AFRICA UNIVERSITY
(A United Methodist-Related Institution)

PREVALENCE OF RIFAMPICIN RESISTANT MYCOBACTERIUM TUBERCULOSIS FROM TUBERCULOSIS PATIENTS ATTENDED AT SALLY MUGABE CENTRAL HOSPITAL IN HARARE, ZIMBABWE: A RETROSPECTIVE STUDY.

BY

TANATSWA JEAN CHINYAMA

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF BACHELOR IN MEDICAL LABORATORY SCIENCES

2024

Abstract

Mycobacterium Tuberculosis (MTB) is among the top ten causes of mortality throughout the world. However, MTB strains that are resistant to rifampicin and other MTB drugs make this global health situation even worse by making MTB management and control a challenge as well as posing a major risk to MTB patients' survival. Rifampicin is one of the first-line drugs used against TB, therefore Rifampicin resistance is a good determinant and predictor of multidrug resistant tuberculosis. Rifampicin resistant Tuberculosis caused an estimated 160,000 deaths in 2022 globally. This laboratory-based analytical cross-sectional study aims to determine in a retrospective manner, the prevalence of Rifampicin resistant Tuberculosis in Harare Zimbabwe from January 2023 to December 2023 based on data from Sally Mugabe Central Hospital in Harare, Zimbabwe with reference to results from the National Microbiology Research Laboratory. The study population were all TB suspected patients who visited the selected health institution. Systematic random sampling method was used in this study and the sample size was 150. To analyse the variables in this study, calculation of frequencies and descriptive statistics for each variable was done. The study had 150 study participants, of whom, 51 had Rifampicin Resistant MTB. The age group that was most affected with Rifampicin resistant MTB was the 41-50 years age group, with 39.2%. No RRTB was found in paediatric patients of 0-10 years. 31.4% of the total Rifampicin resistant patients were females and 68.6% were males. Patients who resided in high density areas made up the highest percentage of RRTB cases of 78.4% of the total number of cases and 21.6% resided in low density areas. 74.5% of the total Rifampicin Resistant patients were HIV positive, 17.7% were HIV negative and the HIV status of 7.8% of them was not known. The risk factors associated with RRTB in this study were middle aged adults, males, HIV positive patients, patients with history of treatment with anti-TB drugs and residing in high density areas. This research demonstrated alarming levels of Rifampicin resistance in Harare, Zimbabwe. The strong association of Rifampicin resistance with previous treatment suggests the need for an improved monitoring of treatment to limit the emergence of drug resistant MTB strains. Therefore there is need to strengthen continuous drug resistance surveillance monitoring systems and the implementation of effective infection control measures in order to reduce the burden of Rifampicin Resistant TB.

Keywords: Mycobacterium Tuberculosis, Rifampicin resistance, Prevalence, Retrospective

Declaration

I, Tanatswa Jean Chinyama, do hereby declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it ever be submitted to another university for the award of a Bachelor of Science degree.

Tanatswa Jean Chinyama	 25 April 2024
Student's Full Name	**Student's Signature (Date)**

Dr Maibouge T.M.Salissou	 08 April 2024
Main Supervisor`s Full Name	**Main Supervisor`s Signature (Date)**

Copyright

Acknowledgements

I would like to acknowledge my mother, Ms Rumbidzai Beta for always being there for me throughout my academic journey, for the support, encouragement and prayers and for funding my degree and project. I want to acknowledge my supervisor Dr Maibouge, for the good advice, constructive criticism and for guiding me through every step of the way in writing this dissertation. I am also grateful to my colleagues for their encouragement and support during the course of my studies.

Above all, I give my utmost gratitude to God Almighty for His grace that has carried me this far. The journey was difficult but God made it possible.

Dedication

I dedicate this dissertation to my mother Rumbidzai Beta for always believing in me. I am very grateful for the sacrifices she made for me.

Abbreviations

TB	Tuberculosis
MTB	*Mycobacterium* Tuberculosis
MDR-TB	Multi-drug resistant tuberculosis
DR-TB	Drug resistant tuberculosis
RR-TB	Rifampicin Resistant TB
RIF	Rifampicin
INH	Isoniazid
DOTS	Direct Observation Therapy Short-course

Table of Contents

List of Tables

List of Figures

List of Appendices

CHAPTER 1: INTRODUCTION

1.0 Introduction

Tuberculosis (TB) is a communicable airborne chronic disease that is caused by an infectious acid fast bacterial agent known as Mycobacterium tuberculosis (MTB). According to the Global tuberculosis control (2003), it is estimated that about a third of the world's population is latently infected with MTB and that TB is among the top ten causes of mortality throughout the world. Multi drug resistant TB refers to TB bacteria that is resistant to at least rifampicin (RIF) and isoniazid (INH), the two most important and most common anti-TB drugs. MTB resistance to anti-TB drugs can be either primary or acquired. Primary drug resistance to MTB is a resistance that is observed among patients with no prior exposure to anti-TB drugs. Acquired drug resistance is a resistance observed among previously treated TB patients (Chegou, Hoek , Kriel , Warren, & Victor, 2011). Occurrence and spread of drug-resistant MTB are a challenge in the African region, specifically in sub-Saharan Africa where TB control is a challenge. This is due to poor health infrastructure, limited resources, and lack of awareness. Furthermore, data on the burden of Drug resistant MTB from Africa is limited due to lack of laboratory facilities, poor reporting procedures, poor surveillance mechanisms and outdated database systems (Molla, Reta, & Ayene, 2022). A report by World Health Organization in 2003 highlighted that about 60,000 MDR-MTB cases which also include RRMTB occur annually in the sub-Saharan region which represents about 14% of the world's DR-MTB burden. According to the existing literature, risk factors of tuberculosis include demographic characteristics such as gender, age, place of residence, education, marital status, bad habits such as alcohol abuse, smoking and infections including diabetes mellitus, HIV, history of tuberculosis and history of anti-tuberculosis treatment are significant risk factors for DR-TB.

1.1 Background to the Study

Rifampicin is one of the most powerful anti-TB drugs used for the management of Tuberculosis. Zimbabwe like many developing countries in sub-Saharan Africa is affected with drug resistant tuberculosis. A research conducted in Zimbabwe (Timire et al., 2019) for the years 2015-2016 proved that the prevalence of MDR-TB in Zimbabwe has remained stable since the 1994 subnational survey. However, the prevalence of rifampicin mono-resistance was double that of MDR-TB. The drug resistant tuberculosis situation over the years has not been described in various regions of the country.

Development of antibiotic resistance leads to treatment failure and emergence of DR-TB. According to new research, key reasons that may be associated with the high prevalence of DR-TB in Zimbabwe include illiteracy, poverty, and inadequate monitoring and control measures ((Metcalfe et al., 2014). Consequently, this study aims to determine in a retrospective manner the Rifampicin drug resistant tuberculosis burden in Harare Zimbabwe from January 2023 to December 2023 based on secondary data generated from Sally-Mugabe Central Hospital and National Microbiology Reference Laboratory.

The findings of the study are envisioned to help in strengthening laboratory drug resistant TB surveillance, improving management of patients with Drug resistant TB and control of the disease. World Health Organization endorsed the Gene Xpert MTB/RIF assay, which is a rapid and automated molecular system that detects both *Mycobacterium* Tuberculosis DNA and Rifampicin-resistance (RR) associated mutations simultaneously.

1.2 Statement of the Problem

According to Metcalfe et al., (2014) the rate of multidrug resistant TB (MDR-TB) including Rifampicin-resistance (RR) in Zimbabwe keeps increasing over the years. About 240 of every 1,000 TB patients (24%) have multidrug resistant TB which is a drastic increase from the previous formal national surveillance for drug-resistant TB in 1995 which was 8.3%. Tuberculosis evades control efforts due to numerous reasons, including the lack of timely access to quality diagnostic and treatment services for vulnerable populations, which has contributed to the spread of drug-resistant tuberculosis. Slow and insensitive diagnostic techniques make it difficult to discover drug-resistant types of the disease and cases in which the patient has a co-infection with the human immunodeficiency virus (HIV). Early identification is crucial to lower the mortality rate and stop transmission, but sensitive approaches' accessibility and impact are constrained by their complexity and infrastructural requirements. The emergence and spread of drug-resistant tuberculosis (DR-TB) is a threat, which complicates diagnosis, treatment and control of the disease. Currently, only few studies explored rifampicin resistance TB in Zimbabwe. One of which is a previous study conducted by Timire et al.,(2019) in Zimbabwe where the prevalence of RR-TB was 4.0% (95% CI, 2.9, 5.4%),where n=42/1043 and 14.2% (95% CI, 8.9, 21.1%;) where n=20/141 among new and retreatment patients, respectively. Hence there is need to update the gap of knowledge with regards to RR-TB prevalence and risk factors in Harare, Sally Mugabe hospital site where more TB cases are still reported in these recent years.

Justification of the study

The findings of this study can provide useful insights to health policy makers to come up with appropriate interventions to reduce the subsequent complications from this disease.

1.3 Research Objectives

- The main objective of this study is to determine the prevalence of RR MTB and associated factors among presumptive pulmonary tuberculosis cases with reference to data from National Microbiology Reference Laboratory and Sally Mugabe Central Hospital laboratory from January 2023 to December 2023.

- To determine risk factors associated with RR MTB among tuberculosis cases from Sally Mugabe Central Hospital and National Microbiology Reference Laboratory Harare, Zimbabwe within the period January 2023 to December 2023.

- To determine the correlation between various factors affecting the prevalence of RRTB at Sally Mugabe Central Hospital with reference to National Microbiology Reference Laboratory from January 2023 to December 2023

- To come up with possible solutions with regards to the data collected in reducing prevalence of RRTB from January to December 2023 at Sally Mugabe Central Hospital and National Microbiology Reference Laboratory.

1.4 Research Questions

- What are the risk factors associated with Rifampicin resistant TB at Sally Mugabe Central Hospital with reference to the National Microbiology Reference Laboratory from January to December 2023?
- What was the prevalence of Rifampicin resistant TB during that specific period and how could it be reduced?
- What was the socio-demographic profile of the TB patients admitted at Sally Mugabe Central Hospital during the period January 2023 to December 2023?

1.5 Significance of the Study

According to the World Health Organization (2021) antimicrobial resistance is a serious issue for public health and is responsible for quite a significant number of deaths globally. Similarly, tuberculosis (TB) strains that are resistant to first and second-line TB medications pose a significant challenge for patients, healthcare professionals, and healthcare systems. Therefore studying the prevalence of drug resistant TB can help us know how big of a problem we are up against.

1.5 Delimitation of the Study

This study includes a large enough sample size and is believed to give representative and updated information on the prevalence of RR-MTB to the regional and national governments.

However, it has its own limitations, there can be lack of important information and data like contact history of RR-MTB and TB, education, residence, and types of non-sputum specimen used for TB detection, and living conditions of patients. This makes it difficult to show the associations between these factors with the outcome variables. Although the study is conducted on a specific sample size, it is limited to one region of the country. Therefore, a larger nationwide study using the Gene Xpert assay will provide a better estimate of the prevalence of Rifampicin resistant TB in the entire nation. On the other hand, this study focused more on patients from urban than from rural areas. This exposes geographical health inequities despite a similar burden of MTB between rural and urban centres as evidenced in this study and the 2014 Zimbabwe National TB prevalence survey (Chipinduro et al., 2022)

CHAPTER 2: REVIEW OF RELATED LITERATURE

2.1 Introduction

Although TB has been substantially eliminated in the Global North and accessible literature shows how this was accomplished, incidence of not just TB but also drug resistant forms of the illness continues to rise in developing countries(Shah et al., 2017). (Shringarpure et al., 2016) suggests that these trends can be attributed to a variety of factors, such as the lack of less harmful anti-TB drugs, severe side effects and protracted treatment timelines, drug stock outs, context-dependent structural, socioeconomic, cultural, and gender-based barriers to treatment adherence, and insufficient or ineffective patient and community education about the illness. Another previous qualitative study (A, Padayatchi, & O'Donnell 2014) reported that the association between a positive HIV-status and RR-TB could be attributed to acquire drug resistance resulting from "preferential adherence" to antiretroviral drugs at the expense of anti-TB drugs among TB co-infected patients.

However, according to (Gupta & Sharma, 2019), multi-drug resistance is man-made as a result of inadequate treatment, ineffective drugs and poor adherence. This study is true to some extent. On the other hand antibiotic resistance in MTB is not a result of a single mutation, but it is due to repeated mutations in several genetic loci. Tuberculosis drug resistance is mainly caused by mutations in genes that codes for anti-TB drug target and the mutations are primary insertions (I, Oudghiri , & EL Mzibri 2018). Acquired drug-resistant TB can be a result of deficient policies and failures in health care, wrong prescription of TB drugs or substandard drugs being used for treatment and patients' poor treatment compliance. On the other hand, primary drug-resistant TB refers to direct transmission of drug resistant *Mycobacterium* tuberculosis strains from person to person.

Covid-19 has had its own fair share in the increase in antimicrobial resistance, this also includes resistance to anti-TB drugs (Yadav, 2022). This is due to the various number of antibiotics that were prescribed to patients with Covid-19. Covid-19 in turn weakened the immune system and also affected people`s lungs leaving some defects in the lungs which may make TB bacteria to thrive in the lungs and may lead to multi-drug resistance.

Drug resistance can develop as a result of inappropriate choice of drugs, irregular drug supplies, and factors related to patients such as poor adherence to treatment and poor compliance with treatment. The WHO recommends DOTS (direct observation therapy short-course) and the Stop TB strategies to address the needs of the poor and vulnerable population. Unless individuals infected with drug-resistant MTB are treated appropriately, they will continue disseminating drug resistant MTB in the community and accelerate the epidemics.

Drug resistant TB can result when the drugs that are used to treat TB are misused or mismanaged. Examples of misuse or mismanagement of drugs include people not completing a full course of TB treatment, health care providers prescribing the wrong treatment (the wrong dose or length of time), drugs for proper treatment are not available and drugs being of poor quality. Drug-resistant TB is more common in people who do not take their TB drugs regularly as well as people who develop TB again, after being treated for TB disease in the past.

The most important way to prevent the spread of drug-resistant TB is to take all TB drugs exactly as prescribed by the health care provider. No doses should be missed and treatment should not be stopped prematurely. People receiving treatment for TB disease should inform their health care provider if they are having trouble taking their medications.

Health care providers can help prevent drug-resistant TB by quickly diagnosing cases, following recommended treatment guidelines, monitoring patients' response to treatment, and making sure therapy is completed. Another way to prevent getting drug-resistant TB is to avoid

exposure to known drug-resistant TB patients in closed or congested places such as hospitals, prisons, or homeless shelters. People who work in hospitals or health-care settings where TB patients are likely to be receiving attention should constantly consult infection control or occupational health experts.

Empirical TB treatment without drug susceptibility testing (DST), which is a common practice in many developing countries, is believed to increase the day to day risk of transmission of drug resistant strains(Gupta & Sharma, 2019). Therefore, routine testing of all patients with TB is widely recognized as the most appropriate surveillance approach for monitoring trends in drug resistant TB.

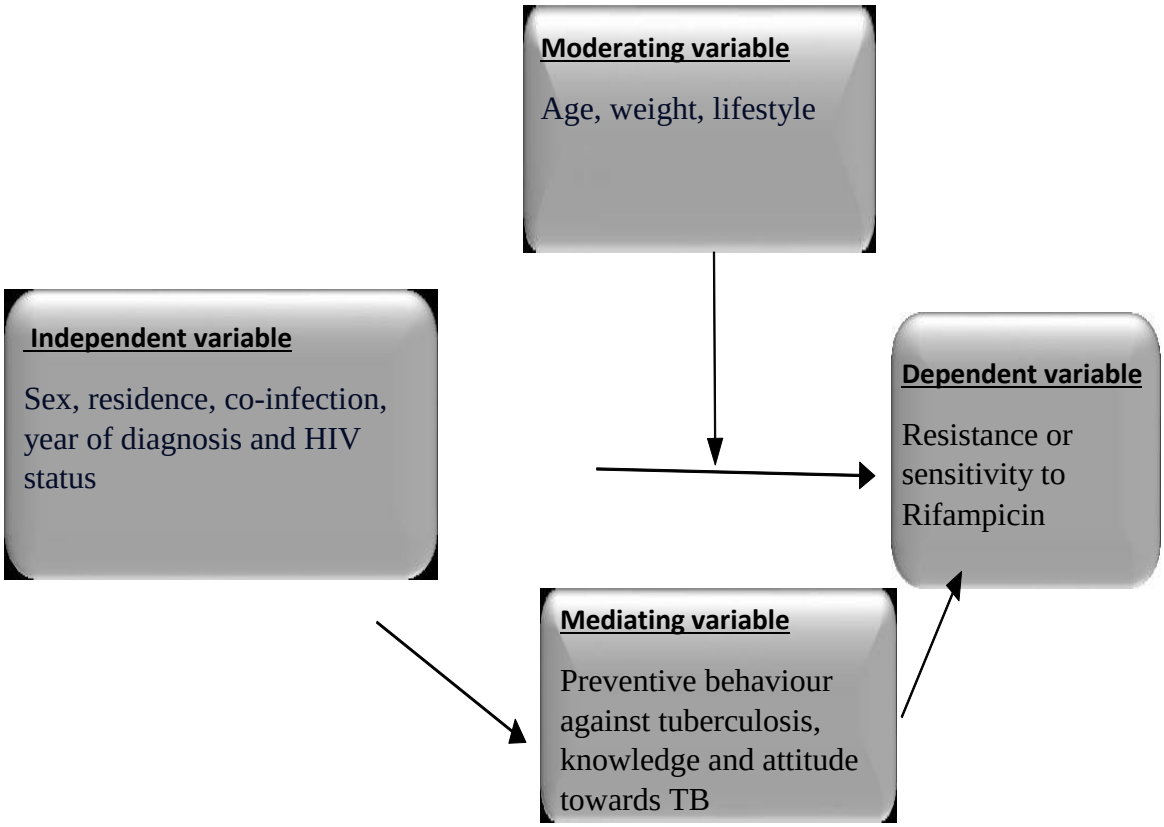

Fig 2.1 Conceptual framework

2.2 Relevance of the Theoretical/ Conceptual Framework to the Study

This shows how the variables are related to each other. In this study, the independent variables are the factors that are associated with the prevalence of Rifampicin resistant TB and the dependent variable is the prevalence of Rifampicin resistant TB. Control variable in this case is the course and dosage of the drugs. Mediating variable is the frequency of occurrence of Rifampicin resistant TB. Moderating variable in this case is the diagnosis of TB. This gives us a clear picture and assessment of how these different factors affect the prevalence and arise of Rifampicin resistant TB as well as assessing which factors are the leading causes to Rifampicin resistant TB.

2.3 Summary

There are many factors that lead to arise and prevalence of Rifampicin resistant TB. Rifampicin resistant TB can arise as a result of gene mutation, misuse and mismanagement of drugs, poor adherence to treatment and poor compliance with treatment. There are other indirect factors that can lead to multi-drug resistant TB, for example Covid-19. Patients should take all drugs as they are prescribed.

CHAPTER 3: METHODOLOGY

3.1 Introduction

Results of persons suspected of having drug-resistant pulmonary TB flagged on the Gene Xpert assay at Sally Mugabe Central Hospital which were then sent to the National Microbiology Reference Laboratory for confirmatory testing are compiled and collected. For logistical reasons, not all polyclinics in Harare could be included. Retrospective study design for collection of data from the archives of laboratory records is used in this research.

Study variables

Dependent variables: Rifampicin resistant MTB;

Independent variables: Factors that could be associated with the prevalence of RRMTB, such as area of residence, history of cigarette smoking, history of treatment with the anti-TB drugs, average monthly income, and history of imprisonment (for patients who were or are in prison), co-morbidities such as HIV, Hepatitis and Diabetes were all considered under the independent variables.

3.2 The Research Design

A Retrospective cross-sectional study design will be used to collect secondary data from January 2023 to December 2023 at Sally Mugabe Central Hospital laboratory and the National Microbiology Reference Laboratory. The study populations are all TB suspected paediatric and adult patients who visited the selected health institution from January 2023 to December 2023. A laboratory-based retrospective analytical cross-sectional study will be used. This is because the patients will not be followed over time but rather, the prevalence is analysed at one moment

in time in a retrospective manner from January to December 2023. Sociodemographic data including age, sex, and residency; low or high density are very crucial in this research and can be accessed from archival data provided by Sally Mugabe Central Hospital Laboratory and the National Microbiology Reference Laboratory records. Logistic regression models can be used to determine the risk factors where a p-value less than 0.05 will be taken as a cut off point.

3.3. Study population

Source population includes all patients suspected of having drug-resistant TB. The study population includes all patients with a history of more than one month of prior treatment (relapse, treatment after default, or treatment failure), or contact with a person with known or suspected drug-resistant TB in Harare during the study period. All persons who previously had smear-positive sputum samples between month 3 and month 5 of anti-TB treatment were enrolled in the study and fulfil the eligibility criteria were also enrolled. Those with suspected drug-resistant TB were defined as persons with persistent cough, fever, night sweats weight loss and either one while under treatment. Furthermore, these persons tested positive for Gene Xpert at Sally Mugabe Central Hospital Laboratory.

3.4 Inclusion Criteria

Patients who were suspected of TB and whose sputum samples were sent to the Sally Mugabe Central Hospital laboratory, based on their clinical presentation were included in the study. Both male and female patients were included in the study.

3.5 Exclusion criteria

Patients' records that had incomplete data, e.g., full name, age, gender, sample type, and TB treatment history were excluded from the study. TB suspected patients who were unable to give sputum samples and complete information initially were excluded from the study.

3.6 Sample size determination

The sample size was determined using a single population proportion formula by taking the prevalence of Rifampicin resistant TB among presumptive TB patients reported from Sally Mugabe Central Hospital with reference to the National Microbiology Reference Laboratory. Margin of error, confidence level and nonresponse rate are determined accordingly in order to determine the sample size. Factors such as treatment history with anti-TB drugs and failure to follow-up are considered to obtain the maximum sample size. The sample size is calculated using Cochran equation;

Where:

N = Minimum sample size;

Z = Constant, standard normal deviation (1.96 for 95% confidence interval);

P = Population proportion with characteristic of interest.

According to the study conducted by (Adhikary , Sinha, Phukan, Debnandi, & Das, 2022) in India the prevalence was 11% therefore we took P= 0.11

For example given that population proportion P is 0.11 from previous studies by Adhikary et al (2022)

Q = 1-P;=1-0.11 = 89

d= Acceptable margin of error;

Z =1, 96, P =0.11, Q= 0.89, d =0.05;

$n=z^2p(1-p)/e^2$

n =150

3.7 Sampling Procedure

Sample collection was done by employing a convenient sampling technique. The most suitable sampling technique is Systematic Random sampling. This technique minimises errors, bias as well as providing a better representation of the population of study. After the samples are collected, these samples can be divided into various age groups and studying the subjects in groups rather than studying all of the subjects at once.

3.8 Data Collection

3.8.1 Instrument

Data is collected from the Sally Mugabe Central Hospital microbiology department and the National Microbiology Reference Laboratory. The raw data will be entered into an excel spreadsheet. Information regarding patient's age, gender and associated factors will be extracted from the patient records at Sally Mugabe Central Hospital Laboratory. No names will be used in this study. The collected data from patients were assigned unique identification for differentiation of patients.

3.8.2 Procedure

Raw data is collected from Sally Mugabe Central Hospital laboratory and the National Microbiology Reference Laboratory records for the period January 2023 to December 2023. The data is then compiled and analysed to come up with a conclusive prevalence of Rifampicin resistant Mycobacterium Tuberculosis from Tuberculosis patients attended at Sally Mugabe

Central Hospital with reference to National Microbiology Reference Laboratory in Harare, Zimbabwe.

3.9 Pilot Study

The pretesting of the data collection form and method was done prior to data collection and after approval of research proposal by AUREC (Africa University Research Committee). The data used for pre-testing was taken from the Sally Mugabe Central Hospital microbiology and the National Microbiology Reference Laboratory records of September to November 2022.

3.10 Analysis and Organization of Data

Descriptive statistics is done for the calculation of frequencies of each variable. All the variables; age, sex, previous TB treatment history, HIV status are included in this study as these are traditional/known risk factors of drug resistance TB and included in the regression model irrespective of their value.

3.11 Ethical Consideration

AUREC (Africa University Research Committee) provides an ethical approval letter which assists in obtaining the clearance from the Sally Mugabe Central Hospital Medical Superintended to conduct my research study at the hospital and the National Microbiology Reference Laboratory located at Sally Mugabe Central Hospital as well. The information which was obtained in this study was kept private and confidential as well as using it for research purpose only

3.12 Summary

Drug-resistant MTB can be controlled by identifying and effectively treating sputum smear-positive cases. Drug susceptibility testing should always be carried out in order to determine how efficient a drug is against a disease, infection or virus, in this case specifically against TB.

A national drug-resistance survey is recommended to determine RRTB prevalence in Zimbabwe

CHAPTER 4: DATA PRESENTATION, ANALYSIS AND INTERPRETATION

4.1 Introduction

This chapter covers the analysis of data collected during this research study and presented in the form of tables and graphs where necessary. The raw data compiled was presented in a format that displayed the prevalence of RRMTB as well as the factors associated with the prevalence of Rifampicin resistant MTB and establish the correlation between various factors affecting the prevalence of RRTB.

4.2 Socio-demographic characteristics of study population

A total of 150 TB patients meeting the inclusion criteria were enrolled in this retrospective study. The age group that was largely affected was the 41-50 age group with 28.7%. The least affected age group was the 81- 90 age group with only 1.3%. The sample was predominantly male, accounting for 81 samples, which is (54%) while females constituted 69 samples, being (46 %). Patients who resided in high density areas made up the highest percentage of MTB cases, making up 79.3% of the total number of cases whereas those who resided in low density areas made up 20.7% of the cases. From the research findings those who resided in high density areas were more vulnerable to TB as compared to patients who resided in the low density areas. There were 67(44.7%) new MTB cases with no previous MTB treatment history. Of the total 150 patients, those with known HIV status were 107 (71.3%) and 43(28.7%) had an unknown HIV status. 74 of the 107 (69.2%) with the known HIV status were positive and 33 of the 107 (30.8%) were HIV negative. Of all the 150 participants, 74(49.3%) were HIV positive, 33(22%) were HIV negative and the HIV status of 43(28.7%) was unknown.

Table 1: Socio demographic factors of all study participants (n=150)

Characteristic	**Frequency n(%)**
Age(year)	
0-10	3(2)
11-20	9(6)
21-30	28(18.7)
31-40	33(22)
41-50	43(28.7)
51-60	16(10.7)
61-70	11(7.3)
71-80	5(3.3)
81-90	2(1.3)
Gender	
Male	81(54)
Female	69(46)
Area of Residence	
Low Density Areas	31(20.7)
High Density Areas	119(79.3)
History of treatment with Anti-TB drugs	
Previous treatment	83(55.3)
No previous treatment	67(44.7)
HIV Status	
Positive	74(49.3)
Negative	33(22)
Unknown	43(28.7)

Note: Data are n (%), unless otherwise stated.

4.3 Prevalence of Rifampicin Resistant MTB and socio-demographic characteristics of RRMTB patients

Out of 150 suspect TB cases that submitted their samples for testing at Sally Mugabe Central Hospital Laboratory, 51 cases were found to have Rifampicin resistant MTB hence giving a prevalence of 51 / 150 (34%) 95% Cl (Confidence level). Their socio-demographic data is summarised in table 2 below

Table 2: Sociodemographic factors of patients with RRMTB (n=51)

Characteristic	Frequency n(%)
Age	
0-10	0(0)
11-20	1(2)
21-30	7(13.7)
31-40	11(21.6)
41-50	20(39.2)
51-60	8(15.7)
61-70	1(2)
71-80	2(3.9)
81-90	1(2)
Gender	
Male	35(68.6)
Female	16(31.4)
Area of Residence	
Low Density areas	11(21.6)
High Density areas	40(78.4)
History of treatment with Anti-TB drugs	
Previous treatment	37(72.5)
No previous treatment	14(27.5)
HIV status	
Positive	38(74.5)
Negative	9(17.7)
Unknown	4(7.8)

Note: Data are n (%), unless otherwise stated.

Table 2 shows of 51 of the total 150 study participants and these 51 had Rifampicin resistant MTB, making up 34% of the total study participants. This is comparably similar to the study conducted in Somalia with a RRTB prevalence of 35% (Ali, Weldegebreal, Kabew, & Urgesa, 2023), However this is much higher compared to a study in Zimbabwe in 2019 with prevalence of RRTB being 4% (Timire et al., 2019). The high prevalence obtained in this study may be due to the different study settings.

Table 2 highlights that in this study the age group that was mostly affected with RRTB was the 41-50 years with 39.2% and there was no RRTB in the age group 0-10 years. Patients with RRTB who were females were 16 from the total of 51 with a percentage of 31.4%. Similar to MTB, males were affected the most with RRTB as well in the year 2023, having 35 males which accounts for 68.6% of the total 51 RRTB participants. This table also highlights how patients who resided in high density areas made up the highest percentage of RRTB cases, making up 78.4% of the total number of cases whereas those who resided in low density areas made up 21.6% of the cases. From the research findings those who resided in high density areas were more vulnerable to TB as compared to patients who resided in the low density areas. Of all the 51 RRTB cases, 38(74.5%) were HIV positive, 9(17.7%) were HIV negative and the HIV status of 4(7.8%) was not known.

4.4 Prevalence of Rifampicin resistant TB by Age

Figure 2 above illustrates prevalence of both MTB AND RRTB by age. The study drew a sample of 150 patients from the records of the total population diagnosed with MTB at Sally Mugabe Central Hospital in 2023. Figure 2, was constructed to assess the prevalence with respect to age groups of ten year intervals. In the sampled data, patient with the lowest age was 6 months and the oldest was aged 86. Moreover, the age group that was most affected with Rifampicin resistant TB was 41-50 and was also most affected with MTB in general. From the

sample, in the 0-10 year's age group there was no patient with Rifampicin resistant MTB, however age groups 11-20, 61-70 and 81-90 years had the lowest prevalence of 2%. From the Figures above, it is evident that RRTB mostly developed in the middle ages adults.

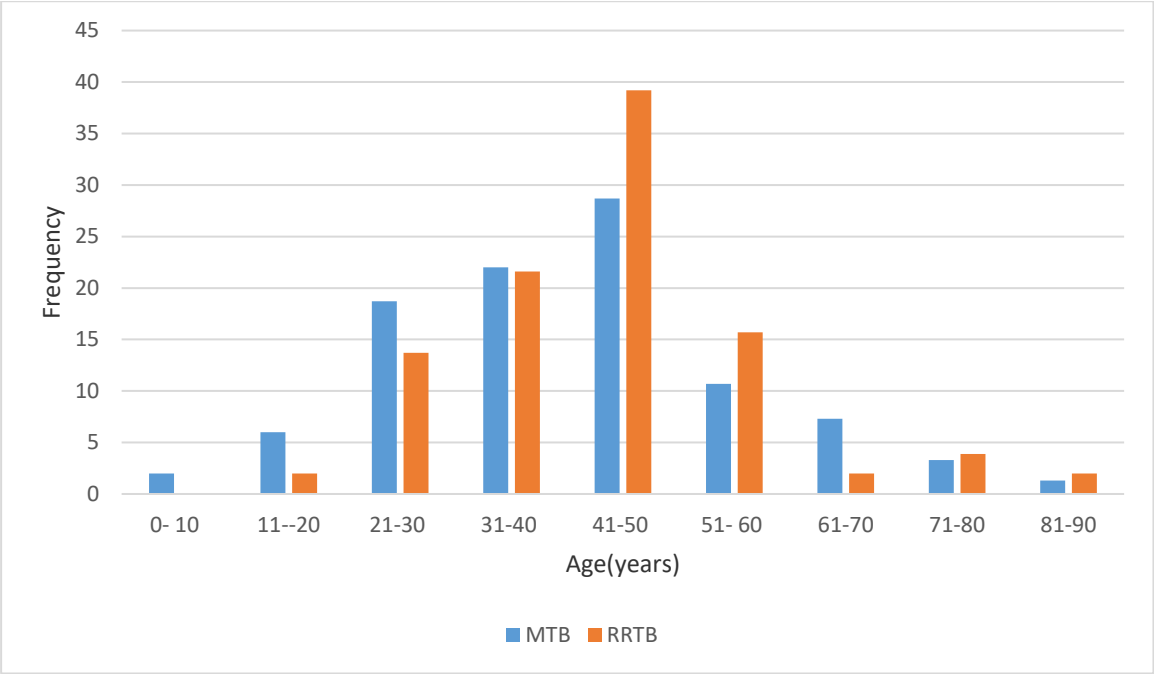

Figure 4.1: Prevalence of RRTB by Age

4.5 Risk factors for RRMTB

Age

Out of all the 150 participants in this study, the total number of participants who were 40 years and below was 73(48.7%) and those who were above 40 years was 77(51.3%). The results of this study proved that, out of the 51 participants who had RRMTB, 19(37.3%) were 40 years and below and 32(62.7%) participants were above 40 years of age. Therefore, according to this study, those who were more than 40 years were more at risk that those who were less than 40

years of age. However some studies (Sah, et al., 2020) did not find age to be a risk factor of RRMTB.

Gender

There were a total of 81(54%) males and 69(46%) females in this study. Out of the 51 participants with RRTB, 35(68.6%) males had RRTB and 16(31.4%) females had RRTB. From the findings of this study, more males proved to harbour RRMTB than females, therefore being a male is a risk factor of RRMTB. However there were more males than females in the study as well.

Area of Residence

Out of the 51 participants with RRMTB, 11(21.6%) resided in low density areas and 40(78.4%) resided in high density areas. Participants who resided in high density areas proved to be more at risk of RRMTB than those who reside in low density areas.

History of treatment with anti-TB drugs

History of treatment with anti-TB drugs has proved to be a risk factor for RRMTB in most prior studies. Findings from a study in Zimbabwe (Timire , et al., 2019) found history of treatment with anti-TB drugs to be a risk factor for RRMTB. Similarly, in this study, 37 out of 51(72.5%) RRMTB participants had previous treatment with anti-TB drugs and 14(27.5%) had no history of treatment with anti-TB drugs. Therefore this proves that having a history of treatment with anti-TB drugs is a risk factor of RRMTB.

HIV status

Quite a significant number of prior studies have found HIV positive status to be a risk factor for RRMTB. A study by Chipinduro, et al., (2022) and another one by Timire , et al., (2019) found HIV positive status to be a risk factor for RRMTB. Out of the 51 participants with

RRMTB in this study, 38(74.5%) were HIV positive, 9(17.7%) were HIV negative and 4(7.8%) had an unknown HIV status. Out the 99 participants with no RRMTB, 36(36.4%) were HIV positive, 24(24.2%) were HIV negative and 39(39.4%) had an unknown HIV status. From the findings of this study, the majority of the participants found with RRMTB were HIV positive and this proves that HIV co-infection with TB is a risk factor for RRMTB (Table3).

Table 3: Risk factors for RRMTB

Variables	RRTB	No RRTB	Total
Age			
≤ 40 Years	19(37.3)	54(54.5)	73(48.7)
>40 Years	32(62.7)	45(45.5)	77(51.3)
Gender			
Male	35(68.6)	46(46.5)	81(54)
Female	16(31.4)	53(53.5)	69(46)
Area of Residence			
Low Density areas	11(21.6)	20(20.2)	31(20.7)
High Density areas	40(78.4)	79(79.8)	119(79.3)
Treatment with Anti-TB drugs			
Previous treatment	37(72.5)	46(46.5)	83(55.3)
No previous treatment	14(27.5)	53(53.5)	67(44.7)
HIV status			
Positive	38(74.5)	36(36,4)	74(49.3)
Negative	9(17.7)	24(24.2)	33(22)
Unknown	4(7.8)	39(39.4)	43(28.7)

4.5 Summary

The chapter examined the research findings of the study. The data was depicted in the form of tables as well as graphs where applicable. Furthermore, a brief explanation or description accompanied every figure and table. The chapter explored the demographic information of the

research participants such as their age and the prevalence rate of Rifampicin resistant MTB from the total MTB patients. Most patients affected by both MTB and RRMTB were male patients and patients of ages 41-50. This chapter also provides an insight of MTB and HIV coinfection and other risk factors.

CHAPTER 5: ONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter summarises the research findings in chapter 4 as well as identifying the gaps in the information. Comparison and contrasting will be made with particular attention to literature review in relation with the research objectives of the study. This chapter also comprises of delimitations, limitations, conclusion and recommendations.

5.2 Discussion

5.2.1 Sociodemographic factors associated with Rifampicin resistant MTB

The study research had a total of 150 laboratory records and results of the MTB patients that attended Sally Mugabe Central Hospital from January 2023 to December in 2023. Socio-demographic determinants such as age, sex, place of residence of the patient, anti-TB treatment history and HIV status of the patient were all assessed for association with the prevalence of RR-TB. Rifampicin resistance is a surrogate marker of Multi-drug resistant MTB (Tembo & Malangu, 2019), therefore should be taken seriously. According to Table 1, MTB was found in all age groups from 0-90 years. With reference to table 2, this study's findings denoted that RRTB was more common in middle aged people of ages 21-60 years making up a percentage of 94% of the total RRTB cases. In this study, men were more affected with RRTB than women. This may be attributed to smoking, alcoholism, strenuous work load, higher exposure of men to outer environment, dusty environments, as well as environments with a lot of smoke and cement. Males also have a wider range of mobility to acquire the TB bacilli as compared to females. This finding, where men are more affect with RRTB may also be due to social and health seeking behaviour difference between men and women, men tend to not seek medical help until it gets serious.

In this study HIV was a major contributor to the prevalence of RRTB. Most patients with RRTB had HIV as well. Patients with coinfection of TB and HIV have a higher chance of acquiring RRTB because of the different medication regimen that may lead to resistance. Drug-Drug interactions may eventually lead to resistance. This may also arise because of a vulnerable and weakened immune system so much that if they come in contact with someone with RRTB, it is very easy for them to acquire it as well.

The World Health Organization (2016) estimates that 3.9% of previously untreated and 21% of previously treated TB cases occurring worldwide in 2015 had MDR/RR-TB (Dennis , Holger , Schünemann, & Harausz, 2016). In this study, the results from table 2 also reflect that previously treated TB patients were more likely to harbour RR-TB than those with no history of treatment with anti-TB drugs, new cases. Previously treated TB case was defined as a patient who had previously taken TB treatment for more than 1 month and included relapses, treatment failure, and treatment after default. The higher prevalence in previously treated patients might be due to treatment failure, non-adherence to anti-Tuberculosis treatment and contact with drug resistant TB patients. This finding may be related to unsatisfactory compliance by patients or clinicians, lack of treatment supervision, improper drug regimens and inadequate or irregular drug supply that make the bacteria to mutate and develop drug resistance. Inadequate treatment regimen prescribed by health staff, poor patient adherence, previous history of exposure to anti-TB drugs were common factors for the prevalence of TB drug resistance. The relative high prevalence of Rifampicin-resistant MTB in our study could also be due to the use of Rifampicin to treat other conditions. Moreover, Rifampicin has several adverse effects which could result in patient non-adherence and hence may lead to the selection of resistant strains.

According to the results in Table 2, patients who resided in high density residential areas were more affected by RRTB as well as MTB, than those who resided in low density residential areas. This may be due to the dusty roads in high density areas and high exposure to dusty environments everyday increases the grip of MTB in the body. Generally, these high density residents are the ones that mostly work in the industries with smoke and for builders inhaling dust from cement every day creates breeding ground for MTB as well as RRTB. RRTB can be easily spread in high density areas because of poor living conditions, poor ventilation and houses being too close to each other. However, Sally Mugabe Central Hospital is a government institution meaning healthcare is cheaper than at most private health institutions; therefore the majority of the patients at Sally Mugabe Central Hospital are presumed to be high density residents.

Another study (Sah et al., 2020) confirmed no association of RR-TB with age, sex, geographical diversity and previous history of treatment failure. However in this study, at Sally Mugabe Central hospital and the National Microbiology Reference Laboratory, the socio-demographic risk factors associated with RRTB were middle aged adults, males, HIV positive patients, patients with history of treatment with anti-TB drugs and residing in high density areas.

RRTB was not prevalent in paediatric patients. RR-MTB was more prevalent among adult TB patients. This could be attributed to lack of adherence to therapy by adult patients. Younger patients of age group 11-20 had a very low prevalence of RR-TB of 2 % as this age group can be easily monitored for treatment therapy adherence by parents or guardians as well and the same goes for older patients. Age group 41-50 had the highest prevalence of RR-TB. The second highest prevalence was in the 31-40 age group, followed by 51-60 years. These are commonly the most productive age groups and age groups that are involved a lot of manual labour

especially for men. These are also the very same industry workers especially in urban set-up, specifically the high density residents. However, a study by Lomtadze, Aspindzelashvili et.el (2009) did not find any significant association between the development of RR-TB and age. These conflicting results shows that there is no well-established association between age and the prevalence of MDR-TB because of different lifestyles in different regions of different countries and also because different studies used different age group cut-off points compared to this study which compared a wide range of age groups from 0-90 years.

5.3 Limitations

This study had its own limitations. Firstly, the study was conducted retrospectively and some of the data was found to be missing including patients characteristics such as age, sex, HIV status, Hepatitis status, Diabetes status and drug susceptibility testing results due to poor documentation. The other limitation is that the current data were only collected from MTB patients' data that met the inclusion criteria and so may not reflect all MTB and RRTB cases in Harare, Zimbabwe. Factors associated with the prevalence of RR-TB were limited only to age, sex, HIV status, previous anti-TB treatment and urban dwellers. Despite these limitations, the study has provided useful information with regards the current burden and the factors associated with the prevalence RRTB which can be used for better planning of TB management in the country.

5.4 Conclusion

The sample size was chosen at random hence it was unbiased. Bias in the sample can lead to misleading conclusions of type 1 or type 2 errors. Therefore, it suffices to remark that the

sample was a fair representative of the total population characteristics. This study has revealed important information on the current prevalence and factors associated with the prevalence of RR-TB in Harare, Zimbabwe. Based on the results obtained, this study has demonstrated alarming levels of RR–TB in Harare, Zimbabwe.

5.5 Recommendations

1. Based on the data obtained, early case detection and prompt initiation of appropriate therapy is required to interrupt further transmission of Rifampicin resistant MTB
2. The Ministry of Health and Child Care should raise awareness about drug resistant strains of TB, especially Rifampicin resistant TB, what can lead to these drug-resistant strains, prevention and control, should be spread among people of all ages and all backgrounds.
3. Implementation of strategies in controlling RR-TB should emphasize on effective implementation of DOTS strategy, involving supervision and follow-up of patients taking their medication.
4. Further interventions should focus on strengthening TB infection control activities, strict adherence to therapy is required to achieve control over the disease.
5. The strong association of Rifampicin resistance with previous treatment suggests the need of an improved monitoring of treatment to limit the emergence of drug resistant MTB strains. Targeted policies for previously treated TB patients can significantly reduce the burden of the disease, prevent the development of new cases of RR-TB and to treat existing patients.

6. Furthermore, there is need to strengthen continuous drug resistance surveillance monitoring systems and the implementation of effective infection control measures in order to reduce the burden of RR-TB.

5.6 Dissemination of results

A copy of the results will be shared with Sally Mugabe Central Hospital Laboratory. Another report of this study (soft and hard copy) will be given to the Africa University College of Health, Agricultural and Natural Sciences.

References

Demelash , M., Endalkachew , N., Hailegebriel , T., Minichil , Z., & Mekonnen, D. (2023). Prevalence of rifampicin resistant pulmonary tuberculosis using. *Heliyon*.

Adhikary , M., Sinha, A., Phukan, J., Debnandi, A., & Das, S. (2022). Prevalence of rifampicin-resistant Mycobacterium tuberculosis by CBNAAT in a tertiary care hospital of West Bengal, India. *Medical Journal of Babylon,*, 362-366. doi:10.4103/MJBL.MJBL_40_22

Chaoui I, Oudghiri , A., & EL Mzibri , M. (2018). Molecular Epidemiology of Tuberculosis and Transmission Dynamics of Mycobacterium tuberculosis. *Mycobacterial Diseases*, 1-2. doi:10.4172/2161-1068.1000268

Chegou, N. N., Hoek , K. G., Kriel , M., Warren, R. M., & Victor, T. (2011). Tuberculosis assays: past, present and future. *Expert Review of Anti-infective Therapy,*. doi:10.1586/eri.11.23

Chipinduro, M., Timire , C., Chirenda , J., Matambo , R., Munemo , E., Makamure, B., . . . Sandy, C. (2022). TB prevalence in Zimbabwe: a national cross-sectional survey, 2014. *nternational Journal of Tuberculosis and Lung Disease,*.

Daftary A, Padayatchi, , N., & O'Donnell , M. (2014). Preferential adherence to antiretroviral therapy over tuberculosis treatment: a qualitative study of drug-resistant TB/HIV co-infected patients in South Africa. *Global public health*. doi:10.1080/17441692.2014.934266

Dennis , F., Holger , J., Schünemann, & Harausz, E. (2016). *World Health Organization treatment.*

Gupta, R. K., & Raju Sharma. (2019). *Imaging in Tuberculosis: Clinicopathological Correlation 1st Edition.* Jaypee Brothers Medical Pub; 1st edition.

Ismail, N., Ismail, F., Omar, S. V., Blows, L., & Gardee, Y. K. (2018). Drug resistant tuberculosis in Africa:Current status, gaps and opportunities. *African journal of laboratory medicine*. doi:10.3201/eid2001.130732

Lomtadze , N., Aspindzelashvili , R., Mirtsk, & Janjgava, M. (2009). Prevalence and risk factors for multidrug-resistant in the republic of Georgia: a population-based study.

Lubumbo, M. (2019, December 5). *Reseach Space*. Retrieved from University of Kwazulu Natal: https://researchspace.ukzn.ac.za/handle/10413/16596

Metcalfe, J., Makamure, B., Makumbirofa, S., Sandy, C., Bara, W., Mungofa, S., . . . Mátyus, P. (2014). Drug-Resistant tuberculosis in High-Risk Groups, Zimbabwe. *Emerging Infectious Diseases*. doi:https://doi.org/10.3201/eid2001.130732

Molla, K. A., Reta, M. A., & Ayene, Y. Y. (2022). Prevalence of multidrug-resistant tuberculosis in East Africa: A systematic review and meta-analysis. *National Library of Medicine*.

Sah, S. K., Pramod, R. B., Anjana, S., Dhami, ,. D., Guruwacharya, D., & Shrestha, R. (2020). Rifampicin-resistant Mycobacterium tuberculosis by GeneXpert MTB/RIF and Associated Factors Among Presumptive Pulmonary Tuberculosis Patients in Nepal,Infection and Drug Resistance. *13*. doi:10.2147/IDR.S263795

Shah, N. S., Auld, S. C., Brust, J. C., Mathema, B., Ismail, N., Moodley, P., . . . Gandhi, N. R. (2017). Transmission of Extensively Drug-Resistant Tuberculosis in South Africa. . *The New England journal of medicine, .*

Shringarpure, K., Isaakidis, P., Sagili, K. D., Baxi, R. K., Das, M., & Daftary, A. (2016). When Treatment Is More Challenging than the Disease": A Qualitative Study of MDR-TB Patient Retention. *PLOS ONE*.

Tembo, B. P., & Malangu, N. G. (2019). Prevalence and factors associated with. *BMC Infectious Diseases*.

Timire , C., Metcalfe, J., Chirenda, J., Scholten, J., Manyame-Murwira, B., Ngwenya, M., . . . Sandy, C. (2019). Prevalence of drug-resistant tuberculosis in Zimbabwe: A health facility-based cross-sectional survey. *International Journal of Infectious Diseases*. doi:10.1016/j.ijid.2019.07.021

World Health Organization. (2003). *Global tuberculosis control.* Geneva: World Health Organization.

World Health Organization. (2021). *Antimicrobial resistance.* World Health Organization.

Yadav, S. (2022). *Starting an All-Oral Longer Regimen in a Primary Multidrug-Resistant Pulmonary Tuberculosis Patient at a District TuberculosisCenter for the First Time: A Rare Case.* Cureus. doi:10.7759/cureus.27146

APPENDICES

Appendix 1: Budget

ITEM	UNIT COST ($USD)	MULTIPLYING FACTOR	TOTAL COST ($USD)
Bond Paper	5.00	1	5.00
Tones	110.00	1	110.00
Airtime	2.00	25	50.00
Transport	20.00	10	200.00
AUREC	15.00	1	15.00
Pens	0.20	3	0.60
Total			380.60

Appendix 2: Grant Chart

Task	Responsible	Nov 2023	Feb 2024	March 2024	April 2024
Study site Approval	Sally Mugabe Central Hospital				
Ethics Approval	AUREC				
Data Collection	Researcher				
Data Analysis and Presentation	Researcher				
Recommendation based on results obtained	Researcher				

Appendix 3: Data Collection Form

Patient	Age	Hepatitis	HIV	Monthly Income,	Gender	TB Status	Residency	History Of Cigarette Smoking	History of Treatment With The Anti-Tb Drug	Diabetes	Resistance/Sensitivity To Rifampicin
A											
B											
C											
D											
E											

Appendix 4: Study Site Approval Letter

Telephone: 621100-19
Fax: 621157

Reference: SMCHEC261023/91

SALLY CENTRAL MUGABE HOSPITAL
P. O. BOX ST 14
SOUTHERTON
HARARE
ZIMBABWE

ZIMBABWE

08 November 2023

Tanatswa J Chinyama
3B Sherydane Lane Strathaven
Harare

REF: PREVALENCE OF RIFAMPICIN RESISTANT AND MULTI –DRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS FROM DRUG- SENSITIVE OR MULTIDRUG –RESISTANT PULMONARY TUBERCULOSIS CASES IN HARARE, ZIMBABWE

I am glad to advise you that your application to conduct a study entitled: **PREVALENCE OF RIFAMPICIN AND MULTI- DRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS FROM DRUG – SENSITIVE OR MULTIDRUG – RESISTANT PULMONARY TUBERCULOSIS CASES IN HARARE ,ZIMBABWE (Ref: SMCHE261023/91),** has been approved by the Sally Mugabe Central Hospital Ethics Committee.

This approval is premised on the submitted protocol. Should you decide to vary your protocol in any material way please submit these for further approval.

You are advised to avail the results of your study whether positive or negative to the hospital through the committee for our information.

Yours sincerely,

HARARE CENTRAL HOSPITAL
DEPARTMENT OF MEDICINE
0 9 NOV 2023
P. O. BOX ST14, SOUTHERTON
HARARE, ZIMBABWE

DR. C. Pasi
Chairman Sally Mugabe Central Ethics Committee

Board Members, Chairman Dr E Chagonda, Deputy Chairperson Ms A Mashamba, Members:- Mr J Makiya, Mrs P Sibanda, Mr. S. Hlatywayo, Dr C. Pasi (Chief Medical Officer)

Appendix 5: Supervisor Approval Letter

Investing in Africa's Future

COLLEGE OF HEALTH, AGRICULTURE AND NATURAL SCIENCES

P.O. BOX 1320, MUTARE, ZIMBABWE Cell: (+263) 780079459 E
MAIL:

11, September , 2023

To whom it may concern
Dear Sir

Re: Permission to submit To AUREC for Tanatswa Jean Chinyama

Program: Bachelor of Medical Laboratory Sciences

This letter serves to confirm that i have supervised the above mentioned student and she has satisfied all the requirements of the college and she is ready in conducting research on Prevalence of Rifampicin Resistant Mycobacterium Tuberculosis From Tuberculosis Patients Attended At Sally Mugabe Central hospital In
Harare, Zimbabwe: A Retrospective Study

Your facilitation in assisting him is greatly appreciated
Thank you

Research Supervisor: Dr Maibouge T.M.Salissou PhD

Endow Chair Pathology and Pathophysiology/ CHANS

Africa University

Appendix 6: AUREC Approval Letter

Investing in Africa's future

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU3096/24

8 February, 2024

TANATSWA JEAN CHINYAMA
C/O Africa University
Box 1320
MUTARE

RE: PREVALENCE OF RIFAMPICIN-RESISTANT MYCOBACTERIUM TUBERCULOSIS FROM TUBERCULOSIS PATIENTS ATTENDED AT SALLY MUGABE CENTRAL HOSPITAL IN HARARE, ZIMBABWE: A RETROSPECTIVE STUDY

Thank you for the above-titled proposal that you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following.

a) Research proposal

- **APPROVAL NUMBER** AUREC 3096/24
  This number should be used on all correspondences, consent forms, and appropriate documents.
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** February 8, 2024
- **EXPIRATION DATE** February 8, 2025
- **TYPE OF MEETING**: Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

AFRICA UNIVERSITY
RESEARCH ETHICS COMMITTEE (AUREC)
APPROVED
P.O. BOX 1320, MUTARE, ZIMBABWE

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE