MANAGEMENT OF MULTI DRUG-RESISTANT TUBERCULOSIS AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

I hereby declare that this research project is entirely my own work and has not been published or submitted for assessment at this or any other University

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This research project has been submitted for examination with my approval as the university supervisor.

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DEDICATION

This research proposal is dedicated to my family and friends for the support they accorded me during my studies.

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LIST OF ACRONYMS

ADR	–	Adverse Drug Reaction
AIDS	-	Acquired Immunosuppressant Disease Syndrome
CCC	–	Comprehensive Care Centre
CSDH	-	Commission for Social Determinants of Health.
DALY's	-	Disability Adjusted Life Years
DOTS	-	Directly Observed Therapy Strategy
DLTLD	-	Division of Leprosy Tuberculosis and Lung Disease
DST	_	Drug Susceptibility Testing
EPTB	-	Extra pulmonary TB
HAART	-	Highly Active Anti Retroviral Therapy
HIV	–	Human Immunodeficiency Virus
HRD	-	Human Resource Development
INH	–	Isoniazid
KNH	-	Kenyatta National Hospital
MDG	-	Millennium Development Goals
MDR-TB	-	Multi Drug -Resistant Tuberculosis
MOH	–	Ministry of Health
MTB	-	Mycobacterium Tuberculosis
MTRH	-	Moi Teaching and Referral Hospital
NHIF	-	National Hospital Insurance Fund
NTP	–	National Treatment Policy
PHS	-	Primary Health System
PPM	–	Public Private Mix
RMP	–	Rifampicin
SCC	-	Standard Short Course Chemotherapy
SDH	-	Social Determinants of Health
TB	–	Tuberculosis
TCRL	-	Tuberculosis Central Reference Laboratory
WHA	-	World Health Assembly
WHO	–	World Health Organization
XDR-TB	-	Extensively Drug resistant Tuberculosis

ABSTRACT

Literature has indicated existence of unprecedented spread of MDR/XDR TB associated with failure to complete TB treatment. Based on this, the study identified factors behind the outcomes of management of multi drug- resistant and extensively drug- resistant tuberculosis at Kenyatta National Hospital. The study made use of secondary data obtained from TB and MDR/XDR specialized clinic records at Kenyatta National Teaching and Referral Hospital which contains factors associated with management of multi drug- resistant and extensively drug- resistant tuberculosis. Specifically, the study sought to determine the demographic and socio-economic factors challenging the outcomes of management MDR/XDR TB patients at KNH, assess the common system deficiencies which affect the outcomes of management of MDR and XDR TB at KNH, and relate the treatment regimen and treatment duration on the treatment and outcomes of the management of MDR /XDR TB at KNH.

The Linear Probability Model (LPM) has been used for estimation of the outcome models. The dependent variable used was TB management outcomes (treatment completion and MDR/XDR status), while the factors that affect outcome include age, sex, education levels of patient, marital status, residence, employment status, drug regimen, treatment duration, system deficiencies, distance and TB-HIV/AIDS co-infection . The study revealed that being married and living far from the MDR treatment centre increased the chance of completing treatment, while co-morbidities and other factors like relocation of patients, death of patients due to treatment complications, absconding from treatment and succumbing of patients to greater illness severity after admission negatively affected treatment completion.

The study indicates a need for prior and immediate focus on rapid identification programmes of patients with MDR/XDR TB using the available technologies .It is also important to invest in developing new technologies to enhance diagnostics which match the developments in therapeutics or prevention. This is because the increased cases of patients succumbing upon being admitted to treat co-morbidities raises the likelihood of not completing treatment. There is a need to develop suitable tests for early diagnosis and ensuring availability of appropriate treatment for MDR/XDR-TB.

CHAPTER ONE

INTRODUCTION

1.1 Background Information

The world Health organization defines Tuberculosis as an infectious lung disease caused any of bacterias belonging to the *Mycobacterium Tuberculosis complex group, Mycobacterium Tuberculi is the most* common causative agent .Other mycobacteria include *Mycobacterium Bovis* which can be transmitted through contaminated milk and its products and *Mycobacterium Africanum* can also cause Tuberculosis. Mycobacteria other than TB (MOTT) may cause a disease similar to typical TB, but that is in rare situations. (DLTLD, 2013).

Davis and Ramakrishnan, (2009), theorize that the bacillus can be transmitted through droplets when an infected person coughs laughs or is involved in any activity that permits aerosolized droplets to pass from person to person. It is important to note all infected persons will have a positive smear after analysis of their sputum. TB infection can therefore also be described to include a situation in which an individual has the TB bacilli in their respiratory tract, but they do not have signs and symptoms of the disease. Incidences of infection in the community, duration of infectiousness, number of contacts over time, population density, poverty, overcrowding and family size are some of the factors contributing to infection with TB.(Rusell, Zumla, et al., 2011).

Once an individual is exposed, the risk of infection is usually high and it directly related to the extend and level of interaction or contact with the tuberculli. Other major risk factors for infection include: bacterial load of infected person, extent of contact with infected person, closeness in distance to infectious case, length of contact with contact environment, air clearance and strength of survival of the Mycobctria in the environment (DLTLD, 2013).

Full blown or active TB can be described as the patient having all the symptoms and there is increased multiplication of the bacteria in the body. If a patient does not receive treatment at this stage, the prognosis of the disease is usually poor and the only thing that may help the patient is the strength of his or her immune system.(Lonnroth et.al 2010). However, a significant proportion of cases of TB do not have any obvious risk factor for disease and unknown biological factors may play a role. Other than the risk factors mentioned earlier, other major risk

factors for infection with TB include; HIV infection, re-infection or relapse, and poor previous treatment .Minor risk factors worth noting include age (at both extremes of), sex (affects males more) ,nutritional status, presence of diabetes, alcohol- related liver damage and tobacco smoking. Other conditions such long term corticosteroid therapy and use of immune suppressing agents may predispose a person TB infection. (WHO/HTM/STB, 2010). TB infection has a poor prognosis if treatement is not started early enough and the outcomes include the following statistics:death within5 years in about 50-60% of the cases, there is spontaneous curing(not understood why) in 20-25% of the cases and 20-25% remain with a chronic infection that significantly impairs their respiratory tract .Initiation of treatment the correct and proper drugs and dosages will reduce mortality to less than 5%(WHO, 2013).

TB infection can be classified into pulmonary TB, which predominantly affects the lungs and the other type is the extra-pulmonary TB that affects tissues outside the lungs. The common sites for extra pulmonary infection are usually the bones, spinal code, the knee, lymph nodes, skin and eye. The only tissue outside the lungs that TB does not affect is the hair and teeth.

1.2. An Overview of MDR and XDR TB

1.2.1. Multi-Drug-Resistant Tuberculosis (MDR-TB)

The World Health Organization (WHO) defines MDR-TB as the form of TB caused by bacteria that is resistant to two of the most powerful first-line TB drugs Isoniazid (INH) and Rifampicin (RMP). WHO estimated in 2013 that of all the TB infections in the world, 5% constituted infection with MDR-TB. 3.5% constituted newly diagnosed cases and 20.5% constituted previously treated cases.The North America and Western Europe regions have are reported to have lower infection rates compared to other similar regions of the world. Russia, the former Soviet Union and parts of Asia are reported to having problems of unprecedented infections levels (WHO/HTM/STB, 2010).On the other hand, 50% of MDR-TB cases are estimated to occur in China and India account for 86% of cases. MDR-TB among new TB cases is most heavily concentrated in Eastern European countries like Russia (16%), Azerbaijan (22%), and other former Eastern Bloc countries, (Gandhi, et al., 2007; WHO, 2010).

There is an estimated 9.4 million cases of new infections every year, the 1.7 million deaths in 2009 are attributed Tuberculosis and these deaths occurred mainly among people in their most productive years, (Gandhi, et al., 2007; Russell, 2009). In the last 15-20 years MDR- TB and

XDR-TB) have become more prevalent and this infection s pose formidable challenges in diagnosis and treatment, Ginsberg and Spigelman, (2007).

Compared to first line treatment, MDR-TB must be treated with second line drugs which are less effective,more expensive and have more side effects (WHO/HTM/TB, 2010).Diagnosis of drug resistance is difficult, especially in low resource countries; diagnosis may take anywhere from 6 to 16 weeks and requires sophisticated lab equipment. It is important, however to note that with proper diagnosis and early treatment,but the challenge comes in the cost of drugs which are 50 to 200 times more costlier than those used for treating normal/ordinary TB, (Ginsberg and Spigelman, 2007). Also the duration of treatment is longer for MDR-TB (18-24 months) and generally there is a high mortality rate compared to ordinary TB.This is attributed due to difficulty in offering treatment to patients with drug resistant TB because highly trained TB clinicians are required and are rarely available,(Zumla, et al., 2011). Secondly treatment should be offered in settings where infection control measures are in place. Thirdly, the complex combination of drugs should be strictly adhered to in the two phases of treatment, that is 8-month intensive phase and an equally important 12- month second phase.Some of the drugs used include inj. kanamycin, tabs prothionamide, tabs levofloxacin, tabs cycloserineand tabs pyrazinamide for the intensive phase, and prothionamide, levofloxacin, cycloserine and pyrazinamide, for the second phase (Barker, et al., 2009).

1.2.2. Extensively Drug Resistant TB

The WHO defines XDR-TB is defined as MDR-TB that also does not respond to multiple second-line drugs and it estimates that 5% of MDR-TB cases lead to XDR-TB. This severe form of MDR-TB requires that it be treated with more expensive and more toxic third-line drugs and the course of treatment that is usually patient .According to Barker et al. (Barker, et al., 2009), most patients with XDR-TB die before such measures can be carried out mainly due to difficulty in diagnosing drug resistance in time.

In the initial years of experience with XDR-TB, there were very few cases and the first case and outbreak was reported in South Africa in 2005, (CDC, 2006). Because XDR-TB is still relatively new, the exact proportion of the population infected is unknown and there in no clear figure on its statistics. According to Legido-Quigley, et al., (2010), it is next to impossible to diagnose it especially in resource scarce settings where drug supply is inadequate and lack of lab testing

facilities. For instance, as of January 2010, 58 countries had reported not less than one case of XDR-TB to WHO. The HIV-positive status of TB is detrimental especially when that patient acquires MDR-TB because of severely impaired immunity. There is evidence that patients are more likely to acquire MDR-TB strains because of their reduced immunity due to HIV/TB co-infection and can be more devastating especially when the TB is drug-resistant, (Ginsberg and Spigelman, 2007;Gandhi, et al., 2007). Due to the complexity of diagnosis and treatment, patients with HIV/MDR-TB co-infection degenerate faster there is a high mortality rate. Legido-Quigley argues that in HIV/AIDs high prevalence areas, it is important to put all measures in place to prevent drug resistant TB. He further suggest that the use of DST and the medical / drug history of the patient as one of the effective methods of preventing infection.

1.2.3. Historical Background of MDR and XDR-TB

In the year 2006, scientists from CDC came up with the term 'extensively drug-resistant tuberculosis' and they based its management on the guidelines by WHO regarding the management of drug resistant TB. Using the guidelines of WHO, these scientists defined MDR-TB as an infection caused by *Mycobacterium Tuberculosis* and it is resistant to Rifampicin and Isoniazid, the two main first line anti-microbials (WHO, 2006). The additional resistance of MDR-TB to a fluroquinolone and a second line injectable antibiotic, results in extensively drug-resistant (XDR) (CDC; WHO, 2006). The diagnosis of MDR and XDR-TB is determined through bacterium isolation as well as anti-microbial drug susceptibility test, and not merely assuming diagnosis upon treatment failure of phase I TB treatment. Therefore, the probability and sensitivity of XDR-TB case-detection in a community are dependent on the coverage and quality of microbiological support services for the management of TB.

Other additional reports from the WHO indicate that the first case of XDR-TB was detected sometime between 1999 and 2003 in Chennai, India. This case was formally reported by India's Revised National TB Control Programme (RNTCP) to WHO. Since then, WHO has recognized 58 countries, including India, in which XDR-TB has been detected (WHO, 2010). Currently surveys are under way in Ahmedabad (Gujarat State) and Chennai to measure the frequency of XDR organisms among MDR TB cases (Ramachandran, et al. 2009).

Since 2006 there have been many papers published in peer reviewed journals from both public and private sector institutions with their data on XDR-TB. These data have been generated from their mycobacteriology laboratories that have been performing 1st and 2nd line mycobacterial DST for many years. Though accreditation is available for 1st line mycobacterial DST, there is none currently available for 2nd line mycobacterial DST. Therefore, the reported XDR-TBisolates in India have not been validated.

When positive XDR-TB diagnosis is confirmed, the individual as well as the community will certainly bear the consequences of this deadly infection. This is mainly because of the limited choice in terms of treatment, the high cost of treatment and limited options in clinical and supportive management of this infection (Mitnick, et al., 2008). Treatment outcome is mostly disappointing and case-fatality rate (CFR) is very high - in one report the CFR was 51 per cent within a month of diagnosis (Gandhi, et al., 2010). When XDR-TB is transmitted to a new host, it accelerates the rate of infection of latent TB after a short period of time and it progresses fast to MDR then to XDR-TB. Therefore, there is an urgent need to prevent secondary transmission at all costs. In some instances it may involve restriction of movement which has resulted in conflict with fundamental human right of movement, but the benefits of restricting movement of infected persons outweigh the benefits of freedom of movement.

1.2.4. Prevalence of XDR-TB/MDR TB

The WHO confirms that the European Regions has some of the highest proportions of drug resistance in the world. The prevalence of XDR and MDR TB in the year 2010 was estimated at 650, 000 cases in the world. For notified proportions, MDR was frequently noted in Baltic states in 2009 (combined MDR TB: 17.4%–28.0%) and Romania (combined MDR TB: 11.2%)(ECDC, 2011). Other countries reported lower levels of MDR TB (0%–8%), where it was generally attributed to foreign origin. In 2008, it was estimated that 440 000 (390 000–510 000) incident cases of MDR TB occurred worldwide, of which 81 000 (73 000–90 000) occurred in the WHO European Region (WHO, 2010).There were 18 365 MDR TB cases reported in the WHO European Region, which accounted for only 23% of the estimated number (ECDC, 2010),WHO 2010

Data obtained from treatment outcomes in the European Union states ,in a 2007 cohort indicated that after 24 months of treatment, 3.2 % had successful outcomes .Treatment default

was seen in 12.7% and treatment failure was seen in 11% among the reported treated patients with MDR TB (ECDC, 2011). The drugs used for second line treatment have more severe side effects and are more costly than the first line. It is therefore important to initiate treatment early enough and put measueres in place to ensure treatment completion and adherence in order to curb the menace of spread of MDT-TB and to increase survival rates.

In Europe, a history of previous treatment presented a strong risk factor for the development of MDR-TB. This backed up by the fact that comparison of infection rates in Eastern and Western Europe suggests Eastern Europe has more transmission rates. (Faustini, Hall and Perucci, 2006). MDR- TB was also associated, although to a lesser degree, to previous treatment and also with being foreign-born. Lack of strict adherence to treatment is another contributing factor and this requires that patients receive adequate and proper counseling on drug and treatment adherence to improve their chances of a cure and ultimately survival.

In the year 2001, the WHO regional office in Europe launched an action plan dubbed "action plan 2011-2015". The main objective of this action plan was to try and check the spread of MDR-TBB in the European region. This plan set goals that by the end of the year 2015, there should be a decrease in the proportions of previously treated MDR patients by at least 20%. Another goal that the plan hoped to achieve was in diagnosis. It hoped to have diagnosed 85% of suspected MDR-TB cases and to treat at least 75% of these cases by the end of 2015.

The trend in Europe that depicted a pattern of upward trend, warranted the need for rapid susceptibility drug testing and proper monitoring of patients using both clinical and laboratory methods such as sputum smear microscopy and bacterial cultures to detect treatment failures early enough.(WHO, 2011). All the proposed actions needed strong political commitment so that the implementation phase of the plan would be successful. Other requirements for the success of the plan was the availability of quality second line drugs as well proper monitoring and evaluation of treatment outcomes that will be used to make informed and better decisions when it comes to treatment of MDR-TB patients (WHO, 2008).

1.3. Treatment of TB, MDR and XDR TB in Kenya

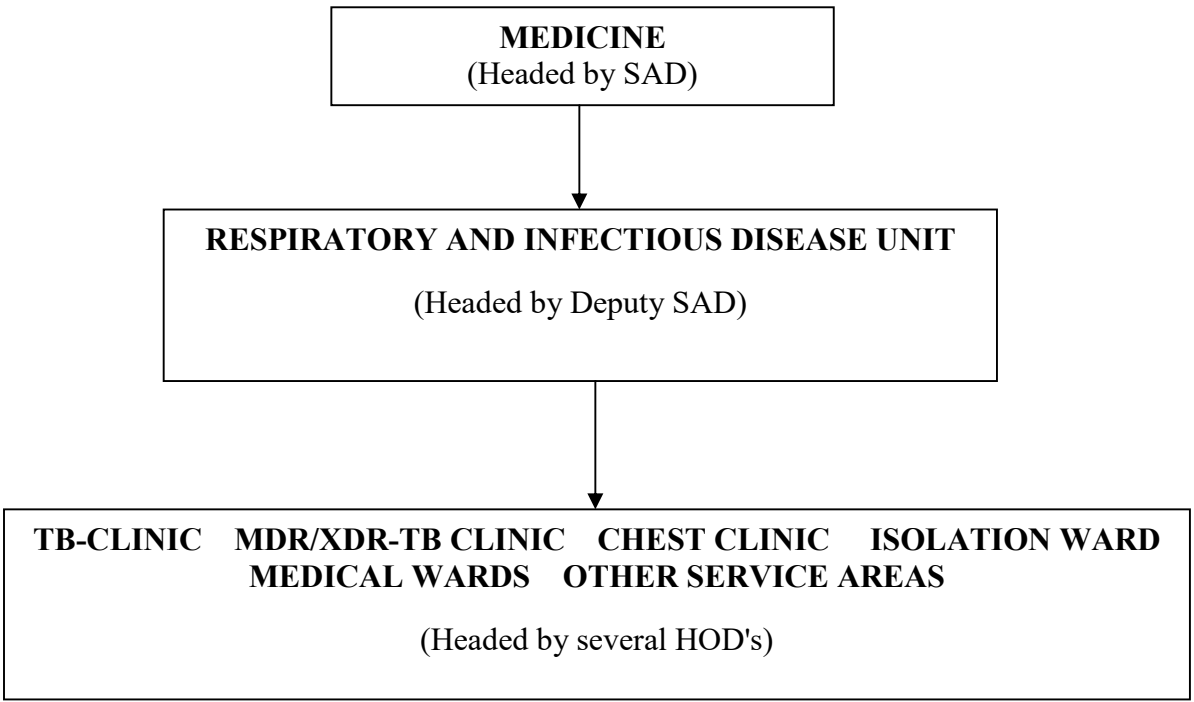
In Kenya, the Division of Leprosy Tuberculosis and Lung Disease (DLTLD) in collaboration with the Tuberculosis Central Reference Laboratory (CRL) is mandated to conduct TB and drug resistant TB surveillance and control on top of setting policies, guidelines and strategies in the control, prevention, diagnosis and management of TB.

Kenyatta National Teaching and referral Hospital has a special TB ward for TB patients and TB clinics. The pediatric ward has isolation rooms for TB pediatric TB patients. It utilizes the national TB management protocol in the management of TB patients. The hospital is located in Nairobi Upper hill. This is one of the oldest Hospital having over 106 years. It was founded in 1901 and in 1952 it was named King George VI hospital. KNH have 50 wards,22 clinics (out-patient) 24 theaters' and a large Accident and Emergency unit. It was renamed Kenyatta National Hospital after independence from the British and it is currently the largest referral and teaching hospital in East and Central Africa.

1.4. The Structure of the MDR-TB Clinic at the KNH

The MDR-TB clinic is under the department of medicine which is subdivided into many other smaller units for the ease of operations. Underthe medicine department, there is the Respiratory and Infectious Disease Unit (RIDU), under which MDR and ordinary TB clinic fall under as service areas. The Medicine department is headed by Senior Assistant Director,(SAD) with several Head of Departments (HoD's)heading the different units under it. The structure is generally as follows:

Figure 1.1: Structure and MDR-TB Clinic at KNH



1.5. Research Problem

MDR and XDR-TB is a growing health concern in the world today, (Ginsberg and Spigelman, 2007; WHO, 2010).In most limited health resources countries including Kenya, the number of MDR cases is on the rise despite the effort, albeit small, that is directed towards tackling this problem, (Legido-Quigley, et al., 2010). According to Ginsberg and Spigelman, (2007) and Gandhi, et al., (2007) MDR and XDR-TB patients face a number of social and economic challenges such as social stigma, lack of food, lack of transport to treatment facility, lack of proper health information as well as effects of drugs/treatment among other challenges.

The health worker on the other hand faces challenges such as lack of adequate equipment, lack of drugs and other consumables, lack of support in terms of specialized training and limited research information, (Kaufmann, Hussey and Lambert, 2010). The influx of refugees into Kenya as well as poor surveillance of the magnitude of MDR/XDR-TB has further complicated it's treatment and management especially in the public health sector. This poor surveillance is due to lack of resources to carry out such exercises, (Hopewell, et al., 2006: Jeon, et al., 2008).

Other challenges that undermine the management of MDR and XDR-TB include the side effects of the drugs due to increased severity such that some patients abandon the treatment before completion. Also the costs associated with the treatment of MDR-TB could be out of reach for many patients. These costs arise from purchase of other drugs and materials to treat other co-infections and for other lab test that are not offered freely in public hospitals (Rajbhandary, Marks and Bock, 2004). This also tied to the fact that most MDR-TB patients are from the lower socioeconomic stratum and therefore they may not afford to pay for all these associated costs of treating MDR -TB and this has a major impact on its management. In some instances the management of this disease is impacted by the lack of proper social support for the patient. In such a situation, the family usually abandons the patient either at home or in the hospital for fear of getting the same problem.

Understanding the challenges faced by the health workers and the patients will go a long way towards solving this problem. Furthermore, MDR and XDR-TB is a relatively new health concern compared to ordinary TB and thus there are very few specialists in the main referral hospitals as well as specifically trained nurses and other medical personnel to manage

MDR/XDR-TB cases (Gupta, Raviglione and Espinal, 2001; Nathanson et al., 2006). Similarly, few studies have given conclusive solution counter this problem, especially in resource scarce settings, (Sharma and Mohan, 2003; Hopewell, et al., 2006; Gandhi, et al., 2007; Jeon, et al., 2008). It is imperative for this study to answer the question; what factors challenge the outcomes of management of MDR/ XDR patients in KNH?

1.6. Research Questions

i. What are the demographic and socio-economic factors challenge the outcomes of management of MDR/ XDR patients in KNH?
ii. What common system deficiencies that affect the outcomes of management of MDR and XDR patients in KNH?
iii. What is the relationship between the treatment regimen and treatment duration and the outcomes of management of MDR /XDR in KNH?

1.7. Objectives of the study

1.7.1. Broad Objective

To determine the emerging challenges in the treatment and management of Multi Drug-Resistant and Extensively Drug- Resistant Tuberculosis at the Kenyatta National Hospital.

1.7.2. Specific Objectives

i. To determine the demographic and socio-economic factors challenging the outcomes of management of MDR/XDR TB patients at KNH.
ii. To assess the common system deficiencies which affect the outcomes of management of MDR and XDR TB at KNH.
iii. To relate the treatment regimen and treatment duration on the treatment and outcomes of the management of MDR /XDR TB at KNH.

1.8. Justification of the study

Drug sensitive TB has been researched extensively but MDR and XDR-TB has not been fully researched and very little information is available about this relatively new epidemic, (WHO, 2011). Most of the studies (Gupta, Raviglione and Espinal, 2001; Johnson, Kagal and Bharadwaj, 2003;Legido-Quigley, et al., 2010) focus on how the disease is spread and no single study has been done to know the problems experienced by both patients and health workers in treatment and management of MDR and XDR–TB. There are many challenges in dealing with

the problem which includes limited range of drugs available for its treatment, relatively long durations of treatment and significant drug side effects leading to poor adherence to drug. This and other challenges have led to the rise of MDR and XDR TB cases and unless a proactive approach is taken, the MDR and XDR-TB will get out of control. The government has not given much support in resources allocation to facilitate proper research and training on MDR and XDR-TB. Much of the findings that inform decision are from international organizations that mostly fund the TB program and as such control the TB program in most African countries.

Thorough understanding of the challenges faced by both the health worker and the patients will help bring forth these to the attention of the government and other stakeholders in the health sector so that relevant policies can be developed to contain it

CHAPTER TWO

LITERATURE REVIEW

2.1. Theoretical Literature

Tuberculosis is among the top ten causes of morbidity and death in the world. (Lim, et al. 2010). Among the goals on health set by the WHO is to eliminate this infection in the 21 century but this goal may not be realized at the expected time line because of emergence of drug resistant TB among world's population, and the control and management is proving to be out of control. The WHO estimated that new diagnosis of TB cases ranged from 300,000 and 600,000 in the year 2012. Among these estimates, WHO say that about 28% of these cases have been reported and also most or the bulk of these cases are traced to Eastern Europe and Central Asia. (WHO, 2013).Among the reported cases of MDR and XDR TB whose figure stood at 83,714, an estimate of 44% which is approximately 36,700 cases, originated from European region.(WHO, 2013). At the time this literature was being written, 92 countries had reported patients with XDR-TB and majority of them were from Eastern Europe (WHO, 2013).Recent studies on MDR-TB from Belarus showed that 35.3% and 76.5% of cases had a first episode and previous treatment respectively. The study also revealed this phenomenon was observed in the whole of Belarus and it represented a high rate of MDR/XDR-TB for a country to be ever documented (Skrahina, et al., 2013).

Various literature and research reports have estimated rates of less than 50 % in most cases but Falzon and Orenstein indicate that success rates in the treatment of MDR and XDR-TB oscillate between 36% and 79% .In the year 2013, a joint surveillance report conducted and released by WHO and ECDC indicated that there was 31.6% success rate treatment outcome for MDR-TB in the European Union (EU)/European Economic Area (EEA). The results from these reports were also compared with results from the period before antibiotics were well in use. (Lassen, 1950). The report also estimated that about 20 % of MDR-TB patients globally received what can be termed adequate treatment. (WHO, 2013).

The unique difference of mycobacterium infections from all other bacterial infections is that mycobacterium infections take relatively longer periods of treatments in order to fully eliminate it. Secondly the drugs used to treat mycobactria infections must be intensively used for relatively

longer periods to enure complete elimination of the offending pathogen and to prevent relapse. The WHO has given guidelines on the acceptable duration or period of treatment and the current guidelines given a duration period of between 20 and 24 months depend ending on the immunity of the patient. (WHO, 2012).Proper adherence should be strictly practiced when treatment with anti-TB microbial is underway. Albeit the efforts put in place to tackle the problem of MDR-TB, factors such as non-adherence, adverse drugs reactions and high costs associated with the treatment of this disease will definitely compromise treatment success.(Soldatou and Davies, 2003; Diel, et al., 2012).

The recent breakthrough and major advances that have enabled rapid identification of MDR-TB patients is a very welcome move, but these important technologies are still not available globally and certainly not in resource poor settings which comprise of most parts of the developing. Therefore the global estimates and statistics on MDR-TB do not match with the developments in therapies and preventionsion (Boehmeet al.2010; Greco et al. 2006). Another breakthrough that would go a long way in combating MDR-TB is the recent licensing of a drug use for MDR-TB in the US by the Food andDrug Agency (FDA).The drug in question was licensed in the year 2013 in the unites states of America, after recommendations from European Medicines Agency (EMA). Another authorization for the European market for two new anti tuberculosis drugs is expected soon and these developments come more than four decades after discovery of the first anti –TB drugs currently in use (FDA 2013).

The alarm that has been prompted by rising MDR-TB infections has seen response from 53 WHO member states who fully went ahead and endorsed a consolidated plan of action for the prevention of MDR-TB especially in the European Union region. The resolutions from the action plan had 6 strategic points and major areas of implementation that would respond to this problem in order to achieve accessibility to diagnosis, treatment of drug resistant TB. (WHO, 2011). The current method of management of MDR is based largely on expert opinion as there is not much evidence based knowledge on it to conclusively address issues such as acceptable duration of treatment, degree of infectivess and the acceptable combination of drugs both for the intensive phase and the second phase of therapy. These are just some of the few problems.

2.2. Empirical Literature Review

Past studies on drug resistant tuberculosis together with the challenges in the management of this relatively new epidemic were the main concern of this study. The study also emphasized on the importance of prompt detection and treatment of existing and suspected MDR -TB cases. There are still variations in the standard practice due to difference in resource availability in different settings. A European Union survey thtat was investigating clinical, public health, and infection control practices in the management of MDR TB and XDR TB patients indicated that there was no proper procedure and the conclusion of the survey is that it failed to meet international set standards. (Sotgiu, et al. 2011)

In the year between 2004 and 2005, a survey was carried by CDC and WHO on prevalence using data collected between the year 2000 and 2004. The report from this survey reported prevalence of 6.6% XDR-TB among all multi-drug resistant tuberculosis isolates worldwide, 6.5% was reported in industrialized countries such United States, and United Kingdom and 13.6% was reported in Russia and Eastern Europe . Prevalence of XDR-TB from Asia and other similar regions was not well defined in this report due to the minimal number of the TB cases taken in this study in comparison to other studied nations.

Other prevalence reports from other regions of the world outside Europe and America reported a prevalence of 1.5% in Bangladesh and Indonesia, and 0.6% was reported in Africa and the Middle East. Korea was reported to have the highest number of XDR cases and this represented 15.4% of cases among all multi-drug resistant tuberculosis patients (Shah et al. 2007). Another aspect of this report is that there is a geographical pattern in the spread of XDR-TB. Data obtained from populations in South Korea, United States and Latvia portrays a more representative picture on the spread of XDR-TB in totally three different regions of the world. These findings confirm that even in settings such as U.S where control measures are stringent, XDR-TB can still spread.

A preliminary descriptive detailed finding on XDR-TB using data from US National TB Surveillance System was released in the year 2006(CDC, 2006). This U.S report indicated that 74 tuberculosis cases captured during 1993-2004 period met the criterion for definition of XDR-TB. Another recent report from Germany and Italy reported that 10.3% and 14.3% XDR-TB isolates respectively among 83 and 43 multi-drug resistant tuberculosis strains respectively were

successfully identified. The report further reveals that these patients had up to 5 times more risk for death, extended hospitalization and treatment periods, indicating a significant association between MDR-TB and death. (Migliori et.al 2007b)

Bouvet,(2007) provide a clear picture of prevalence in France, which was not captured under reported prevalence from Europe. According to Bouvet, the prevalence of XDR-TB in France for those tested for MDR-TB strains was found to be 4% and another report on the same testing from Iran reported a prevalence of 10.9 %. (Masjedi,et al., 2006). Reports from Hong Kong, indicate that 9 out of the 75 MDR-TB strains ,approximately 12% had XDR resistance with severe resistance to some of the major second line drugs such Ethionamide,amikacin, ofloxacin and cycloserine (Kam and Yip, 2004).

Reports from In India, revealed five XDR-TB cases were isolated from 68 MDR-TB strains in a recent study done (Mondal, and Jain, 2007). Despite the fact that this figure was based on a small number of multi-drug resistant tuberculosis patients from North Indian it clearly indicated the reality of XDR and its existence in that region and that the reported figures may not reveal the true picture of the real situation on the ground. This also pointed to the increase in MDR-TB and HIV co- infection and the extent of the risk of MDR associated with HIV in India. India (Narain and Lo, 2004) .During the same period, a new XDR-TB was reported by the TB research centre in Chennai, India (Thomas, et al. 2007).

The nature of resistance of TB is that at any given point it is resistant to more than one chemotherapeutic agents used. This pattern of resistance usually limits the options for treatment because there are very few treatment options or alternative choice of drugs that provide a sure, safer and effective treatment plan. The increasing pattern of resistance to the current drugs in use is becoming a serious global problem .The progressive nature of the spread of MDR-TB can potentially impede TB prevention and care programs and can also affect public health infrastructure, especially in resource scarce set ups which are mostly the developing countries. This does not mean the developed countries are immuned from threats of drug resistant TB. In fact there are reports that developed countries are now under threat albeit the fact that individualized care and treatment costs and larger social and economic disruptions could become major public policy issues.

There are many problems that plague the TB treatment program. These problems or deficiencies result in interrupted drug supply, non- adherence to drug therapy and compounding of complications arising from co-morbidities. (Ginsberg and Spigelman, 2007).These problems can lead to failure in treatment and result in the development of drug resistant strains of MDR-TB. In countries there is a high rate of TB, new drug-resistant cases result from the transmission of already resistant organisms between individuals, (Gandhi, et al., 2007).

Most countries currently do not have profiles of drug resistance therefore it becomes difficult to monitor changes in treatment and therapy is mainly empiric and any change in treatment is only done after initial treatment failures (Barker, et al., 2009).This has had a direct negative impact on patient treatment outcome because there is a lapse of time from the time a patient is infected to the time of confirmed positive diagnosis. Also by this time a patient usually has experienced multiple episodes of TB and their health has deteriorated significantly. In most cases a determination of the drug resistance profile of the infecting mycobacterium is not well determined. For a patient who has been infected with drug-resistant TB, the initial treatment is with standard first line therapy and is switched to a more standardized second line drug regimen only after patients have been considered un-responsive to treatment. This hands-off, standardized and passive approach to TB control and management has led to increased cases of advanced TB disease and death in affected persons.

The global fight against XDR may not be won soon because, even though TB isolates were fully identified in the surveyed regions, their global distribution, and prevalence reports, the consequence for successful treatment is not known due to their limited culture and drug susceptibility testing capabilities in endemic countries. However, current estimates of population-based prevalence suggest that the proportion of MDR TB isolates that meet the definition of XDR is 19 percent in Latvia; 15 percent in South Korea; and 4 percent in the United States (Zignol, et al. 2006; Burgos, et al., 2005). It is important to note that the epidemiological and clinical characteristics, as well as the clinical consequences of MDR and XDR TB likely differ significantly between areas of high and low HIV and TB prevalence.

Zignol, et al. 2006, puts the global estimated cases for MDR-TB at 424,203 and a substantive number of this global estimate occurred mainly in China, India, and the Russian Federation,

and they accounted for 62 % of the burden. MDR TB represented 2.7 % of new and 18.5 % of previously treated Tb cases, an overall of 4.3 %. Despite the fact MDR TB still responds to second line drugs, successful treatment requires not less than two years of therapy, and it involves drug administration in a health facility or a monitored outpatient set up. In addition, MDR TB treatment is not well tolerated, it is about ten times more expensive than treatment of ordinary TB, and its cure rates are often below 60 %. The current costs of treatment for one MDR- TB patient is approximate US $4,000 per patient, while the cost of treatment for one XDR TB patient has been estimated to be at least two to three times this amount, depending on the extent of drug resistance and need for hospitalization (Burgos, et al. 2005; Tupasi,et al. 2006; Rajbhandary, Marks and Bock, 2004).

According to Centre for Disease Control (CDC 2003), the current drug and treatment guidelines for the treatment and management of drug resistant TB have not been fully standardized and are not optimized. The standardization of a particular effective regimen(s) is difficult because of the nature of resistance of the mycobacterium both in phases of treatment. Evidence from an analysis of the global prevalence of all forms of drug-resistant TB indicates the need for further research and studies to determine the distribution, prevalence and consequence of MDR and XDR-TB in order to implement effective TB control activities. Increased research efforts should be urgently put in place expedite the development of new and more effective tools to prevent, diagnose, and successfully treat drug-susceptible and drug-resistant TB in all populations including those co-infected with HIV.

Long term studies and clinical experience have proved that TB is curable if treatment is done well and that MDR-TB is more fatal and cure rates are significantly low. Management of MDRTB is especially difficult, complicated, challenging, and costs more, with the input of highly qualified, specialized and experienced work force. According to a study by Sharma and Mohan, (2006) Tuberculosis was found to be diagnosed easily but MDR-TB diagnosis was not straight forward and was dependent on expensive culturing and sensitivity tests that are not readily available in most parts of the world. Isoniazid and Rifampicin, the key second line drugs for the treatment of MDR TB have severe side effects, more toxic and are expensive in comparison to the others used in first line. (Sharma and Mohan, 2004; Ormerod, 2005).

Research into formulation of newer and better drugs to combat MDR and XDR-TB has also not been forthcoming because the pharmaceutical companies have had a number of constrains when it comes to research and formulation of these drugs. A study by Ginsberg and Spigelman, (2007) found that a number of constraints among drug the companies hinder them from sinking their funds into researching for newer molecules. One of these major constrains is the cost of such a research; simply put research is expensive, difficult and it takes years for its fruits to be enjoyed. The other major problem is that there are few animal -based models that can mimic TB infections in humans much closer. There are several difficulties in designing and development of new drugs with better or superior mycobacterium effects, excellent pharmacokinetics and tolerability. (Tomioka and Namba, 2006).

There is evidence that the growth of resistance has been, ironically, been contributed by the medical personnel, who ideally should be at the forefront in the fight against eradication of drug resistant TB. Mismanagement of the treatment processes has played a major role in the development and the emergence of resistant TB. The main cause and effect of this is in the faulty treatment habits of doctors (Uplekar and Shepard, 1991;Nathanson, et al .2006; Prasad, et al .2002).Secondly, erratic use of the drugs, poor quality drugs, lacked of skilled and experienced ,lack of proper testing facilities and equipment and lastly factors related to cost and access to health care, all have played a role in compounding the problem of drug resistant TB.

Treating MDR-TB has its own share of difficulties. It is difficult, complicated, much costlier, and it needs experienced and skilled workers. In addition, good quality second line anti-TB drugs, standard microbiology testing as well as proper patient management is an essential part of management to ensure a better prognosis of the infection and to improve patient outcome.(Iseman, 1993; Gupta, Raviglione and Espinal, 2001).There is evidence that treating multi-drug resistant tuberculosis with second line drugs may lead to a cure rate of more than 65% and will also help stop any ongoing transmission(Mukherjee, et al. 2004; Van Deum, 2004;Espinal and Dye, 2005). This finding by Mukherjee et al. may not reflect a true picture because most evidences of success in management of MDR-TB is collected from resource rich countries proper treatment in provided by the government.(Espinal and Dye, 2005)

Jeon et.al, 2008, reported in a study in South Korea the strong correlation between development of MDR-TB and previous treatment with second line drugs.Bearing this in mind, the

unprecedented rise in MDR cases undermine all the efforts that have been put in place to curb this problem. The report emphasizes on further strengthening of TB control programs and infection control measures which will be a major role in preventing transmission and survival of resistant strains in the environment. The Green Light Committee of Stop tuberculosis partner provides a global mechanism to help affected countries to achieve these steps. This Korean report further emphasizes the need to strengthen TB control measures through proper implementation of the stop TB strategy and adoption of this strategy by both private and public sectors which is adopted from the new World Health Organization guidelines(Mukherjee, et al., 2004).Based on the findings, it further recommended that vital infection control procedures need to be improved in hospitals to stop XDR-TB from spreading.

From the perspective of health economics it is economically useful to treat TB properly in the first place. The cost of treating TB is US$ 52 compared to US$ 3168 for treatment of MDR-TB including the drugs and hospitalization charges.(Rajbhandary, Marks and Bock, 2004). A study done by Huong *etal., (*2006) from Vietnam suggested that a better way of managing MDR-TB patients is by carrying out directly observed therapy (DOTs),a practice that is recommended and practiced internationally. This study claim that treatment of patients with second line drugs only may not be successful in curtailing the spread of MDR-TB and that DOTs alone may suffice in some settings. This study is based though, on public health perspective and theories. (DeRiemer,Garcia-Garcia and Bobadilla-del-valle 2005)

This clearly shows that inadequate treatment and non adherence is a subject that has not been well addressed in the fight against resistant TB. Non adherence appears to be a problem that underestimated and is difficult to predict. There are certain traits and factors that could be used to predict non adherence and these include alcoholism, homelessness and mental disease. Poor compliance with treatment is also an important factor in the development of acquired drug resistance, (Johnson, Kagaland Bharadwaj, 2003).

The complication of MDR-TB and HIV co- infection is another major concern and setback that is proving to pose a challenge in the management of drug resistant TB. The main problem in treating this co-infection is that each disease on its own has serious implications on its own. The burden of treatment therefore, especially the drug burden and their cumulative adverse effects and events become too much for one body to bear. Coupled with this, the poor outcome and the

prognosis are not always promising. The current information on the drug interactions between MDR-TB drugs and anti-retroviral drugs is very scanty. What is clear though is that second line TB drugs are more expensive, more toxic and less effective.

More studies on co-mobidity and co-infection all give a not so good picture on prognosis.The presence of co-morbidity is of very concern as there is rapid progression of infection and high potential of spread among immune suppressed individuals, greatly accelerating the consequences of a poorly managed TB program (Gandhi, Moll and Sturm, 2006). According to a study by Gandhi in 2006, Co-morbidity with tuberculosis and HIV/AIDS affects close to 11 million people and nearly 200,000 people succumbed in the year 2005. Less than 0.5% of HIV-positive people were screened for tuberculosis that year is of great concern to public health practioners as well the health practioner fraternity in general (Gandhi, et al. 2006). First report of XDR-TB with HIV came from Kwazulu Natal, South Africa (KZN) province. Of 536 TB patients at Church of Scotland Hospital of KZN, which serves a rural area with high HIV rates, 221 had MDR, 53 confirmed an XDR diagnosis, 52 died within 25 days of diagnosis and 44 tested positive for HIV.(Mlambo, et al., 2008).

Results from XDR-TB isolates demonstrated that rising cases of HIV also push up XDR-TB numbers and this correlates to the fact that when a patient has TB, the life time risk of developing XDR-TB is 5-10%, with HIV infection, this figure raises to 5-15% per year. Both MDR and XDR TB treatment success rates are substantially lower in patients with HIV and this may affect negatively the benefits of TB and anti-retroviral treatment programs, more so in areas with high prevalence of HIV and TB infections. (Gandhi, Moll and Sturm, 2006)

2.3. Overview of the Literature Review

From both theoretical and empirical literature reviewed, the study found that MDR/XDR treatment outcomes is associated with treatment regimen and the duration of treatment, demographic and socioeconomic factors, MDR-TB Co-Morbidities and also MDR/XDR management system deficiencies. Given dire consequence of the condition, treatment and management of this disease is proving challenging. Policies and intervention required is stagnating since little is known on factors behind the management and thus elimination or reduction of the disease in the end. This study therefore intents to model factors associated with MDR/XDR TB management outcomes at Kenyatta National Hospital using patient record files.

Lastly, both MDR and XDR TB treatment success rates are very low in patient co -infected with HIV. Areas of high TB and HIV prevalence have the danger of reduced benefits of both TB and HIV treatment programs

CHAPTER THREE

METHODOLOGY

3.1 Introduction

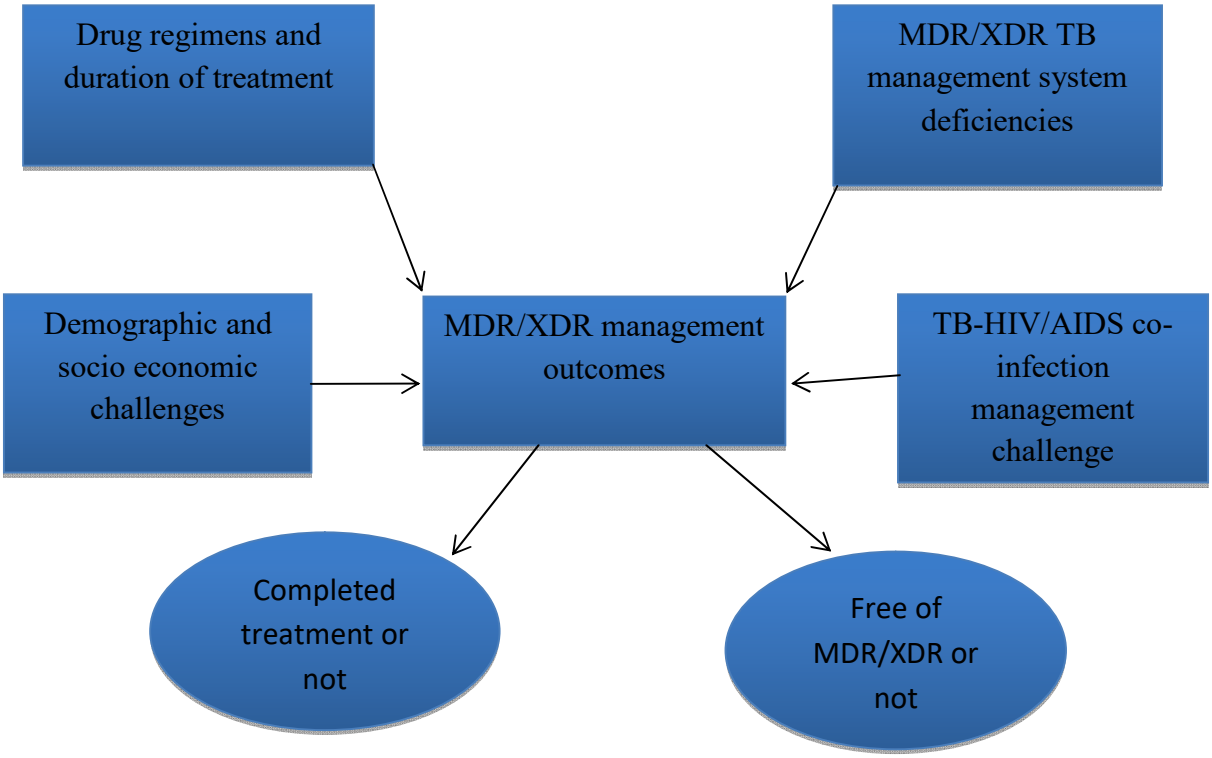
This chapter presents the methodology employed towards the achievement of the set objectives. The research design, conceptual framework, study area and target population, data process and analysis, econometric/estimable model and model specification, definition of study variables and description of data source have been presented.

3.2 Research Design

The study uses Cross Sectional descriptive design in examining the determinants of MDR/XDR TB management outcome in Kenyatta National Hospital (KNH). The proposed factors include demographic and socioeconomic factors, drug regimens and duration of treatment, MDR/XDR management system deficiencies such as incomplete and inadequate treatment of previous TB cases as a result of drug shortages which has emerged as the major common reason for the inadequate initial anti-TB regimen, especially in resource poor settings. Another factor is the poor control of the environments in which resistant strains are transmitted from person to person.

Further, the challenges that face the treatment and the management of MDR-TB include; MDR-TB and Co-Morbidities- the presence of other diseases such as HIV/AIDS, diabetes, and hypertension complicates the treatment and management because of increased cost of treatment, increased mortalities and increased burden of disease to the family. The side effect of the drugs used to treat MDR/XDR-TB is so severe such that patients take off and never return to complete treatment. Before diagnosis is made, the patient is assumed to be infectious such that by the time treatment is received, several people will have been infected and it is always almost impossible to reach these contacts, (WHO, 2010).

3.3. Conceptual Framework



Source: Researcher based on the literature Reviewed

3.4. Study Area and Target Population

The study was carried out in Kenyatta National Teaching and Referral Hospital. This is a not only a national hospital but also a parastatal which is semi- autonomous. The population to be studied included both MDR/XDR TB in and outpatients in the hospital. The patients were selected from the admission register for inpatients and clinic attendance register for outpatients. Other relevant documents with sufficient information on MDR/XDR TB were also used.

3.5. Data processing, analysis and Presentation

Data was then entered in a computer using the STATA program. Descriptive statistics (mean, median, percentage and ratios) will be determined during the analysis. The relationship between the variables was also assessed during cross tabulation of data to econometrically determine the challenges identified in the management of MDR/XDR TB outcome. The study adopted a Linear Probability Model (LPM) in regression since the dependent variable is a binary variable (See

section 3.6 for more details). Data was analyzed and presented in proportions and frequency tables. The results were presented in descriptive form using frequency tables and graphs.

3.6. Econometric Model and Model Specification

The study employed Linear Probability Model (LPM) and Logit models. The model is represented as shown below;

$$P(Y_i = 1/X) = \frac{1}{1+e^{-z}} \quad \text{..... 3.1}$$

$$Where\ z = \beta_0 + \beta' X' + \varepsilon$$

Where Y_i is the probability of observing a certain category for (example completing treatment or a patient becoming free of MDR/XDR)

X' is a vector of independent variables (challenges)

β' are the coefficients to be estimated

ε is an error term

In order to interpret the LPM model, the study computed the marginal effects of each independent variable with regard to treatment outcomes. The interpretation proceeded such that a coefficient were the change in the treatment outcomes (completion/incompletion of treatment or becoming free of MDR/XDR) as a result of a unit change in the explanatory variable holding other factors constant. The model estimated is as specified below;

$$Y = \beta_0 + \beta_1 Age + \beta_2 Gender + \beta_3 Marital\ Status + \beta_4 Employment\ Status + \beta_5 Educational\ level + \beta_6 DR + \beta_7 DRDT + \beta_8 SD + \beta_9 TCMC + \beta_{10} Distance + \varepsilon$$

Y_i is the MDR/XDR management outcomes (In/completing treatment of MDR/XDR TB)

DR is the drug regimens

DT is the duration of treatment of MDR/XDR

SD is System Deficiencies

TCMC is the TB-HIV/AIDS co-infection management challenges

β_s are the coefficients to be estimated

ε is the error term

3.7. Variable Definition and Expected Signs

Table 3.1: Variable definition, measurement and expected signs

Variables	Measure	Expected signs (According to literature)
Dependent Variables		
MDR/XDR TB management outcomes; Completion of Treatment	Treatment outcome: 1 if treatment was incomplete, 0 otherwise	--
Presence of Mycobacterium	Treatment outcome: 1 if mycobacterium free, 0 otherwise	--
Independent Variables		
Age	Complete years	Negative
Gender	Female=1, male=0	Positive
Level of education of patient	None=0 Primary=1 Secondary=2 higher=3	Positive
Marital Status	Married=1, 0 otherwise	Positive
Employment Status	Employed=1, 0 otherwise	Positive
Drug regimen	The number of drugs in a regimen	Negative
Duration of treatment	1 if completed the period of treatment, 0 otherwise	Positive
System Deficiencies	1 if drugs are out of stock, 0 otherwise 1 if there is treatment equipment are insufficient, 0 otherwise 1 if a specialized health worker not available, 0 otherwise	Positive
TB-HIV/AIDS co-infection management challenge	Diagnosed from HIV/AIDS=1, 0 otherwise	Negative
Distance to MDR/XDR TB clinic (Actual kilometers)	Distance≤200=0, Distance≥200km=1	Negative

3.8. Data Source

The study used the secondary data obtained from TB and MDR/XDR specialized clinic records at Kenyatta National Teaching and Referral Hospital with the necessary permissions. In those records, information on the demographics as well as socio economic is captured. This was used to assess the socio economic challenges with regard to MDR/XDR management outcome. Information on different types of drug regimen and duration of treatment of MDR/XDR are recorded for all patients in the clinic together with MDR/XDR TB management system

deficiencies. Also the county of origin or residence of the patient is indicated which was used in this study to proxy for distance.

CHAPTER FOUR

FINDINGS AND DISCUSSIONS

4.1 Introduction

This chapter presents the study results based on management of MDR/XDR treatment outcomes at Kenyatta National Hospital. The LPM model is estimated and findings presented in Tables and figures

4.2 Descriptive statistics

Table 4.2 indicates the summary statistics of the study variables employed in this study.

Table 4.2: Summary statistics

Variable	Obs	Mean	Std. Dev.	Min	Max
Treatment incompletion	122	0.647541	0.479706	0	1
Age	122	37	10.99812	16	60
Sex (male=1)	122	0.3770492	0.4866459	0	1
No Education	122	0.1639344	0.3717427	0	1
Primary education	122	0.295082	0.4579603	0	1
Secondary education	122	0.295082	0.4579603	0	1
Higher education	122	0.2459016	0.4323963	0	1
Married	122	0.5491803	0.4996273	0	1
Residence	121	0.4132231	0.4944597	0	1
Unemployed	122	0.5819672	0.4952696	0	1
Self employed	122	0.1967213	0.3991591	0	1
Employed	122	0.2213115	0.4168416	0	1
Drug regimen	122	1.795082	0.5740752	1	3
Treatment duration (months)	121	16.16529	5.621902	6	24
r1	122	0.1721311	0.3790511	0	1
r2	122	0.1557377	0.3641018	0	1
r3	122	0.0491803	0.2171361	0	1
r4	122	0.1639344	0.3717427	0	1
System deficiencies	120	2.033333	0.6208335	1	3
Comorbidities	120	0.8833333	0.3223687	0	1
Distance to MDR/XDR clinic	120	133.025	210.2349	5	700

The results in Table 4.1 indicate that approximately 64.75% of the respondents never completed MDR/XDR treatment with less than 50% variation. The surveyed respondents were on average 37 years, the youngest being 16 years while the oldest being 60 years. Female population dominated the sample as they formed the majority of the respondents (62.3%) as the males

forming only 37.7%. On education levels, 16.39% of patients were not educated at all while 29.51% of the patients had primary and secondary education levels each and 24.59% of the respondents had higher education levels.

Over 50% of the respondents were married while the rest were not married. The study revealed that 54.92% of the MDR/XDR patients were married while the other proportion was not married. However, it was shown that 41.32% lived within Nairobi county while the rest come from counties away from Nairobi (majority came from the nearby counties such as Kajiado and Kiambu counties).

On economic activities, the study revealed that about 58.2% of the MDR/ XDR patients were unemployed while 19.07% and 22.13% were engaged in self-employment and salaried employment. On the other hand, most respondents were either on the first (28.69%) or second line drugs (63.11%). The total regimens assessed were three. The third is any other drug regardless of the other comorbidities it treats.

Treatment duration was reported in terms of months the disease was treated. On average, it was shown that most respondents received treatment for approximately 16 months with the least attending six months and the maximum patient attending treatment for 24 months. The treatment duration varied approximately for five months among all individuals.

The study found out several reasons as to why patients never completed their MDR/XDR treatment and four outstanding reasons were revealed. They include: first, patients who die before completion of treatment due to complication (r1) who were on average 17.21%; second, patients who were reported to have stopped attending MDR/XDR treatment/ disappeared with no trace (r2) were 15.57%; thirdly, patients who were reported to have relocated to other areas (r3) such as Uganda, Somalia among other areas were 4.92% and lastly patients reported to succumb to death after admission to treat comorbidities (r4) were 16.39%.

Lastly, system deficiencies, comorbidities and distance to MDR/XDR clinic were also assessed. Most of the respondents were seen by the consultant twice as other times the clinical officer attended them. On comorbidities, approximately 88.33% of the respondents were found to have other diseases such as pneumonia, chest disease, diabetes, HIV/AIDs etc. On the other hand, patients were shown to cover a distance of 133 Kilometers on average to access MDR/XDR TB

clinic with the least distance covered being five Kilometers and the largest distance being 700 Kilometers.

4.3 Multicollinearity analysis

When there is perfect linear relationship between the independent variables, then multicollinearity is said to be present. The variance inflation factors are used to determine if any pair of independent variables is highly collinear. Since the results show that all VIF values are less than 10 and their tolerance values are greater than 0.10, Multicollinearity is deemed to be absent. Therefore, the study proceeds to check other estimation issues before conducting actual estimation of the model. Table 4.2 presents details on VIF test.

Table 4.2: Variance Inflation Factors

Variable	VIF	Tolerance
Higher education	3.66	0.273040
Secondary education	3.53	0.283357
Primary education	3.42	0.292440
Age	3.26	0.306388
Married	3.05	0.327555
r1	2.86	0.349166
r2	2.32	0.430616
System deficiencies	2.23	0.447803
r4	2.16	0.462701
Treatment duration	2.13	0.470016
Drug regimen	1.94	0.515039
r3	1.94	0.515511
Residence	1.90	0.526116
Distance to MDR/XDR clinic	1.78	0.561255
Comorbidities	1.57	0.638241
Self-employed	1.52	0.657065
Employed	1.45	0.687990
Sex	1.42	0.705474
Mean VIF	**2.34**	

4.4 Tests for Model specification

Upon conducting tests of goodness of fit to determine if there are any additional independent variables that are significant by chance, the following results are revealed for link test (Table 4.3). The idea behind a link test is to add an independent variable to the equation that is especially likely to be significant if there is a link error.

Table 4.3: Link test

Treatment incompletion	Coefficient	Std. Err.	t	P>t	[95% Conf.	Interval]
_hat	1.852591	0.142616	12.99	0.000	1.570096	2.135086
_hatsq	-0.7391705	0.119253	-6.20	0.000	-0.9753878	-0.5029532
_cons	-0.1033429	0.0336702	-3.07	0.003	-0.170037	-0.0366487
Number of observations= 118						
F(2, 115) = 371.60						
Prob > F = 0.0000						
R-squared = 0.8660						
Adj R-squared = 0.8637						
Root MSE = 0.17754						

First, the p value for the link test regression is 0.0000 indicating that the model has been correctly specified. Second, the quadratic term of the predicted values is statistically significant implying that the linear model specification may not be appropriate. This is because the test is based on the significance of *hatsq*. The study considered another test to determine if there is need to include other important variables in our model. This test reveals that there may be omitted variables which ought to be concluded (See Table 4.4). Considering data limitation and sample size estimation of the linear probability model proceeds.

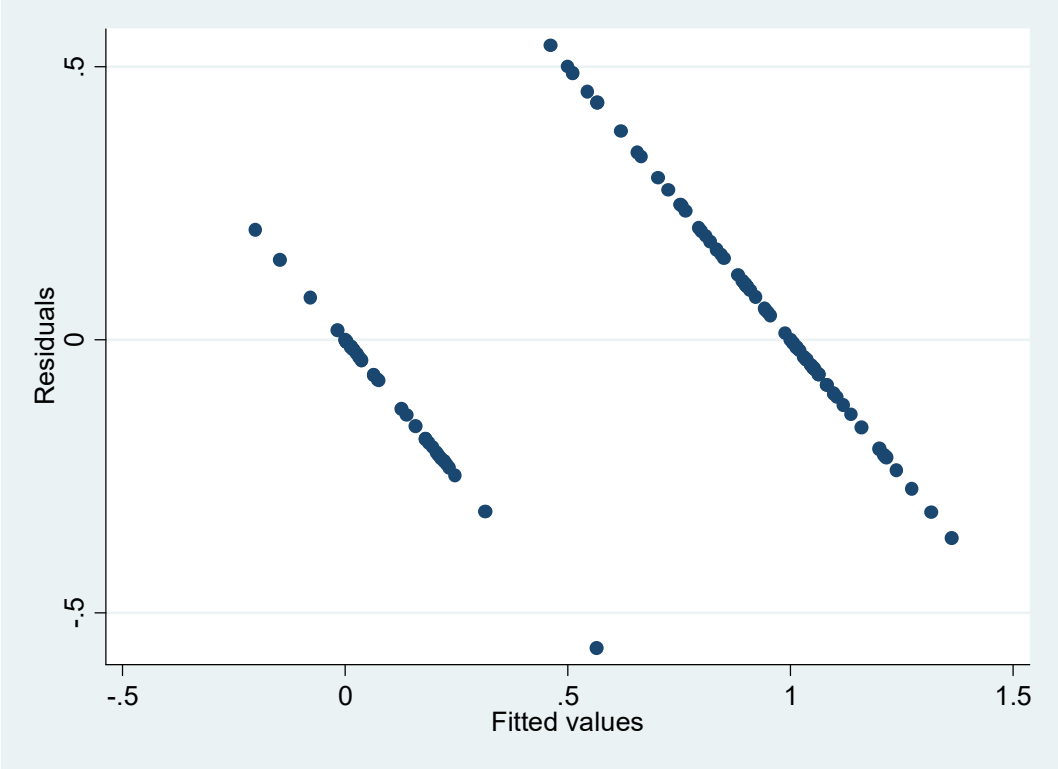
Table 4.4: Ramsey reset test for specification

Ramsey RESET test using powers of the fitted values of treatment incompletion		
Ho: model has no omitted variables		
	F(3, 96) =	60.69
	Prob > F =	0.0000

4.5 Homoscedasticity

The study considered residual plots which involved plotting the squared residuals of the regression model against the predicted values of treatment incompletion or each of the explanatory variables. Absence of heteroscedasticity implies failure to observe systematic pattern between the plotted variables, whereas heteroscedasticity is deemed present, if the plots exhibit a systematic pattern. From figure 4.1, the scatter plots are systematic and thus we fail to reject the null of homoscedasticity. This implies that there no heteroscedasticity.

Figure 4.1: Scatter plots of residual squared against fitted values



4.6 Regression Results

The study estimated an LPM and logit regression model and results are as presented in Table 4.5 and 4.6 respectively. Using results from LPM regression it was found that age, married, residence, treatment duration, r1, r2, r3, r4, comorbidities and distance to MDR/XDR TB clinic were found to be statistically significant factors leading to incompletion of treatment. On the other hand, sex of the patient, all education variables, all employment variables, drug regimen and system deficiencies were shown to be statistically insignificant.

Table 4.5: Regression results of LPM model

Treatment incompletion	Coefficient	Std. Err.	t	P>t	[95% Conf.	Interval]
Age	0.006186*	0.0033902	1.82	0.071	-0.0005409	0.0129129
Sex	0.0551249	0.0496676	1.11	0.270	-0.0434263	0.1536762
Primary education	-0.0188764	0.0823697	-0.23	0.819	-0.1823157	0.144563
Secondary education	0.0398145	0.0836794	0.48	0.635	-0.1262236	0.2058526
Higher education	-0.0542143	0.0894219	-0.61	0.546	-0.2316467	0.123218
Married	-0.1305892*	0.0713558	-1.83	0.070	-0.2721747	0.0109963
Residence	-0.1241678**	0.057298	-2.17	0.033	-0.2378595	-0.0104761
Self-employed	-0.0673629	0.062357	-1.08	0.283	-0.1910927	0.0563669
Employed	-0.0509382	0.0583936	-0.87	0.385	-0.1668036	0.0649273
Drug regimen	-0.0336531	0.0496217	-0.68	0.499	-0.1321133	0.0648072
Treatment duration	-0.0384695***	0.0052776	-7.29	0.000	-0.0489413	-0.0279976
r1	0.540069***	0.0917729	5.88	0.000	0.3579717	0.7221663
r2	0.5553614***	0.0862338	6.44	0.000	0.3842549	0.7264679
r3	0.2630347**	0.1289897	2.04	0.044	0.007091	0.5189783
r4	0.4504716***	0.0797224	5.65	0.000	0.2922851	0.6086581
System deficiencies	-0.0085677	0.0487682	-0.18	0.861	-0.1053343	0.088199
Comorbidities	0.1361585*	0.0787563	1.73	0.087	-0.0201112	0.2924282
Distance	-0.0002223*	0.000133	-1.67	0.098	-0.0004861	0.0000415
Constant	0.8907063	0.205743	4.33	0.000	0.4824675	1.298945
Number of obs= 118						
F(18, 99) = 25.27						
Prob > F = 0.0000						
R-squared = 0.8212						
Adj R-squared = 0.7887						
Root MSE = 0.22101						

Note: Significance at ***1%, **5%, and *10% significance levels

Key: r1,r2,r3,r4r5=reasons for incompletion of treatment.

r1-patient relocation,

r2-death due to treatment complications,

r3- absconding treatment

r4- Succumbing after admission

r5- Death due to infection with co-morbidity

Table 4.5: Regression results of LPM model

Treatment incompletion	Coefficient	Std. Err.	t	P>t	[95% Conf.	Interval]
Age *	0.006364	.003439	1.85	0.067	-.0004597	.0131878
Sex	0.044259	.0495713	0.89	0.374	-.0541009	.1426195
Primary education	-0.02154	.0828747	-0.26	0.796	-.1859771	.1429055
Secondary education	0.025038	.0831951	0.30	0.764	-.1400395	.1901147
Higher education	-0.0561	.0899998	-0.62	0.534	-.2346805	.1224778
Married *	-0.13607	.0716475	-1.90	0.06	-.2782352	.0060931
Residence **	-0.11893	.0576598	-2.06	0.042	-0.23787	-.0045244
Self-employed	-0.06735	.0627713	-1.07	0.286	-.1919001	.0572035
Employed	-0.04305	.0590769	-0.73	0.468	-.1602747	.0741681
Drug regimen	-0.02855	.0506918	-0.56	0.575	-.1291336	.0720335
Treatment duration***	-0.03852	.0053111	-7.25	0	-.0490549	-.0279782
r1***	0.519491	.09102	5.71	0	.3388873	.7000943
r2***	0.538242	.0854003	6.30	0	.3687887	.7076942
r3*	0.255109	.1296603	1.97	0.052	-.0021657	.5123826
r4***	0.452308	.0805159	5.62	0	.2925471	.6120691
System deficiencies	-0.01125	.0500768	-0.22	0.823	-.1106109	.0881156
Comorbidities *	0.133015	.079243	1.68	0.096	-.0242202	.2902504
Distance (<200km)	0.081085	.0654206	1.24	0.218	-.0487235	.210894
Constant ***	0.80987	.2257554	3.59	0.001	.3619222	1.257818
Number of obs= 118						
F(18, 99) = 24.89						
Prob > F = 0.0000						
R-squared = 0.8190						
Adj R-squared = 0.7861						
Root MSE = 0.2239						

Note: Significance at ***1%, **5%, and *10% significance levels

Key: **r1-**patient relocation, **r2**-death due to treatment complications, **r3**- absconding treatment

r4- Succumbing after admission,**r5**-deathe due to infection with co-mobidity

Table 4.5 indicates that all the variables used in the regression significantly fit the model well since the overall p value is less than 1% significant level. The variations in the variables contribute to overall treatment incompletion at 81.90%.In other words, incompletion is explained by 81.90% due variation in variables used in the model while 18.1% of the proportion is attributed to the error term.

Logit regression model

Table 4.6 : Regression results for Logit model

Treatment incompletion	Marginal effects	Std. Err.	z	P>z	[95% Conf.	Interval]
Age	0.0118973*	0.0067801	1.75	0.079	-0.0013914	0.0251861
Sex	0.0248176	0.0397511	0.62	0.532	-0.0530932	0.1027283
Primary education	-0.0093055	0.0747009	-0.12	0.901	-0.1557166	0.1371057
Secondary	-0.0250361	0.0611903	-0.41	0.682	-0.144967	0.0948948
Higher	-0.1694825*	0.0975054	-1.74	0.082	-0.3605896	0.0216246
Married	-0.29603	0.2015934	-1.47	0.142	-0.6911458	0.0990857
Employed	-0.0857649	0.0543718	-1.58	0.115	-0.1923317	0.020802
Drug regimen	0.0992934	0.0806201	1.23	0.218	-0.0587192	0.2573059
Treatment duration	-0.0246309***	0.0060531	-4.07	0.000	-0.0364947	-0.012767
System deficiencies	-0.1111152	0.0987472	-1.13	0.260	-0.3046562	0.0824257
Comorbidities	0.0252269	0.048225	0.52	0.601	-0.0692924	0.1197461
Distance	0.0002349	0.0002089	1.12	0.261	-0.0001745	0.0006444
Logistic regression Number of obs= 119 LR chi2(12) = 132.19 Prob > chi2 = 0.0000 Log likelihood = -11.164905 Pseudo R2 = 0.8555						

Table 4.7: Comparison of the significant variables in the two models.

LPM model

Treatment incompletion	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
Age	0.0135623***	0.0037803	3.59	0.001	0.0060674	0.0210572
Sex	0.0521835	0.0557709	0.94	0.352	-0.0583878	0.1627548
Primary education	0.0866369	0.0888389	0.98	0.332	-0.0894948	0.2627686
Secondary education	0.0598091	0.0864852	0.69	0.491	-0.1116563	0.2312745
Higher education	-0.0873946	0.0941178	-0.93	0.355	-0.2739922	0.099203
Married	-0.2244113***	0.083032	-2.70	0.008	-0.3890303	-0.0597924
Employed	-0.0045151	0.064988	-0.07	0.945	-0.13336	0.1243299
Drug regimen	0.1572979***	0.0508327	3.09	0.003	0.0565171	0.2580787
Treatment duration	-0.0558646***	0.0051553	-10.84	0.000	-0.0660854	-0.0456437
System deficiencies	-0.1535256***	0.05137	-2.99	0.003	-0.2553716	-0.0516796
Comorbidities	0.1876489*	0.0922443	2.03	0.044	0.0047657	0.3705321
Distance	0.0001315	0.0001396	0.94	0.348	-0.0001452	0.0004082
_cons	0.9749883	0.2268799	4.30	0.000	0.5251768	1.4248
Number of obs= 119 F(12, 106) = 21.33						

Prob > F	=	0.0000
R-squared	=	0.7072
Adj R-squared	=	0.6740
Root MSE	=	0.274

4.7: Comparison of the co -efficiencies.

The results for logistic regression model found only three co-efficiencies significantly influencing treatment incompletion. They include; age, higher education and treatment duration while the other co-efficiencies were insignificant in determining treatment incompletion. When the data was analyzed using logit regression, the reasons for treatment incompletion indicated as r1-r4 which include patient relocation (r1), death due to treatment complication, abscondment of treatment (r3) and succumbing after admission (r4) were removed so that the data could give a statically acceptable result.

4.8: Discussion of the study results

Based on the study findings presented in table (4.5), it is clear that if all factors were kept constant, incompletion of MDR/XDR TB treatment was likely to be 82.12% .Similarly, a unit increase in age by one year, increases the probability of incompletion of MDR/XDR TB by 0.6186% holding other factors constant. This implies that an additional year of an individual makes it difficult to adhere to regular schedules of attending the clinic due to old age thus high likelihood of dropping out of the care. Marital status, especially being married reduces the incompletion of MDR/XDR TB treatment by 13.059% holding other factors constant.

Place of residence (urban residence) of a patient reduces the incompletion of MDR/XDR TB treatment by 12.417% holding other factors constant. This may be attributed to access to available health information on management and treatment of MDR/XDR TB.

A unit increase in duration of treatment by a month was shown to reduce treatment incompletion of MDR/XDR by 3.847% holding other factors constant. This implies that an extra month of treatment lowers treatment incompletion. This may be explained by the support provided for those cohorts which utilizes MDR/XDR TB care. According to WHO (2011), the current recommended period or duration for proper treatment of an MDR-XDTR-TB patient is given as a full 20 months, which comprises of combining more than four TB drugs. Studies by Toman (1979) and Rieder, (2002) ascertained that before the year 1970, the standard TB treatment

period was 18 months (1.5 Years) with not less than three drugs. Several random trials have clearly demonstrated that Rifampicin use for TB treatment has significantly reduced the treatment period to 9 months and treatment completion more achievable.

Death of patients as a result of complications associated with MDR/XDR TB significantly raises treatment incompletion at by 55.536% holding other factors constant. This was similar where failure to attend a clinic as a result of relocation. MDR/XDR TB patient relocation within and outside the country increases treatment incompletion by 54.0069% holding other factors constant

The study also revealed that when a patient succumbs after admission to treat co- morbidities, treatment incompletion significantly rises by 45.04716 % holding other factors constant. Lastly, distance to MDR/XDR TB clinic revealed that it reduces treatment incompletion by 0.02223% holding other factors constant. However, it should be noted that this effect is not significant.

CHAPTER FIVE

SUMMARY, CONCLUSIONS AND POLICY RECOMMENDATIONS

5.1 Introduction

This chapter captures the summary of the study findings relating to the set objectives and the literature therein. Substantive conclusions based on the discussed emerging challenges of managing multi drug- resistant and extensively drug- resistant tuberculosis at Kenyatta National Hospital formed the key recommendations and suggestions for further discussion and consideration.

5.2 Summary and Conclusions of the study findings

The study reviewed theoretical and empirical literature to establish the key factors behind emerging challenges in the treatment and management of Multi Drug- Resistant and Extensively Drug- Resistant Tuberculosis at the Kenyatta National Hospital. From the literature, there is continued spread of MDR/XDR TB associated with failure to complete TB treatment. Based on this, the study identified factors behind management challenges of multi drug- resistant and extensively drug- resistant tuberculosis at Kenyatta National Hospital.

The study made use of secondary data obtained from TB and MDR/XDR specialized clinic records at Kenyatta National Teaching and Referral Hospital which contains factors associated with management of multi drug- resistant and extensively drug- resistant tuberculosis. Specifically, the study sought to determine the demographic and socio-economic factors challenging the outcomes of management MDR/XDR TB patients at KNH, assess the common system deficiencies which affect the outcomes of management of MDR and XDR TB at KNH, and relate the treatment regimen and treatment duration on the treatment and outcomes of the management of MDR /XDR TB at KNH. The hypotheses were tested at 1%, 5% and 10% significance levels. The Linear Probability Model (LPM) was used in estimation. The dependent variable used was MDR/XDR TB treatment incompletion outcomes while the independent variables used include: age, sex, education levels of patient, marital status, residence, employment status, drug regimen, treatment duration, system deficiencies, distance and TB-HIV/AIDS co-infection management challenge. The study findings revealed age, being married, residence, treatment duration, distance, comorbidities and reported reasons such as relocation of

patients, death of patients due to treatment complications, absconding of treatment attendance and succumbing of patients after admission as significant determinants of treatment and management of multi drug- resistant and extensively drug- resistant tuberculosis.

Being married, residence and distance to MDR/XDR TB clinic reduces treatment incompletion while comorbidities and factors such as relocation of patients, death of patients due to treatment complications, absconding of treatment and succumbing of patients after admission positively and statistically increased treatment incompletion implying poor management of MDR/XDR TB at Kenyatta National Hospital. In conclusion, to control management of MDR/XDR TB, there is need to consider the study findings obtained and indicated to be statistically significant.

5.3. Policy Recommendations

Kenya has been committed to manage MDR/XDR TB cases through establishment of the Division of Leprosy Tuberculosis and Lung Disease (DLTLD) in partnership with Tuberculosis Central Reference Laboratory (CRL). This institution is tasked with carrying out TB and drug resistant TB surveillance and control while assisting in setting policies, guidelines and strategies in the control, prevention, diagnosis and management of TB. In order to improve on policies which manage MDR/XDR TB cases, there is need to consider age, being married, place of residence, treatment duration, distance, comorbidities, and various reasons revealed.

Considering the study result, there is need to give proper and immediate attention to people in the older age group since a unit increase in age by one year was shown to increase chances of treatment incompletion. This could involve mapping out patients in particular age groups and taking MDR/XDR TB care closer to them. To maintain treatment completion and reduce incompletion there is need to consider individuals who are not married. This could be done through sensitization campaigns. The health specialists should follow up on MDR/XDR TB patients to ensure they complete their treatment schedule and that the drugs are taken as prescribed. This is because the study results revealed disappearance and relocation of MDR/XDR TB patients as contributing to treatment incompletion.

Similarly, there is need to access rural areas frequently and carry out free medical camps so as to manage the unreported cases of MDR/XDR TB cases in such areas. Also comorbidities need to be tackled by development of new vaccines and other morefficacious medicines which can be

used together with the MDR/XDR TB drugs to reduce the treatment incompletion among patients. The MDR/XDR- TB clinic needs to provide sufficient evidence for proper recommendation of preventive measures of MDR and XDR-TB contacts in the public as well as in homes and the sufficiency of these preventive measures.

The government should focus on rapid identification programmes of patients with MDR/XDRTB using the available technologies and also invest in developing new technologies to enhance diagnostics which match the developments in therapeutics or prevention. This is because the increased cases of patients succumbing upon being admitted for treatment of co-morbidities raised the likelihood of not completing treatment. There is an urgent need for development of rapid tests for early diagnosis and availability of appropriate treatment in order to improve the treatment of MDR/XDR-TB. The government, non-governmental organization, the private sector and all the stakeholder in the health sector need to put their heads together and come up with a strategy that will result in proper management and better treatment outcomes for MDRTB patients. Finally, the fact that Tuberculosis is treatable and even curable if drugs are used for sufficient periods, gives hope that with proper management, a patient can overcome TB. Importance should therefore be placed on drug adherence and on having definite confirmatory diagnosis to initiate the correct treatment

5.4. Areas of further study

The study has mainly focused on management of MDR/XDR TB treatment outcomes at Kenyatta National Hospital. Several factors have been considered as contributing to treatment incompletion. However, some other factors such as costs of obtaining services at MDR/XDR TB clinic and even the quality of care were left out yet they are more likely to contribute to increased treatment incompletion. Since the study was conducted at national referral hospital, there is a need for further study in other MDR/XDR TB clinics in the country to have clear national challenges. The small sample covered should be increased to obtain more certain results.

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APPENDIX: DATA USED

Personal number	age	sex (1= M, 2= F)	education level	marital status	residence	occupation status	drug regimen	treatment completion	duration of treatment in Months	Re for inc n tre
1	23	1	1	1	1	1	3	0	13	1
2	37	1	1	4	1	1	2	0	18	2
3	25	2	0	1	1	0	2	0	6	3
4	38	2	1	2	1	3	3	1	24	4
5	52	2	3	2	0	3	2	0	17	1
6	43	1	2	2	0	1	2	1	20	4
7	48	2	0	2	1	0	2	0	13	2
8	16	2	2	1	1	0	1	1	22	4
9	24	1	1	1	1	0	2	0	16	5
10	40	2	2	2	0	2	2	0	12	5
11	27	2	0	1	1	0	3	0	11	2
12	32	2	1	2	1	2	2	1	20	6
14	36	1	2	1	0	2	2	0	18	2
15	56	2	2	2	0	2	1	0	17	7
16	40	2	3	1	1	3	2	1	24	4
17	33	1	0	2	1	0	1	1	24	0
18	60	2	3	2	0	3	2	0	6	5
19	36	2	2	1	1	0	2	0	10	1
20	42	2	1	2	1	0	2	1	24	0
21	47	1	3	2	0	2	1	1	24	0
22	51	1	1	2	0	0	1	0	12	1
23	19	2	2	1	1	0	1	1	20	0

24	26	1	3	1	0	0	2	0	12	3
25	41	2	0	2	1	0	2	0	19	1
26	35	2	1	2	0	0	2	0	12	2
27	47	2	3	2	0	2	1	1	20	0
28	22	1	1	1	1	2	2	0	8	5
29	30	2	1	1	0	1	1	1	22	0
30	44	2	2	2	0	0	2	0	20	5
31	22	1	1	1	1	1	3	0	13	1
32	37	1	1	4	0	1	2	0	18	2
33	26	2	0	1	1	0	2	0	6	3
34	38	1	1	2	1	3	3	1	24	4
35	52	2	3	2	0	3	2	0	17	1
36	45	1	2	2	0	1	2	1	20	0
37	48	2	0	2	1	0	2	0	13	2
38	16	2	2	1	1	0	1	1	22	0
39	24	1	1	1	1	0	2	0	16	5
40	40	2	2	2	0	2	2	1	12	5
41	27	2	0	1	1	0	3	0	11	2
42	32	2	1	2	1	2	2	1	20	6
43	34	1	2	1	0	2	2	0	18	2
44	56	2	2	2	0	2	1	0	17	7
45	41	2	3	1	0	3	2	1	24	0
46	33	1	0	2	1	0	1	1	24	0
47	60	2	2	2	0	1	2	0	6	5
48	36	2	2	1	0	0	2	0	10	1
49	44	2	1	2	1	0	2	1	24	0
50	47	1	3	2	0	2	1	1	24	0
51	49	2	1	2	0	0	1	0	12	1
52	16	2	2	1	1	0	1	1	20	0
53	26	1	3	1	0	0	2	0	12	3

54	41	2	0	2	1	0	2	0	19	1
55	35	2	1	2	0	0	2	0	12	2
56	47	2	3	2	0	0	1	1	20	0
57	22	1	1	1	1	2	2	0	8	5
58	30	2	1	1	0	1	1	1	22	0
59	43	2	2	2	0	3	2	0	20	5
60	22	2	3	1	0	0	2	0	8	8
61	44	2	2	2	0	0	2	0	20	5
62	20	1	1	1	0	1	3	0	13	1
63	48	1	1	4	0	1	2	0	18	2
64	22	1	0	1	1	0	2	0	6	3
65	38	2	1	2	0	3	3	1	24	4
66	52	2	3	2	0	0	2	0	17	1
67	45	1	2	2	0	1	2	1	20	4
68	48	2	0	2	1	0	2	0		
69	16	2	2	1	1	0	1	1	22	4
70	28	1	1	1	1	0	2	0	12	5
71	40	2	2	2	0	1	2	0	12	5
72	30	2	3	1	1	0	3	0	11	2
73	32	1	1	2	1	2	2	1	20	6
74	37	1	2	1	0	1	2	0	18	2
75	54	2	2	2	0	2	1	0	17	7
76	39	2	3	1	0	2	2	1	24	4
77	33	1	0	2	0	0	1	1	24	4
78	59	2	3	2	0	2	2	0	6	5
79	36	2	2	2	0	0	2	0	10	1
80	44	2	0	2	1	0	2	1	24	0
81	43	1	3	2	0	2	1	1	24	0
82	49	2	1	2	0	0	1	0	12	1
83	18	2	2	1	1	0	1	1	20	0

84	24	1	3	1	0	0	1	0	12	8
85	41	2	0	2	1	1	1	0	16	1
86	37	2	1	2	1	0	1	0	12	2
87	47	2	3	2	0	0	1	1	20	0
88	32	1	1	1	0	2	2	0	9	5
89	30	2	1	1	0	1	1	0	12	7
90	43	1	2	2	1	0	2	0	20	5
91	23	1	3	1	0	0	2	0	8	8
92	28	2	3	1	0	1	2	0	11	8
93	44	2	2	2	0	0	2	0	13	1
94	39	1	3	4	1	2	2	0	10	1
95	43	1	1	4	0	1	2	0	18	2
96	42	1	0	1	1	0	2	0	6	3
97	48	2	2	2	0	0	2	1	24	4
98	52	2	3	2	0	1	2	0	17	1
99	45	1	2	2	0	1	2	1	20	4
100	48	2	0	2	1	0	2	0	13	2
101	16	2	2	1	1	0	1	1	22	4
102	26	1	1	1	0	0	2	0	12	5
103	40	2	2	2	0	1	2	0	12	5
104	30	2	3	1	1	0	3	0	11	2
105	32	1	1	2	0	2	2	1	20	6
106	37	1	2	3	1	1	2	0	18	2
107	54	2	2	2	0	2	1	0	17	7
108	41	2	3	1	0	2	2	1	24	0
109	28	1	0	2	0	0	1	1	24	4
110	59	2	3	2	0	1	2	0	6	5
111	34	2	2	1	0	0	2	0	10	1
112	42	2	0	2	1	0	2	1	24	0
113	43	1	3	2	0	2	1	1	24	0

114	46	2	1	2		0	1	0	12	1
115	17	2	2	1	1	0	1	1	20	0
116	24	1	3	1	0	0	2	0	12	8
117	40	2	0	2	1	1	2	0	16	1
118	32	2	1	2	1	0	2	0	12	2
119	47	2	3	2	0	1	1	1	20	0
120	30	1	1	1	0	1	2	0	9	5
121	30	2	1	1	0	1	1	0	12	8
122	43	1	2	2	0	0	2	0	20	5
123	23	1	3	1	0	0	2	0	8	8