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THE PREVALENCE OF ANTIBIOTIC RESISTANT TUBERCULOSIS AT NATIONAL MICROBIOLOGY REFERENCE LABORATORY, 2021 to 2023

BY

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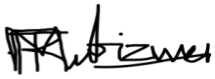
Abstract

Tuberculosis infections have been one of the killer infections with an estimated population of about 10.6 million being affected annually with the severity being increased by anti-microbial resistance. The prevalence of antimicrobial resistance has been reported to be 11.6% (95% Cl: 9.1-14.5%) and some countries in the southern Africa like South Africa, Zambia, Mozambique and Botswana having 8.2%, 20.8%, 12.7% and 9.0% respectively. Zimbabwe has been one of the countries struggling with anti-microbial resistant tuberculosis and according to the study carried out in 2019 there has been a stable increase in antibiotic resistant tuberculosis since 1994 with the prevalence being 8.4%. The purpose of this study was to investigate the prevalence of anti-microbial resistance for the period of 2021- 2023 and to try and find related factors and try to manage the cases. The study is a retrospective study on the prevalence of antimicrobial resistance tuberculosis conducted in 2024 at National Microbiology Reference Laboratory. The study had 108 patients from different regions whose tuberculosis tests were being done at NMRL. The prevalence of antimicrobial tuberculosis was 7.8% in 2021, 7.4% in 2022 and 10.5% in 2023. Mycobacterium tuberculosis was isolated from the patient sputum and grown in Lowenstein Jensen agar. The susceptibility was done using Mycobacteria Growth Indicator Tube (MGIT) with Ethambutol having the highest sensitivity and Pyrazinamide was used on a few samples. Mycobacterium tuberculosis demonstrated resistance in most of the drugs that were used with the most resistance being experienced in Rifampicin and Isoniazid. The percentage frequency of sensitive drugs and antimicrobial resistance was 76.9% and 23.1% respectively. The researcher recommends that there should be awareness programs through the Ministry of Health and Child Care and the Ministry of Information Publicity and Broadcasting to warn and enlighten the nation on antimicrobial resistance and avoid delayed diagnosis, and there is also the need to create ways to closely monitor patients on treatment to deal with issues of adherence. There were some problems which were faced by the researcher which include not all data was recorded, incomplete cases like contamination cases where no other specimen was collected. In conclusion the prevalence of antimicrobial resistant tuberculosis is still on the rise and needs immediate attention for better results in health.

Keywords: Mycobacterium Tuberculosis, Prevalence, Antimicrobial resistance

Declaration Page

I declare that this dissertation proposal 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 degree

Tafadzwa R Mutizwa	
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Main Supervisor's Full Name	Main supervisor's Signature (Date

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List of Acronyms and Abbreviations

AMR	Antimicrobial Resistance
DOTS	Directly Observed Treatment Short course
DRS	Drug Resistance Survey
GoZ	Government of Zimbabwe
MoHCC	Ministry of Health and Child Care
SMCH	Sally Mugabe Central Hospital
TB	Tuberculosis
WHO	World Health Organisation
EMB	Ethambutol
RIF	Rifampicin
L.J	Lowenstein Jensen
NMRL	National Microbiology Reference Laboratory
MGIT	Mycobacteria Growth Indicator Tube

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CHAPTER 1 INTRODUCTION

1.1 Introduction

Tuberculosis is a disease caused by mycobacterium tuberculosis transmitted by airborne particles called droplet nuclei (Tuberculosis Precautions, 2023) which attacks mainly the lungs but is capable of attacking other parts like kidneys, spine and the brain. The disease was first discovered in 1882 by Robert Koch when he found a staining technique that enabled him to stain mycobacterium tuberculosis (Tuberculosis Treatment , 2023). Tuberculosis is now the second leading infectious killer disease after covid-19, according to W.H.O 2022 about 10.6 million got the disease in 2022 with 2 in 5 people with multi-drug resistant tuberculosis getting access to treatment.

There has been an increase in the investments towards new diagnostic techniques such as GeneXpert, Line Probe Assay and Digital Radiology leading to better diagnosis and treatment of tuberculosis and drug resistant Tuberculosis. In 2019 about 6300 succumbed to the disease of the 29000 who fell with 1200 being diagnosed with the drug resistant Tuberculosis in Zimbabwe. The MoHCC and GoZ (Government of Zimbabwe) have acquired mobile trucks for the testing of Tuberculosis and antibiotic resistant Tuberculosis and also raising awareness.

The aim of this study is to determine the proportion of those affected with Antibiotic resistant Tuberculosis across the period of 2021- 2023 NMRL in Zimbabwe (Mugarisi, 2021). The results of this study will be utilised by the MoHCC in the crafting of better treatment plans for example if it is observed that most AMR TB is from retreatment a plan can be devised to closely monitor the medicine uptake by patients.

1.2 Background to the study

Tuberculosis is one many causes of death in the world but more so in developing countries. In the year 2019 there were around 10 million new cases leading above 1.3 million deaths according to W.H.O 2019 (Habibnia, et al., 2019). As the time goes on the resistance against tuberculosis is increasing with the resistance being highest against isoniazid (35%) and cycloserine (44.6%). Although there have been some successful treatments, these treatments are now being affected by the development of new drug resistant tuberculosis strains. The rise in drug resistant strains has to be monitored and through this study it could be achieved and also they can detect which drugs are facing higher resistance.

The multi-drug resistant Tuberculosis is as a result of quite a number of factors which include delayed diagnosis, inadequate treatment regimens, not properly following the proposed treatment plan and mortality according to. In addition, with Tuberculosis being one of the top infectious killer diseases around the globe it is vital to utilize DOTS (Directly Observed Treatment Short Course) during diagnosis and treatment so as to minimise the spread of drug resistant Tuberculosis in the community (Tembo & Malangu, 2019)

The TB drug resistance survey is one of the major processes being done on the global level to try and combat AMR TB. The treatment medicines are divided into first line and second line with the rise in first line resistance increasing the risk of treatment failure. In 2019 there was about 3.3% of new patients with resistance of first line and there was about 20% of new untreated patients with resistance across Europe and Asia (Dean, et al., 2020). In the prevalence rate was 3.9% of the new cases and 21% of those who were on treatment had AMR TB and about 50% of those who were diagnosed with AMR TB died.

1.3 Statement of the problem

Since the discovery of streptomycin which could cure Tuberculosis a few years later it was observed that the bacteria had developed resistance. Although antibiotic resistance has been around for a while, nowadays it is on the rise with antibiotic resistant Tuberculosis being one of the major concerns and unlike in other diseases once one develops antibiotic resistant it will be difficult to treat. In 2019 Zimbabwe recorded a prevalence of AMR TB being 2.0% and 6.4% in new patients and retreatment patients respectively (Timire, et al., 2019). While there have been some breakthroughs in terms of diagnosis the prevalence of antibiotic resistant Tuberculosis is still high. There is need to investigate the prevalence of AMR TB due to the continuous rise in antimicrobial resistant tuberculosis both on the national and global level.

1.4 Research Objectives

1.4.1 Broad objective

Study is to investigate the prevalence of Antibiotic resistant Tuberculosis at National Microbiology Reference Laboratory.

1.4.2 Specific Objectives

- To investigate the prevalence of antibiotic resistant Tuberculosis from 2021-2023 at National Microbiology Reference Laboratory
- To assess the prevalence of antibiotic resistant Tuberculosis in newly diagnosed patients and old patients at NMRL
- To analyse factors leading to antimicrobial resistant Tuberculosis

1.5 Research questions

- What are the factors leading to antibiotic resistant tuberculosis
- What is the prevalence of antibiotic resistant tuberculosis from 2021- 2023
- To what extent is antibiotic resistant Tuberculosis in patients on treatment compared to those newly diagnosed

1.6 Study justification

This study will help the Ministry of Health and Child Care with better diagnosis methods of the disease. In addition, through the treatment of antibiotic resistant tuberculosis it can pave a way to better management and control of the disease not only in Harare but across the whole country. In order to increase the effectiveness of the treatment there is need to know the associated factors leading to the development of AMR TB and this study is designed to identify some of these factors. The knowledge of the factors associated will help in the making of better treatment methods there by mitigating the situation of AMR TB.

1.7 **Study limitations**

There are quite a number of limitations to the study and these include the fact that not everyone has got information on Tuberculosis they will not be able to get the actual data as some of the people do not get tested and just stay home some stay home because they show flue like symptoms hence do not seek medical attention. Furthermore, since National Microbiology Reference Laboratory is a central referral government hospital some people might prefer private health services over government health services hence the data is already limited.

1.8 Study delimitations

The study will be limited to those individuals who would have tested positive for tuberculosis and AMR- Tuberculosis over the period of 2021- 2023 or those who normal tuberculosis which

then mutated to antibiotic resistant tuberculosis before 2021 but was not yet treated. The study is going to be carried out at the National Microbiology Reference Laboratory and those individuals who will test positive for Antibiotic resistant Tuberculosis after 2023 will not be included in the study.

1.9 **Summary**

This chapter introduced the study on the prevalence of antibiotic resistant Tuberculosis and also gave the background of the study. The problem statement, research objectives and questions are clearly outlined. In addition, the reasons why it is vital for this research to be carried out is also mentioned.

CHAPTER 2 LITERATURE REVIEW

2.1 Introduction

This chapter will review literature on antibiotic resistant tuberculosis and the associated factors with the rise in the spread of antibiotic resistant tuberculosis

2.2 Theoretical Framework

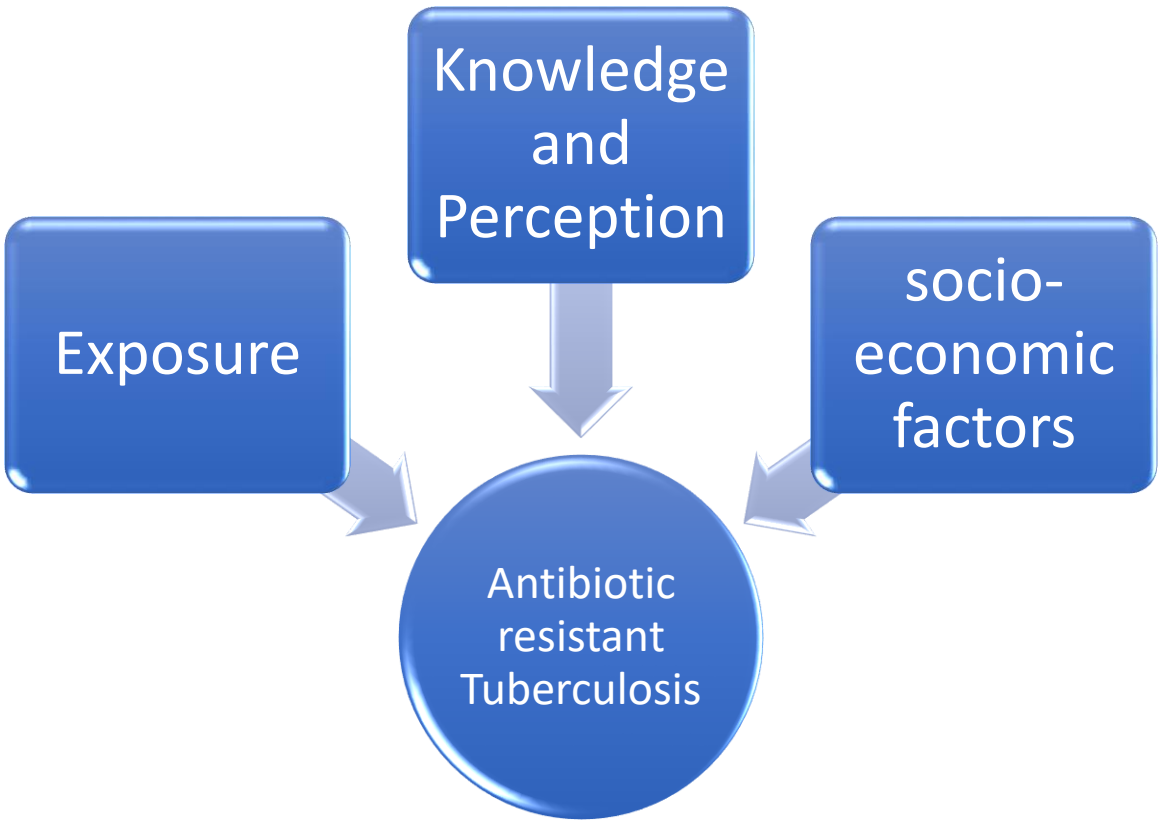

Figure1 Source; Author

2.3 Relevance of the theoretical Framework

The conceptual framework focuses on the factors giving rise to the increase in the prevalence of Antibiotic Resistant Tuberculosis. The framework shows that there are knowledge, perception and attitude related factors on both the physician and patient part leading to the increase in antibiotic resistant Tuberculosis. There is also exposure to AMR Tuberculosis as this determines the type of antibiotics the patient is resistant to and also if there is any possibility of treatment. Finally, the framework depicts the socio-economic factors as one of the causes of the rise in the prevalence of AMR Tuberculosis with those who are socio-economically disadvantaged people being the ones at high risk of getting AMR Tuberculosis.

2.4 Factors leading to Antibiotic Resistant Tuberculosis

Exposure is one of the major factors towards the antibiotic resistant Tuberculosis on a lot of levels from exposure to antibiotic resistant Tuberculosis strains to even access to medication and medical facilities to tackle the Tuberculosis. The incapability to complete an antibiotic treatment there is a higher probability of the patient to develop antibiotic resistant Tuberculosis and this could be due to a number of reasons which include the exposure to all the tuberculosis within the stipulated time period after starting the treatment. Amongst major contributes to antibiotic resistance is overuse and misuse of antibiotics, hence exposing bacteria to low doses of antibiotics overtime leading to the bacteria becoming resistant.

Tuberculosis is one of the diseases that easily spreads and one of the driving factors is through highly populated areas such as overcrowded urban areas and these settings allows for more chances to exposure to antibiotic resistant tuberculosis. Furthermore, the other hotspots to antibiotic resistant tuberculosis are the health facilities as some of the patients come to these

health facilities without resistant strains but overtime at these facilities these patients develop antibiotic resistant tuberculosis (Smith, et al., 2022).

Knowledge and perception are a part of the most important factors leading to the rise in the prevalence of antibiotic resistance Tuberculosis. One of the reasons for the increase in antibiotic resistant Tuberculosis is due to the lack of awareness and knowledge about tuberculosis leading to inappropriate use of antibiotics. Those who contract tuberculosis due to lack of knowledge and awareness the individuals will not seek healthcare early hence delaying diagnosis and lot of them will not adhere to fully finish the course of treatment thereby promoting resistance (Simegn & Moges, 2022).

In spite of knowledge, there is also perception and stigma as part of the leading causes to the rise of antibiotic resistant Tuberculosis. In some cultures tuberculosis is associated with shame and social stigma which means if one contracts the disease they would not seek medical care in time. In adequate infrastructure and resources means that people will only be able to access limited access to proper healthcare, diagnostic tools and effective antibiotics and because of lack of effective resources it will lead to failed treatments and development of antibiotic resistant Tuberculosis as not all the mycobacterium Tuberculosis will be killed leading to resistant strains.

There have been quite a number of reasons pointing to the fact that socio-economic factors are part of the increase in the prevalence of antibiotic resistant Tuberculosis. The increase is ascertained to expensive treatment regimens and the long duration of treatment according to Cannon et al the drug resistant Tuberculosis in Africa is multifaceted illness with expensive treatment regimens and long duration treatments with socio-economic factors like poverty leading to the patient not finishing the treatment regimens, giving rise to resistance.

The antibiotics have been of great assistance from the first time they were discovered in thwarting diseases and at the same time the moment one starts consuming them they will be at risk of having antimicrobial resistance. In line with (Antibiotic Prescribing and Use, 2019) the moment antimicrobials are used there is a chance that they will aide towards resistance as this comes about by the pathogen's exposure to antimicrobials and their resistance mechanisms.

The major causes of the rise in antibiotic resistance tuberculosis is due to antibiotic use on its own and when someone uses antibiotics depending on the way they are utilised some bacteria may die and the resistant ones will survive and due to their nature of taking every chance to proliferate they will multiply. The resistance of the bacteria could be due to overuse of antimicrobials and in this case when someone gets sick usually in developing Countries they go to the pharmacist buy drugs and because the pharmacist wants to make profit there is a greater chance that they will give them the antibiotics without a doctor's prescription.

In addition, there is also the case that some of the tests take a long time for example 8 weeks and alleviate the patient's pain the doctor gives them some drugs and the dosage might not be adequate to kill all the bacteria meaning that some bacteria will be exposed to a low quantity of antibiotics which is not enough to kill the bacteria but will be enough to make the bacteria mutate hence creating a mechanism to escape the effect of the antibiotics in the future. Furthermore, there is the case that due to overuse of drugs this can also help in causing drug resistance because one might be exposed to mycobacterium tuberculosis with very low doses of the antibiotics in their system which means the bacteria will be exposed to these low doses and develop resistance.

In spite of low doses of antibiotics in the system there is also the case of drug addicts, people who take drugs at a higher level to the position that they develop a tolerance towards a certain type of drug. The over intake of drugs will lead to organ failure and weak immune system as

they do not usually take in the required nutrients to stay healthy and may get tuberculosis. Once the drug abuser contracts tuberculosis there is very high risk of them not following the treatment regimen which means that the mycobacterium will develop resistance to the antibiotics which could have been prescribed. In addition, because the drug addicts usually spend their time overcrowded and less aerated spaces they will spread the antibiotic resistant tuberculosis to their peers. (Why Drug and Alcohol Abuse Puts you at High Risk of Suffering from Tuberculosis (TB), 2022)

The other factors leading to is the fact that over time there is spontaneous mutation where the general genetic makeup of bacteria which means that if the genetic makeup which was being targeted by the antibiotics that were being used changes it will not affect the bacteria. Furthermore, although not all the bacteria mutate at the same time the mutation takes place and when the usually curative antibiotics are used the it will kill all the susceptible bacteria leaving the few mutated bacteria and because of reduced population and lack of competition the antibiotic resistant mutated bacteria will proliferate hence there will be antibiotic resistant tuberculosis (Tuberculosis, 2023)

In addition, the other factors leading to antimicrobial resistant tuberculosis is when the patient suffering from mycobacterium tuberculosis fails to use the antibiotics properly and also when one fails to manage the disease properly. The failure to use the prescribed antibiotics aids to the development of antibiotic resistance because when a treatment regimen or course is drafted it is to make sure by the end of the course all the tuberculosis bacteria would have been killed and failure to adhere to that course it will mean that not all bacteria would have been killed off and the remaining bacteria will develop a mechanism to be able to survive in the hostile environment hence developing resistance (Centers for Disease Control and Prevention, 2022).

The other cause of antibiotic resistant tuberculosis is due to mismanagement and this varies it could from the part of the patient, physician and the nation. The mismanagement occurs when the physician prescribes the wrong treatment and this include where the physician prescribes the wrong antibiotic dosage. The prescription of the wrong dosage usually on the low side means that the antibiotic will not be adequate to destroy the mycobacterium but just enough to introduce the drug to the bacterium which means that the bacteria will develop a mechanism against the drug to make sure they are able to survive. In addition, the other wrong treatment is when the doctor gives the wrong length of time for the treatment course which means the treatment dosage could be spread over a long or short period of time which might not be optimal to kill all the bacteria but just allow it to develop resistance and also there is the case of the drugs available are of poor quality and also the necessary drugs for treatment are not available so the physician will just turn to the available medications which because of their quality probably will not eradicate the mycobacterium tuberculosis but rather allow the bacteria to become resistant (Drug-Resistant TB, 2022).

Despite, spontaneous resistance the other factor leading to AMR-TB is due to the transmission of an already resistant mycobacterium tuberculosis strain. In transmitted resistance someone is invaded or gets infected by an already antimicrobial resistant tuberculosis from someone with antibiotic resistant tuberculosis. The person who gets infected by an AMR-TB will have a difficult time as the prescribed medications will not help as the bacteria will not respond to the antibiotics as the mechanism the antibiotics usually attacks might not be available anymore or is no longer relevant in the life of the bacteria (Antibiotic Resistance, 2023)

The other factor leading to the development of AMR-TB is due to the body failing to utilise the drugs as others or what the physician would have anticipated. People have close or similar genetic makeup but there are some who are different and hence will be metabolise the drugs differently from the others which means that when the person takes in the prescribed drug the

drug will not be able to perform as it would have been cleared by the liver or greatly attenuated. The attenuated antibiotics will reach the target in their weakened form and because of that the tuberculosis will develop resistance. (Tuberculosis, 2023)

2.5 Prevalence of Antibiotic Resistant Tuberculosis

One of the major concerns in the health sector is the Antibiotic Resistant tuberculosis. The rise in AMR TB has led to quite a number of studies and there is need to review those studies to find ways to manage the strains. The prevalence of AMR TB has been stable on the national level but there have been a significant rise over the years (Timire, et al.). The prevalence in 2015 was 10,4 million with 3,9% of new cases having AMR TB with 21% being those previously treated patients (Tembo & Malangu, 2019). The prevalence of AMR TB in 1994 Zimbabwe was estimated to be 1.9 % in newly diagnosed patients and 8.3% in the retreaatment patients and as of 2023 the pooled AMR TB prevalence globally was 11.6% which is too high and authorities are advised to consider ways to control and manager tuberculosis.

The prevalence of AMR TB in Zimbabwe is through those Zimbabweans which visit the neighbouring countries like South Africa which was reported to have 4.6% and Botswana which had 6.6% of AMR TB as of 2014 (Timire, et al., 2019). Secondly there have been studies showing that 6% of the new cases that smeared positive they tested negative on the Gene Xpert machine suggesting non Tuberculosis mycobacteria. There have been a number of studies showing the rise in the strains of AMR TB with WHO estimating that there was 630 000 cases in 2013 (Abubakar, et al., 2013). In addition, it was found that there is about 3.6% of Extensively Drug Resistant Tuberculosis amongst the Multidrug resistant Tuberculosis (Keshavjee & Farmer , 2012)

2.6 The risk of Antibiotic Resistant Tuberculosis in newly diagnosed patients and retreatment patients

Tuberculosis has been a major health concern globally for the past decades and with the rise of AMR TB around 1956 it has since become one of the top ranked killer diseases as now a few to no medications can work against it make it difficult to treat and control (Multiple Drug-Resistant Tuberculosis, n.d.). The risk of newly diagnosed patients having AMR TB varies due to factors such as exposure to resistant strains. In the study carried out by (Dean, et al., 2020) it was found that the prevalence of AMR- TB in the newly diagnosed patients was 3.4%.

The patients who have once undergone treatment or are on treatment are at risk of developing resistant strains of TB. The development of AMR TB in patients on treatment is as a result of factors such as inadequate or incorrect treatment regimens and adherence to treatment as incomplete treatment allows the survival of bacteria leading to resistance (Simegn & Moges, 2022). The prevalence of AMR TB in patients on treatment or who were treated is 18% (Dean, et al., 2020). Appropriate treatment regimens based on drug susceptibility tests, early diagnosis and DOTS are essential in reducing the occurrence and spread of AMR TB (Antimicrobial resistance, 2023)

The retreatment patients are those patients who had been on the tuberculosis and then either stopped or finished treatment. The retreatment patients are divided into two categories that is the relapse patients, this is when the disease re-emerges or bacterial activity is noticed after it had been completely eradicated after the patient had followed through with the stipulated treatment course hence had been cured of the disease. The other category is of those who did not finish their treatment course either they were cured or other reasons. In tuberculosis treatment a patient can only be called treated or finished their treatment course if the patient was under direct observation throughout the period of treatment. The disease relapse is usually due to a bacteria population which was not growing or multiplying during the first treatment

and there is a possibility of reinfection and since the bacteria was present during first treatment there is very high risk of it to have developed resistance, the treatment of retreatment is usually done using reinforced first line drugs. The relapse can also mean that the bacteria was not fully eliminated. (Caminero, 2005)

The other risk factors associated with the high prevalence of AMR-TB in retreatment patients is the previous treatment history if the patients who went through treatment once are at higher risk of developing resistance that is if the first time they did not finish the treatment or the treatment was ineffective. The case that the patient did not finish their treatment for the first time due to adherence means that some bacteria remained and had been exposed to antibiotics which mean that there a higher probability that they had developed resistance and hence the higher proportion of AMR-TB in retreatment patients. The case that the drugs were not effective during the first time could mean the person might have had resistance already or the drugs were being cleared at a faster rate from their system hence they have developed resistance since the bacteria was exposed to the antibiotics and survived. (TREATMENT OF TUBERCULOSIS, 2017)

The prevalence of newly diagnosed patients is low because in newly diagnosed the resistance is usually if the patient was exposed a resistant pathogen hence having a Tuberculosis strain which is antimicrobial resistant but there are also other factors that lead AMR-TB in newly diagnosed patients. The exposure of someone to an antibiotic resistant tuberculosis variant is one of the major contributing factors in newly diagnosed patients. In addition, the other contributing factor in the prevalence of AMR-TB in newly diagnosed patients although it might be low is delayed diagnosis. Delayed diagnosis affects and increases the chances of a patient developing resistance in the sense that tuberculosis needs to be diagnosed and receive treatment promptly as delayed diagnosis will lead to more severe and dire consequences as it allows the mycobacteria to multiply and potentially develop resistance (Santos et al, 2021)

In addition, the other factors associated with newly diagnosed patients having or developing AMR- TB include inadequate or lack of adherence to treatment in which that newly diagnosed patients fail to follow through with the prescribed course of treatment for example skipping some doses and abruptly stopping treatment can also lead to the development of resistance. Furthermore, there is also incorrect use of antibiotics for example use of antibiotics in viral or any other infections promotes AMR- TB as there is need proper diagnosis and therapy plans.

In conclusion the factors leading occurrence of resistance in retreatment patients have got high effects compared to those of newly diagnosed patients hence why the prevalence of AMR- TB is higher in retreatment patients compared to newly diagnosed patients.

2.7 Summary

This chapter outlines the conceptual framework for the prevalence of Antibiotic resistant Tuberculosis, identifies gaps in the existing literature and details the factors that may be associated with the rise in the prevalence of AMR tuberculosis as well as other studies done on the Antibiotic resistant Tuberculosis.

Chapter 3 Methodology

3.1 Introduction

Antimicrobial resistance is one of the major concerns health wise on the global scale as it is becoming more and more difficult to counter diseases once they develop resistance to drugs. This chapter describes the study design, sample size and study population data will be collected from. Furthermore, it describes mechanisms to enhance validity and reliability of study findings as well as the ethical considerations to safeguard the study participants

3.2 Research design

For the purpose of this study a quantitative, retrospective descriptive study design will be used. In a descriptive study information is collected without changing the environment and in this research information will be collected at the National Microbiology Reference Laboratory as it reveals patterns and connections that might go unnoticed (Grimes and Schulz, 2002).

3.3 Study Population

The study population will be consisting of patients who are being tested for Antibiotic resistant Tuberculosis, those who have tested positive for Antibiotic resistant Tuberculosis and those undergoing treatment at the National Microbiology Reference Laboratory.

3.4 Exclusion Criteria

Patients who tested positive for AMR tuberculosis before 2021 at the National Microbiology Reference Laboratory will not be part of the study and those who will test positive after 2023 will not be included in the study.

3.5 Inclusion Criteria

The patients who have tested positive for AMR (Antibiotic resistant) Tuberculosis in the period of 2021- 2023, those undergoing treatment or those who tested positive for AMR Tuberculosis before 2021 but they are yet to get full treatment at the National Microbiology Reference Laboratory will be included in the study.

3.6 Sample size

Since sampling is a process of selecting a significant few from the larger population in order to come out with a general outcome regarding the community. Because this study is partly qualitative in nature the size of the population that will be under study will be determined by the data collected in the period of 2021-2023. The sample size (n) is 108.

3.7 Data Collection Procedure

Authority will be sought out from the NMRL Ethics Committee to utilise the AMR-TB and tuberculosis results from the National Microbiology Reference Laboratory data. In order to prevent the loss of data and reduce the amount of errors filters will be used to identify patients that had Tuberculosis which then mutated to Antibiotic resistance tuberculosis and those who had been diagnosed with antibiotic resistant tuberculosis in the period of 2021- 2023 on the database. The selection will give the total population of those who have been diagnosed with AMR TB and these will be used for the study.

3.8 Pilot Study

A pilot study will be done by using a small portion of the sample size from across the years so as to assess the feasibility and reliability of the study before carrying out the actual study using the larger sample.

3.9 Study Setting

The study was carried out at the National Microbiology Reference Laboratory for easier access to records for the period of 2021- 2023. In addition, for better tracking of the patients progress from diagnosis to treatment.

3.10 Data Analysis

Through the use of Microsoft excel data will be cleaned of missing data fields, duplications, errors and out of range data. Descriptive analysis of the participants' characteristics will be done using Statistical Package for Social (SPSS) to generate graphs, tables and frequencies and the characteristics that will be analysed include symptoms, exposure and comorbidities. The Chi square test will be used in the analysis of different variables.

3.11 Ethical considerations

A permission letter will be obtained from the Ethics committee at National Microbiology Reference Laboratory for data collection and also another letter of approval will be obtain from the Africa University Research Ethics Committee (AUREC) to conduct the study. Privacy and confidentiality of the patients will be guaranteed as no names, addresses and contact information will be utilised and the data will be kept in a drive protected by a password.

3.12 Summary

This chapter looked at the methodology of the study through the description of the research design, study population, study setting, the data collection procedure and analysis accompanied by the necessary ethical considerations for the study.

Chapter 4 Data Analysis

4.1 Introduction

This chapter will present the findings of the research study in determining the prevalence of Anti-Microbial Resistant Tuberculosis and any predisposing factors associated with AMR-TB at the National Microbiology Reference Laboratory. Data on the availability of recommended prevention and control intervention will also be presented.

4.2 Laboratory findings

4.2.1 Table 1 showing the Anti-microbial resistance pattern of Tuberculosis

Drug resistance Pattern	All cases (n= 108) Number (%)	Relapse cases (n=74) Number (%)	New cases (n=34) Number (%)
Any Resistance		43 (58.1)	15 (34.9)
EMB	17 (15.7)	7 (16.3)	2 (1.9)
STR	12 (11.1)	2 (1.9)	3 (2.8)
INH	32 (29.6)	14 (32.6)	4 (3.7)
RIF	28 (28.9)	12 (27.9)	5 (11.6)
PZA	8 (7.4)	3 (2.8)	1 (0.9)
MOX	2 (1.9)	1 (0.9)	
CFZ	2 (1.9)	1 (0.9)	
LEV	3 (2.8)	2 (1.9)	
LZD	4 (3.7)	1 (0.9)	
Mono Resistance	14 (13.0)	5 (11.6)	4 (3.7)
RIF	2 (1.9)	2 (1.9)	1 (0.9)
INH	4 (3.7)	2 (1.9)	2 (1.9)
PZA	1 (0.9)		
LZD	1 (0.9)		
STR	4 (3.7)		1 (0.9)
EMB	2 (1.9)	1 (0.9)	
Multi drug Resistance	24 (22.2)	33 (44.6)	8 (7.4)
RIF+INH+EMB	8 (7.4)	9 (12.2)	2 (1.9)
RIF+INH	7 (6.5)	11 (14.9)	3 (2.8)
RIF+INH+STR	2 (1.9)	4 (3.7)	1 (0.9)
RIF+INH+EMB+STR	3 (2.8)	7 (9.5)	2 (1.9)
RIF+INH+EMB+PZA	3 (2.8)	2 (1.9)	

RIF+INH+PZA	1 (0.9)		
Poly drug Resistance	8 (7.4)	4 (3.7)	2 (1.9)
STR+EMB	1 (0.9)		1 (0.9)
INH+EMB	2 (1.9)	2 (1.9)	1 (0.9)
PZA+MOX+CFZ+LEV+LZD	1 (0.9)		
MOX+CFZ+LEV+LZD	1 (0.9)		
INH+PZA	2 (1.9)	2 (1.9)	
LEV+LZD	1 (0.9)		

KEY

RIF: Rifampicin, INH: Isoniazid, STR: Streptomycin, EMB: Ethambutol, PZA: Pyrazinamide, MOX: Moxifloxacin, CFZ: Clofazimine, LZD: Linezolid, LEV: Levofloxacin

4.2.2 Table 2 prevalence of AMR- TB 2021, 2022, 2023

Year	Prevalence
2021	7.8%
2022	7.4%
2023	10.8%

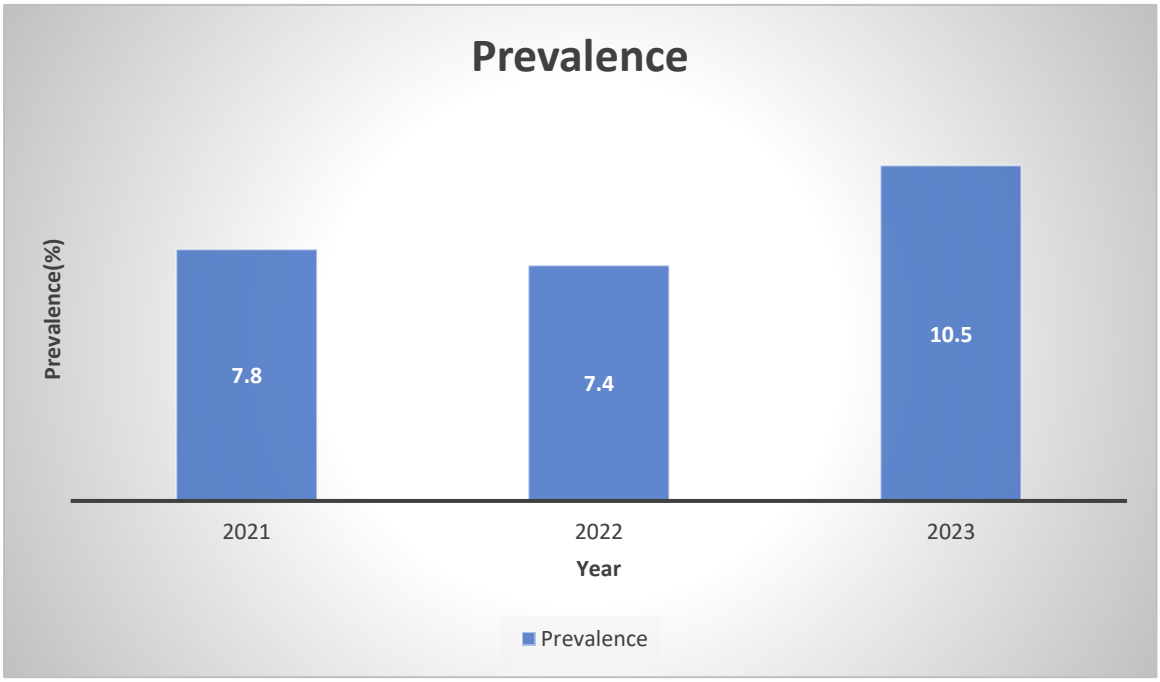

Figure 1: Prevalence of AMR-TB over the period of 2021-2023

Figure 1 summarizes the prevalence of AMR-TB which was calculated from the information obtained from NMRL for those who were tested for AMR-TB between 2021 and 2023.

4.2.3 Analysis of factors leading to Antimicrobial Resistant Tuberculosis

This section summarizes the factors leading to antimicrobial resistant tuberculosis by exploring the patients' results.

The patient results show that the one of the major causes of antimicrobial resistant tuberculosis is the treatment and this is either due to the treatment regimen being wrong or the patients not being able to follow through on the treatment and in the end develop resistance with 74 of 108 patients being retreatment patient which means that there might be issues with adherence to the treatment regimen or misuse of the antibiotics or wrong treatment regimens. However, not all cases were as a result of retreatment the other factors were the case where the patient had contracted an already antimicrobial resistant tuberculosis at the point of diagnosis and this was about 34 of 108 patients.

Chapter 5 Discussion and Recommendations

5.1 Introduction

This quantitative study was conducted amongst Tuberculosis patients who were both positive and negative for Anti-microbial resistant Tuberculosis and shows the prevalence of Anti-microbial resistance tuberculosis at the National Microbiology Reference Laboratory. The exposure accounts suggests that Anti-microbial resistant Tuberculosis is most common amongst retreatment patients rather than newly diagnosed patients. In addition, the study also shows gaps in the knowledge about how AMR TB arises.

5.2 Prevalence of Antimicrobial Resistance Tuberculosis

The anti-microbial resistant tuberculosis was demonstrated as the patients' sputum was cultured in MGIT media and the sensitivity testing was done. Table 1 shows the drugs which were used for the sensitivity testing. The Mycobacterium tuberculosis obtained from the samples was sensitive and resistant to some of the drugs and the table indicated the resistance patterns of AMR-TB in the period of 2021-2023. Mycobacterium Tuberculosis showed a higher resistance in the first line drugs isoniazid (29.6%) and rifampicin (28.9%). The MTB which was resistant to RIF was because they developed a mutation on the DNA-directed RNA polymerase subunit rpoB (Kumar & Jena, 2014) causing the resistance.

The drugs used on MTB had a frequency of 360(76.9%) of the total drugs used were sensitive. This indicates that there are quite a number of drugs that MTB is sensitive to. The used drugs resistance frequency was 108(23.1%) with Isoniazid having the highest resistance frequency, which indicates a slightly higher AMR towards TB which results in the difficulties in controlling or even eradicating the pathogen hence forth placing quite a number of the

population at variable risk of getting infected. The virulence factors of TB causes the AMR of this organism which has been shown by Table 1.

The Table 2 shows prevalence for Antimicrobial resistance tuberculosis for each year that is 2021, 2022 and 2023. The prevalence of AMR Tuberculosis had a noticeable increase from 7.4% in the year 2022 to 10.5% in 2023. The AMR-TB in the year 2023 increased due to a number of reasons which include the fact that in the year 2021 and 2022 there was still the Covid-19 pandemic and some of the TB cases were treated as Covid cases which means that not everyone did not get the chance to be tested for Tuberculosis hence the reason why the prevalence is in 7^{th} percentile. In addition, there is also there is the case that all those who did not get tested for TB in the years 2021 and 2022 could have also developed AMR-TB as they could have received treatment through the use of proper treatment regimens and this could also be the other reason why prevalence of AMR-TB was in the 10^{th} percentile in the year 2023. The prevalence of AMR-TB in the period of 2021-2023 is 9.5% on the basis of the National Microbiology Reference Laboratory.

Prevalence of AMR-TB Between newly diagnosed and retreatment patients

This study was able to concur with evidence coming from other studies that retreatment patients are at high risk of getting AMR-TB compared to newly diagnosed patients. The prevalence of this study is higher than in Matabeleland and Bulawayo by (Dumisani, et al., 2017). The study findings are in line with other studies which show that most retreatment patients tend to have resistance against a specific type of drug (Adane, et al , 2015) in this case Rifampicin (RIF).

The study although in some regions it does not align with those studies as these studies targeted first line drugs like Isoniazid and Rifampicin in which case because of the switching between different drugs it does not show the full picture. However, there is still the fact that retreatment patients are the ones having higher percentage of prevalence compared to newly diagnosed

patients with the prevalence of MDR-TB being 6.4% and 2.0% for retreatment and newly diagnosed patients (Timire, et al., 2019).

Factors leading to Antibiotic Resistant Tuberculosis

Antimicrobial resistance has been a major concern in the health sector and with its emergency on the Tuberculosis side of the sector it has increased the virulence and the difficulty in treatment by a considerable amount. Generally Antimicrobial resistance is influenced by a number of factors which include poor healthcare facilities, lack of awareness and knowledge, lack of access affordable and quality drugs and also diagnostics. In the case of Antibiotic resistance in tuberculosis it varies as there are some which apply on the global scale and some which apply on the national level for instance Zimbabwe.

The system in this study data had mixed information on Anti-microbial resistant Tuberculosis, there is the case that in certain cases since there is no follow up of results go unsolved for example when the sample is reported as contaminated without follow up of results no other sample will come for that patient. In addition, there is the case that some of the patients who were tested were not admitted at the hospital with some of them travelling long distances it is most likely that the doctor would give them some medication as they wait for the results which in some cases can go up to 8 weeks.

In the midst of having the right information there were also misconceptions which needed correcting. The existence of correct information without confronting wrong beliefs may continue to facilitate the rise in AMR- TB infection and pull back treatment. Misconceptions about TB which are common include that some believe it is just a common cold or flue. In addition, although generalised through different treatment some believe once relieved of the disease symptoms there is no longer the need to adhere to the treatment course. Furthermore, there is also misuse of drugs as one of the factors leading to antimicrobial resistance and this

concurs with (Salam, et al., 2023) as overuse and misuse of antibiotics eventually results in resistance.

5.3 Limitations of the study

The study findings should be interpreted in context of some limitations. The prevalence is based on the data of those who came for Tuberculosis testing and there is also some bias in the fact that around 2021 there was the covid-19 pandemic as such some Tuberculosis patients could have misdiagnosed as Covid-19 patients hence did not get tested for Tuberculosis. In addition, the sampling was guided by the already present data. Lastly, this research since it was centralized it does give the full view of the nation also there is the fact that not everyone comes back for retreatment if the disease persists.

5.4 Conclusion

This study shows that there is a general increase in spread of AMR-TB and this is attributed to a number of reasons and these include lack of awareness on the part of the community. Furthermore, although the prevalence is a little bit high through this study it shows that there are certain steps that can be utilized to reduce the rise of AMR-TB. The findings of this study shows that there is need for some interventions so that patients are able to understand and follow through with the treatment regimen. There is need to take into consideration of certain socio-economic factors when trying to control AMR-TB. The study findings may be of aide to the MoHCC in the development of programmes to control AMR-TB.

5.5 Recommendations

The patients newly diagnosed with Tuberculosis should be placed in good treatment programmes or given a proper treatment regimen depending on the type of drug (that is if it takes a certain drug 6 months to eliminate TB then the regimen should be 6 months long) being used to try and avoid the development of resistance. Since it has be proven that prevention is

better than cure it will be good to create programmes through the Ministry of Health and Child care and the Ministry of Information, Publicity and Broadcasting to raise the community's awareness towards Anti-microbial resistance.

Bibliography

(n.d.).

Abubakar, I., Zignol, M., Falzon, D., Raviglione, M., Ditiu, L., & Masham, B. S. (2013, JUNE). Drug-resistant tuberculosis: time for visionary political leadership. *THE LANCET infectious Diseases, 13*(6).

Adane, K., Ameni, G., Bekele, S., Adebe, M., & Aseffa , A. (2015, June 20). Prevalence and drug resistance profile of Mycobacterium tuberculosis isolated from pulmonary tuberculosis patients attending two public hospitals in East Gojjam zone, northwest Ethiopia. *BMC Public Health*. doi:10.1186/s12889-015-1933-9

Antibiotic Prescribing and Use. (2019). Retrieved from Centers for Disease Control and Prevention: https://www.cdc.gov/antibiotic-use/antibiotic-resistance.html#:~:text=Anytime%20antibiotics%20are%20used%2C%20they,and%20their%20mechanisms%20of%20resistance.

Antibiotic Resistance. (2023, October 19). Retrieved from Cleveland Clinic .

Antimicrobial resistance. (2023, November 21). Retrieved from World Health Organisation : https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance#:~:text=Priorities%20to%20address%20AMR%20in,surveillance%20of%20AMR%20and%20antimicrobial

Bhembe , N. L., Nwodo, U. U., Govender, S., Hayes, C., Ndip, R. N., Okoh , A. I., & Green, E. (2014). Molecular detection and characterization of resistant genes in Mycobacterium tuberculosis complex from DNA isolated from tuberculosis patients in the Eastern Cape province South Africa . *BMC Infectious Diseases*.

Caminero, J. A. (2005). Management of multidrug-resistant tuberculosis and patients in retreatment. *European Respiratory journal*.

Cannon , L.-A. L., Oladimeji, K. E., & Goon, D. T. (2021). Socio-economic drivers of drug-resistant tuberculosis in Africa: a scoping review. *BMC Public Health*.

Dean, A. S., Zignol, M., Cabibbe, A. M., Falzon, D., Glaziou, P., Cirillo, D. M., . . . Floyd, K. (2020). Prevalence and genetic profiles of isoniazid resistance in tuberculosis patients: A multicountry analysis of cross-sectional data. *PLOS MEDICINE*. doi:https://doi.org/10.1371%2Fjournal.pmed.1003008

Drug-Resistant TB. (2022, October 13). Retrieved from Centers for Disease Control and Prevention .

Dumisani, H. M., Chirenda, J., Juru, T., Mugurungi, O., Shambira, G., Tshimanga, M., & Gombe, N. (2017). The epidemiology of drug-resistant tuberculosis in Bulawayo and Matabeleland South provinces, Zimbabwe 2017. *National Library of Medicine*. doi:10.1016/j.ijregi.2022.03.004

Goyal, V., Kadam, V., Narang, P., & Singh, V. (2017). Public Health. *Prevalence of drug-resistant pulmonary tuberculosis in India: systematic review and meta-analysis*, 1-2.

Habibnia, S., Zaker, S., Nasiri, M. J., Doustdar, F., Ghalavand, Z., Ghalami, M., & Eslami, G. (2019). Prevalence of Multidrug-Resistant Tuberculosis: A Six- Year Single-Center Retrospective Study in Tehran, Iran. doi:https://doi.org/10.5812/archid.82828

Keshavjee, S., & Farmer , P. E. (2012). Tuberculosis, Drug Resistance, and the History of Modern Medicine. *The NEW ENGLAND JOURNAL of MEDICINE*.

Kumar, S., & Jena, L. (2014, December). Understanding Rifampicin Resistance in Tuberculosis through a Computational Approach. *Genomics and Informatics*. doi:10.5808/GI.2014.12.4.276

Mugarisi, V. (2021, March 31). *Zimbabwe scores gains in Tuberculosis (TB) treatment and control despite COVID-19 disruptions*. Retrieved from World Health Organisation Africa : https://www.afro.who.int/news/zimbabwe-scores-gains-tuberculosis-tb-treatment-and-control-despite-covid-19-disruptions

Multiple Drug-Resistant Tuberculosis. (n.d.). Retrieved from A Brief History of TB: https://sphweb.bumc.bu.edu/otlt/MPH-Modules/PH/MDR-TB/MDR-TB2.html#:~:text=In%201956%20strains%20of%20TB,resistant%20TB%20or%20MDR-TB.

Ogari, C. O., Nyamache, A. K., Nonoh, J., & Amukoye, E. (2019). Prevalence and detection of drug resistant mutations of Mycobacterium TUBERCULOSIS anong drug naive patients in Nairobi, Kenya. *Infectious Diseases*, 1-3.

Oudghiri, A., Karimi, H., Chetioui, F., Zakham, F., Bourkadi , J. E., Elmessaoudi, M. D., . . . El Mzibri1, M. (2018). Molecular characterization of mutations associated with resistance to second-line tuberculosis drug among multidrug resistant prevalence tuberculosis city in Morocco. *Infectious diseases* , 1.

Prevalence of drug-resistant tuberculosis in Zimbabwe: A health facility-based cross-sectional survey. (2019). *Pub Med*. doi:10.1016/j.ijid.2019.07.021

Reta, M. A., Alemnew, B., Abate , B. B., & Fourie, P. (2021). Prevalence of drug resistance-conferring mutations associated with isoniazid- and rifampicin-resistant Mycobacterium tuberculosis in Ethiopia: a systematic review and meta-analysis. *Journal of Global Antimicrobial Resistance*.

Rostamian , M., Kooti, S., Abiri, R., Khazayel, S., Kadivarian, S., Borji, S., & Alvandi, A. (2023). Prevalence of Mycobacterium tuberculosis mutations associated with isoniazid and rifampicin resistance: A systematic review and meta-analysis. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*.

Salam, A., Al-Amin, Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A., & Alqumber, M. (2023). Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *PubMed Central* .

Santos, J. A., Leite, A., Soares, P., Duarte, R., & Nunes, C. (2021). Delayed diagnosis of active pulmonary tuberculosis - potential risk factors for patient and healthcare delays in Portugal. *BMC Public Health*.

Simegn, W., & Moges, G. (2022). Awareness and knowledge of antimicrobial resistance and factors associated with knowledge among adults in Dessie City, Northeast Ethiopia: Community-based cross-sectional study. *PLOS ONE*.

Smith, J. P., Modongo, C., Moonan, P. K., Dima, M., Matsiri, O., Fane, O., . . . Oeltmann, J. E. (2022). Tuberculosis attributed to transmission within healthcare facilities, Botswana—The Kopanyo Study. *Infection Control and Hospital Epidemiology*.

Tembo, B. P., & Malangu, N. G. (2019). Prevalence and factors associated with multidrug/rifampicin resistant tuberculosis among suspected drug resistant tuberculosis patients in Botswana. *BMC Infectious Diseases*.

Tembo, B. P., & Malangu, N. G. (2019). Prevalence and factors associated with multidrug/rifampicin resistant tuberculosis among suspected drug resistant tuberculosis patients in Botswana. *BMC Infectious Diseases*.

Timire, C., Metcalfe, J. Z., Chirenda, J., Mutunzi, H., Kalisvaart, N., Sandy, C., . . . Matambo, R. (2019, October). Prevalence of drug-resistant tuberculosis in Zimbabwe: A health facility-based cross-sectional survey. *Pub Med*. doi:10.1016/j.ijid.2019.07.021

TREATMENT OF TUBERCULOSIS. (2017). Retrieved from World Health Organisation: www.who.int/tb

Tuberculosis. (2023, March 22). Retrieved from Mayo Clinic : https://www.mayoclinic.org/diseases-conditions/tuberculosis/symptoms-causes/syc-20351250

Tuberculosis Precautions. (2023, November). Retrieved from WISCONSIN DEPARTMENT of HEALTH SERVICES .

Tuberculosis Treatment . (2023). Retrieved from History of Tuberculosis: https://globaltb.njms.rutgers.edu/abouttb/historyoftb.php#:~:text=In%201882%2C%20Robert%20Koch%20discovered,deadliest%20enemy%20could%20really%20begin.

Why Drug and Alcohol Abuse Puts you at High Risk of Suffering from Tuberculosis (TB). (2022, February 3). Retrieved from Centre of Health Solutions: https://chskenya.org/why-drug-and-alcohol-abuse-puts-you-at-high-risk-of-suffering-from-tuberculosis-tb/#:~:text=Drug%20and%20alcohol%20abusers%20may,ventilated%20homes%20or%20social%20venues.

Appendix 1 Work Plan

	January	February	March	April
Proposal writing				
Topic Presentation				
Request for permission to conduct study				
Submission and correction of proposal				
Submission to AUREC				
Data collection				
Data analysis				
Report writing				
Submission of final report				
Dissemination of findings				

Appendix 2 Budget

Item	Unit Cost	Quantity	Total cost in USD
Transport	30	-	30
Application fee	10	-	10
Airtime and Data	140	-	140
Total Cost			180

13374 UNIT N

SEKE

CHITUNGWIZA

09 January 2024

The Ethics Office

Sally Mugabe Central Hospital

Post Office Box ST14

Southerton

Harare

Dear Sir/Madam

RE: APPLICATION LETTER TO GET PERMISSION TO COLLECT DATA AT NATIONAL MICROBIOLOGY REFERENCE LABORATORY SALLY MUGABE CENTRAL HOSPITAL.

I have written this letter asking for permission to gather data at the National Microbiology Reference Laboratory for my research regarding the prevalence of Antibiotic resistant tuberculosis from the period of 2021 to 2023. The results of the study will be able to aide the Ministry of Health and Childcare in the fight against drug resistant Tuberculosis strains.

I hope you will able to help me

Thank you

Yours sincerely

Tafadzwa R Mutizwa

Telephone: 621100-19
Fax: 621157

Reference: SMCHEC090124/09

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

ZIMBABWE

15 January 2024

Tafadzwa Runyararo Mutizwa
13374 Unit N
Chitungwiza
Harare

REF: THE PREVALENCE OF ANTIBIOTIC RESISTANT TUBERCULOSIS AT SALLY MUGABE CENTRAL HOSPITAL FROM 2021 TO 2023

I am glad to advise you that your application to conduct a study entitled: **THE PREVALENCE OF ANTIBIOTIC RESISTANT TUBERCULOSIS AT SALLY MUGABE CENTRAL HOSPITAL FROM 2021 TO 2023** **(Ref: SMCHE090124/03),** 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.

HARARE CENTRAL HOSPITAL
DEPARTMENT OF MEDICINE
16 JAN 2024
P. O. BOX ST14, SOUTHERTON
HARARE, ZIMBABWE

Yours sincerely,

DR. C. Pasi
Chairman Sally Mugabe Central Ethics Committee

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: AU3169/24

March, 2024

TAFADZWA R MUTIZWA

C/O Africa University

Box 1320

MUTARE

RE: **THE PREVALENCE OF ANTIBIOTIC-RESISTANT TUBERCULOSIS AT SALLY MUGABE CENTRAL HOSPITAL FROM 2021 TO 2023**

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** AUREC3169/24
  This number should be used on all correspondences, consent forms, and appropriate documents.
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** March 11, 2024
- **EXPIRATION DATE** March 11, 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.

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE