DETERMINANTS OF PERSISTENT SPUTUM SMEAR POSITIVITY AFTER INTENSIVE PHASE CHEMOTHERAPY AMONG PATIENTS WITH TUBERCULOSIS AT RHODES CLINIC, NAIROBI, KENYA

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Determinants of persistent sputum smear positivity after intensive phase chemotherapy among patients with tuberculosis at Rhodes clinic, Nairobi, Kenya

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

This work is dedicated to my family. Without your support I would not have made it this far. This is a testament that hard work is rewarding, and so is the outcome of this research.

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ABBREVIATIONS AND ACRONYMS

AFBs	Acid Fast Bacillus
AIDS	Acquired Immune Deficiency Syndrome
BCG	Bacille Calmette Guerin
CDC	Center for Disease Control
CNR	Case Notification Rate
DLTLD	Division of Leprosy Tuberculosis and Lung Diseases
DOT	Directly Observed Treatment
DOTS	Directly Observed Therapy Short Course
EPI	Expanded Program on Immunization
ETB	Extra Pulmonary Tuberculosis
IPT	Isoniazid preventive therapy
SDGs	Sustainable Development Goals
MDR-TB	Multi-Drug Resistant Tuberculosis
MOPHS	Ministry of Public Health and Sanitation
PLWHA	People Living with HIV and AIDS
PTB	Pulmonary Tuberculosis
RHZE	Rifampicin, Isoniazid, pyrazinamide and Ethambutol
RCC	Rhodes Chest Clinic
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively Drug Resistant Tuberculosis

OPERATIONAL DEFINITIONS

Adherence – Compliance to treatment requirement including taking medication on time and required dosage, a practice often reinforced by counseling

Cases – in this study refers to persons included in the study on the basis of having a positive sputum result after intensive phase of Tb treatment

Continuation phase – TB treatment period for a period (often four months) where a patient receives 2 anti TB drugs

Control – in this study refer to people involved in the study on the basis of having sputum negative results in which case the desired sputum results after two months of Tb treatment

GeneXpert – an improve TB diagnostic equipment with advance technology to detect drug resistance.

Intensive phase chemotherapy – treatment of tuberculosis with multiple drugs that include Isoniazid, Rifampicin, pyrazinamide and Ethambutol for a period of two months.

Persistent sputum positivity – existence of mycobacterium tuberculosis bacterium in sputum after two month of TB treatment.

Sputum conversion – desired treatment outcome where the sputum does not have mycobacterium tuberculosis bacterium after two month of Tb treatment

ABSTRACT

Tuberculosis is a global health challenge that according to World Health Organization (WHO) resulted in the deaths of 1.6 million people including 230,000 children in year 2017. (WHO, 2017). Sputum smear testing is recommended procedure for effective monitoring TB treatment success, with negative sputum testing results being the key signifier of successful treatment. Conversely, positive sputum smear results are an indicator of failure of treatment. This study was conducted to determine the factors that contribute to persistent sputum smear positivity after intensive treatment. The study took place at the Rhodes Clinic, Nairobi, a health facilities operated by the Department of Health (City county of Nairobi) and National Ministry of Health to primarily treat tuberculosis and lung diseases as well as acquired immune efficiency disease (AIDS). This case control study compared patients who were sputum positive (cases) to those who were sputum negative (controls) after completion of two months of intensive chemotherapy with TB medication. The sample population was 71, 25 of whom were cases and 46 were controls. Data was collected analyzed and results tabulated using SPSS. Skipping medication doses which is treatment non adherence was significantly associated with sputum positivity ($p=0.01$). Also, treatment practices were found to affect treatment outcome in that patients who were sputum positive at the end of the two-month period were more likely to have taken longer before seeking treatment compared to those who were sputum negative by median (IQR) 8 (3 -12) and 4 (3 – 8) weeks respectively. Similarly, patients who took longer to seek treatment were significantly more likely to miss their medicine. The study concluded that factors such as non-adherence to medication, and delayed diagnosis, and socio-economic factors contributed to persistent sputum positivity two months after intensive treatment.

CHAPTER ONE

INTRODUCTION

1.1 Background information

Tuberculosis is an ancient disease that continues to plague the modern world. The disease was known as the 'captain of men's death' due to the high mortality resulting from the disease in the late nineteenth century Europe (Schaf, Zumla, Donald, 2009). The high burden of this disease has shifted from the developed nations and has become one of the top 10 leading causes of death in the world. According to the recent WHO statistics, South East Asia has the highest incidence of the disease with 4,440,000 reported cases of the disease in 2017. The second region after South East Asia is Africa with 2,480,000 reported TB cases in the same year. In spite of the global collaborations and efforts to end TB, the disease continues to adapt and prevail around the globe. In 2017, TB lead to approximately 1.3 million deaths among HIV negative individuals and an additional 300,000 deaths of HIV positive people (WHO, 2018). There are incidences of the disease in all countries across all age groups with the severity varying across countries.

The incidence of Tuberculosis has been on the decline in Sub-Saharan Africa. Back in 2000, the incidence of the disease in the region was at 333 per 100000 people. In 2012, however, the incidence was at 292 per 100000 (World Bank Group, 2018). The latest recorded trend was in 2016 with 246 people per 100000 exhibiting the disease. Efforts towards increased surveillance, collaboration across health care organizations and NGOs as well as affordability of drug treatment contributed to the decline across the decade. Conversely, TB continues to present new challenges due to its co-association with HIV as well as the rise in drug-resistant TB. In 2017, approximately 920,000 people infected with HIV fell ill of TB in Sub-Saharan Africa (WHO, 2018). The rise in immune disrupting long-life infections such as diabetes impede on the recent global commitment to end TB across the globe.

A global strategy that aims to end TB across the world by year 2035 was launched in year 2014 by WHO with the aims of ending global TB epidemic, reduce TB deaths

by 95% and cut new cases by 90% between 2015 and 2035. (WHO, 2015) One of the ways to achieve this goal is through innovation and research. TB is a disease that is caused by the bacteria Mycobacterium tuberculosis. There is extensive research on the factors contributing to the spread of the disease. Research on tuberculosis has informed practice as well as strategies aimed at curbing the disease. However, there is a growing recognition that the fight against TB calls for an adaptive approach that actively responds to the factors that fuel the disease. Drug resistant tuberculosis is increasingly becoming an issue. In Kenya, for instance, multidrug resistant TB is an issue (Ministry of Health, 2016). Multi-drug Resistant Tuberculosis (MDR-TB) is a form of the disease resulting from mycobacteria that do not respond to the two first line drugs, Isoniazid and Rifampicin used in TB treatment

All the member states in the UN and WHO have committed to the goal of ending TB by 2030. Kenya is one of these member states. The country ranks 14 out of the 22 high TB burden countries that collectively contribute to 80% of world T.B cases. In 2015, the country recorded the lowest prevalence rate of 82000. Since then, the smear positive cases have maintained a narrow range of 15.1% to 18.2% (Ministry of Health, 2016). A recent assessment of the status of TB in the country revealed that there are limited resources for data collection, planning, and implementation of evidence-based interventions and programs. County respondents indicated that some of their TB budgets have been significantly reduced thereby deterring successful TB programming.

The NTLP program under the Ministry of Health in Kenya was launched in 1980. Since then, the program focuses on guidance and supervision of leprosy and tuberculosis in the country. According NTLP's recent report, the country has a high burden of TB co-occurring with HIV of 35.6% (Center for Health Solutions Kenya, 2019). About 1% of the TB cases are from prisons. Also, 28% of the TB cases are from refugees. The prevalence of diabetes is presenting a new threat. Studies indicate that diabetes mellitus increases the risk of developing TB threefold (KELIN, 2018). Diabetes mellitus is associated with delayed innate immunity to TB. As a result, diabetic patients are more likely to develop pulmonary TB rather than extra-

pulmonary TB.

In a bid to curb the prevalence of tuberculosis, the World Health Organization recommended the adoption of directly observed therapy (DOTS) strategy for control of tuberculosis(World Health Organization. 2010). This involves administration of effective chemotherapy namely Ethambutol, Isoniazid, Rifampicin and Pyrazinamide, for the first two months (referred to as intensive phase), followed by a four-month course of daily Rifampicin and Isoniazid (referred to as continuation phase) to patients under supervision of health care worker or community health care worker. The regimen adopted in Kenya is 6 months for new cases and 8 months for re-treatment. In spite of this change, drug resistant TB has become a core issue in the country. According to a 2015 survey, the prevalence of MDR TB cases among new cases and previously treated cases is 0.7% and 2.1% respectively (Ministry of Health, 2016). In 2015, approximately 368 out of 433 DR TB cases were rifampicin resistant. Twice as many males exhibited TB compared to females. Moreover, 2.3% of the MDR TB cases were children below 15 years.

In 2019, Kenya launched a National Strategic plan for tuberculosis. TB is the fourth leading cause of death in the country (Ministry of Health, 2016). Although Kenya has made significant investments to fight the disease in the last two decades, the prevalence for TB has increased from 223 per 100,000 in 205 to 348 per 100,000 in 2016 on adult population. The highest burden of the disease is on 25-34 year olds with the disease occurring at a higher rate in males than in females. Kenya has a higher burden of the disease among the urban population (760 per 100000) compared to the rural population (453 per 100000) (Ministry of Health, 2016). The 2019-2023 National Strategic Plan for Tuberculosis identifies patient centered approach to TB diagnosis, prevention and treatment as the best approach to minimizing the burden of the disease. The country seeks to treat 597000 people with TB by 2030. This includes the treatment of 55,000 children, 542,000 adults, and 4500 people who have the multi-drug resistance TB (Center for Health Solutions Kenya, 2019). One of the strategies utilized in the country is the elimination of fees associated with diagnostic

testing including the chest radiography services for TB. However, there is still much more to be done as the condition is affected by various comorbidities.

1.2 Statement of the Problem

This study examines the issue of persistent sputum smear positivity after intensive phase chemotherapy among patients with tuberculosis. The switch to free anti-TB medication did not lead to positive cure rates and desirable treatment outcomes. There has been a rise in multi-drug resistance strains which are associated with high mortality and morbidity (O'Donnell *et al.*,2014). At the end of the treatment period, health workers are required to assess whether the disease is cured, whether the treatment is complete or whether the therapy was a failure. Monitoring the progress of medication involves clinical assessment, weight monitoring and sputum microscopy and culture. According to WHO recommendation, persistent sputum positivity after intensive phase for a period of one month calls for a continuation of intensive phase of treatment (WHO, 2010). Whereas there is sufficient information regarding the relationship between TB, HIV, and drug adherence, there is limited information regarding factors relating to persistent positive sputum smear after intensive phase of TB treatment. Most defaults happen in the first two months of treatment. This may be due to drug side effects, drug load or other factors that were subject of this study. The highest MDR-TB treatment success outcome was achieved in Ethiopia (Meressa *et al.*,2015). The success of this treatment had to do with intensive treatment of adverse side effects, nutritional supplementation, adherence interventions, and collaboration with various stakeholders.

1.3 Justification

Tuberculosis is a curable disease despite the fact that it is highly infectious and treatment period with multiple antibiotics is long (6-8 months). If untreated, each person with active TB can infect 10–15 other people through close contact over the course of a year. Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die(WHO, 2016). The goal of treatment must therefore be to achieve optimum desirable cure rate.

Kenya has been achieving TB cure rates of approximately 80% on average in the recent past(WHO,2016).This shows that approximately 20% of patients do not achieve desirable treatment outcomes. This is against a back drop of free TB treatment offered in all government and private health institutions. A key pillar in tuberculosis treatment monitoring is sputum smear microscopy and culture. To assess treatment progress, sputum smears are taken at 2, 5 and 6 months. This is in line with guidelines by International Union against tuberculosis and lung diseases (IUATLD) (Enarson *et al*., 2004). Multi drug resistant form of tuberculosis (MDT-TB) which is resistance to both Rifampicin and Isoniazid has been reported to be on the rise. MDR TB strains have emerged in all regions of the world (WHO. 2010). Cain *et al.,* 2015 reported TB drug resistance not only in Kenya but across the East Africa region (Cain *et al*., 2015). To guard against expensive to treat form of drug resistant TB, success with first line treatment must be optimized. An early reliable indicator of treatment outcome is sputum smear status.

This study was conducted in the months of June to September of year 2011 and sought to outline factors that are associated persistent sputum positivity after intensive phase of TB treatment among patients on medication in Rhodes Chest Clinic

The findings can help improve clinical outcomes and help care providers and policy makers in designing appropriate TB management and monitoring interventions. The findings will also help clinicians optimize sputum conversion and thus improving care outcomes during and after intensive phase of treatment of tuberculosis.

1.4 Research Questions

i. What are the socio-demographic characteristics of patients receiving medication for TB at Rhodes Chest Clinic, Nairobi are associated with sputum conversion?
ii. What adherence, attitude and practice aspects regarding TB management do patients receiving medication at Rhodes chest clinic have?
iii. What are the predictors of sputum positivity after intensive phase of TB medication at Rhodes Chest Clinic?

1.5 Objectives

1.5.1 General Objective

The purpose of this study is to determine the factors associated with persistent sputum positivity after intensive phase of treatment among patients on TB Medication at Rhodes Chest Clinic in Nairobi.

1.5.2 Specific Objectives

1. To establish attitude and practice factors associated with sputum conversion after intensive phase of treatment among patients receiving TB chemotherapy at Rhodes chest clinic
2. To evaluate adherence factors associated with sputum conversion after intensive phase of treatment among patients receiving TB chemotherapy at Rhodes chest clinic
3. To determine the predictors of sputum positivity after intensive phase of TB treatment at Rhodes Chest Clinic in Nairobi.

1.6 Scope

This is a clinic based study undertaken in Rhodes Clinic, Nairobi from June to September 2011. The population of interest was patients who had been started on TB treatment and had completed the intensive phase of treatment (two months).

CHAPTER TWO

LITERATURE REVIEW

Tuberculosis is a disease of global importance. This is due to its global prevalence, incidence and mortality among those who contract it. A recent Global TB report 2017 released by WHO indicated that there were 6.3 million new TB cases in year 2016 up from 6.1 in year 2015 this is equivalent to 61% of estimated global TB incidence of 10.4 million(World Health Organization 2016) . Globally , an estimated one-third, (1/3) of the world population is infected with *mycobacterium tuberculosis* the bacterium that causes TB(World Health Organization 2014). It is further reported that an estimate average of 10 million people get sick from the active form of the disease every year(World Health Organization 2014). There were over 2 million deaths from the disease according to reports from Centre for Disease Control (CDC)(CDC 2014). Tuberculosis in the same report is cited as the lead killer among HIV positive persons.

2.1 History of tuberculosis

Tuberculosis is a disease with a long history. Though the disease may date back to the 3000 BC, its description and devastation was witnessed in the 16^{th} to 19^{th}century when most of Europe and America population started living in urban dwellings whose poor living conditions and increase population density promoted the spread of the disease (Daniel, 2006). 1n 1650, tuberculosis is reported to have been the leading cause of death in Europe. The cause of the disease was largely unknown and thus referred by various names depending on signs and symptoms interpretation. Such names as ‘consumption’ derived from wasting or weight loss associated with disease, white plague, phthisis, scrofula any many other were in use until Robert Koch in 1882 discovered cultured and isolated *mycobacterium tuberculosis* as the disease causative agent. The disease was thus described as Koch’s disease. His work was further improved on by Ziehl and Neelson who developed staining methods for sputum.

In the early 19th century, Théophile Laennec set the ground work for understanding of the pathogenesis of the disease. Laennec described the pulmonary lesions

characteristic in patients who had died from TB (Van Zyl, L., Du Plessis & Viljoen, 2015). Laennec's work was advanced by a demonstration of the transmissibility of the TB bacteria by Jean-Antoine Villemin in 1865. In the 20th century, significant advances and discoveries were made in the treatment of tuberculosis. Albert Calmette and Camille Guerin in 1906 using attenuated bovine strains of the mycobacterium developed vaccine, to date referred to as Bacille Calmette Guerin (BCG). In 1944, Albert schatz, Elizabeth Bugie and Selman Waksman isolated *streptomyces griseus* (streptomycin) the first antibiotic against tuberculosis. In 1952, the development of Isoniazid and thereafter Rifampicin in 1970 helped improve treatment of TB.

2.2 Biology, Pathogenesis, Etiology, Transmission and Natural History of TB

Tuberculosis is caused by *mycobacterium tuberculosis*, a rod shaped bacterium with a protective waxy coat lipid cell wall. This Mycolic acid cell wall makes it resistant to mild antiseptics as well as contributing to its virulence. This bacterium thrives in human host whereas other varieties like *mycobacterium bovis* are found in cattle. This bacterium takes 15- 20 hours to multiply which is relatively longer than other bacteria. It is identified by its red color on acid fast-staining.

The pathogenesis of TB involves the interaction between the host and the pathogen. Infection occurs when one inhales droplet nuclei containing tubercle bacilli. The tubercle bacillus reaches the lungs where they are ingested by the alveolar macrophages. The bacteria use a variety of strategies to survive in the host's body. One strategy is the ingestion of the bacteria by the alveolar macrophages by means of phagocytosis (Welin, 2011). The bacteria are ingested by the tissue dendritic cells and the resident alveolar macrophages. The infected cells in turn release the pro-inflammatory cytokines. This release leads to the infection of more dendritic cells as well as neutrophils and monocytes from the blood stream. Once infected, the blood carrying the infected cells moves to the lymph nodes where they activate a specific T cell. The cytokines of the infected cells release IL-12 and IL-18. This induces NK cell activity and the NK cells release IFN-γ which activates the release of TNF-α from the macrophages. Through the process of cytokine and chemokine signaling, other immune cells are disrupted leading to the formation of TB infected granuloma.

Macrophages in the granuloma differentiate further to epitheloid cells that agglomerate to form one giant cell (Welin, 2011). Lymphocytes surround the cells along with fibroblasts and extracellular matrix proteins. The bacilli remain in the granuloma until it fails as a result of immunosuppression.

The host's ability to garner an effective immune response is a key influencing factor in the natural history and progress of the disease. The T-Lymphocytes are central to the control of TB (Welin, 2011). As a result, severe impairment of cell mediated immunity due to HIV infection can trigger active tuberculosis. Studies reveal that active TB in people infected with HIV is directly associated with CD4+ count and indirectly with other factors such as the duration of infection. A HIV infection influences the natural history and clinical presentation of the disease. For instance, a patient suffering from early HIV infection cannot be distinguished from patients with TB but are HIV negative. However, after the HIV infection progresses, there is a higher proportion of sputum smear negative extrapulmonary and pulmonary TB (Raviglione, 2016).

Transmission of the microorganism; The bacillus is transmitted from person to person through aerosolized droplets from an infected person through coughing, sneezing, Spitting, or talking (Nikolayevskyy *et al.,* 2016). Whereas the main mode of transmission is airborne, the microorganism can be transmitted through ingestion of unpasteurized dairy products. Infection is primarily the lungs but can also infect other organs. The bacteria multiply in the body weakening host immune system.

2.3 TB Scale of the Problem

TB is significantly linked to poverty. Poor people are less likely to receive adequate care and face many health system barriers, economic, social and cultural barriers that impede on efficacy of treatment. In a study by Oxlade and Murray, the researchers observed that poor people are at a greater risk of getting tuberculosis due to the various factors characteristic with this social condition. These factors include rural versus urban dwelling issues, health insurance, HIV status, and substance abuse (lifestyle issues). Kenya has chronic levels of poverty. Furthermore, approximately 75% of Kenya's population lives in rural areas. Although global statistics indicate

that TB burden is higher in urban areas, rural areas also present a unique challenge. In rural areas, there is the issue of poverty and limited access to health facilities (Stop TB.org, 2015). Also, the adherence to treatment might compete with other factors such as jobs. In China, 80% of the population is located rurally. As a result, the prevalence of pulmonary TB is eight times higher in rural areas than in the urban region. The same is true for Kenya as rural areas face the challenge of inadequate care and poor post-treatment follow-up.

There are barriers to diagnosis and treatment of tuberculosis. One of the barriers is shortage of health workers (Stop TB Org, 2015). Whereas 50% of the world's population lives in rural areas, less than 38% of health care workers are located in these settings. In the recent WHO health workforce requirements for the shift towards universal health coverage, Kenya was listed as one of the 57 countries facing a shortage in health workers (WHO, 2016a). This shortage contributes to poor TB care outcomes. Some studies have indicated that when faced with the responsibility of delivering supportive treatment in rural areas, some health workers forgo this responsibility due to high patient burden and other constraints. As a consequence, people infected with tuberculosis in rural areas who have complicated diagnosis or MDR-TB have a difficult time accessing health care facilities in their location (Stop TB.org, 2015).

The WHO recognizes that Kenya has made progress in the fight against tuberculosis. The country no longer depends on WHO data to determine prevalence of the disease. Furthermore, the move towards providing free TB treatment in public health facilities has contributed in terms of ease of accessibility of treatment. Some of the control strategies implemented in the country include implementation of TB/HIV collaboration activities, the adoption of a national strategy in collaboration with the global move to end TB, and public-private mix strategies (Ministry of Public Health and Sanitation, 2009). However, the country has a long way to go in minimizing the prevalence of the disease.

2.4 Tuberculosis Epidemiology

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* an acid-fast bacillus (bacteria) The bacillus its transmitted from person to person through aerosolized droplets from an infected person through coughing, sneezing, Spitting, or talking. Majority of persons infected with tubercle bacillus have their immune system able to contain the infection and thus bacillus remain dormant and does not lead to disease. The persons at a higher risk of tuberculosis infection include the old, under five years of age, malnourished and those with poor immune status like HIV infected, diabetics, substance abusers (alcohol, drugs), smokers, those on steroids or those on immunosuppressive treatment. Overcrowding like in slums, prisons, poorly lit and ventilated dwellings are some of the environments that promote the spread of tuberculosis.

2.5 HIV and Tuberculosis

The advent of HIV has had a significant impact to the prevalence of tuberculosis. Africa has largely been hit by this twin epidemic with a significant proportion of TB patient having HIV infections. People living with HIV and AIDS (PLWHA) are a major subgroup with increased incidence of tuberculosis. Current data shows that on average, 44% of tuberculosis patients in Kenya tested positive for HIV among 79% of notified cases(Ministry of Health and sanitation 2009). This also points at a significant number of people with tuberculosis yet are not HIV positive. Besides HIV infection, poor social economic status overcrowding, informal settlement, poor nutrition and limited access to health services are risk factors to tuberculosis infection and have been attributed to tuberculosis morbidity.

2.6 Classification of Tuberculosis

Most infections in human are largely asymptomatic and thus produce a latent form of TB. With lowered immunity, the infection progress to active disease in one out of ten persons with latent TB. It is worth noting that latent form of TB cannot be transmitted. The clinical form of Tb can be transmitted easily.

Tuberculosis is clinically classified as either pulmonary tuberculosis (PTB), one that

involves the lungs or extra-pulmonary tuberculosis (EPTB), tuberculosis outside the lungs. Pulmonary TB or PTB is the most common form accounting for about 80 % of all cases of TB. It is also of public health concern since smear positive cases can transmit the infection. Extra pulmonary tuberculosis can affect any body organ or tissue except the hair and teeth.

There have been incidences of drug resistant tuberculosis over the years. Multi-drug resistant tuberculosis (MDR) is resistance to both Rifampicin and Isoniazid two main drugs used in TB treatment. In Kenya 353 MDR-TB cases were reported at the end of year 2008(Ministry of Health and sanitation 2009). Extensively Drug Resistant (XDR) TB involves resistance to a wide range of drug use in treatment of resistant form of TB that is Rifampicin, Isoniazid, fluoroquinolone and either Kanamycin, Amikacin and Capreomycin.

2.7 TB Diagnosis

The diagnosis of tuberculosis can be through clinical assessment, clinical signs and symptoms, histopathological laboratory analysis or through radiological examination. Detailed physical examination can be used to elucidate TB disease. Clinical symptoms and signs include weight loss, loss of appetite, night sweats, fever and fatigue. For pulmonary TB the signs and symptoms include cough for more than three weeks, hemoptysis (coughing up blood) and chest pain. Confirmatory bacteriological diagnosis (that include microscopy, culture and polymerase chain reaction (PCR) is the gold standard while other tests such as tuberculin test, Interferon-Gamma Release Assays (IGRAs) and chest radiology can also be useful. To evaluate susceptibility to TB infection, recent contact with infected persons, infectious signs and symptoms, work place environments, infection with immune suppressing diseases among others factors contributing to disease can be gathered from a detailed medical history.

2.8 Tuberculosis prevention and control strategies

Prevention is based on various interventions. Immunization with BCG is part of expanded program of immunization (EPI) in Kenya for all children at birth. Other strategies include screening and prompt treatment for infected persons, Isoniazid

Preventive Therapy (IPT) for all HIV infected persons and other high-risk individuals, providing laboratory and diagnostic services, collecting and analyzing data, and providing training and education, ensuring that patients who have TB receive appropriate treatment until they are cured.

2.8.1 Administrative Control Measure

The first and most important level of control is the use of administrative controls to prevent droplet nuclei from being generated and thus reducing the exposure of health care worker and patients to *M. tuberculosis*. Important administrative measures include early diagnosis of potentially infectious TB patients, prompt separation or isolation of infectious TB patients, and the prompt initiation of appropriate anti-tuberculosis treatment. Other important measures include an assessment of the risk of transmission in the facility, the development of an infection control plan that details in writing the measures that should be taken in a given facility, and adequate training of health care workers to implement the plan.

2.8.2 Environmental Control Measures

The TB infection control program are based on a three-level hierarchy of control measures and include, Administrative measures, Environmental controls and Use of respiratory protective equipment. This is according to Centre for Disease Control, tuberculosis infection control guidelines (CDC Tuberculosis Control)(CDC 2014). Since the exposure to infectious droplet nuclei usually cannot be eliminated, various environmental control methods can be used in high-risk areas to reduce the concentration of droplet nuclei in the air. Such measures include maximizing natural ventilation and aeration. (CDC Tuberculosis Control)(CDC 2014).

2.8.3 Personal Respiratory Protection

The third recommended control measure is the protection of the health care worker from inhaling infectious droplets through the use of personal respiratory protective devices which are designed to fit over the mouth and nose and filter out infectious TB particles. The type of surgical masks (cloth, paper) commonly used by HCWs do not filter out infectious droplet nuclei, although they may be of some use if placed on patients to prevent the generation of TB droplet nuclei when coughing or talking.

2.9 Tuberculosis treatment

Tuberculosis is curable. Latent form of tuberculosis can be treated in a number of people at risk of developing active form of tuberculosis. This include those with HIV infection, those who have had prolonged contact with TB infected persons, residents and employees of high-risk congregations e.g. prisons and chest clinics and hospital, and laboratory employees. The most common form of treatment of latent tuberculosis is by use of daily dose Isoniazid for period of 9 months. This is in line with guidelines for treatment of latent form of Tuberculosis infection(CDC 2014).

Taking several antibiotics for at least 6 months can cure tuberculosis. Left untreated however, tuberculosis is a disease with high mortality rate and is also highly infectious. An infected person has a potential to transmit the infection to 10-15 persons in a year. All patients previously not an TB therapy should have two months intensive phase of treatment with Isoniazid, Rifampicin, Pyrazinamide and Ethambutol followed by a continuation phase of Ethambutol and Isoniazid for six (6) months or Isoniazid and Rifampicin for four (4) months. This is often abbreviated as 2RHZE/6EH or 2RHZE/4RH(CDC 2014). These drugs have common side effects that include hypersensitivity hepatitis, vasculitis, fever and abdominal pain associated with Rifampicin, hypersensitivity and lack of mental concentration associated with Isoniazid, two of the drugs that are key in tuberculosis management(CDC 2014), (Walker & Colledge, 2013).

2.10 Tuberculosis and sustainable development goals

The Millennium Development Goals that ended in 2015 were succeeded by Strategic Development Goals (SDGs). The SDG's that will run until 2030 prioritize the end of TB in the society. In Kenya, the strategy set in place to attain this goal includes the prioritization of patient centered approach to treatment in a bid to ensure quality treatment outcomes (Stop TB Partnership Kenya, 2018). Also, Kenya aims to prioritize the use of evidence-based methods such as Genexpert and other newly available TB medicines to successfully diagnose the disease. The country seeks to attain the universal access to rapid molecular tests as recommended by WHO as the first line of treatment for suspected cases of TB. Included in the treatment strategy

are new drugs and combination therapies recommended by WHO to treat drug resistant TB (Stop TB Partnership Kenya, 2018). The main targets are quality treatment for the purpose of preventing prevalence and death. The country seeks to treat at least 70% of incident smear-positive cases and that at least 85% of incident smear-positive cases.

2.11 Factors associated with tuberculosis treatment outcome

There are a host of factors that determine tuberculosis treatment outcome. Munro and colleagues identify knowledge, motivation, believes and attitude, interpretation of illness and wellness, healthcare service delivery as factors that influence tuberculosis treatment outcome(Munro *et al.*, 2007).To improve adherence to tuberculosis treatment, Thiam and colleagues pointed out that reinforced counseling through improved communication between healthcare personnel and patients, decentralization of treatment, choice of directly observed therapy supporter by the patient, and reinforcement of supervision activities were important interventions(Thiam *et al.*, 2007).

Tuberculosis is associated with significant weight loss among the patients. Traditional interventions in tuberculosis management included food. Food rations and supplements have been included in several tuberculosis treatment programs with varying results. Martins *et al.* found no significant relationship between food supplementation and tuberculosis treatment outcome(Martins, Morris, & Kelly, 2009). It is surprising to note that in this study there was a significant gain in weight and sputum bacillary clearance was fast among patients who received food rations. Despite these favorable secondary indicators, food incentives did not translate to beneficial effects of treatment completion. In another study conducted in Tanzania, Villamor *et al.* found that micronutrients supplementation improves tuberculosis treatment outcomes among patients on chemotherapy(Villamor *et al.*, 2008). Therefore, there is need to consider the effect of food and micronutrient supplement on treatment outcome at the intensive phase of tuberculosis treatment.

Treatment adherence to TB medication is associated with desirable treatment outcome. Health care worker in the various treatment programs often emphasis

treatment adherence. There are many factors that influence TB treatment completion that have been researched on in varying depth. Study in Mbagathi Hospital Kenya by Roguenauld and others identified, not having enough pills to last until the appointment date caused by delays due to work or family reasons, needing to seek money for transport and losing some pills as some of the main reason to non-adherence. The same study however observed high treatment adherence to tuberculosis treatment(Raguenaud *et al*., 2008a).

Disclosure of HIV status to sexual partners, friends or relatives is useful for prevention and care as reported by Banjunirwe and others on their research on relationship between disclosure of disease status and adherence (Bajunirwe *et al.*, 2009). However, there are no studies found in Kenya to show the effects of disclosure about TB on treatment outcomes. Treatment adherence has often been associated with treatment outcomes with a number of factors that include health service factors (organization of treatment and care) social context factor and personal factors contributing to treatment adherence. Default due to treatment non-completion especially during continuation phase was found to be related to physical access to the health centers in study in southern Ethiopia (Shargie & Lindtjorn, 2007).

Overcrowding has been singled as a risk factor to infection with tuberculosis. Home environments that are well lit and ventilated are suited for recovery and also for risk reduction of infection.

2.12 Conceptual framework

The diagram below (figure 2.1) is a conceptual framework presentation of TB treatment and the factors associated with TB treatment outcomes.

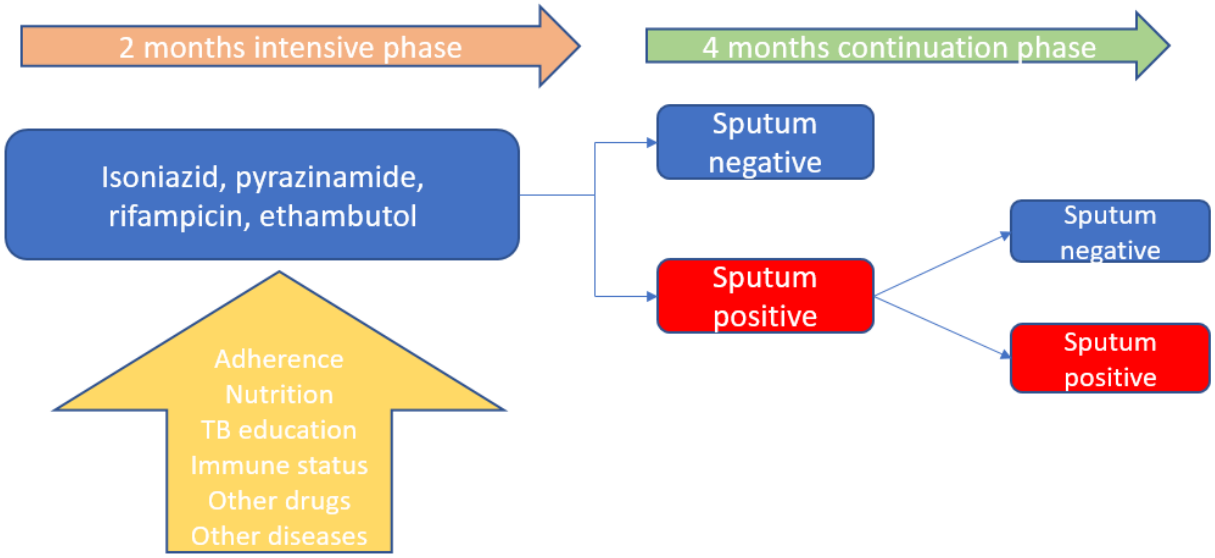

Figure 2.1: Diagrammatic Conceptual framework of TB treatment and factors associated with sputum conversion after intensive treatment

2.13 TB treatment monitoring

Patients on TB treatment should be monitored for clinical outcomes and bacteriological responses. Clinical outcomes include: weight, resolution of signs and symptoms of TB while bacteriological responses include: sputum tests at 2, 5 and 6 months for patients on Rifampicin and Isoniazid at continuation phase or 2, 5 and 8 months for patients on Ethambutol and Isoniazid at continuation phase.

2.14Factors associated with sputum smear and culture conversion.

Characteristics of patients who exhibit positive smear results after intensive phase of TB treatment are largely unknown. Horne *et al.*, 2009 points at sputum smear and culture test sensitivity and specificity as factors responsible of increased cases of sputum positivity(Horne, Spitters, and Narita, 2011). Guler and others in their work on TB sputum conversion identifies factors such as old age, numerous bacilli on initial sputum smear examination, presence of multiple cavitary diseases, male sex, smoking and thrombocytosis to be significantly associated with sputum smear conversion time(Guler *et al.*, 2007).TB medication compliance has been identified as a significant risk factor for persistent sputum positivity after intensive phase. Raguenaud in his work on TB compliance identified missing medication as

significantly related to non-compliance and hence unsuitable treatment outcome(Raguenaud et al. 2008b). Another study in India by Banu *et al* indicated that pulmonary cavitation is associated with persistent sputum positivity after intensive phase chemotherapy. Important factors associated with smear and culture non-conversion after 2 months include increasing age, chest radiographic features (cavitation and extent of disease), and higher sputum smear and culture grading at diagnosis (Banu *et al.*, 2007).

CHAPTER THREE
MATERIALS AND METHODS

3.1 Study Area

This study was conducted at Rhodes Chest Clinic that provides diagnostic, treatment and monitoring for tuberculosis. The health facility in is in Nairobi, the capital city of Kenya with an estimated population of 4 million residents. The Rhodes chest clinic is located in Starehe constituency, Nairobi Central ward, within Nairobi County (see figure 3.1).

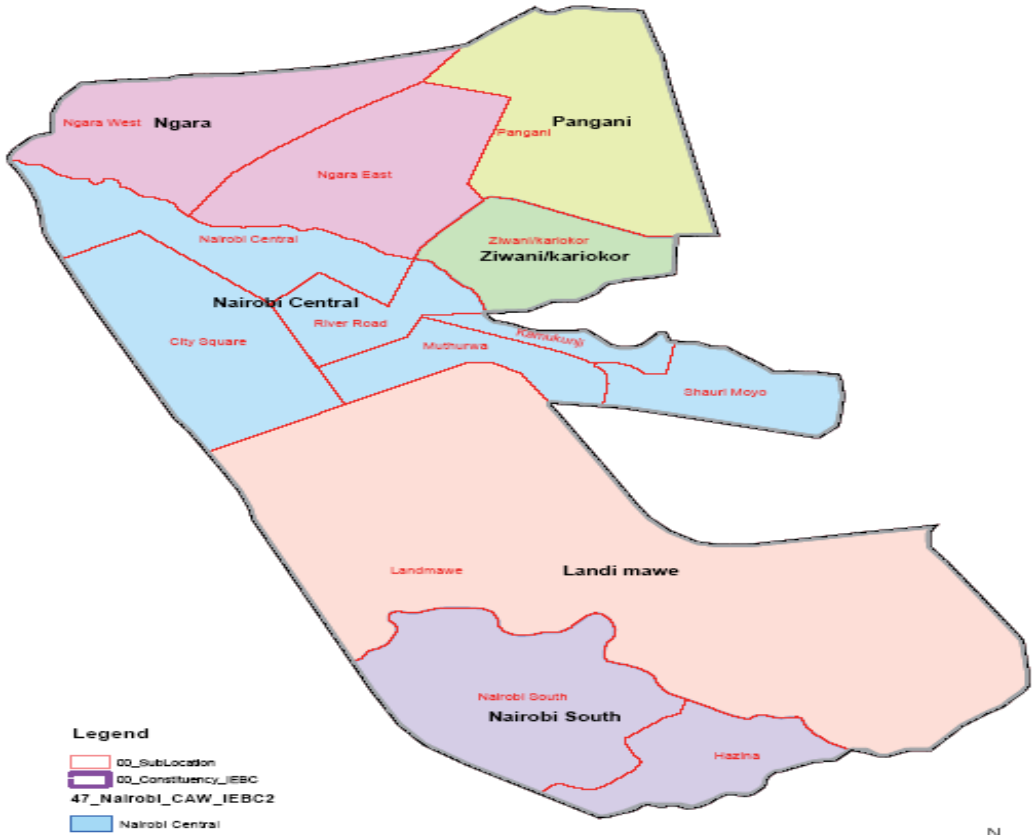

Figure 3.1: Map of Starehe constituency in Nairobi County where Rhodes Clinic is located

Starehe constituency is one of seventeen constituencies in Nairobi County. It consists of central to north areas of Nairobi. The entire constituency is located within Nairobi City county area. Starehe electoral wards are Nairobi Central, Ngara, Pangani, Landimawe and Nairobi South (South B). Rhodes chest clinic is located in Starehe constituency, in the central business district next to the Technical University of

Kenya formerly known as Kenya Polytechnic. The dispensary is run by Ministry of health with master facility listing code 13163.

Rhodes chest clinic;

This clinic is located in the in Nairobi adjacent to Central Business District in Starehe constituency. It is run by the city Council of Nairobi. Services offered include, Antenatal, Family Planning Growth Monitoring and Promotion Immunization, Prevention of Mother to Child transmission of HIV, Tuberculosis Labs and radiology services. It is an important facility for TB diagnosis, treatment and treatment monitoring. It also acts as a referral for several city council of Nairobi clinics for diagnosis, treatment and monitoring of tuberculosis. The TB workload for the period 2011 to 2015 derived from District Health Information System (DHIS2) is captured in table 3.1 below.

Table 3.1: TB case workload for Rhodes chest clinic from year 2011 – 2015

RHODES CHEST CLINIC OVERALL TB ANNUAL WORKLOAD					
Period / Data	TB cases detected	Smear positive TB	Smear negative TB	Re-treatment TB patients	Extra-Pulmonary TB patients
2011	383	208	87	43	41
2012	612	364	148	80	67
2013	94	58	19	17	19
2014	105	78	25	15	19
2015	47	20	11	6	10

3.2 Study Design

This was a case control study. Cases were patients with positive sputum results after intensive phase of treatment. Controls were patients with sputum smears negative results after intensive phase of treatment.

Figure 3.2 below is a diagrammatic presentation of the study design. The population of interest is the patient on medication for TB who had completed two months of treatment.

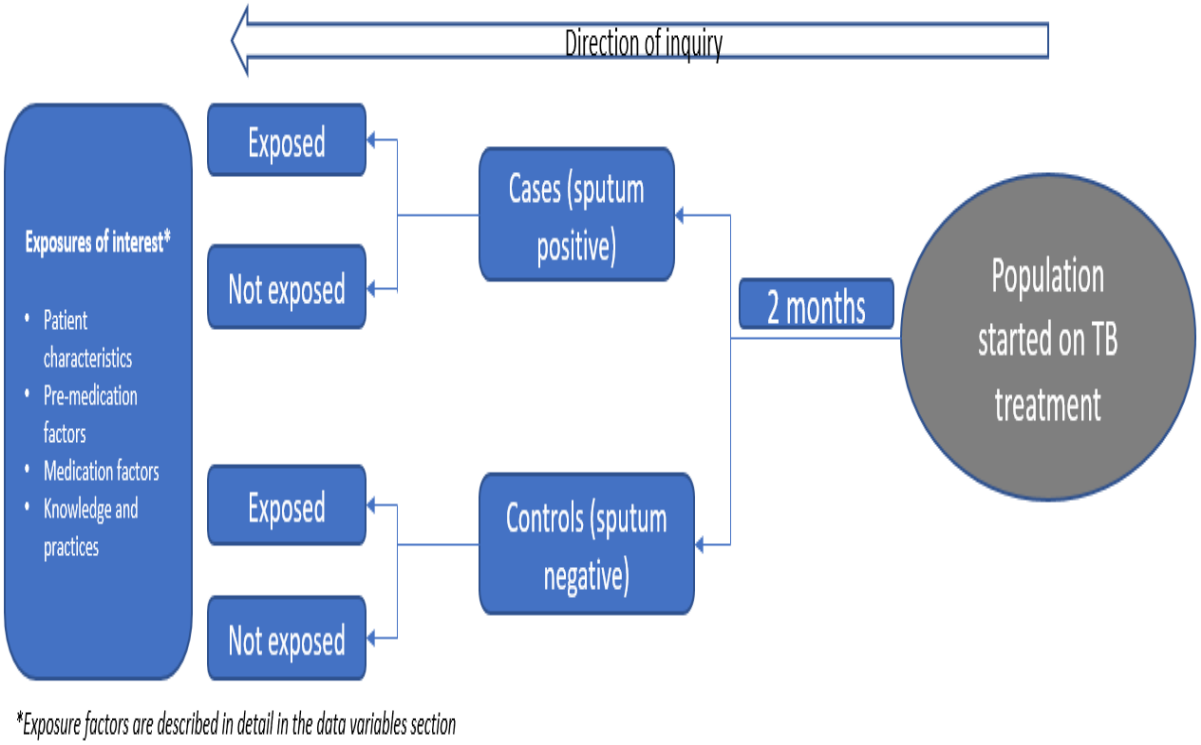

Figure 3.2: The case control design of the study

3.3 Study Population

The study population were TB treatment naïve patients (previously not on TB treatment) who had completed 2 months TB treatment intensive phase as per the national TB guidelines and enrolled in the Rhodes clinic for follow-up. Both males and females aged 18 years and over formed the population of the study. The study participants were sampled from patients on tuberculosis treatment willing and consenting to participate in the study.

3.4 Sample Size Determination.

TB medication compliance has been identified as a significant risk factor for persistent sputum positivity after intensive phase (Raguenaud *et al*., 2008b).I postulate that among the controls (sputum negative), 20% will be non-compliant. Assuming a power of 80% and alpha of 0.05 with ratio of 1:2 for cases and controls,

we had a sample size of 69.

$$n = (\frac{r+1}{r}) \frac{(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

n = required sample size

For 80% power, Z_{β}=.84

For 0.05 significance level, Z_{α}=1.96

r=2 (1 case for 2 controls)

P_2 =The proportion that are non-compliant to medication in the control group is 20%

P_1 = The proportion of cases that are compliant to medication – to get this, the formula below was used:

$$p_{case\exp} = \frac{OR p_{controls\exp}}{p_{controls\exp}(OR-1)+1} \qquad p_{case\exp} = \frac{4.0(.20)}{(.20)(4.0-1)+1} = \frac{.80}{1.60} = .35$$

Where:

$P_1 = P_{\text{case exposed}}$ = proportion of cases in the exposed

OR = Expected Odds ratio to be detected/estimated

$P_{\text{controls exposed}}$ = proportion of non-compliance in control group

Therefore, applying the formula

$$n = (\frac{r+1}{r}) \frac{(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

$$n = 1.5 \frac{(.35)(1-.35)(.84+1.96)^2}{(.35-.20)^2} = 23$$

N = a minimum of 69 study participants (23 cases and 46 controls)

3.5 Sampling procedure

For health facility entry, permission was first sought from the Rhodes Clinic management and Nairobi City County (now department of health, County Government of Nairobi). At the start of the study, a presentation outlining the study objectives, procedures and data collection approaches was done to the hospital staff as guided by the Scientific and Ethical Review committee of KEMRI. All cases were selected on the basis of their positive sputum microscopy status at enrollment,

provided they met the inclusion and exclusion criteria stated below. Identification of case and controls followed the following steps.

Step 1: Patients who had completed 2 months of intensive phase of treatment were identified.

Step 2: Cases, who were patients who had positive sputum result after the intensive phase were identified. Due to the low numbers of cases systematic sequential selection of cases was undertaken. This involved, enrolling patients with positive sputum results as they were identified over the study period. Upon identification as a case, data collection through interview was scheduled in their subsequent scheduled appointment.

Step 3: Controls were randomly selected from a pool of patients who had converted to sputum negative after intensive phase. To allow sufficient numbers of for randomization and reduce the risk of recall bias, patients who were sputum negative were pooled over a six-week periods when randomization was done and patients scheduled for interviews in the next scheduled appointment.

Both cases and controls were required to be able to communicate in English or Swahili as the data collection tools were available in either of these languages (see appendix II for Swahili translation of tools).

3.5.1 Criteria for selection of cases

The inclusion criteria for cases included all persons on TB medication after their intensive phase who must have tested sputum smear positive after intensive phase of TB treatment. They were required to be adults (18 years) and consented to taking part in the study and must have been on the recommended 1st line regimen TB management.

The exclusion Criteria included:

- Patients on re- treatment for tuberculosis
- Patient with multidrug resistant (MDR) or extensive drug resistant (XDR) forms of tuberculosis
- Unable or unwilling to give consent
- Patients not on TB therapy

3.5.2 Criteria for selection of controls

The inclusion and exclusion criteria for the controls is as described below:

Inclusion Criteria

- All persons on TB medication after their intensive phase
- Must have tested sputum smear negative after intensive phase of TB treatment
- Must be adults (18years) and consenting to taking part in the study.
- Must be in recommended 1st line regimen TB management

Exclusion criteria

- Sputum positive patients
- Patient with multidrug resistant (MDR) or extensive drug resistant (XDR) forms of tuberculosis
- Unable or unwilling to give consent
- Patients not on TB therapy

3.6 Data Collection

3.6.1 Tools

Interviewer-administered questionnaires, (Appendix II) were used to gather information on TB treatment progress. To ensure reliability of this tool, pretesting was done in a sampled group of cases and controls. The questionnaire was reviewed by an expert in DLTLD. Existing patients' records were used to gather information of patients at baseline (at onset of treatment) and sputum results at completion of intensive phase of treatment. Clinical outcomes were recorded on the same questionnaire. Three clinical field assistants, (a clinical officer and a nurse and a records clerk) were recruited and trained on data collection procedures and were the once who administered the questionnaires.

3.6.2 Procedure for data collection

No pre-scheduled interview appointments and patients presenting as part of routine follow-up visits to the health facilities were requested to participate in the study. Patients were requested to participate, if the inclusion and exclusion criteria were

met. Interviews were conducted within the Rhodes clinic, in a venue that guaranteed privacy and confidentiality. The study was then explained and if the patient agreed to participate they signed the consent form. Upon completion of the interview, complementary clinical outcome data were extracted from the patient medical records. Sputum microscopy results were extracted from records to verify sputum positivity at end of intensive phase in addition to the weight at onset of treatment, one month and two months. For the controls, verification of sputum negativity at end of intensive phase was done. Same procedure as for cases above was followed. Questionnaires were store in a lockable cabinet within the Rhodes Clinic. At the of every week, I reviewed the questionnaires for completeness, I then took the questionnaires for data entry if complete. When questionnaires were found to be incomplete, the research assistants were tasked to make follow-up in the subsequent visits to ensure data completeness. Data was entered in a password protected database while the questionnaires were archived in lockable cabinet where only I had access to.

Validity of the study

There was a deliberate effort to ensure construct validity at design level of the questionnaire and further external validity of the study finding. The study tools were piloted at the Mbagathi TB clinic and the results from the pilot phase informed further refinement of the data collection tools and training procedures. The selection and information bias that are common with case control design were avoided by random selection of controls and by strict adherence to inclusion and exclusion criteria. In addition, the research assistants were trained on the data collection tools and study procedures with Standard Operating Procedures (SOPs) that guided this process to limit interviewer bias. I reviewed 5% of the data collected against medical records to explore for deviations in the SOPs. To limit on the recall bias, aimed to interview both cases within a 7-8 week period after completion of the intensive phase. The objectives and hypothesis were not explained to the patients to limit the interviewee bias. Confounding was controlled at design level by randomization at selection of cases and controls. In the analysis, confounding was controlled by stratification and matching.

3.7 Data Variables

3.7.1 Independent variables

The independent variables considered in this study include: gender, Age, Income, Residence, Occupation, Alcohol abuse, adherence to medication, HIV status, nutrition, weight at start of treatment, and knowledge about TB, time to TB diagnosis and TB treatment

3.7.2 Dependent variables

The outcome of interest for this study was sputum status; positive or negative for AFBs at 2 months after completion of the intensive phase.

3.8 Data Management and Analysis

Data was entered and analysed using IBM SPSS Statistics for Windows Version 20.0 (IBM Corp). Each questionnaire had a unique identified to allow validation. Descriptive and inferential statistics were calculated for various social demographic characteristics, risk factors and treatment outcomes. For descriptive analysis proportions are reported for categorical variables while mean and standard deviation or median and interquartile range for continuous normally and non-normally distributed data respectively. To explore for any associations between the various socio-demographic and risk factors with sputum conversion, cross-tabulation was undertaken and associations explored using a chi test for categorical variables. For continuous variables, association between sputum positivity was explored using a student t-test for normally distributed data and Kruskal-Wallis for non-normally distributed data. Univariable logistic regression was used to examine the association between the primary outcome (persistent sputum positivity after intensive phase) and all pre-specified covariates. A multivariable predictive model for persistent sputum positivity after intensive phase was then developed. Age and gender were included as *a priori* independent risk factors for persistent sputum positivity with additional variables identified in univariate analysis as associated with persistent sputum positivity ($P<0.05$) added into the model starting with those with the strongest

association. Variables were retained in the model if a likelihood ratio test (LRT, p value of <0.05) supported improved model fit. For the univariable and multivariable analyses the odds ratios, accompanying 95% confidence intervals and Wald test p values (two-tailed) are reported.

3.9 Ethical Considerations

Participation in this study was voluntary. Consent was sought from all study participants with a signed consent form preceding all interviews, minors and those too sick to participate were excluded from the study. There were no benefits or incentives to the participants. Long term benefit to society is anticipated as results of this survey may be of medical importance. Confidentiality was guaranteed for all information obtained from study participants. Informed Consent Document *Appendix 1* that details all information required by the participant were signed by participants after familiarizing themselves with all ethical issues relating to this study. Approval for the study was sought and granted by KEMRI's Scientific and Ethical Review Committee (SERU) vide approval number **2043**. .

CHAPTER FOUR

RESULTS

A total of 71 patients participated in the study after meeting the inclusion criteria of whom 25 Patients (Cases) were sputum positive after intensive phase of treatment while 46 patients (controls) were sputum negative after intensive phase of treatment.

4.1 Social demographic characteristics

The results indicate that the sex distribution of the respondents were such that males were three quarters (77%) . In respect to marital status, patients who were married constituted 52% (37) of the respondents while 44% (31) and 4% (3) were single and separated respectively.

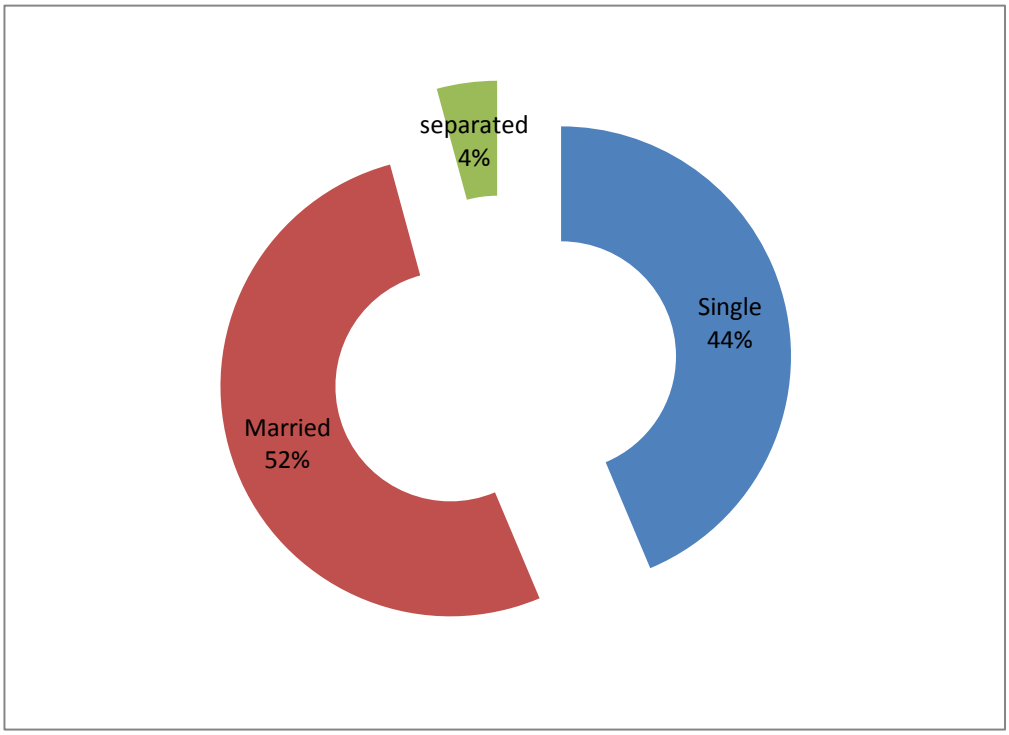

Figure 4.1: The marital status of the patients

Christians accounted for 97% of respondents while Muslims and other religions contributed 1% each while the remaining one percent had no response (figure 4.2).

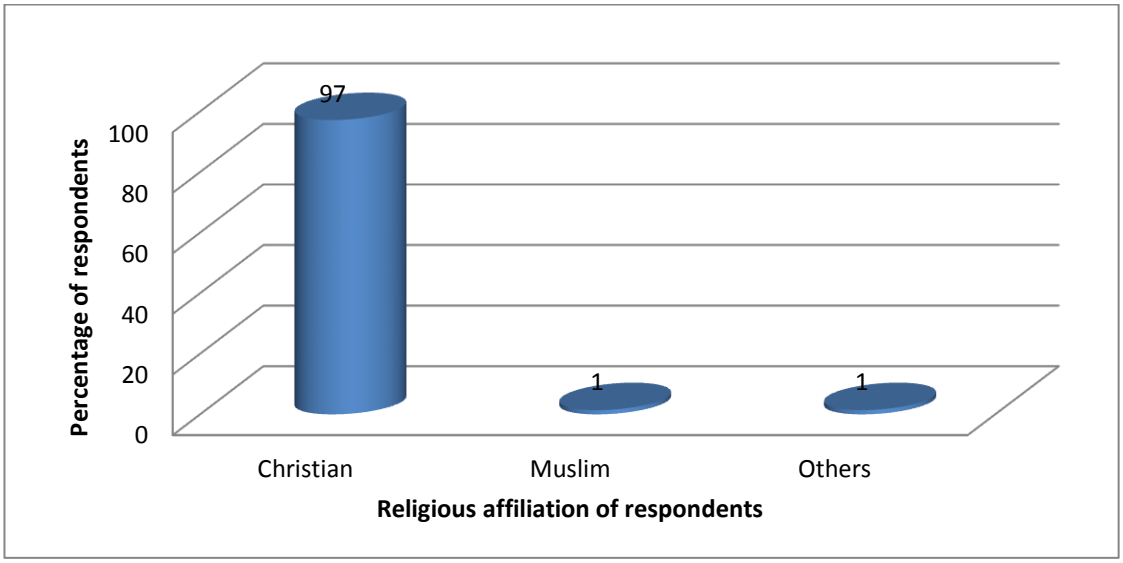

Figure 4.2: Religious affiliations of the respondents

Patients who were in informal employment constituted the majority 45% (32) with those in in-formal employment being 28% (20) and the rest were the unemployed 27% (19)

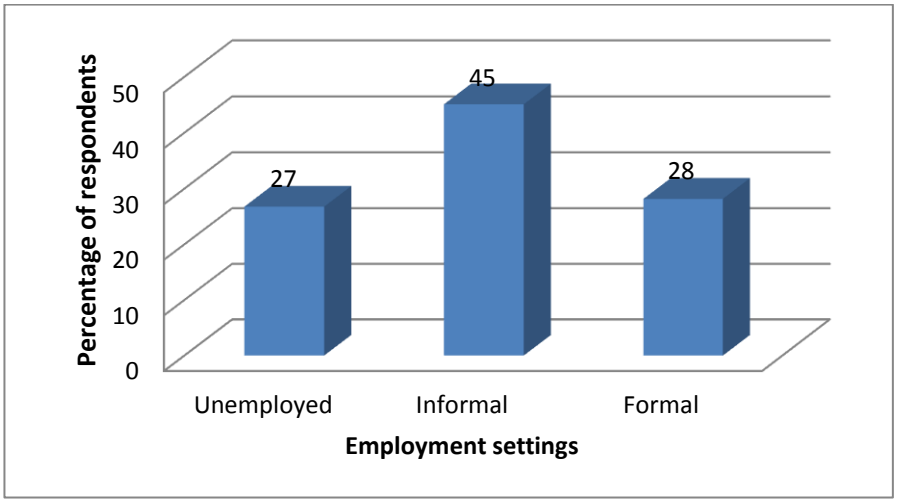

Figure 4.3: Occupation of the respondents

Majority of the patients 45% (32) had an income of Kenya shillings <10,000 while the least 7% (5) had an income of >40,000. Those with an average income of 20,000 – 30,000 and 10000 – 20000 were 10% (7) and 23% (16) respectively. However, 15% of the patients did not give their income (Figure 4.4).

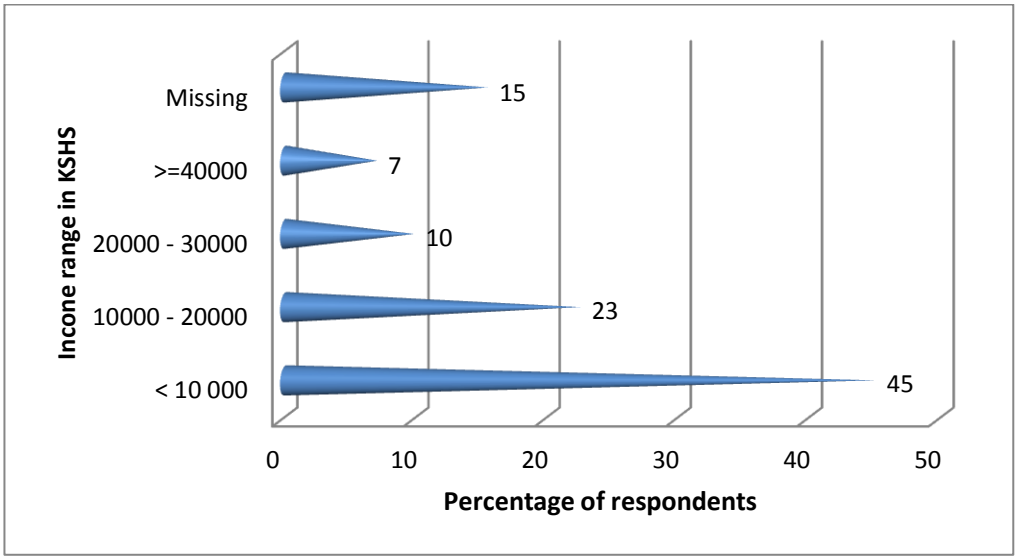

Figure 4.4: Income categories of the respondents

Across all the categorical socio-demographic factors, none of them was significantly associated with sputum results after the intensive phase (Table 4.3). The direction of effect was however noted and the need to undertake more research using a large sample size.

For all cases no significant socio-demographic factors were found to affect the outcome of the sputum conversion. (Table 4.1)

Table 4.1: Demographic characteristics of respondents with a sputum positive result

--		Sputum positive (n=25)
Gender		
	male	22 (88.0)
	female	3 (12.0)
Marital status		
	single	12 (48.0)
	married	11 (44.0)
	separated	2 (8.0)
Religion		
	Christian	24 (96.0)
	Muslim	0 (0.0)
	others	1 (4.0)
Education level		
	primary	10 (40.0)
	secondary	11 (44.0)
	tertiary	3 (12.0)
	university	1 (4.0)
Occupation		
	unemployed	7 (28.0)
	informal	13 (52.0)
	formal	5 (20.0)
Monthly income		
	< 10 000	14 (56.0)
	10000 - 20000	4 (16.0)
	20000 - 30000	1 (4.0)
	>=40000	1 (4.0)
	Missing	5 (20.0)
House live in		
	own house	1 (4.0)
	rental house	24 (96.0)
	Missing	0 (0.0)
Duration to treatment		
	Median (IQR) weeks	8 (3 -12)

For controls no socio-demographic characteristics of study participants was found to affect sputum conversion. (Table 4.2)

Table 4.2: Demographic characteristics of respondents who had a sputum negative result

		Sputum negative' (n=46)
Gender		
	Male	33 (71.7)
	Female	13 (28.3)
Marital status		
	Single	19 (41.3)
	Married	26 (56.5)
	Separated	1 (2.2)
Religion		
	Christian	45 (97.8)
	Muslim	1 (2.2)
	Others	0 (0.0)
Education level		
	Primary	15 (32.6)
	Secondary	18 (39.1)
	Tertiary	9 (19.6)
	University	4 (8.7)
Occupation		
	Unemployed	12 (26.1)
	Informal	19 (41.3)
	Formal	15 (32.6)
Monthly income		
	< 10 000	18 (39.1)
	10000 - 20000	12 (26.1)
	20000 - 30000	6 (13.0)
	>=40000	4 (8.7)
	Missing	6 (13.0)
House live in		
	Own house	0 (0.0)
	Rental house	45 (97.8)
	Missing	1 (2.2)
Duration to treatment		
	Median (IQR) weeks	4 (3 – 8)

Table 4.3: Chi square test for association between sputum results and the various variables

		Sputum positive (n=25)	Sputum negative (n=46)	Chi value	P value
Gender					
	male	22 (88.0)	33 (71.7)	2.45	0.117
	female	3 (12.0)	13 (28.3)		
Marital status					
	single	12 (48.0)	19 (41.3)	1.95	0.376
	married	11 (44.0)	26 (56.5)		
	separated	2 (8.0)	1 (2.2)		
Religion					
	christian	24 (96.0)	45 (97.8)	2.39	0.303
	muslim	0 (0.0)	1 (2.2)		
	others	1 (4.0)	0 (0.0)		
Education level					
	primary	10 (40.0)	15 (32.6)	1.4	0.705
	secondary	11 (44.0)	18 (39.1)		
	tertiary	3 (12.0)	9 (19.6)		
	university	1 (4.0)	4 (8.7)		
Occupation					
	unemployed	7 (28.0)	12 (26.1)	1.35	0.51
	informal	13 (52.0)	19 (41.3)		
	formal	5 (20.0)	15 (32.6)		
Monthly income					
	< 10 000	14 (56.0)	18 (39.1)	4.11	0.391
	10000 - 20000	4 (16.0)	12 (26.1)		
	20000 - 30000	1 (4.0)	6 (13.0)		
	>=40000	1 (4.0)	4 (8.7)		
	Missing	5 (20.0)	6 (13.0)		
House live in					
	own house	1 (4.0)	0 (0.0)	2.39	0.303
	rental house	24 (96.0)	45 (97.8)		
	Missing	0 (0.0)	1 (2.2)		
Duration to treatment*					
	Median (IQR)	8 (3 -12)	4 (3 – 8)		0.342

*Kruskall Wallis test

4.2 Adherence, attitude and practice regarding treatment

When patients were evaluated on the Morisky adherence scale, majority reported an adherence of 89% or more for all the indicators of adherence with the specific indicators on never failing to comply with treatment 89% (63), never forgetting to take medication 92% (65), and 93% (66) for never feeling worse and stopping medication (Figure 4.5).

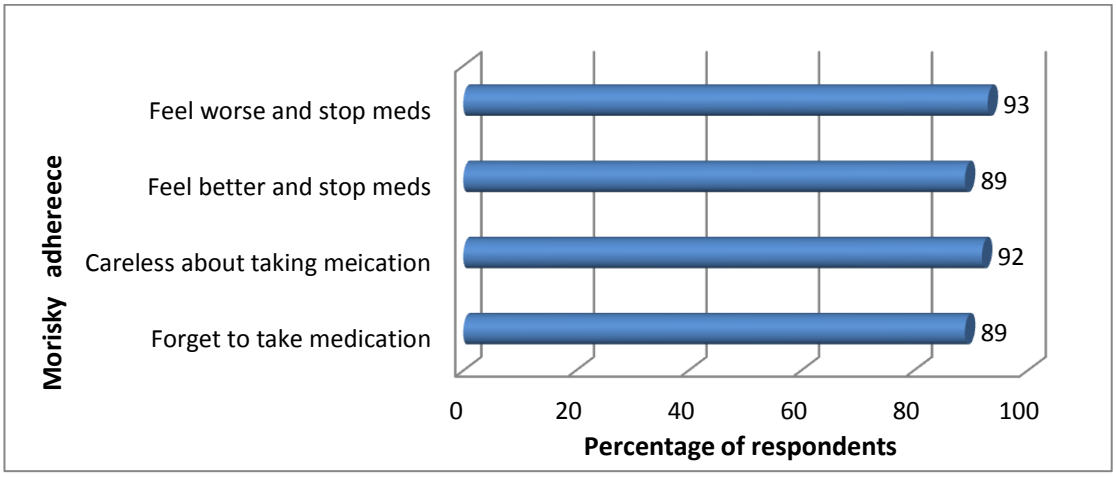

Figure 4.5: Reported Performance on Morisky adherence scale

Majority 89% of the respondents never forgot to take their medication with 3% (2) and 8% (6) forgetting to take their medication sometimes and rarely respectively (Figure 4.6).

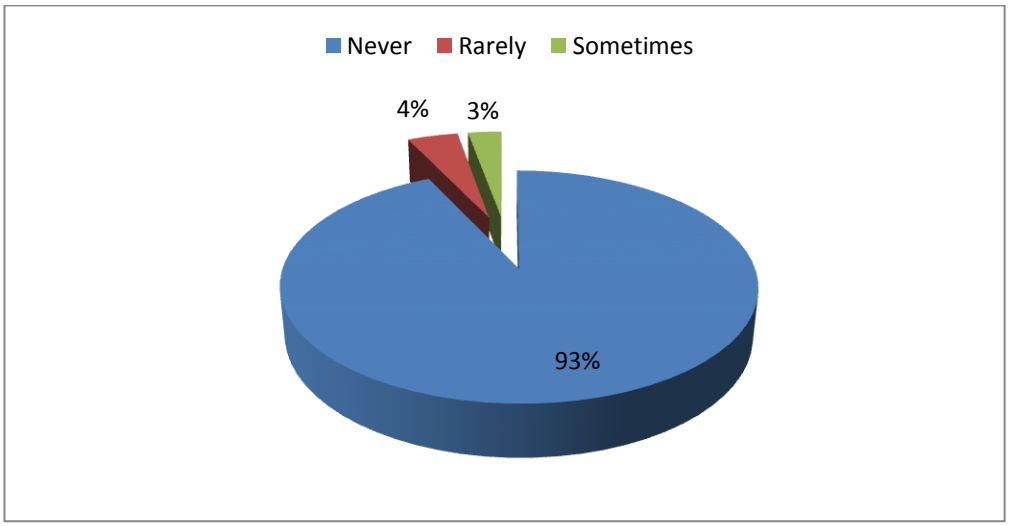

Figure 4.6: Frequency of missing medication

Very few patients were rated as being careless about taking their medication with majority 92% reporting never being careless.

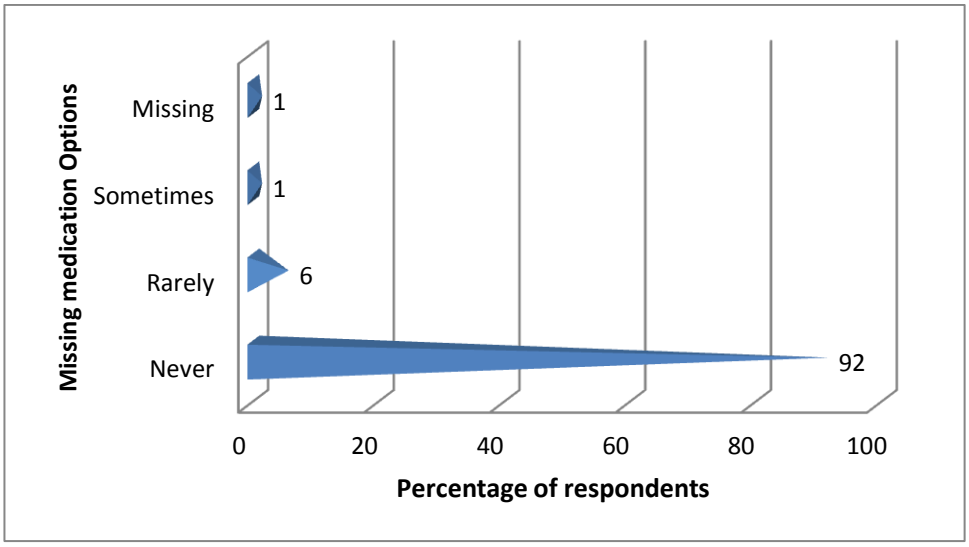

Figure 4.7: Careless about taking medication

Most 89% of the patients were adherent to treatment with less than 1% reporting either missing or sometimes stopping treatment if they felt better. In rare occasions 8% of patients who felt better missed to take medication.

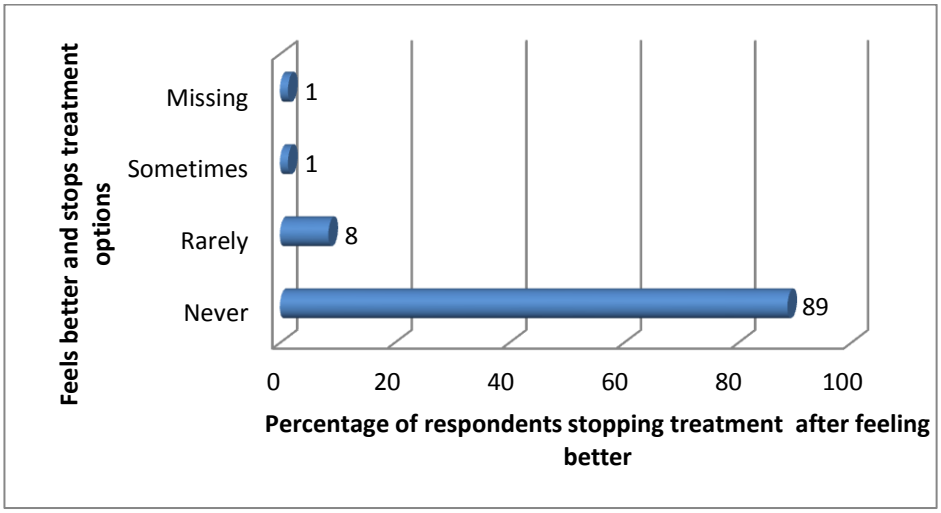

Figure 4.8: Feeling better and stopping treatment

Similarly, patients did not feel worse and stop treatment further reinforcing treatment adherence at 93% reporting never stopping treatment if they felt worse and less than 7% reported that they sometimes or in rare occasions stopped treatment if they felt worse

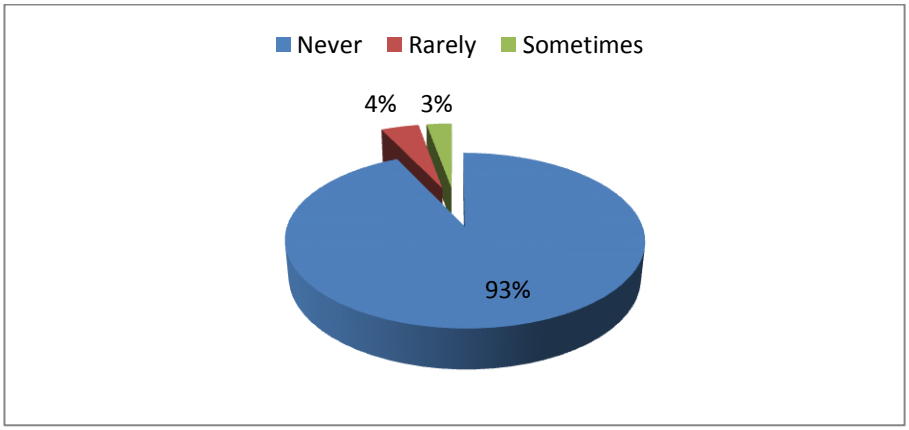

Figure 4.9: Feeling worse and stopping medication

Thirty-percent (21) of the patients had missed their medication at some point during treatment. Of those who missed treatment, 62% (13) only missed treatment for one day, 14% (3) missed treatment for two days while 14% (3) missed treatment erratically.

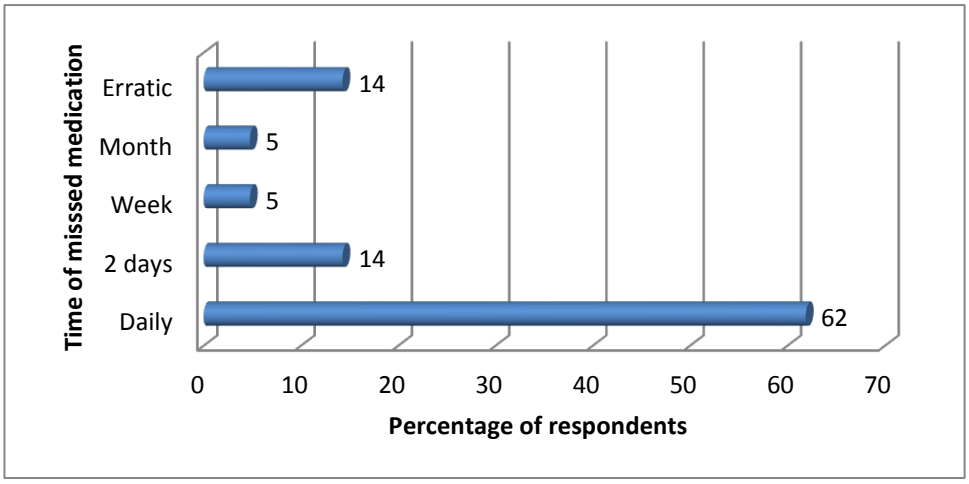

Figure 4.10: Time Length of missed medication among non-adherent respondent

When factors that worry patients about treatment were explored, having a relapse was the leading cause of worry 42% (30) while length of treatment, side effects and stigma and discrimination was worrying for 25% (18), 18% (13) and 10% (7) of the patients respectively. However, 4% (3) did not answer the question.

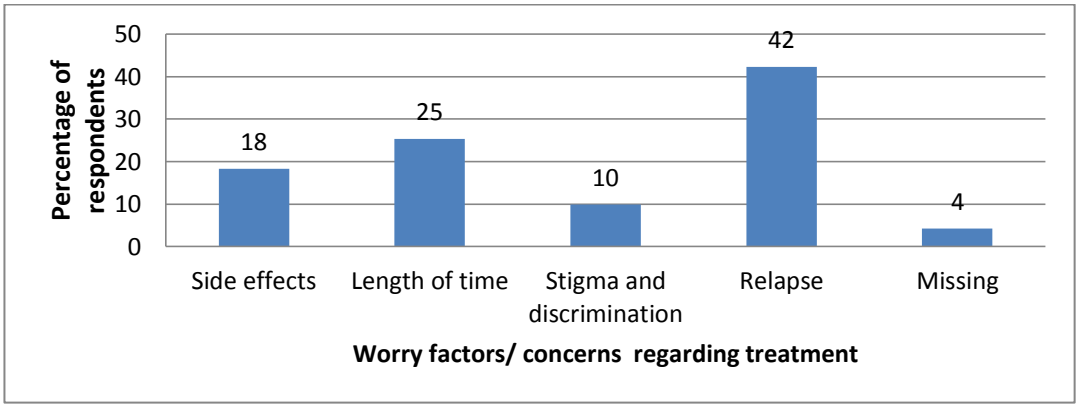

Figure 4.11: Patients concerns regarding treatment.

Government hospitals were the main diagnostic facilities 69% (49) while local authority health facilities provided a diagnosis for 24% 917) of the patients while private and mission hospital provided a diagnosis for 6% (4) and 1% (1) of the patients respectively.

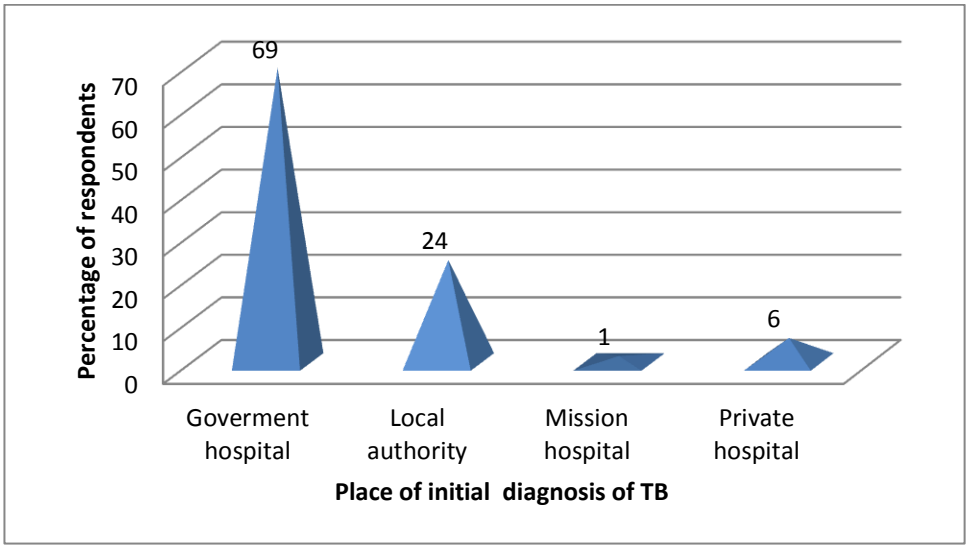

Figure 4.12: Diagnostic Institutions

Information regarding TB facts was given to at least 54% of the patients with information on spread and infection being given to 80% (57) and 85% (60) of the patients respectively while the least information given was on sputum disposal and was provided to 54% (38) of the patients.

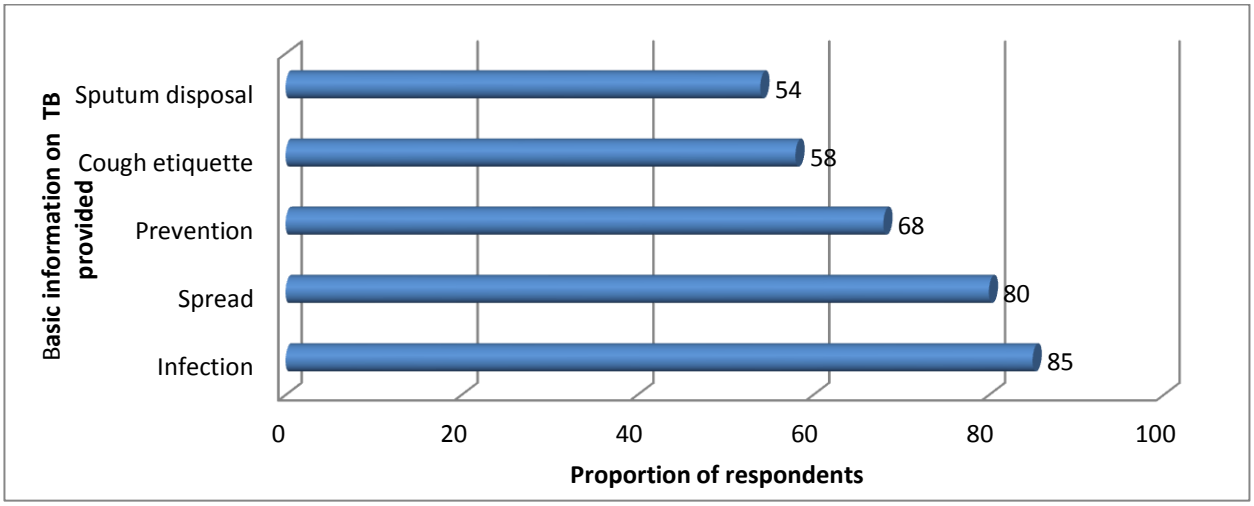

Figure 4.13: Patients information on TB basic facts given at the clinic

Information regarding duration of treatment was given to 94% (67) of the patients, 62% (44) received information on treatment outcome, 66% (47) on adherence, 62% (44) on nutrition, 55% (39) on side effects and 49% (35) on the need for a treatment supporter.

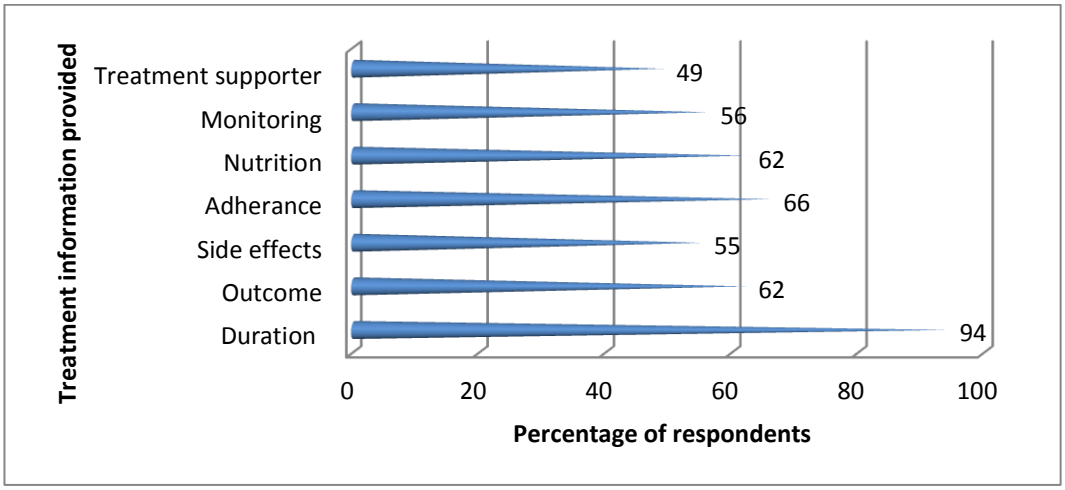

Figure 4.14: Information given to patients regarding treatment for TB

Services that were described as negative (stigmatizing and discriminatory) were reported by only 1%(1) of the patients while services that were deemed positive were reported by at least 60% of the patients with the greatest 83% (59) being reported as educative services while friendly and educative services and fast and timely services were reported by 62% (44) and 61% (43) of respondents respectively

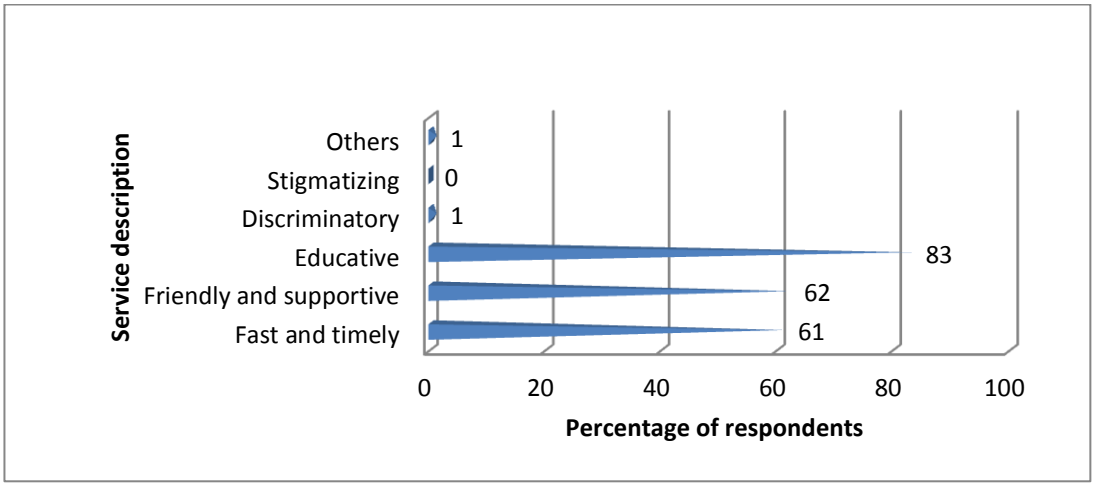

Figure 4.15: Patients description of nature of service at the clinic

For the categorical treatment-related factors, only ever missing medication was significantly associated with sputum results (P value 0.012). All other variables investigated such as nutrition, alcohol consumption and occupation were not statistically associated with sputum conversion at 2 months as indicated in the table.

Table 4.4: Adherence, attitude and practices for treatment related factors

	Sputum positive (n=25)	Sputum negative (n=46)	Chi value	P value
Ever missed medication				
yes	12 (48.0)	9 (19.6)	6.29	0.012
no	13 (52.0)	37 (80.4)		
Reason missed medication				
side effect	3 (30.0)	2 (33.3)	0.02	0.889
forgot	7 (70.0)	4 (66.7)		
Ever abardon treatment				
yes	3 (12.0)	3 (6.5)	0.63	0.428
no	22 (88.0)	43 (93.5)		
Required a treatment supporter				
yes	18 (72.0)	32 (69.6)	0.9	0.638
no	3 (12.0)	9 (19.6)		
dont know	4 (16.0)	5 (10.9)		
Hiv status when starting TB treatment				
yes	3 (12.0)	3 (6.5)	0.65	0.724
no	15 (60.0)	30 (65.2)		
dont know	7 (28.0)	13 (28.3)		
Disclose TB status to anybody				
yes	21 (84.0)	43 (93.5)	1.64	0.201
no	4 (16.0)	3 (6.5)		
Take alchohol while on medication				
yes	8 (32.0)	7 (15.2)	2.74	0.098
no	17 (68.0)	39 (84.8)		
Ever go without food during medication				
yes	4 (16.0)	7 (15.2)	0.01	0.931
no	21 (84.0)	39 (84.8)		
Screened TB - cough				
yes	13 (52.0)	31 (67.4)	1.63	0.202
no	12 (48.0)	15 (32.6)		
Screened for TB- weight loss				
yes	17 (68.0)	28 (60.9)	0.35	0.551
no	8 (32.0)	18 (39.1)		
Screened for TB - night sweat				
yes	14 (56.0)	26 (56.5)	0	0.966
no	11 (44.0)	20 (43.5)		

4.3 Associations between sputum positivity and the various risk factors

Patients who were sputum positive were likely to have taken longer before seeking treatment compared to those who were sputum negative in median weeks (IQR) 8 (3 -12) and 4 (3 – 8) weeks respectively although this difference was not statistically significant (Krusskal Wallis P value 0.342 for difference in medians). However, patients who took too long before seeking treatment were significantly (student t test p value =0.002) likely to miss their medication with those who ever missed medication having a median (IQR) 8 (6 -12) duration to seeking treatment while those who never missed medication had a duration of 4 (3 -8) weeks.

There was an increase in the odds of persistent sputum positivity by 1.02 (95% CI 0.97-1.08) times for every increase in one year of age although this effect was not significant. Women had a lower odds of 0.32 (95% CI 0.08 – 1.26) times of being sputum positive after intensive phase when compared to males although this association was not significant. With primary education as the reference group, there was a trend for a decrease in the odds of being sputum positive with increase in education level. Patients with secondary education had a decreased odd of 0.78 (95% CI 0.26-2.81) times of being sputum positive while those with tertiary education and university education had0.42 (95% CI 0.09 – 1.95) and 0.32 (95% CI 0.03 – 3.27) decreased odds of being sputum positive, however this association was not significant.

Patients in formal employment had a decreased risk of 0.57 (95% CI 0.14- 2.78) of being sputum positive while those in in-formal employment were 1.33 times likely to be sputum positive after the intensive phase when compared to those who were unemployed as the reference group. With patients with an income of <10 000 as the reference group, patients earning 10000 – 20000 had a 0.38 (95% CI 0.10 – 1.42) decreased risk while those with an income of 20000- 30000 and >40000 had a decreased risk of being sputum positive after intensive phase by 0.19 (95% CI 0.02 – 1.75) and 0.28 (95% CI 0.03 – 2.82) times respectively, however these associations were not significant. For every increase in one room in the house the risk of being sputum positive after intensive phase decreased by 0.80 (95% CI 0.4 – 1.53) times

although this association was not significant. Although not significant for every extra person in the house there was a 0.90 (95% CI 0.71 – 1.16) times decreased risk in being sputum positive after intensive phase (Table 4.4)

Table 4.5: Univariate logistic regression analysis for the association of socio-demographic factors between sputum results and covariates

		Odds ratio	Upper CI	lower CI	p value
Age					
	Age in years	1.02	0.97	1.08	0.345
Gender					
	male	Ref			
	female	0.32	0.08	1.26	0.103
Marital status					
	single	Ref			
	married	0.76	0.28	2.06	0.590
	separated	3.17	0.26	38.84	0.367
Education					
	primary	Ref			
	secondary	0.78	0.26	2.31	0.651
	tertiary	0.42	0.09	1.95	0.271
	university	0.32	0.03	3.27	0.335
Occupation					
	unemployed	Ref			
	informal	1.33	0.42	4.27	0.628
	formal	0.57	0.14	2.26	0.425
Income					
	< 10 000	Ref			
	10000 - 20000	0.38	0.10	1.42	0.151
	20000 - 30000	0.19	0.02	1.75	0.143
	>=40000	0.28	0.03	2.82	0.282
No of rooms					
	rooms	0.80	0.42	1.53	0.496
No of persons per house					
	persons	0.90	0.71	1.16	0.430

Table 4.5 shows the association between sputum conversion after two months intensive phase and treatment related factors. With those who reported never forgetting to take their medication as the reference group, those who rarely/sometimes missed their medication were1.04 (95% CI 0.23 – 4.72) times more likely to be sputum positive after the intensive phase however this association was not significant. Similarly, those who rarely/sometimes got careless about medication were 2.93 (95% CI 0.46 – 18.86) times more likely to be sputum positive after the intensive phase when compared to those who reported being careless about taking medication, however this association was not significant.

Patients who reported to rarely/sometimes feeling better and stopping treatment were 1.40 (95% CI 0.29 – 6.81) times more likely to be sputum positive after intensive phase compared to those who reported never stopping treatment although this association was not significant. Patients who reported to rarely/sometimes feeling worse and stopping treatment were 2.80 (95% CI 0.44 – 18.00) times likely to be sputum positive after intensive phase compared to those who reported never stopping treatment. Patients who never missed drugs had a significantly decreased risk by 0.29 (95% CI 0.10 – 0.84; p value 0.023) times of being sputum positive after intensive phase when compared to those who ever missed drugs.

With patients who missed drugs because of side effects as the reference group, patients whose reason for missing medication was because they forgot had non-significant increase in the odds of being sputum positive by 1.17 (95% CI 0.13 – 10.22) times. Patients who did not know about a treatment supported were 1.42 (95% CI 0.34 – 5.98) times likely to be sputum positive while those who felt they did not have/want a treatment supported had a decreased risk of 0.89 (95% CI 0.23 – 3.37) times of being sputum positive after the intensive phase, however both of these associations were not significant when compared to those with patients who reported having a treatment supporter as the reference group. With patients who were requested for a HIV test as part of TB care as the reference group, patients who were not requested to have a HIV test had a non-significant increase in the odds of being positive after the intensive phase

When patients who knew their HIV status were set as the reference group, patients who did not know their HIV status had a decreased odds of 0.33 (95% CI 0.07 – 5.33) times. Patients who never disclosed their TB status were 2.55 (95% CI 0.52 – 12.40) times likely to be sputum positive when compared to those who disclosed their status although this was not significant. Not taking alcohol with medication resulted in a decreased non-significant odd of 0.41 (95% CI 0.13 - 1.32) of being sputum positive after the intensive phase when compared to those who took alcohol with medication. With patients who ever went without food as the reference group, patients who did not go without food had 1.04 (95% CI 0.27 – 3.96) odds of being sputum positive after the intensive phase however this association was not significant.

Patients who were screened for cough were 2.21 (95% CI 0.82 – 5.99) times likely to remain sputum positive when compared to those who were not screened although this association was not significant. Similarly, there was no significance for an association between screening for night sweats or weight loss, however there was an increased odds of 1.17 (95% CI 0.44 – 3.10) of being sputum positive if a patient was not screened for night sweats and a 0.87 (95% CI 0.02 – 2.39) decreased of being sputum positive if a patient was not screened for weight loss when compared to those who were screened as the reference group.

Table 4.6: Univariate logistic regression analysis for the association of treatment related factors between sputum results and covariates

	Odds ratio	Upper CI	Lower CI	P value
Forget to take medication				
never	Ref			
rarely/sometimes	1.04	0.23	4.77	0.956
Careless about taking medication				
never	Ref			
rarely/sometimes	2.93	0.46	18.86	0.257
Felt better and stopped treatment				
never	Ref			
rarely/sometimes	1.40	0.29	6.81	0.679
Felt worse and stopped treatment				
never	Ref			
rarely/sometimes	2.80	0.44	18.00	0.277
Ever missed drugs				
yes	Ref			
no	0.29	0.10	0.84	0.023
Reason for missing drugs				
side effect	Ref			
forgot	1.17	0.13	10.22	0.889
Ever abandoned treatment				
yes	Ref			
no	0.55	0.10	2.94	0.482
Require a treatment supporter				
yes	Ref			
no	0.89	0.23	3.37	0.862
don’t know	1.42	0.34	5.98	0.631
Requested HIV test as TB care				
yes	Ref			
no	1.76	0.11	29.38	0.694
HIV status at starting TB treatment				
yes	Ref			
no	0.55	0.10	3.06	0.496
don’t know	0.33	0.02	5.33	0.437
Ever disclose TB status				
yes	Ref			
no	2.55	0.52	12.40	0.247
Take alcohol with medication				
yes	Ref			
no	0.41	0.13	1.32	0.136
Ever go without food				
yes	Ref			
no	1.04	0.27	3.96	0.954
Screened for cough				

yes	Ref			
no	2.21	0.82	5.99	0.117
Screened for weight loss				
yes	Ref			
no	0.87	0.32	2.39	0.79
Screened for night sweats				
yes	Ref			
no	1.17	0.44	3.10	0.748

4.4 Multivariable analysis

After successful iterations, a predictive model for sputum positivity after intensive phase was built. The factors identified as being predictive for sputum positivity were age (continuous variable), gender, income, taking alcohol when on medication and having been screened for cough. However, after adjusting for all other factors in the model, only gender was significantly associated with a positive sputum result after the intensive phase with females having a significantly decreased odds of 0.16 (95% CI 0.03 – 0.93; p value 0.042) times for a positive result when compared to males (Table 4.5).

Table 4.7: Model 1: Multivariable model for demographic factors that predict sputum positivity

		Odds ratio	Lower CI	Upper CI	P value
Age					
	Age in years	1.05	0.99	1.11	0.12
Gender					
	Male	1.00			
	Female	0.16	0.03	0.93	0.042
Income					
	< 10 000	1.00			
	10000 - 20000	0.24	0.05	1.14	0.073
	20000 - 30000	0.20	0.02	2.07	0.177
	>=40000	0.29	0.02	3.91	0.351
	Missing	2.28	0.45	11.56	0.319
Take alcohol on medication					
	Yes	1.00			
	No	0.62	0.16	2.45	0.496
Sreened for cough					
	Yes	1.00			
	No	1.84	0.55	6.18	0.324

CHAPTER FIVE

DISCUSSSIONS, CONCLUSIONS AND RECOMMENDATIONS

Sputum conversion at 2 months is a significant indicator of treatment success with sputum positivity after intensive phase of TB treatment having been identified as an early indicator or potential drug resistance. Adherence and TB treatment practices were found to affect treatment outcomes at two months of intensive chemotherapy. These results are discussed in detail.

5.1 Summary of key findings

The main findings from this study were that non-drug adherence was significantly associated with sputum positivity while patients who were sputum positive were likely to have taken longer before seeking treatment when compared to those who were sputum negative which is consistent with findings from other studies.

5.1.1 Attitude and practices affecting sputum conversion

Considerations of patient's socio-demographic and treatment-related factors have been found to be significant determinants of tuberculosis treatment outcome. In this study, there is a suggestive trend for a decrease in the risk of sputum positivity with increase in education level although this association was not significant. However, these results compare with those from Panambuco, Brazil by Maruza and colleagues which highlighted that complete or incomplete secondary or university education was associated with a lower risk of defaulting from TB treatment(Maruza et al. 2011). It is believed that a low level of education hinders perception of the seriousness of the disease and causes difficulties in understanding medical guidelines. Further, the more one is educated the higher the chance of conceptualizing the danger of non-adherence and the importance of treatment compliance.

Although TB medication is free, other indirect costs associated with TB infection like lost income, transport, food costs due to the extra nutritional requirements

among others may hinder treatment uptake and adherence. This could therefore explain the decreased risk of sputum positivity associated with medication adherence among individuals in formal employment and those having an income of greater than ksh 10 000 (ksh100 =1 USD)

The decrease in the risk of being sputum positive after intensive phase for every increase in one room in the house may allude to the assumption that with congestion, there are chances of re-infection with the mycobacterium if the patient is living in enclosed environment where they may have infected other people living with them.

5.1.2 Adherence factors affecting sputum conversion.

There were adherence, attitude and practice issues that seem to have a bearing on the outcome of sputum microscopy results after intensive phase of tuberculosis treatment. Not disclosing TB status had a two-fold increase in risk of sputum positivity while not being offered HIV services alongside TB treatment increased risk of sputum positivity. Which highlight the possibility of reinforcing messages that are given during counseling on importance of treatment and adherence which are common in both HIV and TB. This finding highlights the fears that people have regarding disclosure of the illnesses and hence the need for disclose to a suitable person who could provide the role of a treatment supporter actively or passively. It also shows that stigma and discrimination may be related to tuberculosis.

With regards to practices at the health facility, respondents provided positive feedback on the services at the health facility. Majority of patients rated the services they receive as educative and friendly. However, the services provided were sub-optimal with more than a third of the respondents reporting that they did not receive information on treatment outcome, adherence, nutrition, side effects and the need for a treatment supporter. Further, only about 50% of the respondents had the right knowledge on sputum disposal and cough etiquette which are two key factors that influence the spread of TB infection. This calls for intensified training of health workers on the importance of patient health education regarding adherence as it is found to have a profound effect on treatment outcome. A more positive finding was

that over 80% of the respondents reported receiving information on spread and infection. Ayisi *et al,* in a study in western Kenya explored potential reasons that patients might discontinue their treatment before completing it. Reasons included being unaware of the duration of TB treatment, stopping treatment once symptoms subsided, and lack of family support(Ayisi *et al.,* 2011). This therefore highlights the need for adherence counseling, patient education about tuberculosis and treatment support is important factors in TB treatment programs.

5.1.3 Risk factors to tuberculosis treatment sputum non-conversion

A great challenge to a tuberculosis control programme is ensuring that TB patients seek diagnosis in a timely manner and, once diagnosed, adhere to treatment. Central to this inquiry was the assessment of adherence to treatment medication using Morisky adherence scale(Morisky *et al*., 2008). Missing drugs was significantly associated with sputum positivity. Those who poorly complied with medication had an increased risk of sputum positivity i.e. rarely/sometimes careless about drugs, forgot or even stopped medication. These finding may be explained on the basis of low or suboptimal levels to suppress multiplication of the mycobacterium tuberculosis. Several studies have been undertaken on the relationship between adherence to medication and persistent sputum positivity(Calver *et al*., 2010; Chang, Leung, & Tam, 2004; Munro *et al*., 2007).

Time from onset of symptoms to diagnosis and initiation of tuberculosis chemotherapy has in this study been found to be significant to persistence in sputum positivity after intensive phase. The longer one takes to have a diagnosis and initiate treatment, the higher the chance of sputum positivity after completion of intensive phase. A Study in Gambia reported the median delay from onset of symptoms to commencement of treatment was 8 weeks (range 4–12) in the urban area which compares with the similar median of 8 weeks and IQR of 3 to12 week reported in this study(Lienhardt *et al.,* 2001). The study in Gambia however did not establish a relationship between duration of delay to treatment and cure rate, but longer delay did increase the risk of death(Lienhardt *et al,.* 2001). Banu and colleagues in India indicated that pulmonary cavitation is associated with persistent sputum positivity

after intensive phase chemotherapy(Banu Rekha *et al.,* 2007). Though this study did not seek to establish the extent of the disease by the time of initiation of medication, it is possible that delayed diagnosis and treatment initiation leads to adverse effect to the lung tissue.

These findings are consistent with those from another recent study in South Africa by Calver and others which showed that Diagnosis delay and inappropriate therapy facilitate disease transmission and drug-resistance(Calver *et al.,* 2010). This finding therefore calls for implementation of rapid diagnostics and enhanced active screening strategies, for all with coughs for other signs and symptoms of tuberculosis. All persons with unexplained weight loss, unexplained persistent cough for more than 2 weeks, and unexplained night sweats should be investigated for tuberculosis.

In this study, it was further established that patients who took long (median time of 8weeks) to seek diagnosis and treatment had higher likelihood of missing medication during treatment. It is possible that the delay in seeking treatment may be characterized by denial that may spill over to the treatment phase. This calls for adherence counseling and for close monitoring of this category of patients by health care providers.

In summary, this study sought to determine factors that are associated with sputum positivity after intensive phase of chemotherapy in people with tuberculosis. It was a retrospective study conducted in Rhodes chest clinic, a health unit in Nairobi County that specializes in treatment of chest infections. The participants were sampled from clinic attendants who had completed two months of intensive phase TB chemotherapy and meeting inclusion criteria. Descriptive statistics and inferential statistics for the association between sputum positivity after the intensive phase and the various patient, knowledge and practice factors are reported. Seventy-one participants were included in the study. Of these, 25 (36%) were sputum positive at the end of the two months intensive phase. Social demographic characteristics of study participants were not significantly associated with sputum conversion. This is despite the fact that overcrowding is often associated with TB spread and re-infection. Study participants exhibited significant knowledge about TB treatment,

duration of treatment, adherence to treatment, anticipated side effects , what to expect during treatment relating to signs and symptoms including diseases remission. A patient skipping doses which is a non-adherence factor was significantly associated with sputum positivity (P =0.012). Patients who were sputum positive at the end of the two-month period were more likely to have taken longer before seeking treatment compared to those who were sputum negative by median (IQR) 8 (3 -12) and 4 (3 – 8) weeks respectively. This is can be seen from a knowledge, attitude or practice issue. Similarly, patients who took longer to seek treatment were significantly more likely to miss their medicine. The significant predictive factors for sputum positivity after the intensive phase were age, gender, income, taking alcohol and having been screened for cough. Patients who had not disclosed their TB status had a two-fold possibility of remaining sputum positive at the end of intensive phase. Public health practitioners should advise on adherence to treatment and have patient seek prompt diagnosis and treatment for signs and symptoms of tuberculosis.

5.1.4 Limitations of the study

Finally, these findings need to be interpreted in light of the following limitations. Firstly, due to the limited nature in which additional testing is done, culture results were not taken into account as it is not done routinely. Therefore, there is a possibility that some of the bacilli detected in the sputum were dead, however the action on whether to institute additional period for intensive phase are based on sputum microscopy findings in developing world. Secondly, I did not attempt to have sputum samples re-read to validate the findings, however the laboratory in which these investigations were carried out is accredited. Other general limitations are the draw backs associated with a case control design such as recall bias. Lastly, the sample of 69 patients limited the scope of the analysis and caution is required in interpreting the results as evidence by the wide confidence intervals. Despite the above mentioned limitations the following strengths reinforce my arguments. There was a deliberate effort to ensure construct validity at design level of the questionnaire and further external validity of the study finding. The selection and information bias that are common with case control design were avoided by random selection of study participants and by strict adherence to inclusion and exclusion criteria.

5.2 Conclusions

An early reliable indicator of treatment outcome is sputum smear status. Whereas many factors were included and evaluated for their effect to TB treatment in this study, Adherence to TB medication and the practice related to seeking treatment early were identified as determinants of TB treatment outcomes and I thus conclude as follows.

- Important but not significant socio-demographics predictive factors for sputum positivity after the intensive phase were age, gender, income. dwellings, gender and level of education . I thus conclude that health social demographics have a potential to affect TB treatment outcomes .
- Adherence in this study had a bearing on the outcome of sputum microscopy results after intensive phase of tuberculosis treatment. A patient skipping doses which is a non-adherence factor was significantly associated with sputum positivity (P =0.012) The study participants had significant treatment and adherence knowledge regarding their treatment and what to expect if there is treatment adherence. There was significant knowledge on treatment duration and challenges associated with skipping medication. I therefore conclude that adherence has an effect on TB treatment outcomes and adherence counseling and training need to be sustained for effective TB programming.
- This study further established that time to diagnosis which is a knowledge and practice issue had an effect on treatment outcome. I therefore conclude that reducing the time taken to seek medication for TB will have a positive effect on treatment outcomes.
- Further, more research is required to explore how social demographics characteristics of study participants , other adherence issues besides skipping medication , knowledge and attitude overly affects TB treatment outcomes

5.3 Recommendations

Arising from the conclusions and discussions above I made the following recommendations:

I. There is need to provide enhanced counseling and treatment related education to patients with low literacy education promote adherence to TB treatment.

II. That there is need for enhanced or innovative approaches for improving and reinforcing treatment adherence knowledge, side effects and duration of treatment as these attributed to treatment success.

III. Patients continue receiving educative, fast and friendly services devoid of stigma and discrimination as these were identified as some of the strengths of the practice in the facility.

IV. More efforts to provide information, education and communication materials to the public to encourage prompt care seeking for individuals with potential for signs and symptoms of tuberculosis for screening.

V. Health care workers should be more vigilant in to identify and screen patients presenting with suspected signs and symptoms for tuberculosis patients to ensure early diagnosis.

VI. Further studies should be undertaken on much bigger population and more varied settings to determine the overall effect of non-adherence to treatment and time to diagnosis on TB treatment outcomes at the end of two months and six months treatment period.

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APPENDICES

Appendix I : Consent Form

Part A

Study title:

Determinants of persistent sputum smear positivity after intensive phase chemotherapy among patients with tuberculosis at Rhodes Chest Clinic, Nairobi, Kenya**.**

Introduction

Tuberculosis is a disease of concern to health workers and to the Public because its infectiousness. You are requested to participate in this study in order to improve care provided to the patients who contract tuberculosis. I seek to identify what promotes quick recovery as indicated by sputum conversion from positivity to negativity for AFBs among patients on intensive medication for tuberculosis. The information that you will provide is vital and will be confidential.

It's your choice to be in the study

This consent form gives you information about the study that am undertaking, the risks and benefits and the process. All this will be explained to you before you choose to be or not to be in the study. Once you understand and agree to take part in this study, you will be requested to sign or make your mark on this form. You will retain a copy of this form.

Take note of the following;

Your participation of this study is entirely voluntary

You may decide to withdraw from this study at any time without any Consequences

Purpose of the study

The purpose of this study is to assess factors associated with sputum smear conversion among patients on intensive phase tuberculosis medication in Mbagathi district hospital. This will be achieved by a questionnaire to participating persons, routine clinical health assessment and review of patient's records.

What to expect during the interview

I will guide you in filling a simple questionnaire regarding your medication, food habits and your social and family life. I will also do a clinical assessment to check on your current health status.

If you choose not to participate or to leave the study

You choose to or not to participate in this study. If you choose not to participate in this study or to leave the study during the interview process, you may do so freely without consequences against you.

Risks and / or discomforts

I do not anticipate any risks or discomfort to you during this study. Your assessment will be at the clinic and will be private as routinely done any time you seek medication. All information regarding your family and social history will be confidential.

Benefits participating in the study

By participating in this study, you help us understand the needs of patients on medication for tuberculosis and the strategies to be put in place to improve treatment outcomes. There are no costs to you in participating in this study neither are incentives for participation. The results of this study will however assist tuberculosis program officers and policy makers improve on care to tuberculosis infected patients.

Your records will be private

All information that you provide will be confidential. Information regarding your health assessment will also be confidential. You will be identified only by a code. No personal will not be personally identified in any publication about this study. Every effort will be made to keep all your information confidential, absolute confidentiality may however not be guaranteed. Your records may be reviewed by **study investigator** or **ethical committee at KEMRI**

No harm because of participating in this study

It is unlikely that any form of harm could happen to you as a result of being in this study. If you have questions regarding this study, contact David Wambugu Maingi, the **Principal investigator** on cell phone number 0722241490 Email wambugudav@gmail.com

If you have any questions of concerns regarding this study and would like to talk to someone else other than the researcher, you may contact the following;

The Director,

Institute of Tropical Medicine and Infectious Diseases (ITROMID)

Jomo Kenyatta University Of Agriculture and Technology

P.O. Box 6200-00200 Nairobi

Telephone number 067-52711

E-Mail; itromid@nairobi.mimcom.net

Or

The Director

ITROMID-KEMRI OFFICE

Kenya Medical Research Institute

P.O.Box 54840 00200

Telephone number 020-2722541/4

Or

Chairman

KEMRI National Ethical Review Committee

P. O. Box 54840 -00200 Nairobi Kenya.

Telephone +254 020 2722541, 2713349, 0722-205901, 0733-400003

E-Mail: info@kemri.org

Consent Form (Part B)

Read information sheet (Part A) or have the information read to you carefully before completing and signing this consent form. If there are any questions regarding this study, kindly feel free to ask the investigator prior to signing your consent form

DECLARATION OF THE VOLUNTEER

I , Mr., Miss, Mrs……. Hereby give consent to Mr. David Wambugu Maingi to include me in the proposed study entitled Factors associated with sputum smear positivity for AFBs after intensive phase chemotherapy among patients on tuberculosis medication in Mbagathi district hospital and city Council health centre. I have read the information sheet concerning

this study. I understand the aim of the study and what will be required of me if I decide to take part in the study. The risks and benefits have been explained to me. Any questions concerning the study have been adequately answered. I understand that at any time that I may wish to withdraw from this study I can do so without giving any reasons and without affecting my access to normal healthcare and management. I realize that that I will be interviewed once. I consent voluntarily to participate in this study.

Your name (Respondent)……
Signature……...

Name of person taking consent…….
Signature ……

Name of investigator …….
Signature ……

Date……

Appendix II: TB Research Questionnaire

Serial Number …… Date……

Part one

Social demographic characteristics

1. Age ……yrs

2. Gender Male □ Female □

3. Marital Status
    1. Single □
    2. Married □
    3. Divorced □
    4. Separated □
    5. Widowed □
4. Religion
    1. Christian □
    2. Muslim □
    3. Traditional African □
    4. Others □ (specify) ……
5. Education level
    1. None □
    2. Primary □
    3. Secondary □
    4. Tertiary/ mid-level college □
    5. University □
6. Occupation
    1. Unemployed □
    2. Informal employment □ (business/ artisan / farming)
    3. Formal employment □

7. Monthly income …….(thousand Kenya shillings)

8. Dwellings
    1. Own house □
    2. Rental house □

       Number of rooms……
9. Number of residents in house…….

Part Two

Adherence assessment

10. Morisky adherence scale

Subjects to be asked:

"Thinking of the medication PRESCRIBED to you by your doctor(s), please Answer the following questions."

Response options: never=0; rarely=1; sometimes=2; often=3; always=4

Do you ever forget to take your medications? ……

Are you careless at times about taking your medications? ……

When you feel better, do you sometimes stop taking medications? …….

Sometimes, if you feel worse when you take your medications, do you stop taking them? .....

Adapted from Morisky DE, Green LW, Levine DM, Concurrent and predictive validity of a self –reported measure of medication adherence. Med Care 1986; 24; 67-74

11. If you ever missed your medications

a) What time length dosages did you miss?

1. Daily dosage □
2. 2 day dosage □
3. Week dosage □
4. Month dosage □
5. Erratic dosage □

b) What were the reasons not to take medication?

1. Medicines side effect/ made me more sick □
2. Forgot to take medicine □
3. Felt better./ symptoms were gone □
4. Medicine were many □
5. Didn't like taste of medicine. □

12. Did you ever abandon your treatment all together?

- Yes □
- No □

a) If yes, for how long……(weeks)

What were the reasons?

1. Felt better / no symptoms □
2. Prayed for / belief was cured □
3. Taking herbal / other medicines for TB □
4. Medicines made me sicker/ unpleasant □
5. Just needed a break from medication □
6. Displaced from home health facility □
7. Others □ (specify) ……

b) If no, what was the reason?

1. Health worker instruction to complete □
2. Wanted to get cured □
3. Knew of dangers not completing treatment □
4. Was getting better / no symptoms □
5. Medical certificate needed □
6. Others □ (specify) ……

13. Besides the medicine for T.B what other drugs do you often take

    1) Drugs for HIV/AIDS □
    2) Drugs for cough (cough syrup) □
    3) Herbal remedies □
    4) Other □ (Specify) ……..

14. What worries you most when you think about your medication?

    1) Side effects □
    2) Length of the medication (time) □
    3) Stigma and discrimination □
    4) Relapse □

Part three

Health care facility.

15. Where were you diagnosed with tuberculosis?

    a) Government hospitality / health centre □
    b) Mission hospital □
    c) Local authority □
    d) Private clinic □

16. How long in months did you have signs and symptoms that culminated in you as having

    Tuberculosis diagnosis ……

17. What is the distance (in kilometer) from house to health facility you attend? ……

18. What information regarding your disease condition did you receive at the health facility

    Basic facts about TB

    - Mode of infection □
    - Mode of spread □
    - Prevention. □
    - Cough etiquette □
    - Sputum disposal □

Treatment

- Duration □
- Outcome □
- Side effects □
- Adherence □
- Nutrition □
- Monitoring and follow up □
- Importance of treatment supporter □

19. Did you require treatment supporter?

- Yes □
- No □
- Did not know about it. □

20. Were you ever requested to take a HIV test as part of your TB care?

- Yes □
- No □

21. What was your HIV status at the time you were initiated on TB Medication?

1. Positive □
2. Negative □
3. Don't know □
4. Decline to answer □

22. Description of service you received at the health facility

(Marked as appropriate)

1. Fast and timely □
2. Friendly and supportive □
3. Educative and informative □
4. Discriminatory □
5. Stigmatizing □
6. Others □ (specify) ……..

Part four

Social aspects

23. Did you ever disclose your disease (TB) status to anybody?

- Yes □
- No □

a) If yes who was the disclosure made?

1. Friend □
2. Relative □
3. Sibling □
4. Child □
5. Employer □
6. Community health care worker □
7. Others □ (specify)

b) If no why was disclosure not made?

1. Fear of losing confidentiality □
2. Avoid discrimination □
3. Fear of losing job □
4. Fear of stigmatization □
5. Fear of losing friends □
6. Just didn't want to □
7. Others □ (specify)

24. Did you take alcohol while on medication for tuberculosis?

- Yes □
- No □

a) If yes did alcohol interfere in anyway in your medication?

1. Forgot to take medication □
2. Forgot / missed clinic appointment dates □
3. Abandoned treatment □
4. Lost/ misplaced my medicine □
5. No interference with medication □

25. Did you ever receive education about alcohol at the clinic?

- Yes □
- No □

Part five

Nutrition

26. Did you ever go without food during your medication period?

- Yes □
- No □

a) If yes on average, how long in a week did you miss food ?

1. One day in a week □
2. Two days in a week □
3. Three days in a week □
4. Others □ (Specify)……

b) If yes why

1. Didn't have food at all □
2. Didn't have fuel to prepare □
3. I was too sick/ weak to prepare □
4. Medicines affected my eating □
5. Others □ (specify) …….

27. What nutritional services did you receive from your nutritionist/ nurse/doctor at the clinic?

1. Nutritional education about balance diet □
2. Weight □
3. nutritional supplements □
4. Food by prescription □
5. Others □ (specify) …….

28. From records

- Wt. …… Kilograms at treatment onset
- Wt……. Kilograms at one month
- Wt…….. Kilograms at 2 month
- Wt…….. Kilograms now

Part six.

Sign and symptoms

29. Screening for tuberculosis

	Yes	No
- Cough		
- Wt Loss		
- Night sweat		

30. Sputum screening at two (2) months (end of intensive phase)

Positive for AFBs □

Negative for ABFs □