which reduces its excretion. Ototoxicity manifesting as hearing loss, dizziness and vertigo were due to Kanamycin and capreomycin which damages the auditory nerve and the prevalence was higher than from a Korean study (Yang et al., 2017). Visual impairment was reported by 30.4% of the participants which was higher than that from an Ethiopian study (Bhardwaj et al., 2015). Ethambutol is the culprit since it damages the optic nerve. Hepatotoxicity occurred in 26.1% of the participants which was higher than that from a Korean study (Yang et al., 2017) and drugs responsible were protionamide, isoniazid, and pyrazinamide which are known to damage the hepatocytes. Nephrotoxicity occurred in 26.1% of the participants which was higher than that observed in Ethiopia ((Mohammad et al., 2015) and the drugs responsible were kanamycin and capreomycin. The damage to the kidneys was the main cause of hyperkalemia, hypokalemia, and changes in the frequency of urination. Anemia that occurred in 39.1% of the cases and was likely due poor feeding habits and myelosuppression which usually occurs in chronic illnesses.

The health-related quality of life was assessed according to the domains described in chapter 3. The effects of sociodemographic characteristics and adverse drug reactions on these domains were scored accordingly. Physical health scored 40.5% indicating that majority of the participants were unable to optimally conduct their daily activities due to lack of energy, fatigue, pain and discomfort, inadequate sleep and dependence on the drugs. Characteristics that enhanced physical health included; improved body mass index (BMI), having a spouse, and being in the continuation phase of MDR-TB therapy. Increase in BMI is usually accompanied with increased muscle mass

and energy stores which enables the victim to engage in the daily activities easily. Having a spouse provides solace and a helping hand and the continuation phase of therapy uses fewer drugs which impacts lesser side effects were probably the reasons for the improvement. Malnutrition, previous TB infection,use of alcohol and previous hospitalization had a negative effect on physical health. All these attributes are associated with loss of body weight and decreased energy. The adverse drug reactions that had a deleterious effect on physical health were anemia,hearing impairment, hepatotoxicity and electrolyte imbalance.

Psychological health had a score of 45.8% which was low. This domain is concerned with the perception of the participants on bodily image and appearance, feelings, self-esteem, religion and ability to think, learn, memorize and concentrate. The score suggests that majority of the participants had low self-esteem. The perception is usually a combination of environmental influence and a person's locus of control. This may explain why males, improved body mass index and increasing age had a positive effect on psychological health. The duration of treatment was accompanied with an improved physical appearance which had a positive psychological effect. HIV infection, malnutrition,use of alcohol and hospitalization had a negative impact on psychological health probably due to the social stigma and negative physiological effect associated with them. The adverse drug effects that had negative effects on psychological health were;hearing impairment, visual disturbances, and anemia which decrease the ability to engage in many socioeconomic activities.

The social relationship which is concerned with personal relationships, social support, and sexual activity had a score of 48.4%, which suggests that most participants had poor interpersonal relationships. The characteristics that enhanced this domain were; increase in BMI, having a

spouse, previous hospitalization, and having been in therapy for some time. Improved bodily image impacts confidence and esteem while having a partner provides an avenue of sharing life experiences. Male sex had a negative effect probably because men do not like sharing their issues often than women. Previous TB infection, malnutrition, anduse of alcohol have a stigma associated with them.

The environment score was below average at 48%. Most of the participants lived in low-class estates which were overcrowded with limited social amenities and a lot of mixed economic activities such bars, shops and service businesses. Traffic congestion was present every day and lack of appropriate disposal services for the refuse made the environment filthy. Most of the participants did not have a regular source of income because they had to attend the clinic daily to receive the medicines. Others were very ill and were not able to engage in the meaningful economic activity. The environment score was enhanced by an increase in BMI, being male, having a spouse, increasing age and duration of treatment. This domain was negatively affected by social habits such as smoking anduse of alcohol as well as HIV infection and relapsed TB. Previous hospitalization and low level of education had a negative effect. The adverse drug reactions which reduced the environment score werehearing impairment, skin rash and hepatotoxicity.

8.4 Conclusion

Drug-resistant tuberculosis was more common in males than females. Many participants suffered from the adverse effects of drugs which became less severe as the treatment progressed from intensive to the continuous phase. These side effects manifested in all body systems with the nervous and gastrointestinal tract being most affected. The health-related quality of life was low

across all the domains and was affected by sociodemographic characteristics and adverse drug reactions in different ways. Generally, increase in body mass index and having a spouse increased the quality of life.

8.5 Recommendations

8.5.1 Policy and practice

1. Appropriate monitoring of the adverse drug reactions should be instituted regularly in all health facilities handling MDR-TB patients. It was observed that most of the facilities were ill-equipped to detect drug toxicity early in order to prreactions permanent disability like completehearing impairment that was witnessed in some participants.

2. Adequate drug information should be given to patients concerning the side effects and measures to be taken to reduce their severity, especially gastrointestinal disturbances. A well-informed patient will be able to report the adverse reactions before they inflict debilitating harm to the body.

3. Since the daily observed therapy was used to administer drugs, the TB program should provide regular incentives to the patient to avoid a loss to follow up. The current arrangement for giving monthly stipend is inadequate since the financial assistance is not regular.

4. A number of the participants had peripheral neuropathy which is mainly caused by isoniazid and protionamide and can be reversed with administration of pyridoxine. The dose of pyridoxine should be individualized to ensure optimization of therapy.

5. Kanamycin should be discontinued in the treatment of drug-resistant tuberculosis. Patients who hadhearing impairment were on kanamycin and therefore capreomycin which is less ototoxic should be used.

6. Malnutrition was observed to negatively affect all domains of the quality of life. Patients should be counseled on balanced diet and where possible food supplements to all patients on treatment should be provided.

8.5.2 Research

1. A cohort study should be carried to investigate the adverse drug reactions and quality of life among patients using the current WHO recommended nine-month regimen for the treatment of drug-resistant tuberculosis. This approach will enable the detection of side effects in the course of therapy and assist in the development of a protocol for monitoring treatment.

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CHAPTER 9: SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

9.1 Introduction

This study investigated the risk factors for pulmonary tuberculosis and knowledge level, adverse drug reactions and quality of life among patients on the first line and those on MDR treatment for tuberculosis in Nairobi City County. This chapter summarizes the main findings of the study. It also incorporates the general conclusions and recommendations as well as limitations encountered. The new contribution to the body of knowledge.

9.2 Conceptual/Theoretical framework

The overall goal of treating patients with tuberculosis is to enhance their quality of life which involves improvement in social relationships, psychological health, environmental health, physical

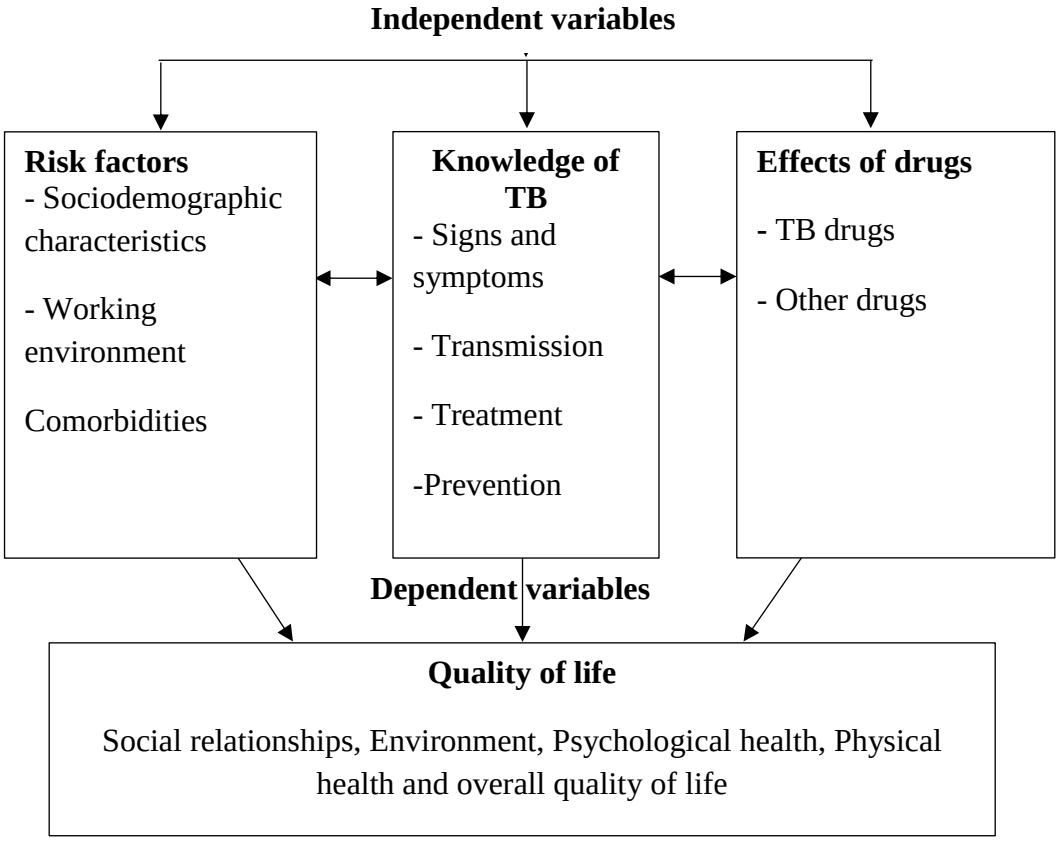

Fig 9.1 Conceptual framework **Source: Author, 2017**

health and overall quality of health according to WHO QOL-BREF. Physical health is assessed by

evaluating the effects of the diseases on the daily activities, dependence on medicinal substances and medical aids, level of energy and fatigue and interference with mobility. The presence and effect of pain and discomfort in the body are also assessed. The sleeping behavior, resting times and ability to work are also assessed in this domain. The components that are assessed in psychological health include bodily image and appearance. The emotional feelings which may be positive or negative are considered. Personal beliefs, religion, ability to think and learn as well as self- esteem are also assessed. Social relationships assess the availability of social support, ability to nurture personal relationships and engage in sexual activity. The environment domain is assessed by looking at financial status, physical safety, security and the extent of freedom an individual has. It also encompasses health and social care where quality and accessibility are considered. The status of the home environment and opportunities for acquiring skills and new information are explored. The other aspects included are the conditions of physical environment, leisure/ recreation activities and mode of transport. The quality of life in this study was used as the dependent variable.

The quality of life of patients with tuberculosis is dependent on several factors which may be endogenous or exogenous. Risk factors for pulmonary tuberculosis have a direct bearing on the quality of life. Among them includes sociodemographic characteristics and comorbidities. The former involves sex, age, education level, marital status, income, types of housing, working environment as well as lifestyle habits such as smoking and use of alcohol among others. These factors affect perceptions about life and feelings of self-worth. Comorbidities often have a negative effect on health thereby decreasing the quality of life of individuals. Risk factors were considered as independent variables in this study.

Tuberculosis is a curable disease and the drugs used are known to precipitate undesirable effects. When patients are put on TB therapy, they improve clinically and in their quality of life. However due to undesirable effects associated with treatment some patients' experience a downward trend in their well- being and quality of life decreases. This often involves several systems and may cause residual disability which can be temporary or permanent. Concurrent diseases, as well as the genotype of the patient, may influence the severity of the adverse reactions. Genetic predisposition to adverse reactions has been documented and mainly caused by the metabolites of drugs. Accumulation of metabolites occurs due to rapid production among patients who are fast acetylators (Stettner et al., 2015) or decreased excretion due to kidney damage. Concurrent administration of TB drugs with other drugs increases the possibility of adverse drug reactions. The effects of drugs in the participants were considered as independent variables in this study.

The quality of life is largely influenced by the knowledge people have about tuberculosis. This is because they are able to understand the management and prognosis of the illness. Social perceptions which are associated with stigma is improved when the society is informed thereby supporting the victims to regain their sense of self-worth. Early detection and treatment of tuberculosis are critical for adequate recovery and reduction of residual disability. This can be achieved if the society is informed about the signs and symptoms, mode of transmission, treatment, and prevention of the disease. Knowledge about tuberculosis was considered an independent variable in this study.

Risk factors, knowledge and effects of drugs are closely intertwined and therefore interacts to influence the quality of life. Knowledge facilitates the understanding of how the risk factors and drug affect the treatment of tuberculosis. In addition, the adherence to therapy and early detection

of adverse reactions, as well as prreactionsive strategies, depends on the patient knowledge and willingness to abide by the instructions given by the healthcare givers.

The conceptual framework **(figure 9.1)** above depicts the how the different variables in the study are connected with the quality of life and the subsequent chapters endeavors to describe their effects singly or in combination.

9.2 Summary

The risk factors for pulmonary tuberculosis were several **(Chapter 4)**. Males were more predisposed to the disease than females due to their genotypic and phenotypic characteristics. Overcrowding was a risk factor since the disease is transmitted mainly through droplets. HIV infections destroy the body immune system making it easier for the pathogen to enter the body. Smoking anduse of alcohol are known to depress the body immune system in different ways. Aging was also a risk factor. The more the risk factors a patient has, the higher the possibility of contracting pulmonary tuberculosis. The most important risk factor in the study population in Nairobi was male gender. This finding has not been demonstrated in previous studies and a new contribution to the body of knowledge.

Knowledge was assessed in four dimensions, namely; signs and symptoms, transmission, treatment and prevention **(Chapter 5).** Generally, the level of knowledge in increasing order was; signs and symptoms, disease prevention, transmission, and treatment. Participants with tuberculosis were more knowledgeable than those without the disease probably because of the experience and counseling rendered by health care providers in the course of treatment. A cough was recognized as the most common symptom of tuberculosis. The predictors for knowledge on signs and symptoms as well as treatment were HIV and tuberculosis infections. Sex was a strong

predictor for knowledge on prevention. Level of education,use of alcohol, and TB infection were strong predictors for the overall level of knowledge. These findings have not been demonstrated before and therefore an addition to the body of knowledge

The study also investigated the adverse drug reactions and their impact on adherence to first line anti-tuberculosis therapy. The most common gastrointestinal side effects were a loss of appetite, nausea, and vomiting **(Chapter 6)**. Neurological problems were weakness, numbness, tingling sensations and depression. Skin rash, arthralgia, and blurring of vision were common. The rate of adherence was mainly medium or high. Independent predictors of adherence were mental depression,use of alcohol, arthralgia and peripheral neuropathy. This has not been demonstrated in previous studies.

Health-related quality of life of participants on first line anti-tuberculosis therapy was assessed **(Chapter 7)**. The mean scores for the domains in ascending were; environmental health, the overall quality of life, physical health, psychological health and social relationships. Generally, level of education, body mass index, impaired vision, and duration of treatment were independent predictors of all the domains of health-related quality of life. This has not been demonstrated in previous studies.

Participants on drug-resistant therapy for tuberculosis were investigated to determine the adverse drug reactions and health-related quality of life **(Chapter 8).** The prevalence of the adverse reactions in ascending order according to the body systems involved the skin, liver, renal, electrolytes, eyes, hematological, endocrine, cardiovascular systems, ENT, respiratory systems,

musculoskeletal systems, gastrointestinal tract and nervous system. The mean scores for the different domains of health-related quality of life in ascending order were; overall quality of life before treatment, social relationships, environmental health, the overall quality of life during treatment, psychological health, and physical health. Independent predictor of physical health was malnutrition and those of psychological health were; malnutrition, previous hospitalization, and hepatotoxicity. Social relationships were associated with malnutrition,use of alcohol, and previous hospitalization and nervous system disturbances. Body mass index and previous hospitalization were predictors for the overall health-related quality of life. This has not been demonstrated in previous studies.

9.3 General conclusions

1. The risks of contracting tuberculosis are genetic, environmental and behavioral. Males are more at risk than females. Smoking anduse of alcohol and overcrowding are also risk factors. The knowledge about the disease is inadequate among residents of Nairobi City County. Patients on anti-tuberculosis drugs suffer from diverse side effects. The most prevalent ones involve the gastrointestinal, nervous and musculoskeletal systems. Some of these adverse effects cause permanent residual disability such ashearing impairment. The health-related quality of life is lower in patients with tuberculosis which is an additive effect of the disease and drugs. Patients who were on treatment for drug-resistant tuberculosis had lower mean scores of the different domains of the health-related quality of life compared to those on first-line treatment for non-drug-resistant tuberculosis.

9.4 General recommendations

Wide-scale health promotion regarding tuberculosis should be carried out to empower people with information. This approach will dissuade the public from engaging in lifestyle habits that

predispose them to the disease. Protocols should be developed to assist in monitoring the adverse effects of drugs. This may help to optimize therapy and reduce the incidence of adverse effects of drugs. The morbidity and mortality due to drugs may be detected early and managed accordingly. The quality of life should be assessed in the course of treatment. This may provide a holistic approach to management of the disease.

9.5 Study limitations

The limitations encountered during the study were;

a. Recall bias

   Some of the questions required the participants to remember what happened in the past. The responses, therefore, were dependent on the individual memory. Occasionally it was difficult to do so especially on the questions pertaining to the quality of life.

b. Loss to follow up

   Some patients absconded in the course of treatment. This involved participants on drug-resistant TB therapy where universal sampling was applied. This reduced the number of participants targeted.

c. Ineffective communication

   Challenges were encountered during the interviews due to impaired hearing among patients on drug-resistant tuberculosis therapy. A few of these participants were completely deaf and communication was through writing questions for them to read and respond accordingly. No oral explanation was possible and therefore the answer is given depended

on the understanding of the participant. Some participants were very sick and communication was difficult.

d. Incomplete patients' records

Comprehensive data was lacking in the records of patients. This mainly involved laboratory results because samples collected were sent to one organization charged with the responsibility for analyzing them. Therefore results which were crucial for the study were not available. This aspect mainly involved participants who had drug-resistant tuberculosis and were being followed up daily in the respective health facilities.

9.6 Dissemination plan

The findings of this study will be disseminated through the various ways;

1. Publications in refereed journals

Two articles have already bee published in the Pharmaceutical Journal of Kenya. These are;

i. ***P.N.Karimi , A.N. Guantai , C. Kigondu , T. Ogaro.*** Adverse drug reactions among patients being treated for Multi-Drug Resistant Tuberculosis in Nairobi City County Health Facilities. *Pharmaceutical Journal of Kenya Vol. 23, (2); 2017*: 56-60.

ii.***P.N.Karimi , A.N. Guantai , C. Kigondu , T. Ogaro***. prevalence of adverse events of anti-tuberculosis drugs and their impact on adherence to Treatment in Nairobi City County. *Pharmaceutical Journal of Kenya Vol. 23, (2); 2017*: 61-65.

Three more articles are being revised for submission to other journals.

2. Presentations in conferences and workshops

The findings will be presented in local and international conferences in future.

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APPENDICES

Appendix 1. Consent Form

Principal investigator

Dr. Peter. N. Karimi, Department of Pharmaceutics and Pharmacy Practice, UON, Tel: 0722436019

Introduction

I am Dr. P.N. Karimi, a student at the University of Nairobi, pursuing Doctor of Philosophy degree in Clinical Pharmacy. As you might be aware, Tuberculosis is a serious disease and therefore quick and appropriate treatment is necessary. The purpose of this study is to identify the risk factors and adverse reactions of drugs used to treat tuberculosis and their effect on the quality of life. I am therefore requesting you allow me to ask you questions and examine the body to assess the adverse drug effects on different systems and also peruse through your medical records to assess the the relevant laboratory test results. Once you agree to take part in the study, I will request you to sign your name or make your mark on this form. We will offer you a copy to keep if need be. Kindly oblige.

Your participation is voluntary

Your participation in this study is voluntary. Your refusal to take part in the study will not affect the quality of treatment accorded to you in the health facility. Your values will be respected.

Risk and /or discomfort

There is no major risk involved. There will be no financial obligation on your side. During the assessment, precautions will be taken to ensure your privacy and comfort.

Benefits

The results obtained from the assessment, results will be shared with your clinician and may be used to effectively manage your condition. In addition, any information concerning the disease will be offered at no financial cost. The results may be used by the government to predict the incidences of side effects associated with TB drugs. Therapy may be altered to ensure that the adverse drug effects are minimized.

Confidentiality

Effort will be made to keep your personal information confidential. The information will be kept under lock and key and only be used to facilitate your treatment and for academic purposes. However, confidentiality may be broken at your request or when a court of law asks for it.

Justice

You will be given the same treatment like other participants regardless of the outcome. Your social status, gender, culture or lifestyle will not negatively affect the treatment. There will be no discrimination.

Veracity

I will be truthful with all the information given. The importance of each question will be explained if requested for.

Dissemination of information

The information generated from the data will be published in reputable journals to enhance wide circulation. In addition, the information will be presented at conferences and seminars. The Ministry of health through the TB program will be informed about the results.

Problem or questions

If you have any questions about the research study or you have any research-related injury, you should contact DR. P.N. Karimi on Telephone number 0722436019.

If you have any questions about your right as a research participant, you should contact Prof M. Chindia, Secretary, University of Nairobi Kenyatta National Hospital Ethics and Research committee on Telephone number 2726300. Ext 44102

Participant's statement

I have read this form or had it read to me. I have discussed the information with those concerned. All my concerns have been addressed. I comprehend that my decision to take part in the study is voluntary. By signing this form, I do not give up any rights that I have as a research participant.

Participant Name/ _____ Participant Signature _____ Date _____

Thumb Print

Investigator's statement

I have taken the participant through the entire consenting process and obtained his/her consent without coercion. I will maintain confidentiality and give guidance to the participant where necessary.

Investigator's Name_____ Investigator signature ____ Date_____

Appendix 2.Assessment of risk factors and knowledge of tuberculosis (Case-control study)

a. Socio-demographic characteristics and risk factors of tuberculosis

1. TB patient (1) Non –TB patient (0)
2. Sex

Male	Female
1	0

3. Age----------

4. Age Category

Age Category (Years)	Code
18- 30	0
31 and above	1

5. Marital status

Category	Code
Married	1
Single	0

6. Highest Education Level

Category	Code
Primary level	0
Secondary level and above	1

7. Number of occupants in the house

No of occupants in the house	Code
1-2	0
3 and above	1

S/No	Risk factor	Absent	Present
8	HIV infection	0	1
9	Poorly treated previous TB	0	1
10	Malnutrition	0	1
11	Diabetes mellitus	0	1
12	Alcoholism	0	1
13	Tobacco smoking	0	1
14	Immune suppressive therapy	0	1
15	Corticosteroid therapy	0	1
16	Previous contact	0	1
17	Overcrowding	0	1
18	Hospitalization	0	1

19. Number of risk factors

Number	Code
0	1
1	2
2	3
3	4

4	5
Above 4	6

b. Assessment of knowledge about tuberculosis

Dimension of knowledge on signs and symptoms (DKSS)

21. Coughing with or without blood for at least three weeks	Yes (1)	No (0)
22. Chest pain	Yes (1)	No (0)
23. Shortness of breath	Yes (1)	No (0)
24. Loss of appetite	Yes (1)	No (0)
25. Weight loss	Yes (1)	No (0)
26. Fever with night sweats	Yes (1)	No (0)

Dimension of Knowledge about Transmission (DKT)

27. Is TB communicable?	Yes (1)	No (0)
28. Can TB be communicated through sneezing?	Yes (1)	No (0)
29. Can TB be communicated through coughing?	Yes (1)	No (0)
30. Can TB be communicated through sharing of things Of affected people?	Yes (1)	No(0)

Dimension of Knowledge about Treatment (DKTr)

31. Is treatment available	Yes (1)	No (0)
32. Does regular intake of medicine cure patient	Yes (1)	No (0)
33. Does irregular intake of medicine cause death/MDR	Yes (1)	No (0)

Dimension of Knowledge about Prevention (DKP)

34. Is vaccine available	Yes (1)	No (0)
35. Does one need to be far away from affected people when sneezing	Yes (1)	No (0)
36. Should one avoid using things of affected people	Yes (1)	No (0)
37. Should one always get clean	Yes (1)	No (0)

Themes

37. DKSS

Adequate knowledge (1) Inadequate knowledge (0)

38. DKT

Adequate knowledge (1) Inadequate knowledge (0)

39. DKTR

Adequate knowledge (1) Inadequate knowledge (0)

40. DKP

Adequate knowledge (1) Inadequate knowledge (0)

Appendix 3. Assessment of adverse drug reactions, adherence and quality of life among patients on first-line TB therapy (Cross-sectionalalal study)

a. Socio-demographic characteristics

1. BMI

Category of BMI	Code
Below 18.5	1
18.6-25	2
Between and 30	3
Above 30	4

2. Duration of treatment

Month	Code
1	1
2	2
3	3
4	4
5	5
6	6

3. Sex

Male	Female
1	0

4. Age----------

5. Age Category

Age Category (Years)	Code
18- 30	1
31-40	2
Above 40	3

6. Marital status

Category	Code
Married	0
Single	1

7. Highest education Level

Category	Code
No formal education	1
Primary level	2
Secondary level	3
Tertiary	4

8. Employment status
   1. Formal ( )

   2. Nonformal ( )

9. 1ncome per month

Income (ksh)	Code
10,000 and below	1
Between 10,000 to 20,000	2
Above 20 000 to 30000	3
Above 30,000	4

S/No	Risk factor	Present	Absent
10	HIV infection	1	0
11	Poorly treated previous TB	1	0
12	Malnutrition	1	0
13	Diabetes mellitus	1	0
14	Alcoholism	1	0
15	Tobacco smoking	1	0

Phase of treatment

No of drugs	Code
Continuation phase	1

Intensive phase	2

Adverse drug reactions

	Adverse drug reactions	Present	Absent
17	Loss of appetite	1	0
18	Nausea, vomiting	1	0
19	Tiredness or weakness	1	0
20	Clumsiness or unsteadiness	1	0
21	Numbness	1	0
22	Tingling	1	0
23	Burning or pain in the hands or feet	1	0
24	Sore throat	1	0
25	Unusual bleeding and bruising	1	0
26	Skin rash	1	0
27	Arthralgia	1	0
28	Seizures	1	0
29	Mental depression	1	0
30	Psychosis	1	0
31	Muscle twitching	1	0
32	Blurred vision	1	0
33	Loss of vision	1	0
34	Inability to distinguish green and yellow	1	0
35	Eye pain	1	0
36	Chills,	1	0

37	Pain and swelling of joints especially big toe, or knee, hot skin over affected joints	1	0
38	Greatly increased or decreased frequency of urination or amount of urine	1	0
39	Increased thirst	1	0

Assessment of adherence

Eight-item Morisky medication adherence assessment scale

		Response	
	Morisky Medication Adherence Scale (MMAS-8) questions	**Yes (1)**	**No(0)**
i	Do you sometimes forget to take your medication?		
ii	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?		
iii	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
iv	When you travel or leave home, do you sometimes forget to bring along your medicine?		
v	Did you take all your medicine yesterday?		
vi	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
vii	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
viii	How often do you have the difficulty of remembering to take all your medicine? □Never/rarely □ Once in a while□ Sometimes □ Usually □ All the time		
40	**Grading of the score** High adherence (score=8) (1) Medium adherence score 6-7 (2) poor adherence (below 6) (3)		

Quality of life (WHOQOL-BREF)

i. How would you rate your quality of life?

Please identify the rating				
Very poor	Poor	Neither poor nor good	Good	Very Good
1	2	3	4	5

ii. How satisfied are you with your health?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

*The following questions ask about **how much** you have experienced certain things in the **last two** weeks.*

iii. To what extent do you feel that physical pain prreactions you from doing what you need to do?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

iv**.** How much do you need any medical treatment to function in your daily life?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount

1	2	3	4	5

v**.** How much do you enjoy life?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

vi. To what extent do you feel your life to be meaningful?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

vii. How well are you able to concentrate?

Please identify the rating				
Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

viii**.** How safe do you feel in your daily life?

Please identify the rating				
Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

ix. How healthy is your physical environment?

Please identify the rating

Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

*The following questions ask about **how completely** you experience or were able to do certain things in the last two weeks.*

x. Do you have enough energy for everyday life?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

xi. Are you able to accept your bodily appearance?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

xii**.** Have you enough money to meet your needs?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

xiii. How available to you is the information that you need in your day-to-day life?

Please identify the rating

Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

xiv. To what extent do you have the opportunity for leisure activities?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

xv. How well are you able to get around?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

*The following questions ask you to say how **good** or **satisfied** you have felt about various aspects of your life over the **last two** weeks.*

xvi. How satisfied are you with your sleep?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xvii. How satisfied are you with your ability to perform your daily living activities?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied

1	2	3	4	5

xviii**.** How satisfied are you with your capacity for work?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xix. How satisfied are you with yourself?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xx. How satisfied are you with your personal relationships?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xxi. How satisfied are you with your sex life?

Please identify the rating

Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xxii**.** How satisfied are you with the support you get from your friends?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xxiii. How satisfied are you with the conditions of your living place?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xxiv. How satisfied are you with your access to health services?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

xxv. How satisfied are you with your mode of transportation?

Please identify the rating

Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

*The following questions refer to **how often** you have felt or experienced certain things in the **last two** weeks.*

xxvi. How often do you have negative feelings, such as blue mood, despair, anxiety, depression?

Please identify the rating				
Never	**Seldom**	**Quite often**	**Very often**	**Always**
1	2	3	4	5

S/NO	DOMAIN	SCORE (%)
41	Physical health domain	
42	Psychological health domain	
43	Social relationship domain	
44	Environmental health domain	
45	Overall quality of life	

Appendix 4. Assessment of adverse drug reactions and quality of life of patients with drug-resistant tuberculosis (Longitudinal study)

Socio-demographic characteristics

1. Weight---------- Height----------

   BMI below 18.5 (1) Between 18.5 to 25 (2) Between 25 to 30 (3) Above 30 (4)

2. Sex

Male	Female

1	0

3. Age----------

4. Age Category

Age Category (Years)	Code
18- 30	1
31-40	2
Above 41	3

5. Duration of treatment

Month	Code
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20
21	21

6. Religion

Category	Code
Christianity	1
Islam	2
Hinduism	3
Others	4

7. Marital status

Category	Code
Married	1
Single	0

8. Highest education Level

Category	Code
No formal education	1
Primary level	2
Secondary level	3
Tertiary	4

9. Number of children in the family

No of occupants in the house	Code
2 and below	0
3 and above	1

S/No	Risk factor	Present	Absent
10	HIV infection	1	0
11	Poorly treated previous TB	1	0
12	Malnutrition	1	0
13	Diabetes mellitus	1	0
14	Alcoholism	1	0
15	Tobacco smoking	1	0
16	Immune suppressive therapy	1	0
17	Corticosteroid therapy	1	0
18	Previous hospitalization	1	0

19. **Treatment regimen**

Drug combination	Code
8km,lev,PTO,CS,Z,Pyridoxine	1
Cm,lev,PTO,CS,Z,Pyridoxine	2
lev,PTO,CS,Z,Pyridoxine	3
H,E,Z,Kn,Mfx,PTO,Cfz,	4
H,E,Z,Kn,Mfl,PTO,Cfz	5
Z,Mfx,PTO,Cs,cfz,DLM	6

20**. Drugs used to treat HIV**

Regimen	Code
TDF/AZT+3TC+EFV	1
AZT+3TC+ABC/TDF	2
TDF/AZT+3TC+EFV	3

Adverse drug reactions

	Sign and symptom	**Present**	**Absent**
21	Nephrotoxicity	1	0
22	Hypothyroidism	1	0
23	Hyperkalemia	1	0
24	Hypokalemia	1	0
25	Anaemia	1	0
26	Hepatotoxicity	1	0
27	Nausea	1	0
28	Vomiting	1	0
29	Abdominal pain	1	0
30	Flatulence	1	0
31	Excessive salivation	1	0
32	Diarrhea	1	0
33	Constipation	1	0
34	Abdominal cramps	1	0
35	Loss of appetite	1	0
36	Black tarry stool	1	0
37	Dry mouth	1	0
38	Mouth ulcers	1	0
39	Palpitations	1	0
40	Headache	1	0
41	Dizziness	1	0
42	Confusion	1	0
43	Irritability	1	0
44	Nightmares	1	0
45	Drowsiness	1	0
46	Convulsions	1	0
47	Speech problems	1	0
48	Thoughts of suicide	1	0
49	Tingling sensation,numbness,burning sensation of feet	1	0
50	Insomnia	1	0
51	Mental depression	1	0
52	Agitation	1	0
53	Cough	1	0
54	Chest pain	1	0

55	Dyspnoea	1	0
56	Painful urination	1	0
57	Blood in urine	1	0
58	Frequent urination	1	0
59	Decreased urine production	1	0
60	Pain in the joints	1	0
61	Backache	1	0
62	Pain in the big toe	1	0
63	Muscle spasms	1	0
64	Fullness of the ears	1	0
65	Inability to hear properly	1	0
66	Vertigo	1	0
67	Sore throat	1	0
68	Gynaecomastia	1	0
69	Sexual dysfunction	1	0
70	Hypoglycemia	1	0
71	Bleeding	1	0
72	Tiredness	1	0
73	Jaundice	1	0
74	Visual impairment	1	0
75	Weight gain	1	0
76	Fever	1	0
77	Paleness of the skin	1	0
78	Bleeding from the gums	1	0
79	Tremor	1	0
80	Rash	1	0

Assessment of quality of life

During treatment

1a. How would you rate your quality of life?

Please identify the rating				
Very poor	Poor	Neither poor nor good	Good	Very Good
1	2	3	4	5

2a**.** How satisfied are you with your health?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

Before treatment

1b. How would you rate your quality of life?

Please identify the rating				
Very poor	Poor	Neither poor nor good	Good	Very Good
1	2	3	4	5

2b**.** How satisfied are you with your health?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

*The following questions ask about **how much** you have experienced certain things in the **last two** weeks.*

3. To what extent do you feel that physical pain prreactions you from doing what you need to do?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

4**.** How much do you need any medical treatment to function in your daily life?

Please identify the rating

Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

5**.** How much do you enjoy life?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

6. To what extent do you feel your life to be meaningful?

Please identify the rating				
Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

7. How well are you able to concentrate?

Please identify the rating				
Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

8**.** How safe do you feel in your daily life?

Please identify the rating				
Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

9. How healthy is your physical environment?

Please identify the rating				
Not at all	slightly	A moderate amount	Very much	Extremely
1	2	3	4	5

*The following questions ask about **how completely** you experience or were able to do certain things in the last two weeks.*

10. Do you have enough energy for everyday life?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

11**.** Are you able to accept your bodily appearance?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

12**.** Have you enough money to meet your needs?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

13. How available to you is the information that you need in your day-to-day life?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

14. To what extent do you have the opportunity for leisure activities?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

15. How well are you able to get around?

Please identify the rating				
Not at all	A little	Moderately	Mostly	Completely
1	2	3	4	5

*The following questions ask you to say how **good** or **satisfied** you have felt about various aspects of your life over the **last two** weeks.*

16**.** How satisfied are you with your sleep?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

17. How satisfied are you with your ability to perform your daily living activities?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

18**.** How satisfied are you with your capacity for work?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

19. How satisfied are you with yourself?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

20. How satisfied are you with your personal relationships?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

21. How satisfied are you with your sex life?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

22**.** How satisfied are you with the support you get from your friends?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

23. How satisfied are you with the conditions of your living place?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

24. How satisfied are you with your access to health services?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

25. How satisfied are you with your mode of transportation?

Please identify the rating				
Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
1	2	3	4	5

*The following questions refer to **how often** you have felt or experienced certain things in the **last two** weeks.*

26. How often do you have negative feelings, such as blue mood, despair, anxiety, depression?

Please identify the rating				
Never	**Seldom**	**Quite often**	**Very often**	**Always**
1	2	3	4	5

SCORE

S/NO	DOMAIN	SCORE (%)
81	Physical health domain	
82	Psychological health domain	
83	Social relationship domain	
84	Environmental health domain	
85	Overall QOL before treatment	
86	Overall QOL during treatment	

Appendix 5. List of public health facilities in Nairobi City County

A. National Hospitals

1. Kenyatta National Hospital
   Location: Ngong Road

2. Mathari National Hospital
   Location: Thika Road

B. District Hospitals

1. Mama Lucy Kibaki District Hospital
   Location: Umoja, Off Kangundo Road

2. Mbagathi District Hospital
Location: Mbagathi way

3. Pumwani Maternity Hospital
Location: General Waruinge Street, Eastleigh

C. Health Centers and Dispensaries

DISTRICT	FACILITIES	SATELLITE CLINIC
1. KAMUKUNJI	1.Eastleigh H/C Location: Eastleigh Section 7	2.Biafra clinic Location:Biafra estate
	3 Pumwani Majengo H/C Location: Gikomba Open air market	4. ShauriMoyo Location: Shauri Moyo estate shopping center 5. Muthurwa Location: Muthurwa market/bus terminus
	6. Bahati H/C Location: Bahati Estate	7. Jerusalem Clinic Location: Jerusalem estate
2. STAREHE	8. Ngaira H/C Location: Off Hailesellasie Avenue, next to government press	9. Rhodes Chest clinic Location: Ngaira health center, next to government press
	10. Ngara H/C Location: Park Road	11. Kariokor Clinic Location: Opposite Ziwani shopping center
	13. STC Casino H/C Location: Off River Road	12. Pangani Clinic Location: Pangani estate
	14. Huruma Lions H/C Location: Huruma Estate, next to Huruma grounds	
	15. Lagos Rd. Disp. Location: Lagos Road, next Marble Arch Hotel	
	16. Mathare Police Depot Location: Mathare Police Post shooting range	
3. KASARANI	17. Mathare North H/C Location: Mathare North estate	

	18. Kariobangi North H/C Location: Old Kariobangi estate	
	19. Kasarani H/C Location: Kasarani DC's office	
	20. Kahawa West H/C Location: Kahawa West estate	
	21. Babadogo H/C Location: Babadogo road, Ruaraka	
	22. NYS H/C Location: National Youth Service H/Q, Ruaraka	
	23. GSU Hq H/C Location: GSU hq Ruaraka	
	24. Kamiti Prison H/C Location: Kamiti	
	25.Ruiru PSTC Location: Ruiru prison	
	26. CID Hq's Disp. Location: Nairobi Area Police Hq	
	27. GSU Ruiru Disp. Location: Ruiru GSU camp	
4. WESTLANDS	28. Westlands H/C Location: Westlands	
	29. Kangemi H/C Location: Waiyaki way, Kangemi	
	30. Highridge H/C	
	31 Karura H/C Location: Kiambu rd next to Muthatiga golf club	
	32. Lady Northey H/C Location: State House rd	33. State House. Clinic Location: State House
	34. Kabete Approved Sch. H/C Location: Kabete Approved Sch	
	35. State Hse. Dispensary Location: State Hse Girls school	
	36. Lower Kabete	

	Location: Lower Kabete	
	37. MjiwaHuruma Disp. Location: MjiwaHuruma, Runda	
	38. KARI 9Muguga) h/C Location:Muguga, Naivasha Road	
	39.Waithaka H/C Location: Waithaka suburb	
	40.Riruta H/C Location: Riruta shopping centre	
	41. Ngong Rd H/C Location:Karen	42. Woodley Clinic Location: Woodley estate Mugo Kibiru rd
DAGORETI	43. Dagoreti Approved Sch. h/C Location: Dagoreti Approved Sch	
	44. Langata H/C Location: Otiende estate	45. Jinnah Clinic Location: Langata
	46. Karen H/C Location: Hardy, Karen	
	47. Kibera DO H/C Location: DC's office	
	48. Langata Women Prison H/C Location: Langata Women	
	49. Nairobi West Prison H/C Location: Nairobi West Prison	
	50.Uhuru camp H/C Location: Uhuru AP camp	
	51.Kibera DO H/C Location: Kibera slums	
	52. Kibera Amref H/C Location: Kibera laini shaba	
	53. GSU Kibera H/C	

	Location: GSU Kibera quarters	
7.EMBAKASI	54. Kayole 1 H/C Location: Kayole 1 estate	
	55. Kayole II H/C Location: Kayole II estate	
	56. Umoja H/C Location: Umoja II estate	
	57. Embakasi H/C Location: Embakasi village	
	58. GSU Embakasi H/C Location: GSU Training School	
	59.APTC Embakasi H/C Location: APTC Embakasi	
8.NJIRU	60. Dandora 1 H/C Location: Dandora 1 estate, Komarok road	
	61. Dandora 11 H/C Location: Dandora II estate	
	63. Njiru H/C Location: Njiiru shopping center, Kangundo rd	
	64. Kariobangi South Disp. Location: Kariobangi South estate	
9. MAKADARA	65. Makadara H/C Location:Jogoo rd, Hamza estate	66. Mbotela Location: Mbotela estate, jogoo rd
	67. Jericho H/C Locatio	68. Hono Clinic Location: Hono Cresent Jericho 69. Ofafa 1 Clinic Location: Ofafa 1 70. Maringo Clinic Location: Maringo
	71. Loco H/C Location: Nairobi Railway Station, Industrial area	72 MOW Dispensary Location: MOW sports club

	73. Kaloleni Dispensary Location: Kaloleni estate shopping center	
	74. Railway training Institute (South B) Dispensary Location: Railway training Institute (South B)	75. South B Clinic Location: South B, next to shopping center 76. Police Band Dispensary Location: South C
	77. LungaLunga H/C Location: LungaLunga informal settlement	
	78. Nairobi remand Home H/C Location: Industrial area	

Appendix 6. Letter of ethical approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/146

31st March, 2015

Peter Ndirangu Karimi
Pharmaceutics and Pharmacy Practice
School of Pharmacy
University of Nairobi

Dear Peter

Research Proposal: Risk Factors of Tuberculosis Resistance and the Effect of Chemotherapy on the Quality of Life (P736/12/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 31st March 2015 to 30th March 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

Appendix 7. Approval from Nairobi City County

NAIROBI CITY COUNTY

elegrams: "PRO-MINHEALTH", Nairobi
elephone: Nairobi 217131/313481
x: 217148

hen replying please quote

ef. No. CHS/PH/109/24

COUNTY HEALTH OFFICE
NAIROBI
NYAYO HOUSE
P.O. Box 34349-00100
NAIROBI

COUNTY HEALTH SERVICES

Dr Peter Ndirangu

Department of pharmaceutics and Pharmacy

RE: RESEARCH AUTHORIZATION

Following your application dated 14th April, 2015 for authority to carry out research on **"Risk factors of Tuberculosis Resistant to Drugs and Effects of Chemotherapy on the Quality of Life in Nairobi,"** I am pleased to inform you that you have been authorized to undertake research in Nairobi County.

On completion of the research, you are expected to submit **two hard copies and one copy in PDF** of the research thesis to our operational research technical working group.

Mr R. K Muli ,

For County Director of Medical Services

Cc

- All DMOHs
- Medical superintendent

Mbagathi Hospital

Mama Lucy Hospital