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Assessment of Multidrug Resistance Among Tuberculosis Patients in Lesotho

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Abstract

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Jerry Yakubu Yahaya

MS, Brandeis University, 2010

BA, University for Development Studies, 2004

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

The emergence of multidrug-resistant tuberculosis (MDR-TB) jeopardizes the tremendous efforts in the fight against tuberculosis in Lesotho. To understand the occurrence of MDR-TB, it is important to identify the associated risk factors and how to address them. There is a literature gap on the sociodemographic risk factors associated with MDR-TB in Lesotho. This study assessed whether there is any significant association between age, employment, income, sex, education, place of residence and MDR-TB. The association between HIV and MDR-TB was also evaluated. Guided by the health belief model and social cognitive theory, a retrospective case-control study design and a proportionate stratified random sample were employed to gather primary data from 306 randomly selected participants from 12 TB clinics between March 2021 and February 2022. Confirmed TB patients who were 18 years of age or older were included in the study. Chi-square and multivariate logistic regression analysis were performed to identify the risk factors that moderate MDR-TB status. The results revealed that increased age beyond 18–26 years and income levels above $1,026.00 significantly decreased the odds of the risk of MDR-TB (*OR* = 0.8, 95% *CI* [0.673, 0.991], *p* = 0.040; *OR* = 0.5, 95% *CI* [0.222, 0.943] *p* = 0.034). Not having a caregiver was associated with increased odds of the risk of MDR-TB by 80% (*OR* = 1.8, 95% *CI* [1.039, 3.110], *p* = 0.036). The findings highlight the need for a public health campaign and education to enhance caregivers' and young TB patients knowledge on infection prevention and control of MDR-TB. It is important to improve the socioeconomic drivers of MDR-TB among TB patients by targeting those that are poor and vulnerable.

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Dedication

This dissertation is dedicated to my wonderful boys: Jordan Borenyiche Yahaya and Josiah Kenyiwale Yahaya.

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Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Introduction

Tuberculosis (TB) is a disease caused by an infectious bacterium called *Mycobacterium tuberculosis*, which mostly affects the lungs and is transmitted from one person to another through the air by the propelling of TB germs when a person coughs, spits, or sneezes (World Health Organization [WHO], 2019a). Recent reports published by the WHO (2018) revealed that about a quarter of the world's population has latent TB, which implies that though these people are infected by the TB bacteria, they are mostly not ill with the disease and cannot transmit the disease. Additionally, people infected by the latent TB bacteria have a 5–15% lifetime risk of falling ill with TB. People with active TB have mild symptoms such as night sweats, coughs, fever, and/or weight loss for many months, which lead to delays in seeking care and eventually result in the transmission of the bacteria to others. The danger associated with people with active TB is that they can infect 10–15 other people through close contact within a year. For this reason, transmission in high-incidence settings is attributed to community and household contacts of case-patients to those exposed to the disease in the household (Brooks-Pollock et al., 2011). The disease can also spread quickly in crowded settings such as prisons and hospitals (WHO, 2018). The problem is further exacerbated by the increasing surge in the number of multidrug-resistant TB (MDR-TB) cases, and this has become a major concern of TB control programs worldwide (WHO, 2008). For instance, the MDR-TB at an incidence rate of 41/100,000 population (WHO, 2019b) in Lesotho is a major challenge to TB prevention and control in the country.

Although TB is fully curable, prevention and early detection are considered the ideal method of controlling the disease and increasing the survival of patients. For instance, during the period 2000–2017, about 54 million people's lives were saved through effective diagnoses and treatment (WHO, 2018). Nonetheless, it is estimated that on average, one person dies from TB every 15–16 seconds (Corbett et al., 2003). In 2017, over 1 million children were ill from TB, with 230,000 of them dying from the disease (WHO, 2018). One third of TB cases are unreported and unknown to the health system and are not receiving any treatment (Holmes et al., 2017). The WHO proposed the End TB Strategy in 2012 with an aim to reduce the burden of TB by 2035 and ultimately eradicate TB. In pursuit of this goal, the strategy adopted was to promote house contact investigation to broaden TB case findings (WHO, 2012). Though the incidence of TB fell by 2% per year, this decline was not enough to reach the planned 2020 milestone (WHO, 2018). On the contrary, an annual decline of 4–5% would have been needed to reach the 2020 milestone of the End TB Strategy. Ending TB by 2030 is included in the targets of the Sustainable Development Goals, but a substantial annual reduction in TB incidence and the number of deaths will be necessary to meet the strategic targets for 2030 and 2035. This requires 3.5 billion U.S. dollars per year to fill the resource gap for implementing TB interventions worldwide, which has been found to be high (MacNeil et al., 2019).

Due to inadequate knowledge about risk factors associated with MDR-TB in Lesotho, a better comprehension of the risk factors associated with the disease is significant to the development of health promotion and intervention strategies. Therefore, in this quantitative study, I examined the socioeconomic, demographic, and behavioral risk factors associated with MDR-TB in Lesotho. The findings from this study can be used to allocate resources more efficiently toward specific health programs and interventions targeted at the population affected and impacted by MDR-TB. The study contributes to the body of knowledge for potential interventions aimed at reducing the risk factors associated with MDR-TB among TB patients in Lesotho. Finally, developing countries with a similar population can adopt the findings from this study and dovetail them to fit their specific situation and need. Chapter 1 of the study is devoted to giving the introduction and background to the study. It also includes a discussion of the problem statement, purpose of the study, research questions, hypotheses, theoretical framework, nature of the study, significance of the study, and basic definitions of terms used in the study.

Background

Globally, there is an increasing prevalence of drug-resistant tuberculosis (DR-TB; Bell et al., 2014), and this is undermining global efforts to combat the disease (Long et al., 2016). The WHO, for instance, reports that Lesotho has a high prevalence of TB, with an estimated incidence of 665 cases per 100,000 population, higher than the global incidence of 133 cases per 100,000 population (WHO, 2018). Among persons infected with the disease, men are disproportionately affected (61.9%) compared to women (38.1%), and returning migrant workers in South African mines have been identified as the key drivers of TB (WHO, 2018). While 74% of all reported TB cases in 2015 were treated successfully, an estimated 4.8% of new cases and 14% of previous cases were identified to be resistant to multidrug treatment in Lesotho (WHO, 2018). The prevalence of drug resistance demonstrates that treatments have been compromised, and this is of great concern to global public health (Kelly & Davies, 2017). Drug-resistance is associated with lengthy stays in hospitals, with its associated cost and high risk of mortality and morbidity (Founou et al., 2017; Gulen et al., 2015). TB has emerged as a top disease to control in Lesotho. Located next to and surrounded by South Africa, Lesotho is among the 30 highly TB-burdened countries, and TB is among the leading causes of morbidity and mortality in the country (WHO, 2016). Lesotho shares a similar epidemiological situation as the Republic of South Africa. Many of the MDR-TB patients report a history of working in South Africa and in the mines. With an estimated incidence rate of 665/100,000 people (WHO, 2019), Lesotho experiences a disproportionate burden of TB compared to other African countries. MDR-TB, at an incidence rate of 41/100,000 population (WHO, 2019), is a major challenge to TB control in Lesotho. It should be noted that TB control and elimination programs rely on the early detection of active TB cases, prompt treatment of TB patients, and identification of risk to exposure and prevention of infection from secondary TB cases (Lönnroth et al., 2015). Besides medical factors, there is increasing evidence of the role of socioeconomic and other risk factors in health (Braveman & Gottlieb, 2014; Epstein et al., 2009) and the epidemiology of TB (Hargreaves et al., 2011; Lönnroth et al., 2009). To this end, an understanding of the socioeconomic determinants of health, such as social and economic conditions in which people are born, develop, live, work, and grow (Solovic et al., 2017; WHO, 2011), is essential for the development of epidemiological theories and interventions to prevent

MDR-TB and promote health. Socioeconomic and health risk behaviors such as income, occupation, educational levels, alcohol consumption, age, gender, or HIV status have been the focus of a plethora of interventions and studies (Hall & Elise, 2016). While socioeconomic and demographic variables are important in understanding the health status of individuals and populations, few studies have investigated the relationship between MDR-TB and sociodemographic variables in Lesotho. Similarly, quantitative description of a problem or a disease in social epidemiology through data such as incidence, mortality, and morbidity by age, sex, and other related variables provides essential inputs for burden of disease analysis and interventions (Garg, 2016). To this end, this study was set to fill the literature gap and at the same time serve as an important source of information for policymaking, planning, and resource prioritization in MDR-TB prevention and control initiatives in Lesotho.

Problem Statement

To understand the occurrence of MDR-TB, it is imperative to understand the risk factors associated with the disease and how the information can impact future strategies in addressing the problem. Risk factors such as nonadherence, lack of access to quality health care, lack of quality TB medication, and environmental and biological factors can take shape in determining the outcomes of the disease (WHO, 2018). The proposal that socioeconomic and demographic determinants are associated with MDR-TB in Lesotho, if established will be pertinent or essential for effective TB control and eradication interventions. While there is extensive literature on MDR-TB, these studies were conducted in developed countries. Indeed, there were no elaborate studies that elucidated the socioeconomic and demographic risk factors associated with MDR-TB among TB patients in Lesotho. This study was designed to identify the socio-demographic risk factors associated with MDR-TB in Lesotho.

Purpose of the Study

The purpose of the study was to use quantitative methods to examine the association between the socioeconomic, behavioral, and demographic risk factors associated with MDR-TB among TB patients in Lesotho. Specifically, the study assessed the association between income levels, level of education, employment status, and place of residence of patients with MDR-TB status. Age, sex, and HIV status of study subjects were also examined to understand how they moderate MDR-TB. Having a caregiver and multiple sex partners were examined for potential confounding. A case-control study design was used to gather primary data for the study. The data were then used to create and refine approaches to identify appropriate measures for the control of MDR-TB challenges in Lesotho.

Research Questions and Hypotheses

To carry out the task of assessing the socioeconomic, behavioral, and demographic risk factors associated with MDR-TB outcomes, the following overarching research question was formulated to guide the study: What socioeconomic, behavioral, and demographic factors are associated with MDR-TB outcomes in Lesotho? The specific research questions and associated hypotheses that were set for the study are listed below. The hypotheses were tested based on observations from the data:

Research Question 1: Do sociodemographic factors (age, employment status, education status, income, place of residence, and sex) contribute to MDR-TB status among TB patients in Lesotho?

Null Hypothesis (H_0) 1: Sociodemographic factors (age, employment status, education status, income, place of residence, and sex) do not contribute to MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 1: Socio-demographic factors (age, employment status, education status, income, place of residence, and sex) do contribute to the MDR-TB status among TB patients in Lesotho.

Research Question 2: Is the HIV status of participants associated with a high risk of MDR-TB status among TB patients?

Null Hypothesis (H_0) 2A: HIV status of participants is not associated with MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 2: HIV status of participants is associated with MDR-TB among TB patients in Lesotho.

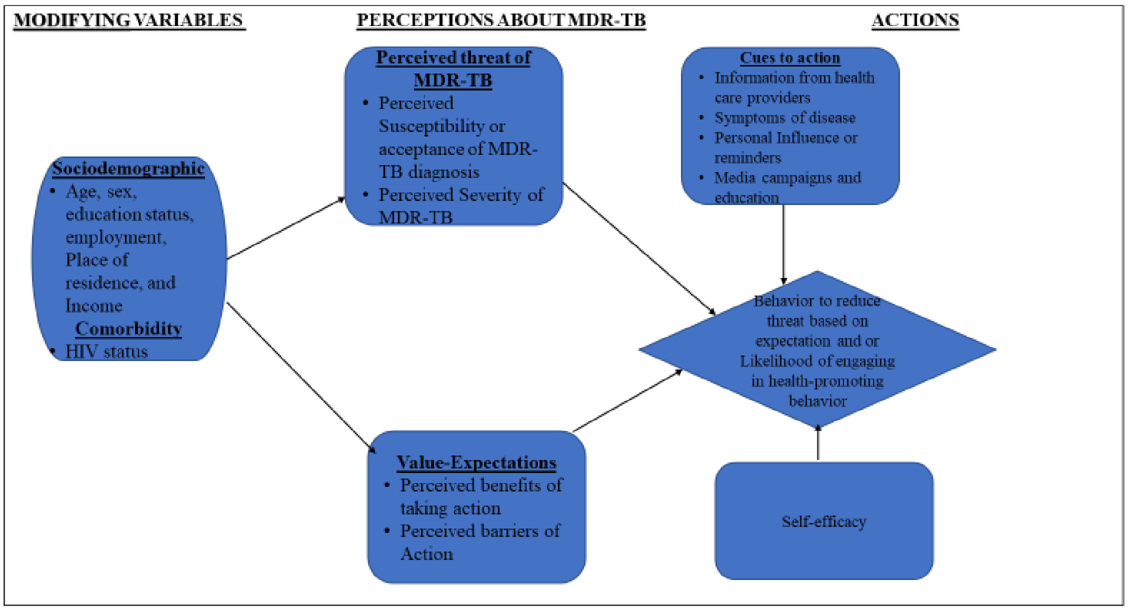
Theoretical Foundation

Through this study, I aimed to contextualize the experiences of the participants within a social determinants of health frame to highlight the broader social factors shaping individual health actions that give rise to factors associated with MDR-TB. Specifically, social cognitive theory (SCT) and the health belief model (HBM) were used to provide explanations of the risk factors associated with MDR-TB and how to prevent and control it. SCT, as articulated by Bandura (2004), explains how human behavior results from the interaction between personal factors and environmental influence. The emphasis of the theoretical tradition is on the concept of social influence or position, as well as external and internal reinforcement as a strong determinant of disease outcome (Krieger, 2001). The adoption of SCT enabled me to assess and understand, interpret, and explain social risk factors such as the sex, age, community of residence, income, and employment status of the study subjects in relation to susceptibility to MDR-TB. Conclusions were anchored on arguments of SCT and could be used to support the design of policy frameworks for public health interventions in a resource-constrained setting such as Lesotho.

The HBM, on the other hand, guided me to understand and predict health-related factors associated with MDR-TB and was used as a guide to craft possible interventions for better health outcomes. As a theory, the HBM addresses health decision-making in an attempt to explain the conditions under which a person will engage in individual health behaviors such as preventive screening and/or seeking treatment for a health condition (Rosenstock, 1974). The underlying concepts of the HBM to explain or predict why individuals will take actions to prevent, control, or even screen for MDR-TB are illustrated in Figure 1.

Figure 1

A Health Belief Model Hypothesizing the Links Between Sociodemographic Factors and Multidrug-Resistant Tuberculosis



Note. Adapted from "The Health Belief Model and Preventive Health Behavior," by I. Rosenstock, 1974, *Health Education Monographs*, *2*(4), p. 354-386 (https://doi.org/10.1177/109019817400200405). Copyright 2019 by Society for Public Health Education.

Figure 1 demonstrates how to prevent MDR-TB through the sick role and the use of TB treatment clinics. Sick role behavior can be thought of as someone who has TB and is adhering to the first line of treatment after seeing a professional. Additionally, the framework is thought of as the likelihood of developing MDR-TB due to an individual's risk factors based on their sociodemographic characteristics or behavior (Glanz et al., 2008). In other words, a wide range of sociodemographic factors can impact the perceptions of an individual in the way they behave to reduce the risk of MDR-TB. The sociodemographic factors in the model include age, sex, education, employment, income, and place of residence of TB patients. It is important to note that there are aspects of some disease comorbidities that can increase the risk of TB patients to predict MDR-TB. Thus far, HIV has been included in the model as a mediating factor to predict MDR-TB.

The sociodemographic factors in the model are exacerbated by an individual's perception of severity and personal susceptibility and the barriers and benefits of TB treatment. This application fits the description of the construct by Glanz et al. (2015), who explained that people are more likely to act if they perceive themselves to be susceptible to a condition such as MDR-TB. Perceived severity in the figure describes the belief about the seriousness that an individual attaches to treatment after knowing their TB diagnosis and the consequences of developing MDR-TB. The model merges these two concepts and calls them threats.

The next item on the model is the construct on perceived benefits or the belief in the advantages of the methods suggested for reducing the risk of MDR-TB, such as medication adherence, reduction in alcohol use, and not having comorbidities such as HIV while on treatment for TB. This part of the theory is related to the desire for a person to avoid MDR-TB (illness) and the value of getting well from TB. The other part deals with perceived barriers, with an emphasis on the belief that a specific action available to a person would prevent MDR-TB (expectation). All things being equal, it is important to reduce the potential barriers, impediments, and cost of action taken as much as possible. The construct indicates that a belief in taking action will reduce a person's susceptibility to the condition or its severity. In other words, the construct takes into consideration an individual estimate of personal susceptibility to MDR-TB and the likelihood of being able to reduce that threat through personal action.

Finally, the cues to action construct of the model involves aspects that prompt change or the likelihood to change. Put differently, individuals are exposed to factors that prompt them to take action (cues to action), and they are confident in their ability to successfully perform an action (self-efficacy). The cues to action in the model include information from media campaigns, information from health professionals, symptoms of the disease, and self-reminders on actions to take to respond to the treatment regime and reduce the risk of MDR-TB. Self-efficacy describes the confidence in one's ability to rightly engage in a behavior that will result in the desired outcome. Therefore, it not only explains basic behavior, but also allows the model to explain and predict more complex outcomes and behavior (Rosenstock et al., 1988).

In applying this theory to this study, I sought to understand how the sociodemographic factors of individuals infected with TB influence their behavior toward their susceptibility to MDR-TB, whether they believe that MDR-TB is serious, and whether they believe in taking certain actions that can reduce the threat of the problem at an acceptable cost. In other words, the models suggest that sociodemographic factors are modifiable variables that may influence an individual to engage in certain health behaviors for positive outcomes. The HBM can be interpreted from the relationship between each of the constructs. All the arrows are directed toward the desired behavior. Sociodemographic factors, for instance, influence perceived susceptibility, severity, benefits and barriers, and self-efficacy. Threats, expectations, and cues to action, on the other hand, are factored into the decisions to engage in healthy behavior.

The theories selected for this study encouraged me to think critically and systematically about the integral connections between social determinants and disease occurrence. From these theories, one can gain insight, responsibility, and accountability to translate the vision of a healthier society into a reality. The predictive capacity of the selected theory will contribute to the quality of the study by identifying the necessary elements for inclusion. The predictive capacity serves to identify a range of possible evaluation indicators, while the explanatory capacity of the theory allows generalization to be made and enhances understanding of the results.

Nature of Study

Using a quantitative retrospective case-control design, the study aimed at establishing a statistically significant association between the socioeconomic, behavioral, and demographic risk factors that account for MDR-TB among TB patients in Lesotho. This was carried out through the collection of numeric and categorical data that that were used to test the hypotheses in the study. Subsequently, the hypotheses were either accepted or rejected based on the measurement and observation of the data. Nine predictive variables were selected to test for their association with the dependent variable, MDR-TB. The independent variables included in the study were age, sex, income, level of education, employment status, place of residence, have a caregiver, have multiple sex partners, and HIV status of study subjects. MDR-TB status was the dependent variable in the study. Given that the independent variables were many, multivariate logistic regression procedures were applied to identify which of the variables contributes most to predict the dependent variable (MDR-TB) while controlling for all the other variables. Selected risk factors that did not establish statistical significance were not considered as risk factors to the dependent variable.

The study subjects included all clinically confirmed TB patients in Lesotho. The cases in the study included a sample of confirmed MDR-TB patients, and the controls constituted a sample of confirmed pulmonary TB cases listed on the TB clinic register from 2020–2022. The data for the study were collected directly from the study participants through a telephone survey. In other words, using random sampling, primary data were collected from enrolled subjects through a telephone survey questionnaire.

The study variables and the aim of the study were consistent with the conditions of a quantitative study; hence, the study was deemed appropriate. The dependent and independent variables were clearly defined and measurable, the study variables were in numeric data, and control observation of participants was employed to ensure that the findings produced had high levels of reliability (Leedy & Ormrod, 2015). Furthermore, the quantitative data analysis allowed for a broader study of the problem involving a greater number of subjects to enable the generalization of the results. Similarly, the quantitative method ensured that data summaries were provided that would support the generalizations of the study to the entire population.

The choice of a case-control research design was appropriate to answer the research questions, given that the method was used to identify the demographic, socioeconomic, and behavioral risk factors associated with MDR-TB. Additionally, MDR-TB is a rare condition with a long latency period; hence, the case-control design was the only feasible approach for this type of study. The approach allowed the study subjects to be retrospectively assessed on the multiple exposures that are associated with the outcome variable.

Definitions

Some important terms have been referenced throughout the dissertation, and for the avoidance of doubt, the terms are defined below for clarity and for the purposes of this study:

Tuberculosis (TB): Applied to non-MDR-TB patients with culture-proven or confirmed *M. tuberculosis* that is fully sensitive to the first-line anti-TB drug. Also called *active TB* or *pulmonary TB.*

Multidrug-resistant tuberculosis (MDR-TB): MDR-TB is used generically to apply to TB patients with confirmed *M. tuberculosis* that is proven to be resistant to both isoniazid (INH) and rifampicin (RIF) with or without resistance to other drugs. It also includes all cases of extensive drug-resistant tuberculosis (XDR-TB)—that is, TB caused by a strain of *M. tuberculosis* that is resilient to at least two first-line drugs, to second-line fluoroquinolone, and to second-line injectable drugs such as amikacin, kanamycin, or capreomycin. MDR-TB is generically used in this study to include any drug-resistant TB. Therefore, MDR-TB, a dependent variable, was measured as a binary variable (i.e., 0 = have MDR-TB and 2 = do not have MDR-TB).

Risk factors: Selected independent variables used in the study that predict MDR-TB. They include age, sex, educational level, place of residence, employment status, and income level. Age in this study was treated as a covariate and was ordered into the following categories 0 = 18–29, 1 = 30–39, 2 = 40–49, 3 = 50–59, and 4 = 60+. Additionally, the sex of subjects was treated as a binary variable of 0 = male or 1 = female. Predictor variables such as educational levels were put in ordered categories, namely 0 = no education, 1 = elementary school, 2 = high school education, 3 = college education, and 4 = higher education (postgraduate and professional education). Information on place of residence was solicited from subjects concerning whether they lived in a rural or urban setting. This variable was put into binary categories of 0 = rural and 1 = urban. Yearly income levels were put into ordered categories of 0 = below $ 1,026 (low income), 1 = $1,026 to $3,995 (lower middle income), 2 = $3,996 to $12,375 (upper middle income), and 3 = $12,376 or more (high income). Employment was coded into a finite categorical variable of 0 = employed, 1= unemployed, 2 = retired, and 3 = not answered.

Comorbidity: HIV coinfection. The HIV status of participants was treated as a binary variable (i.e., 0 = positive and 1 = negative.

Cofounders: The variable multiple sex partners (MSP) pertained to whether the participant engaged in sexual activities with two or more people within the last year. It measured whether a participant had multiple partners or not. Thus, this variable was prepared as a dichotomous category of 0 = have one partner or no partner and 1= have two or more partners. The variable caregiver, on the other hand, applied to a family member who shouldered the duties and responsibilities of caregiving for a TB patient at home. As a binary variable, it was divided into 0 = have a caregiver and 1 = do not have a caregiver.

Assumptions

The study was based on some assumptions that influenced the validity of the final findings. First, it was assumed that the variables identified and discussed in the literature review were operationalized in ways that represented the intent of the measures in the reviewed studies. Further, it was assumed that the sampled subjects for the study had correct and reliable contact information in TB clinic registers. Additionally, it was assumed that the study respondents provided accurate information about themselves in the survey to the best of their ability.

Scope and Delimitations

The scope of the study was limited to individual risk factors of study subjects and how they were associated with MDR-TB status in Lesotho. The target population for the study consisted of TB patients who received treatment in government hospitals in Lesotho. Therefore, the findings from the study may not necessarily be applied to similar geographic settings. Moreover, many variables have been reviewed in previous studies that may be of equal or greater importance than the variables included in the literature review as potential risk factors associated with MDR-TB. Primary data collection did not cover some variables due to time constraints and associated limited resources available for data collection.

Limitations

The main challenge with the study was how to have access to the TB clinic register that was used as the sampling frame. Furthermore, there is a limitation associated with self-report studies wherein bias can be introduced to the study. To overcome the challenges, I ensured that I communicated formally with the National Tuberculosis Programs (NTP) and the Lesotho Health Service to allow me to have access to TB clinic registers that were used as the sampling frame for the study. I also ensured that during the design of the survey instruments, the questions were not ambiguous and were pretested before the actual study took place.

Significance

No previous studies were identified in the literature that investigated the relationship between socioeconomic variables and MDR-TB in Lesotho. This study addressed the gap by providing relevant information about the association between MDR-TB and some selected sociodemographic variables. This allowed for the identification of the risk factors associated with the outcome variable and provided a better understanding of how to address the problem through control initiatives at both national and global levels. Using multivariate logistic regression analysis, the study contributed to the understanding of the sociodemographic risk factors that predict MDR-TB in order to identify better prevention options in the elimination of MDR-TB. To this end, the study elicited social change through findings that provided recommendations on how to engage relevant stakeholders in TB prevention and control initiatives.

Summary

The purpose of this study was to determine the socioeconomic and demographic risk factors associated with MDR-TB in Lesotho. The introductory chapter of the study gave a global overview of TB and a background to the MDR-TB situation in Lesotho. The chapter also laid the groundwork on how the study was conducted, including the methods and the theoretical basis of the study. In the next section of the dissertation, I review the literature on factors related to MDR-TB.

Chapter 2: Literature Review

Introduction

Despite 90 years of vaccination and 60 years of chemotherapy, TB remains the leading cause of death from a single infectious disease agent worldwide, with an estimated 10 million people falling ill from the disease and 1.6 million recorded deaths in 2017 (WHO, 2018). About one third of the global population is infected with TB bacteria that persist latently for many years without showing any clinical symptoms. Given that TB is widespread, the development of strategies is imperative, especially in a country such as Lesotho, where incidence is as high as 665 cases per 100,000 population, which is higher than the global incidence of 133 cases per 100,000 population (WHO, 2018). Worldwide, Lesotho had the fourth highest prevalence of TB in 2014 (WHO, 2014). Prozorov and colleagues (2012) described the situation as serious due to the development and prevalence of drugs that are resistant to mycobacteria, with new resistance that often combines with an existing one to produce multidrug resistance. Though drug-resistant forms of TB are a major risk of global health security research (Floyd et al., 2018), the epidemiology of MDR-TB is not well understood, given that few studies have assessed the prevalence, determinants, and treatment outcomes of DR-TB, with inconclusive findings (Girum et al., 2018). To prevent the development of drug resistance, Masterton (2008) recommended an approach to surveillance that involves monitoring antimicrobial use. However, the epidemiological features and factors associated with DR-TB are broad and vary from place to place, and a one-size-fits-all solution might not be desirable. Additionally, the literature on the trends of DR-TB is unclear in most settings (Van

Gemert, 2014); therefore, consistent surveillance or surveys that give accurate data on characteristics of patients with DR-TB is essential to develop measures and establish policies to control the problem in a developing country such as Lesotho. In particular, the sociodemographic factors driving the rapid increase of DR-TB have not been fully elucidated, and the knowledge gap in this area underscores the urgent need for public health interventions or approaches to tackle the scourge of the disease.

To halt the danger of antibiotic resistance, it is imperative to have effective preventive and control measures. However, addressing drug resistance requires a proper understanding of the problem through research to optimize the findings to ensure sustainable investment in countering drug resistance for a disease such as TB. This chapter provides a review and synthesizes the literature on MDR-TB to find gaps. Specifically, this chapter provides a summary update of the literature on MDR-TB and the sociodemographic factors that are associated with treatment outcomes of the disease. In this chapter, I review the study variables to determine how other researchers have operationalized them in similar and related investigations. The review began with an introduction to the chapter that gave a global overview of the epidemiology of TB. This is followed by a description of the literature search and the various search engines that were used to locate and identify materials for the review. The theoretical framework used for the study is concisely described in the review. The chapter also contains descriptions of the clinical prognosis of TB and the various forms of DR-TB, the challenges in addressing the problem, and what has been done to overcome the challenges. Moreover, an overview of the situation of TB and DR-TB in the study community is presented.

Additionally, the sociodemographic and other risk factors of MDR-TB, namely income, HIV comorbidity, educational status, place of residence, gender, age, have a caregiver, have multiple partners, and employment, are identified and described. Finally, this chapter concludes with a summary.

Literature Search Strategy

The combined databases CINAHL and MEDLINE were used to conduct searches for relevant studies on the topic. Additionally, searches were conducted using the ScienceDirect database. The references that were deemed useful for the bibliographies of relevant tests and journal articles were included. The inclusion criteria encompassed seminal literature, WHO reports, and peer-reviewed articles that provided information about the determinants and risk factors of MDR-TB from the period 2015 to 2019. The key search terms included *tuberculosis*, *drug resistant*, *multi-drug resistance*, *socioeconomic*, *nonadherence*, *demographics*, *Lesotho*, and *risk factors*. These terms were used individually and in various combinations to identify relevant literature. Furthermore, observational studies such as cross-sectional, case-control, retrospective, and prospective cohort studies that reported associations and those that did not confirm any association of sociodemographic risk factors and MDR-TB among TB patients were included in the review. Some ecological studies were also included. All eligible studies published in English from 2015 to 2019 were included in the study.

Application of Health Belief Model in the Prevention of Multidrug-Resistant Tuberculosis

A theoretical framework explains the path of research and grounds it firmly in theoretical constructs (Adom et al., 2018). A framework makes research findings meaningful and consistent with the theoretical constructs in research fields while ensuring generalizability. While stimulating research, it also ensures the extension of knowledge by providing direction and impetus to a research inquiry. A theoretical framework enhances the empiricism and rigor of research. Imenda (2014) described both theoretical and conceptual frameworks as giving life to research.

The HBM is one of the oldest and most widely used models to explain health behavior. The model was first used by Hochbaum (1958) and Rosenstock (1960, 1966) to explain the impact of beliefs and attitudes concerning protective health behaviors such as immunization and chest x-rays for TB. Becker (1974) and Rosenstock (1990) further developed the model, which has since been applied to several health-related problems, including health promotion behaviors. In this regard, some studies have demonstrated how to apply the constructs of the HBM to understand how sociodemographic variables influence specific health outcomes.

The HBM framework as applied to disease prevention or condition is influenced by four beliefs: perceived susceptibility, perceived severity, perceived benefits, and perceived barriers. Perceived susceptibility involves an individual's belief that they are at risk of contracting a certain disease or condition such as TB or MDR-TB. On the other hand, perceived severity refers to an individual's belief in the seriousness of a disease or condition in question if infected or left untreated. Perceived benefits refer to the belief that an individual's engagement in a preventive action will lower the risk of contracting the disease. Perceived barriers are largely the obstacles that individuals believe they might encounter and that might deter them from taking preventive measures. Furthermore, the model asserts that for preventive actions to take place, the benefits must outweigh the barriers. In addition to the beliefs, cues to action (e.g., stimuli to take medication) such as fear of the condition or symptoms of the disease and publicity, or educational materials are needed to trigger an appropriate action. Finally, modifying factors have been identified and applied to the framework in studies to understand disease prevention and health promotion. Modifying factors can influence other factors; they include sociodemographic factors such as age, education, income, ethnicity, race, place of residence, and structural factors such as knowledge about the disease and prior experience with the disease.

The HBM was identified as the most widely used theory in health education, health promotion, and disease prevention. Kaur and colleagues (2019), for instance, used the HBM framework to explore patients' perspectives about the factors with a loss to follow-up, relapse, and treatment failure in TB patients based on the HBM framework. The authors concluded that though TB treatment was free, the side effects from TB medications were disabling factors for completing treatment. Additionally, low socioeconomic status, family liabilities, and challenges associated with losing income from work contributed to noncompliance with TB treatment. The authors used the HBM to demonstrate the factors responsible for a loss to follow-up, treatment failure, and relapse in TB patients. This shows that the model was beneficial, especially in providing a framework for the study that explored patients' perspectives related to follow-up, relapse, and treatment failure in TB patients. Azizi and colleagues (2018) indicated that the HBM is a suitable framework for predicting therapeutic adherence in TB patients. In investigating the factors associated with adherence to TB treatment using the HBM, the authors identified that the variables of perceived threat, benefits, barriers, and self-efficacy accounted for 42% of the variance in therapeutic adherence. The results from the study emphasized the centrality of self-efficacy in TB treatment, which health educators should consider when developing programs to motivate patients to adhere to treatment. To understand TB infection control in healthcare facilities in Georgia, Mirtskhulava and colleagues (2015) conducted a survey study based on the HBM framework. The authors identified four aspects of the HBM model framework: the perceived susceptibility of ill-health, perceived severity of ill-health, perceived health benefits of behavior change, and perceived barriers to taking action. In the end, findings from the authors in using the model suggested that individuals assess the net benefits of changing behavior and decide whether to act. The evidence from the study supports the understanding that knowledge is a facilitator of compliance interventions (Palanduz et al., 2003; White et al., 2002). This was particularly useful to the current study, which identified education as a potential variable that predicts MDR-TB. Moreover, the HBM is a good tool for studying diseases and health conditions, given that the model offers a theoretical framework that can be used to assess how individuals can prevent diseases such as TB and, if the disease is present, ensure that the condition is improved such that it does not get to the level of drug resistance, as in cases of MDR-TB.

Treatment of Tuberculosis and Antibiotics

Antibiotics have saved the lives of people worldwide and have often been referred to as medicine's "magic bullet." Indeed, the discovery of penicillin by Sir Alexander Fleming in 1928 heralded the beginning of the antibiotic revolution (Fleming, 1980). With the purification of penicillin by Ernst Chain and Howard Florey in 1942, it was widely made available outside the Allied Army in 1945, marking the beginning of the antibiotic era (Science History Institute, 2017). The discovery of antibiotics was considered the greatest achievement in modern medicine and public health with many improvements and modifications to existing antibiotics (Aminov, 2010). Over time, however, the "magic bullets" have been losing their power due to decades of overuse (Davies, 2007), which has created a public health crisis with a growing inability of bacteria to resist the effects of antibiotics (Lushniak, 2014). Antibiotic resistance results when bacteria undergo a genetic change that reduces or eliminates the effectiveness of drugs such that they are not able to cure or prevent infection. Though the use of antibiotics as the most effective drug therapy began in the 1940s, with over 20 drugs developed to date, the treatment of TB remains complex (Shenoi & Friedland, 2009). Prozorov and colleagues (2012) explained that due to the formation of resistant strains, antibiotics for TB treatment are grouped into complex lines where the medications are alternated in an order to treat TB. Usually, the first-line drugs (such as rifampicin) are the most effective with the least side effects. On the other hand, second-line drugs are used against the strains that are resistant to first-line drugs. Third-line drugs are used against strains of extensive DR-TB over a prolonged period.

Drug-Resistant Tuberculosis

Even though TB is curable, many people continue to die from the disease. In a 2018 WHO TB report, India, China, and Russian Federation accounted for almost half of the global burden of DR-TB, and about 8.5% of all DR-TB cases had extensive drug-resistant TB (XDR-TB) in 2017. The report stated that, globally, about 55% of MDR-TB patients are successfully treated. The disease is complex, with the largest burden located in low-resource settings with weak health care systems and consequently low capacity for diagnosis and treatment (Koch et al., 2018). While many approaches have been developed, such as standardized diagnoses and treatment algorithms (WHO, 2017), which have undoubtedly contributed to increased access and survival rates, there has been widespread resistance to anti-TB drug use (Keshavjee & Farmer, 2012). In other words, one of the reasons for the ongoing TB epidemic is its resistance to antibiotic drugs. Since the discovery of the first TB drug (streptomycin), drug resistance, a biological phenomenon, has been observed when streptomycin is used to treat *Mycobacterium tuberculosis* (*M. tuberculosis*; Seung et al., 2015). Many patients who almost died were brought back to life after taking streptomycin injection, which temporarily cleared their sputum of *M. tuberculosis* (Brennan, 1949). Despite receiving treatment, the patients began to excrete bacilli that demonstrated resistance to streptomycin in the laboratory (Brennan, 1949).

The emergence of strains of *M. tuberculosis* that are resistant to one or more anti-TB first-line drugs (isoniazid and rifampicin) has posed a huge challenge to global public health efforts to control the TB epidemic (Afshari et al., 2018; Van Gemert, 2014). Drug resistance is associated with both high death rates and high treatment costs (Kipkoech et al., 2015). The WHO (2019) has reported that the misuse of anti-TB medications through patients stopping medications prematurely, physicians prescribing medications incorrectly, and manufacturers producing poor-quality drugs are to be blamed for the existence of drug resistance. This supports Kipkoech and colleagues' (2015) earlier work, which identified nonadherence to therapy, poor quality of drugs, and poor prescribing practices as the factors responsible for DR-TB. In a similar study, Pedro and colleagues (2015) demonstrated that TB treatment is associated with drug resistance, with most DR-TB cases occurring due to irregular treatment and treatment dropout.

Afshari and colleagues (2018) reported that about 8.1 per 100,000 population globally experienced DR-TB in 2016, of which 4.1% were new cases and 19% had a history of previous treatment. The authors found that persons with a history of a previous TB significantly associated with DR-TB in Iran (*OR* = 16.55, 95% *CI* [2.83, 96.89]). Globally, 556,000 people are resistant to rifampicin, the most effective first-line drug, of which 82% had MDR-TB (WHO, 2019). Results from a recent study conducted in Russia suggest that MDR and XDR-TB have become common in recent years and treatment efficacy is declining in the face of extensive drug resistance (Yunusbaeva et al., 2019). To control DR-TB, the WHO (2018) has recommended that facilities cure TB during the first round of treatment, provide access to diagnostic services, and ensure adequate control and appropriate treatment with second-line drugs. There are two forms of DR-TB, namely MDR-TB and XDR-TB. These are briefly described below.

Multidrug-Resistant Tuberculosis

MDR-TB is defined as a laboratory-confirmed case of resistance to the most first-line TB drugs, namely isoniazid and rifampin (Frieden et al., 1995). The WHO (2018) has described MDR-TB as caused by bacteria that do not respond to isoniazid and rifampicin. Multidrug resistance continues to emerge and spread due to mismanagement of TB treatment and person-to-person transmission (Seung et al., 2015). MDR-TB is treatable and curable by using second-line anti-TB drugs. The challenge with this form of treatment, however, is that it has limited treatment options and requires extensive chemotherapy that can take up to 2 years with medicines that are expensive and at the same time toxic. In some cases, complications and more drug resistance can develop as a result. The continuing spread of MDR-TB is urgent and a daunting challenge to global TB control (Zumla et al., 2012; Zumla et al., 2013). The reason is that not only is the incidence of MDR-TB high in many areas with a consequence of curtailing the ability to meet targets for TB control, but the treatment of MDR-TB puts an economic burden on NTP, accounting for over 50% of annual NTP budgets (Schnippel et al., 2013). Additionally, the number of people with active MDR-DR highly outpace the number of people placed on treatment (Falzon et al., 2013). For instance, of the 480,000 people who developed MDR-TB, 300,000 of them were notified of having TB, but fewer than 100,000 of them were placed on treatment (WHO, 2015); this situation has left many people with infectious MDR-TB in many places. In a setting such as Ethiopia, the odds of developing MDR-TB are high in patients with previously treated TB, those with a history of having contact with a known TB patient, those with a history of alcohol consumption, and those without jobs (Desissa et al., 2018). In Moldova, treatment default is associated with increased mortality and increased drug resistance, and this could contribute to the high MDR-TB incidence in the country (Jenkins et al., 2013).

The number of people with untreated MDR-TB represents an important point of transmission and spread of the disease. Even though the diagnoses time for MDR using the rapid test is fast, a degree of delay can prevent the initiation of treatment after diagnoses in a country like Bangladesh where patients experience a health system delay of a median of 7.1 weeks to initiate treatment (Rifat et al., 2015). Globally, there is an emphasis on treatment as prevention for many infectious diseases like HIV (Mayer et al., 2013), malaria (Gosling et al., 2011), and TB (Reid et al., 2015). Therefore, strategies for MDR-TB control are largely focused on clinical outcomes (Weiss et al., 2014) and cost (Korenromp et al., 2012). Hence, it is unlikely that MDR-TB programs will be successful since most people with MDR-TB are not on treatment. To this end, Kendall and colleagues (2017) stated that current treatment practices continue, and a majority of MDR-TB patients remain untreated, then the global MDR-TB is expected to rise. The authors, however, estimated that if 85% of all previously treated TB patients are identified and placed on appropriate MDR-TB treatment, then MDR-TB incidence could be reduced by over 25% in 2025.

Drug-Resistant Tuberculosis in Lesotho

The WHO (2017) estimates of the MDR-TB burden show that 4.8% of new TB cases and 14% of previously treated TB patients were found to have MDR-TB in Lesotho. The above estimates are similar to a previous anti DR-TB survey conducted in Lesotho between 2008-2009 where the result showed that 3.1% (n = 984) of the new cases and 12.8% of the retreated TB cases had MDR-TB (Maama-Maime et al., 2015). Though the authors acknowledge logistical, operational, and data management challenges may have affected the reliability of the results of the survey, the findings suggested the presence of DR-TB strains among TB patients in Lesotho.

In a follow-up study conducted by the National TB Programme of Lesotho (2017) between 2013-2014, the prevalence of MDR-TB among new cases (3.2%) was consistent with the previous study which was at 3.1% (National TB Programme of Lesotho, 2017). The National TB Programme of Lesotho (2017) estimated the national prevalence of MDR-TB among new cases at 3.2% (95% CI: 2.3, 4.1), and previously treated cases were 6.9% (95% CI:3.9, 9.8). The majority (66%) of the MDR-TB cases were found among males and 60% of them were HIV positive. Persons within the 0-14 and 45-54 age groups were significantly associated with MDR-TB in Lesotho (OR = 5.8; 95% CI [1.2, 28.5]; p = 0.03 and OR = 3.0; 95% CI [1.5, 6.2]; $p < 0.01$ respectively). Though both studies established the pattern of TB in Lesotho, they did not identify socioeconomic variables that might be associated with DR-TB in the country.

Mugomeri and colleagues (2017) conducted a study on treatment outcomes in Lesotho and included socioeconomic and demographic predictive variables. Using multivariate logistic regression analysis, the authors found that males had significantly higher unsuccessful treatment outcomes compared with females (*aOR* = 1.4, 95% *CI* [1.0, 1.8], $p = 0.046$). The study did not find age to be significantly ($p = 0.055$) associated with treatment outcomes. But persons between 31-60 years old had the highest treatment outcomes (34.5%), and young children between the ages of 1-12 years had the lowest proportion of unsuccessful treatment outcomes. Moreover, employment status was not significantly associated with treatment outcomes in a multivariable analysis, but it was significant (*OR* = 5.0, 95% *CI* [3.4, 7.4], $p < 0.001$) in the univariate analysis. Meanwhile, results from a cross-sectional analysis for 2014 Demographic and Health Survey in Lesotho (LDHS) pointed out that overall knowledge of TB in the general population in Lesotho was adequate at 59.9% (Luba et al., 2019). The multivariate logistic regression from the study showed that sex, age, educational level, marriage status, occupation, and mass media exposure were strongly associated with respondent knowledge towards TB (*aOR* = 2.45, 95% *CI* [2.10, 2.86], $p < 0.001$; *aOR* = 1.75, 95% *CI* [1.29, 2.41], $p < 0.001$; *aOR* = 6.26, 95% *CI* [3.90, 10.06], $p < 001$; *aOR* = 1.42, 95% *CI* [1.10, 1.85], $p < 0.008$; *aOR* = 1.20, 95% *CI* [1.00, 1.44], $p < 0.049$; *aOR* = 1.33, 95% *CI* [1.08, 1.64], $p < 0.008$ respectively). The action taken to prevent TB, and the association between sociodemographic variables and respondents' knowledge regarding TB suggest that there could be similar associations with the MDR-TB status of patients. Meanwhile, in an earlier study, Malangu and Adebanjo (2015) described the level of knowledge about MDR-TB amongst health workers in Lesotho as unacceptable since some were observed to be using unsafe practices such as not wearing protective gear and not following the MDR-TB treatment guidelines. Subsequently, the inability of health workers to follow the guidelines has affected MDR-TB treatment, control, and preventive measures in Lesotho.

Biosocial and Economic Risk Factors Associated With Tuberculosis

Social determinants represent the broader non-medical conditions into which individuals are born into or live, and these social conditions put certain individuals at high risk for the disease (Link & Phelan, 1995; 2002). Additionally, these social conditions play a major role in the epidemiology of TB and are considered as part of the bold policies and supportive systems of the *End TB strategy* (Lönnroth et al., 2010; WHO, 2015). Furthermore, they are high on the causal pathway that links poverty and socioeconomic status to the factors that increase the risk of exposure to the infectious source of developing TB (Lönnroth et al., 2009). Globally, TB prevalence and mortality are unequally distributed in many countries and have an inverse relationship with wealth. Similarly, there is evidence to demonstrate that TB has a negative impact on the socioeconomic status of patients and their families (Dye et al., 2009).

In their position paper, the American College of Physicians stressed the need to increase efforts to identify the social mechanisms which are responsible for the many health disparities including TB infection among populations (Daniel et al., 2018). To effectively understand and address the health needs of populations at risk of disease, it is important to adopt strategies that take into consideration the socioeconomic, cultural, and demographic reality of the population. However, the biomedical model which is based on the principles of biology and biochemistry (Mulinari, 2014), continues to be dominant in health-care practices. Paul Elrlich coined the term “magic bullet” therapy to describe how medication has the power to attack the pathogenic invader without affecting the human host (Travis, 2008). Critiques of biomedical reasoning, however, argue that it is elitist, acts as the final authority on what is normal, and is historically associated with the Victorian notion of the body as a machine (Clarke & Shim, 2010; Slatman, 2014). There are many criticisms that have come from the medical community, medical sociologists, and practitioners who believe that the governance, delivery, and evaluation of health care should not revolve around the traditional medical model (Bury & Gabe, 2013). For instance, Engel (1977) critiqued the traditional medical approach which assumes that disease is accounted for by deviations of the norm of measurable biologic variables. This approach does not leave room to include the social, psychological, and behavioral dimensions of the illness framework. Engel argued that to provide a basis for understanding the determinants of health, a medical model should take into account the patient, the social context in which they live, and the supporting infrastructure designed by society to deal with the destructive effect of illness as in the role of the physician and the health system, which in effect requires a biopsychosocial model (Engel, 1977). This means that the biomedical approach should be broadened to include psychosocial variables without compromising the advantages of the biomedical approach (Engel, 2017). When this happens, patients will continue to be cared for from the biomedical standpoint, and that the same time, their psychosocial and social information would be given attention in the care process (Smith et al., 2013).

Different pathways can be used to establish the association between socioeconomic, demographic, and behavioral risk factors to DR-TB. Given the increasing attention to the social determinants of TB by the scientific world and the public health community (Lönnroth et al., 2009; Rasanathan et al., 2011), it is imperative to have a comprehensive review of the literature to understand what the data says about the determinants. Therefore, the next pages of this chapter will review a wide range of literature on topics related to the socioeconomic, demographic, and behavioral risk factors that may be associated with DR-TB diagnoses and treatment outcomes. The review first discussed age and sex as the demographic risk factors. The remaining chapter was devoted to discussing the socioeconomic risk factors associated with MDR-TB namely, place of residence, education, income levels, HIV, and employment.

Age

Numerous studies from different populations have established that the risk of developing TB increases with age (Chadha et al., 2012; Rao et al., 2012; Wang et al., 2014). Some researchers have theorized that the weak immunity of older persons predisposes them to an increased rate of progression from latent TB infection to reactivation of TB disease (Thrupp et al., 2004). In a population-based cross-sectional study conducted in China, Zhang and colleagues (2019) reported that almost half (48.8%) of diagnosed TB cases in China's Fifth National Prevalence Survey were older people. In their multivariable regression analysis, age 75-84 (OR = 1.59, 95% CI [1.17, 2.17]) and age group ≥ 85 (OR = 2.05, 95% CI [1.25, 3.36]) were shown to have a high risk of TB compared to lower age groups. This supports an earlier study conducted in the United

States that found TB rates increase with age among adults aged 65 years and above (Hochberg & Horsburgh, 2013). Elduma and colleagues (2019) reported similar results in a case-control study. In their multiple regression analysis, they found that age groups between 25-44 and 45-64 years were at high risk of MDR-TB (*aOR* = 3.86; 95% *CI* [2.30, 6.48], $p < 0.00$) and (*aOR* = 4.29, 95% *CI* [2.13, 8.28], $p < 0.001$) respectively compared to the 18-24 and 65+ (*aOR* = 2.09; 95% *CI* [0.79, 5.59] $p = 0.136$) years groups. In a study conducted in China using an ecological design, Liu and colleagues (2013) performed a multiple logistic regression analysis to assess the risk factors for DR-TB and found that compared to those 65 years or older, the risk of MDR-TB was significantly associated with the age of patients (*aOR* = 2.224, 95% *CI* [1.158, 4.273]). In another study using a case-control design, Workicho and colleagues (2017) found a statistically significant association between age and MDR-TB among TB patients (*aOR* = 7, 95% *CI* [2.40, 21.07], $p = 0.001$). The study demonstrated that those aged 30 years and above were seven times more likely to have MDR-TB compared to respondents below 30 years. Though the study designs are different, they provide consistent results supporting that an increase in TB cases is associated with an increase in age. But such increases in TB cases with age have not been convincingly demonstrated in some studies. Whereas some of the associations are weak, some were found to be very strong, and others were observed in the opposite direction. For instance, a cross-sectional descriptive study conducted in Pakistan by Ullah and colleagues (2016) found that age is a major risk factor for the development of DR-TB. Using multivariable logistic regression analysis, the study observed a statistically significant association between individuals who were

10-25 years and DR-TB (*aOR* = 0.607, 95% *CI* [0.420, 0.878], $p < 0.008$). Though there is an association in this study, it is a very weak one. Raazi and colleagues (2017) established that the young age of patients is a risk factor for MDR-TB compared to non-MDR TB patients ($x^2 = 19.956$ $df = 2$, $p = 0.05$). Mixed results were produced in an ecological study conducted in Brazil where the authors used a multilevel model to reveal that persons aged 15-59 years had a higher risk (*IRR* = 1.75, 95% *CI* [1.40, 2.11]) of DR-TB compared with those aged 60 years and above (Jacobs et al., 2018). Those who were below 15 years had a low risk of DR-TB (*IRR* = 0.02, 95% *CI* [0.008, 0.05]).

In contrast, many studies did not produce any link between age and TB. Demile and colleagues (2018) found no association between age and MDR-TB among armed force members (*OR* = 5.1, 95% *CI* [0.8, 31.2], $p = 0.079$) and civilian patients (*OR* = 2.4, 95% *CI* [0.14, 38.9], $p = 0.546$) in a cross-sectional study conducted in Ethiopia. Furthermore, Stosic and Colleagues' (2018) bivariate analysis of sociodemographic risk factors of TB in Serbia revealed that age did not predict MDR-TB (*OR* = 1.36, 95% *CI* [0.59, 3.10] $p = 0.536$). Moreover, results from a multivariate analysis in an observatory and exploratory study conducted in South Africa demonstrated that age ≤ 40 years did not show any significant association (*cOR* =1.308, 95% *CI* [0.392, 4.368], $p = 0.533$) with MDR-TB (Maharjan et al., 2017). Based on the data on this review, it is obvious that there are mixed results on the association between age and development of DR-TB among TB patients. The reason might be that most of the studies reviewed here do not cover a wide population of TB patients. The data are largely from small populations such as a single TB facility or a few TB facilities. Therefore, the findings in the studies should be interpreted with a major limitation of the small number of patients enrolled. This limitation was addressed in the current study given that the sample size was big and was randomly selected from the population. With a population from the widely distributed geographical area, it is believed that the findings from the present study reflected the impact of age on MDR-TB in Lesotho. Moreover, the association between age and MDR-TB is not well established because different studies used different age group cut-off points. Thus far, age-related differences in medication compliance could be a possible reason, as most patients within the age-group10-25 years have active lifestyles compared to older patients (Kim et al., 2019). Therefore, an understanding of age disparities associated with MDR-TB is crucial in providing insight into the development of targeted measures, improving access to health care, and reducing the risk of drug-resistance by age in a population-based study.

Sex

Infectious diseases rarely affect the male and female genders equally (Guerra-Silveira & Abad-Franch, 2013), and TB is not an exception. Conflicting results have been reported in the literature about sex and MDR-TB (Ejaz et al., 2010; Lomtadze et al., 2007). The susceptibility to MDR-TB may differ for gender because of differences in access to healthcare (Liu et al., 2013). In a systematic review, Faustini and colleagues (2005) found that men are more likely than women to be associated with MDR-TB in Europe (*OR* = 1.38, 95% *CI* [1.16, 1.65]), but the reverse is the case for a study conducted by Ejaz and colleagues (2010) who performed a logistic regression analysis on a passive case finding. The authors used a sample of sixty-four participants and found that the female gender was independently associated with MDR-TB (*OR* = 3.12, 95% *CI* [1.40, 6.91]). Although the cause of this is not certain, Nhamoyebonde and Leslie (2014) suggest that epidemiological factors have historically been considered as the driving force. In a population-based prospective study conducted in Mexico, Jimenez-Corona (2006) report the incidence rate of TB to be 58% higher in men (31.79 cases per 100,000 person-years) than in women (20.13 cases per 100,000 person-years, $p < 0.001$), and men were more likely than women to default from treatment (*aOR*: 3.30, 95% *CI* [1.46, 7.43]), to retreat (hazard ratio (*HR*): 3.15, 95% *CI* [1.38, 7.22]), and to die from TB (*HR*: 2.23, 95% *CI* [1.25, 3.99]). These results are confirmed in a retrospective study in Israel where males are found to be more at risk for MDR-TB (*aOR*: 1.2, 95% *CI* [1.0, 1.5], $p < 0.001$) than females. The World Health Organization supported these findings in their report, which stated that the number of men with TB was close to 6 million TB in 2017 compared to an estimated 3.2 million women infected with TB (WHO, 2017). The above reports demonstrate that gender is a risk factor for TB and that men are significantly more at risk of contracting TB than women. As noted by some researchers, men predominantly work in the mines and indulge in risky behaviors (such as smoking and alcohol abuse) which may explain the higher TB rates and treatment outcomes among men (Negm et al., 2016; Seung et al., 2009).

But in an exploratory and descriptive study, Maharjan and colleagues (2017) applied multivariable logistic regression analysis and identified the female gender to be significantly (*cOR* = 9.237, 95% *CI* [1.032, 82.705], $p = 0.05$) associated with MDR-TB in Nepal. This suggests that females are 9 times more likely at risk of developing MDR-

TB than males. The authors indicated that women spend more time caring for family members who have MDR-TB both in household and clinic settings and this might account for the association. Also, a descriptive cross-sectional study in Pakistan used multivariable logistic regression analysis and found the female gender to be associated (*aOR*:1.004, 95% *CI* [0.75, 1.34]) with MDR-TB (Ullah et al., 2016). This finding is similar to results in a case-control study conducted in Sudan where Elduma and colleagues (2019) found that the risk of acquiring MDR-TB among females was twice high as among males (*aOR* = 1.98, 95% *CI* [1.26, 3.09], $p = 0.003$). Results from a retrospective study in South Africa report that only female gender (*OR*: 1.38, 95% *CI* [1.11, 1.73]) were independently associated with XDR TB (O'Donnell et al., 2011). The findings in the study also indicated that women are predominantly affected by DR-TB in the KwaZulu-Natal region of the country given that they were 38% more likely than men to have XDR-TB. It must be noted here that irrespective of the study design, sample size, and type of methodological analysis, the positive association between gender and MDR-TB remained. Though the reasons for the association are not known, it could be hypothesized that the association were in part due to the fact the women spend more time caring for the sick both at home and in the healthcare settings (Liu et al., 2013). The direction of the associations is however mixed given that whereas some studies indicate that men are more at risk of MDR-TB, others proved otherwise. The reason might be that the study population differs relative to gender roles in different communities.

Unlike the studies that found an association between gender and MDR-TB, Ullah and colleagues (2016) used a chi-square analysis in a study in Pakistan and did not find a statistically significant association between gender and MDR-TB (*aOR* = 1.004, 95% *CI* [0.753, 1.338], *p* = 0.981). Also, in a cross-sectional study conducted in Ethiopia by Demile and colleagues (2018), sex was not a predictor of MDR-TB among force members (*OR* = 1.0; 95% *CI* [1.0, 1.1], *p* = 0.153) and civilians (*OR* = 1.1, 95% *CI* [0.1, 17.4], *p* = 0.965). Gender was not also a predicting factor of MDR-TB (*OR* = 1.22; 95% *CI* [0.50, 2.97], *p* = 0.658) in a case-control study conducted in Serbia (Stosic et al., 2018). The results presented here suggest that more work remains to be done to identify and understand gender differences in patients with TB and how this influences MDR-TB to improve diagnosis, treatment, and prevention for MDR-TB within specific populations. Further, studies are needed to confirm the magnitude of the association between gender and MDR-TB.

Educational Levels

Factors outside the healthcare system such as educational attainment are consistently associated with health outcomes and have featured prominently in explaining health disparities by geographic and demographic characteristics (Adler et al., 1994). But the relationship between education and health is not a simple one. There are a variety of studies about education and health inequalities with frequently different conclusions (Cutler & Lleras-Muney, 2006). Nonetheless, there appears to be a consistent association between education and health outcomes observed in many countries, at different periods, and for different health measures. Zimmerman and Woolf (2014) reported that studies have consistently identified education status as a strong predictor of health outcomes in their meta-analysis. Hahn and Truman (2015) observed that more educated people are less likely to suffer from acute and chronic diseases than less educated people. In a case-control study conducted in Henan province in China, the researchers reported that the odds of having MDR-TB was almost 2 times in people with less education compared to those with more education (*aOR* = 1.87, 95% *CI* [1.27, 2.69], *p* = 0.000) (Zhang et al., 2015). This is consistent with a recent similar study in India which confirmed an association (*aOR* = 1.63, 95% *CI* [1.03, 3.11], *p* = 0.01) between low or no formal education and MDR-TB (Sharma et al., 2019). In contrast, while another case-control study in Ethiopia established an association between education and MDR TB, the direction of the association was different. The researchers determined that education above grade 12 is statistically associated (*aOR* = 2.04, 95% *CI* [0.85, 4.89], *p* = 0.005) with MDR-TB status (Assefa et al., 2017). This is confirmed in Khan and colleague's (2017) case-control study in Myanmar where educational status was established as a risk factor for MDR-TB. The study discovered that the risk of MDR-TB was high among TB patients with a high educational background compared with patients who only have primary school education or less (*aOR* = 1.78; 95% *CI* [1.01, 3.13], *p* = 0.046). Despite the association in both studies, the statistical significance is weak and can not be used as a strong predictor of MDR-TB. The difference in the results of the association might be due to a difference in sample size and populations used for the various studies. As expected, what remains clear is that all the studies found education as a determining factor of MDR-TB.

Zimmerman and Woolf (2014) indicated that the obvious explanation for the association between education and health is that education produces benefits that predispose the recipient to better health outcomes. Another explanation for the relationship is that people with more education can access medical care and use it to improve their health (Nutbeam, 2000). Other authors have given evidence to show that those with more education are better able to access health care (Burgard & Hawkins, 2014; Cho et al., 2008). DeLuca and colleagues (2018) demonstrated in a study in India that populations with a high risk of TB do not have the knowledge and understanding of how TB transmission occurs. Most of them do not know what a positive skin test means. Even though most of the households were willing to utilize preventative therapies, they did not know how to implement preventive measures. Some studies demonstrate that people with high levels of education and knowledge have a higher tendency to take appropriate action about their health, such as regular screening and/or adherence to taking their medication. Results from a study found that MDR-TB patients with low educational attainment have a higher risk of death during treatment (Chung-Delgado et al., 2015) and that it was associated with adherence to treatment as it increases the awareness in levels of knowledge of patients regarding the disease (Franke et al., 2008).

Despite the above findings and explanations, a previous case-control study conducted in Botswana and using multivariate analysis did not observe any association ($aOR = 0.43$, 95% CI [0.14, 1.30], $p = 0.13$) between education and MDR-TB (Zetola et al., 2012). In a similar study conducted in Sudan, educational status was not a significant risk factor associated ($OR = 0.6$, 95% CI [0.3, 1.2, $p = 0.17$]) with MDR-TB (Ali et al., 2019). Both studies used similar study designs and sample size and not surprisingly, the results and conclusion are similar. Both studies suggest that there is no statistically significant difference between persons with low or no education and those with education relative to their risk to MDR-TB. The review demonstrates that the results are mixed about the relationship between education and DR-TB, nonetheless, educational attainment could be an important leverage factor that could potentially help to address the problems that give rise to increasing health disparities in DR-TB among populations.

Income Levels

The mechanism through which income inequality is linked to average health and health disparities has been established. Many researchers have demonstrated that income inequality affects the health of individuals (Fletcher & Wolfe, 2014; Truesdale & Jencks, 2016). There is a graded association between income and health such that higher income is typically associated with better health. But this idea has been debated. Wilkinson (1992) argued that in developed countries, higher levels of income inequality lowered the average lifespan of individuals. Therefore, it is often recommended that improving the incomes of the poor in society will improve their health, and subsequently reduce health inequalities. However, for health interventions and policies to be effective, it is imperative to understand how income influences health. Benzeval and colleagues (2014) identified four key theories that explain how income influences health. First, they theorized that individuals with good income can afford health-promoting goods and engage in lifestyles that promote good health and healthy living. Second, they identified psychosocial mechanisms that can impact their health. For instance, the stress of not having money can eventually have a negative impact on a person’s health. Moreover, behavioral factors such as people living in disadvantaged environments and circumstances due to poverty may more likely impact their health behavior negatively. Indeed, when compared with people with higher incomes, those with low incomes are more likely to adopt unhealthy behaviors. Finally, the author explained that poor health may affect a person's ability to have a good education and employment opportunities in ways that will even make their condition worse. This situation can best be described as reverse causation whereby poor health leads to low income, and low income affects a person's health.

Specifically, poverty is associated with the risk of TB infection, but the relationship between income and MDR-TB outcomes is not well understood. There is evidence from many studies that highlights the relationship between TB and economic levels among different populations (De Castro et al., 2018; Harling & Castro, 2014). De Castro and colleagues (2018) argued that absolute poverty, disease concentration, and transmission among vulnerable populations may explain the slow pace of TB reduction. The researchers further observed that in most countries, the probability of contracting TB is significantly higher among socially disadvantaged and economically vulnerable populations such that populations with greater income inequality experienced greater TB incidence (De Castro et, al., 2018). Results from a cross-sectional study in Sri Lanka found TB to be significantly associated (*aOR* = 4.06, 95% *CI* [2.1, 7.775]) with low economic status (Senanayake et al., 2018). In a case-control study conducted in Serbia, Stosic and colleagues (2018) found family income to be a statistically significant independent predictor of MDR-TB in multivariate analysis (*OR* = 3.71, 95% *CI* [1.22, 11.28], $p = 0.021$). Sharma and colleagues (2019) in their case-control study in India noted that people belonging to lower per capita income groups had higher odds of developing MDR-TB (*aOR* = 1.82, 95% *CI* [1.21, 2.59], *p* = 0.41). In contrast, Khan and colleagues (2017) did not find any statistically significant association between low income and high income to the and risk of developing MDR-TB (*aOR* = 1.05, 95% *CI* [0.61, 1.81], *p* = 0.0866) and (*aOR* = 1.01, 95% *CI* [0.57, 1.78], *p* = 0.0966) respectively in their case-control study conducted in Myanmar. These findings from this study should be interpreted with caution due to potential bias in the selection of the cases and controls. Whereas only 16% of the MDR-TB cases in the study were smear-negative, a very limited number of the smear-negative were included in the control group which might not be representative of the population. Like this finding, Rifat and colleagues (2014) used a chi-square analysis in a case-control study in Bangladesh and did not find any association between income levels and health systems delays in treatment among MDR- patients (95% *CI* [-0.001, 0.002], *p* = 0.71). Though poverty might hinder as well as delay TB patients from seeking correct treatment and adhering to treatment, it is important to always investigate and establish the exact factors that predispose individuals within a population to the risk of developing MDR-TB.

Undeniably, for patients who are already poor, the risk of falling into deeper poverty due to diagnoses of TB and MDR-TB is high as demonstrated in a study in Indonesia where it was reported that 32% of TB patients and an extra 69% of MDR-TB patients who had income-earning jobs lost their jobs after diagnosis (Fuady et al., 2018). In a prospective cohort study, Djibuti and colleagues (2014) demonstrated that TB patients in Georgia with low household income were at a high risk of TB treatment outcomes relative to those with high incomes (*aOR* = 6.18, 95% *CI* [1.83, 20.94]). Besides imposing an economic burden on affected patients and their families, the high cost related to TB can create access and adherence barriers (Fuady et al., 2018: Van den Hof et al., 2016). Variable costs (such as travel costs, food, nutritional supplements, and income losses) contributed significantly to the total cost. Victora and colleagues (2000) showed that in populations where income inequality exists, those with higher socioeconomic levels benefit more from health resources than the poor, resulting in increased health disparities. To this end, there is a greater agreement regarding how economic heterogeneity can explain disparities in the incidence of TB among populations. Therefore, understanding the mechanisms that link income to health is imperative for designing policies that reduce disparities in MDR-TB outcomes.

Human Immunodeficiency Virus Coinfection

HIV is a strong risk factor associated with the increased incidence of TB, and it underlines the synergy between the progress of HIV and TB (Adeiza et al., 2014). Indeed, the global burden of HIV has had an impact on the epidemiology of TB, and this has implications on the health outcomes and treatment options. In particular, the resurgence of TB in sub-Saharan Africa has been fueled by the HIV pandemic (Swaminathan et al., 2010), and the WHO African region bears the highest burden of the disease accounting for 82% of HIV-positive incident TB cases in 2010 (Adeiza et al., 2014). While many epidemiological studies have been equivocal about the statistical significance of the association between HIV and DR-TB (Suchindran et al., 2009), several studies have found that the risk of developing DR-TB is greatly increased by HIV coinfection

(Mishkin et al., 2018; Van den Hof et al., 2016). The strong association between HIV and TB is responsible for the increased incidence of TB observed in the region in the last 20 years (Idh et al., 2008; Keshinro & Diul, 2006). In a case-control study involving multiple regression analysis of risk factors of MDR-TB among TB patients, Workicho and colleagues (2017) determined that respondents who are HIV positive were 3 times more likely to have MDR-TB when compared to persons without HIV infection (*aOR* = 3.1, 95% *CI* [1.02, 9.40], *p* = 0.046). Though this study suggests that the risk of MDR-TB is three times more likely among people infected with HIV than those without HIV, the statistical significance is marginal and therefore HIV is not a strong predictor of MDR-TB in the study. Mulisa and collegues (2015) reported a stronger association between HIV and the existence of MDR-TB in a study involving multivariate analysis to report an association between HIV and the existence of MDR (*OR* = 2.7, 95% *CI* [1.43, 5.06], *p* = 0.01). Similar findings were reported by Elmi and colleagues (2015) and Assefa and colleagues (2017) in two separate studies. The researchers found statistically significant association between HIV and MDR-TB (*aOR* = 0.22, 95% *CI* [0.08, 0.61], *p* = 0.001; *aOR* = 1.95, 95% *CI* [1.13, 3.35], *p* = 0.001). Sharma and colleagues (2019) also reported an association (*aOR* = 9.45, 95% *CI* [6.8, 15.9], *p* = 0.008) between HIV and MDR-TB. Their study revealed that persons with HIV were nine times likely to be a risk of MDR-TB than those who are HIV negative.

Despite this observation, a cross-sectional study conducted in South Africa found that HIV is not a significant and independent risk factor for infection and development of DR-TB (*OR* = 3.10, 95% *CI* [0.85, 11.33]). A retrospective case-control study in Korea, Lee and colleagues (2016) demonstrated similar results where the rate of DR-TB in Southeast Korea was 11.1%, and DR-TB was not significantly associated with HIV coinfection (*OR* = 1.40, 95% *CI* [0.54, 3.61], *p* = 0.42). Moreover, Baya and colleagues (2019) did not find any significant association with HIV coinfection and MDR-TB (*OR* = 0.82, 95% *CI* [0.34, 1.94], *p* = 0.65). Like this study, Ali and colleagues (2019) used a multivariate logistic analysis model and did not find a significant association between DR-TB and HIV (*OR* = 0.1, 95% *CI* [0.02, 1.1]). Similar studies in Thailand, Malasia, and Uganda did not find HIV as a factor associated with MDR-TB infection (Chuchottaworn et al., 2015; Elmi et al., 2016; Lukoye et al., 2013). The conflicting reports in these reviews suggest that the risk of MDR-TB is manifested differently in different settings. In other words, the different sample sizes and sample selection might account for the different findings in the various studies. Determining the association between HIV as a risk factor for MDR-TB will ensure the prioritization of patients to achieve optimal DR-TB prevention, diagnoses, and treatment in resource-limited settings.

Employment Status

Many studies have reported an association between employment and health, with unemployment being associated with poor health outcomes (Emerson et al., 2018). In some ways, the association appears to be accounted for by processes such as health selection and benefits associated with employment (Bartley, 1994; Van Rijn et al., 2013). Health selection takes place when a person’s health status has a profound impact on their ability to be actively engaged in a paid workforce. In other words, poor health plays a major role in early retirement, exit from employment due to a disability, and unemployment (Schuring et al., 2007; Schuring et al., 2013; Van den Berg et al., 2010). On the other hand, employment is known to improve health by increasing social capital, enhances psychological well being, provides income, and reduces the negative impact of economic hardship (McKee-Ryan et al., 2005; Paul & Moser, 2009; Ross & Mirowsky, 1995).

TB has been recognized as a disease that affects the poorest of the poor and the epidemiological analysis of the disease shows that a risk factor such as unemployment may increase the likelihood of the disease (Krawiecka, 2014). While some studies have identified an association between TB and unemployment, others did not. Desissa and colleagues (2018) found that the odds of developing MDR-TB were high in patients without jobs ($OR = 2.4$, 95% CI [1.06, 5.42], $p < 0.001$). A similar finding was reported in China where the association between TB and unemployment was observed to be statistically significant ($OR = 1.30$, 95% CI [0.78, 2.52], $p = 0.007$) (Zhang et al., 2015). In a multivariate analysis, Sharma and colleagues (2019) found that labor occupation was strongly associated ($aOR = 2.15$, 95% CI [1.18, 3.90], $p = 0.01$) with MDR-TB in their case-control study. De Castro et al. (2018) also found a strong statistically significant association between the unemployment rate and MDR-TB ($aOR = 7.27$, 95% CI [3.102, 11.445], $p = 0.003$). In another case-control study conducted in Bangladesh with a sample of 1000 participants (250 cases and 750 controls), Rifat and colleagues (2014) found individuals with occupations in the service and business industry to be associated with MDR-TB ($OR = 2.88$, 95% CI [1.29, 6.44] and $OR = 3.71$, 95% CI [59, 8.66] respectively) compared to individuals who do not have any professional work. The literature reviewed demonstrates that employment status is associated with MDR-TB. However, the extent to which employment status is a risk factor for MDR-TB is not clear. The possible reason might be that the small sample size coupled with methodological limitations might account for the inability to establish the extent of the relationship. Therefore, the study used population-based data with a large sample size to test the hypothesis on how employment status mediates the relationship between employment status and MDR-TB.

Place of Residence

Eberhardt and Pamuk (2004) reported that rural-urban health patterns differ and that the individuals residing in rural and urban have higher rates of harmful health effects compared to suburban areas. In a multivariate analysis, Ali and colleagues (2019) found that living in a rural area was an independent predictor of MDR-TB in Sudan (*aOR* = 3.11, 95% *CI* [1.2, 8.2], $p < 0.01$). Also, Mulisa and colleagues (2015) found that TB patients in rural settings had a 2.7 times increased risk of MDR-TB in the multivariate analysis compared to those living in urban settings (OR = 2.7, 95% *CI* [1.54, 4.85]). Similarly, Zhang et al. (2015) reported that distance to a health facility is associated with the risk of MDR-TB in China (*aOR* = 6.66, 95% *CI* [5.92, 7.72], $p = 0.000$). The increased risk is MDR-TB is typically found in rural areas due to patients having to travel long distances to access healthcare. The study indicated that it took patients an average of 3 hours to reach the nearest health center. Moreover, Mulu and colleagues (2015) used a multivariate analysis to establish an association (*aOR* = 0.5, 95% *CI* [0.25, 0.92], $p = 0.03$) between living in an urban area and MDR-TB. This is confirmed in a recent study where living in a rural setting was associated (*OR* = 5.6, 95% *CI* [2.14, 14.46], *p* = 0.001) with MDR-TB. These studies reported a strong association that provides strong support that living in a rural setting is associated with MDR-TB. Basingnaa et al., (2018) reported contrary results in a study conducted in Ghana, which showed that MDR-TB was found to be high among people living in the urban areas than in rural areas (x^2 = 12.946, *p* = 0.005). However, in a recent retrospective cohort study in Botswana with a sample of 2568, Tembo and Malangu (2019) did not find any association between place of residence and DR-TB (*OR* = 758, 95% *CI* [0.480, 1.197], *p* = 0.234). Ashari and colleagues (2018) demonstrated similar results in a case-control study with a sample of 22 cases and 78 control in Iran. Using multivariable regression analysis, the authors demonstrated that there was no statistically significant association between place of residence (*OR* = 0.93, 95% *CI* [0.31, 2.84], *p* = 0.905) and DR-TB. The difference in the results might be due to differences in sample size and representativeness of the sample population. In summary, a key feature of this section of the review is that the risk of MDR-TB seems to exhibit a monotonic pattern where populations in rural communities are most affected as evidenced in the statistical significance obtained in the many studies. Nonetheless, more studies are needed to examine the association between MDR-TB disparities and place of residence.

Summary and Conclusion

The literature review suggests that while sociodemographic factors are imperative in predicting MDR-TB, some of the variables are not strong predictors of MDR-TB. While the biosocial and economic variables included in the review mediates MDR-TB, the literature on HIV status and age demonstrated a strong association with the outcome variable. Additionally, gender was a strong mediator of MDR-TB, however, both genders were strongly associated with MDR-TB depending on the population the study took place. Moreover, whereas some of the literature demonstrated an association between income, employment, place of residence, education status, and MDR-TB, other studies did not. The results from the analysis of the review varied in many ways and this is due in part to the fact that the study designs varied, different analytical methods were used, and findings were based on different sample sizes. As the results in the various studies differ, conducting further studies with an appropriate population that is broad and country-specific to identify appropriate strategies to optimize control measures to DR-TB is warranted. The study filled some research gap by way of identifying the socioeconomic, demographic, and behavioral risk factors associated with MDR-TB in Lesotho.

Chapter 3: Research Method

Introduction

The purpose of this study was to use quantitative methods to examine the association between the socioeconomic, behavioral, and demographic risk factors associated with MDR-TB among TB patients in Lesotho. The study employed a case-control study design to analyse data from TB patients at TB clinics in Lesotho between 2021 and 2022. Data on nine independent variables (employment status, education level, have a carer, have multiple sex partners, income level, and place of residence of patients, age, HIV status, and sex), and one independent variable (MDR-TB status) were analysed in the study. The confounders included in the study were having a caregiver and multiple sex partners. The main purpose of the study was to examine how the independent variables, both individually and in combination, are associated with MDR-TB. Therefore, the case-control research design was used to analyse the determinants of MDR-TB and describe some features of the population. The method was useful for establishing preliminary evidence in planning for future advanced studies.

The methodology of this study began with assumptions about the nature of reality and knowledge, values, and theory and practice of the study of social determinants of a disease such as TB. Building on this methodology, the study started with a standpoint of questions relative to what informed the paradigm, theoretical framework, research approach, data collection and analysis, ethics, and validity of the study. The assumption here is that the risk of exposure to TB, progression to MDR-TB, and cure of MDR-TB constitute a process affected by several risk factors. However, along with several known factors such as age, sex, and HIV comorbidity status of patients, emerging risk factors such as income level, level of education, employment status, and place of residence of patients play a significant role in the increased susceptibility of MDR-TB infection and treatment outcomes. This quantitative study was aimed at addressing the literature gap of the sociodemographic risk factors and comorbidities associated with MDR-TB among TB patients in Lesotho. Therefore, the sociodemographic risk factors—namely, age, education level, employment status, income status, place of residence, and sex—were examined in relation to their association with MDR-TB status of TB patients in Lesotho.

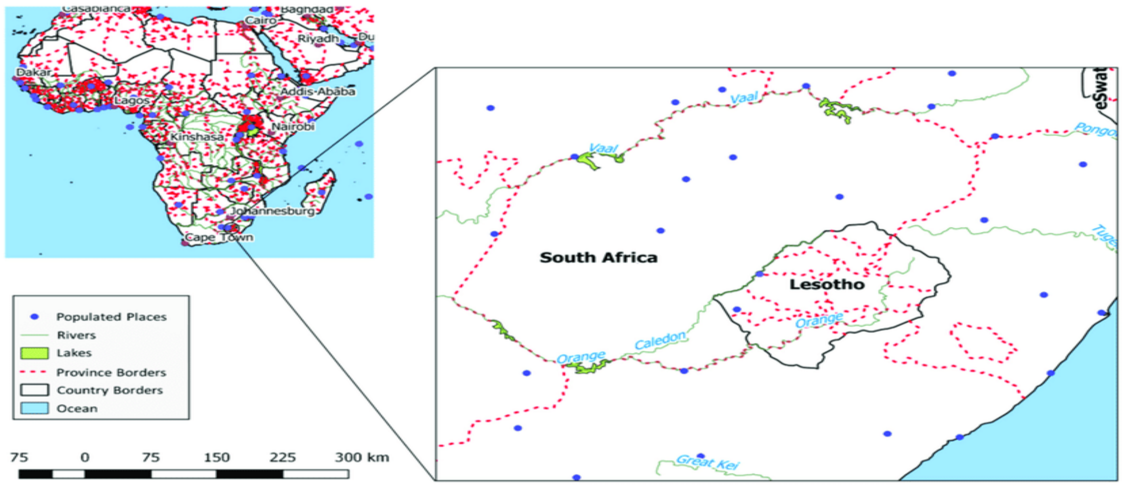
The goal of Chapter 3 is to provide a clear and complete description of the specific steps undertaken to address the hypotheses and research questions to enable the study to be replicable. The chapter contains an overview of the methods, strategies, and techniques that were used to obtain and analyze the data. This section also details the design that was used for the study. Specifically, the section focuses on the research design and rationale, target population, sampling techniques and sample size, power estimation, data collection techniques, instrumentation or measures, and the plan for analyzing the data. Moreover, the chapter gives an operationalization of the study variables, research questions, and hypotheses. Finally, a presentation is made on how the data were statistically treated and the ethical considerations regarding the protection of the study subjects.

Study Site

The study was conducted in Lesotho, a small and mountainous southern African country that is completely surrounded by the Republic of South Africa (Figure 2).

Figure 2

The Kingdom of Lesotho Within the Country of South Africa



Note. From *The World Factbook*, by the Central Intelligence Agency, 2020 (https://www.cia.gov/the-world-factbook/countries/lesotho/map). In the public domain.

Figure 3

Map of Lesotho Showing Its 10 Administrative Districts

Note. *Note*. From *The World Factbook*, by the Central Intelligence Agency, 2020 (https://www.cia.gov/the-world-factbook/countries/lesotho/map). In the public domain.

Over 80% of the country is 1,800 meters above sea level. Because of its mountainous nature, the country is popularly referred to as the *kingdom in the sky*. With an estimated population of about 2.7 million people (Bureau of Statistics, 2019), Lesotho has an estimated TB prevalence of 665/100, 000 population and TB mortality of 46/100,000 population (Centers for Disease Control and Prevention, 2019). This means that Lesotho has one of the highest per capita burdens of TB in the world. The NTP is responsible for managing the control of MDR-TB in Lesotho. Thus, the NTP develops policies, standards, and plans and gives guidance for TB control and prevention at all levels of government in 10 administrative districts of the country. As expected of a low-income country, the Basotho people are peasants, with others working in factories largely in the national capital, Maseru. Others also travel to relatively developed neighboring South Africa to offer their labor in South African mines.

Research Design and Rationale

As indicated earlier, the study used a quantitative case-control research design to address the research questions. This involved the measurement of observable variables and the performance of statistical analysis on a body of numerical data. The quantitative approach in this study applied the positivism paradigm to research whereby the researcher cannot go beyond the boundaries of what is observed (Park et al., 2020). In other words, positivism as a research strategy is rooted in the ontological principle and doctrine, which explains that truth and reality are free and independent of the researcher (Aliyu et al., 2014). Therefore, in this study, I applied the positivist paradigm with the assumption that there is an objective reality that can be measured objectively and explained scientifically by using reliable and valid measurements. Following the underlying principles of the positivist paradigm, the study used repeatable and generalizable procedures to isolate the effects of the study variables.

The rationale for the choice of a case-control study design enabled me to use methods that would determine the relative importance of the predictor variables in relation to the presence or absence of MDR-TB. The study involved primary data collection from TB clinics that were randomly selected across the country. The sample included patients with active TB and MDR-TB. The assessment of the multiple etiologic factors was accomplished through telephone and person-to-person surveys.

A total of seven independent and two confounding variables and one dependent variable were examined in the study. The dependent variable for the study was TB status (MDR-TB). The independent variables (sociodemographic variables) for the study were educational level, employment status, income level, place of residence (rural/urban), sex, and age. The other risk factors used as controls in the study included having multiple sex partners, having a caregiver, and HIV status. It should be noted that after a random sample of the TB clinics, stratified sampling was used to select and enroll the study participants. A standard survey questionnaire was used to obtain sociodemographic information from the study subjects via telephone and in-person interviews. Subsequently, the data collected were cleaned and used for the study analysis. Because the primary data were randomly collected nationally, the data were considered appropriate for this study. In other words, the data were current, offered a large sample size representation of the population of interest, and were of guaranteed quality.

Given that the research questions involved the identification of biosocial and economic risk factors, the choice of a case-control research design was appropriate. This observational study was important in answering critical health promotion questions that can further the understanding of a range of risk factors related to MDR-TB. Additionally, due to its ability to assess multiple types of exposures, the case-control design was considered appropriate and cost-efficient for this study, especially given that MDR-TB is a rare disease. Results from this study could be used to design interventions that will minimize the risk factors associated with MDR-TB in Lesotho. The results could also be used to support Lesotho's efforts to strengthen surveillance, monitoring and evaluation, and management systems needed for the national TB response.

Methodology

Population

A case-control quantitative study was conducted at TB clinics in Lesotho. The complete list of people who received treatments at TB referral centers in Lesotho between January 2018 through January 2022 constituted the study population. The target population, on the other hand, was composed of people with confirmed TB cases in Lesotho who were 18 years of age and above. The study sample consisted of individual TB patients who were responding to first-line anti-TB treatment drugs and those who had MDR-TB. A random stratified sample of 306 TB patients were selected for the study. The sample included patients who had showed resistance to first-line treatment with anti-TB medications such as rifampicin and isoniazid while on treatment for TB. Patients who were responding to first-line anti-TB treatment drugs were also added to the study.

Sampling and Sampling Procedure

Study participants were recruited from health clinics in Lesotho that provide TB services. The inclusion criteria took into consideration all individuals with confirmed TB at designated TB health facilities who were on the TB register. This included all patients who were actively on anti-TB treatment, patients who were still alive, and patients who had defaulted on treatment during the study period. Eligible patients were adult outpatients with active TB and/or MDR-TB. Participants needed to be 18 years age or older and have a working knowledge of Sesotho and/or English. The exclusion criteria included anyone with unconfirmed TB and anyone who was not receiving any form of treatment at designated TB clinic during the study period. Moreover, patients who were below 18 years of age were excluded.

A random sample of the participants was contacted either directly or enrolled through phone calls for data collection. The process began by dividing the whole population into homogenous subpopulations or strata based on the community of location of TB clinics. From there, I selected individuals randomly from each stratum. In other words, a random sample from each stratum was drawn to the stratum's size when compared to the population. Thus, the proportionate stratified random sample was obtained by dividing the sample size over the population multiplied by the stratum size ([sample size/population] * stratum size). The subsets of the strata were then pooled together to form a random sample. To select participants from each stratum, individuals were first assigned with numbers starting from 1 through the last name on the list on the TB register at each selected TB clinic. Using Microsoft Excel, random numbers were generated from the list. TB patients who were randomly selected from each list were recruited for the study. The use of a probability sample method ensured that each TB patient in the target population was given an equal chance to be selected to participate in the study.

Sample Size Estimation

Sample powering was conducted to determine the number of participants needed to power the test statistic for the study. The factors that were taken into consideration in calculating the sample size for the study were the alpha level (α), desired statistical power, anticipated effect size, predictor variables, and covariates considered for the study. The dependent variable for this study was dichotomous (presence or absence of MDR-TB); therefore, a logistic regression analysis was considered appropriate for the regression analysis. The required sample size and the effect size were determined using a G*Power software developed by Faul et al. (2009) for an analysis of logistic regression and a binomial predictor. The G*Power analysis assumes a desired power set at (β) = 0.80 and an alpha level of (α) ≤ 0.05. Odds ratios (*OR*) were reported for the effect size statistics. Based on the G*Power analysis, the odds ratio was detected at *OR* = 2.3, and a total sample size of 186 was required to achieve a statistical power of (β) = 0.80. However, a 25% (46.5) contingency of the sample size was added to account for multiple comparisons and missing data. This suggests that there was an 80% chance of correctly rejecting a null hypothesis that a particular value of a predictor variable was not associated with the value of the outcome variable (presence or absence of MDR-TB). However, in all, there were 306 participants in the study, and this ensured that the 80%

power considered for the study was able to detect a difference in the predictive factors to determine MDR-TB and was adequate to accept or reject the null hypothesis accurately. This means that the possibility of false-negative results was 20%. Put differently, the study accepted one in five times (20%) that a real difference would be missed. Whereas the conventional *p*-value of 5% ($p = 0.05$) considered for the study provided a determination of whether an association is a chance occurrence, the effect size ($OR = 2.3$) is the empirical value to judge whether statistically significant results are meaningful at the practical level. Specifically, the effect size was used to capture the impact of an association by using the *OR*s to measure how many times bigger the odds of an outcome were for one value of an independent variable compared to another value. In other words, for any single increase in an independent variable, the odds of the dependent variable would be 2.3 times as big, after controlling for other predictors.

Procedures for Recruitment, Participation, and Data Collection

Access to Datasets

This quantitative study used primary data sources only. To have access to TB patients, I sought permission from the Lesotho Health Services through the Lesotho National TB Program. Once permission was granted to access health facilities, I sought further clearance from managers of the individual health facilities. Upon approval, TB data managers provided access to the TB register, which had the list of TB patients and their phone contacts. Where possible, selected individuals were contacted by phone for recruitment and subsequently interviewed. In some cases, individuals were recruited on TB clinic days.

Data Collection

The number of TB patients on TB registers at TB clinics constituted the sample frame. Information for the independent variables was gathered on the sociodemographic characteristics of sampled participants directly in the field. In other words, information was collected from a stratified random sample of the population through a structured telephone survey questionnaire. The primary survey questionnaire was used to solicit basic information from study subjects on age, sex, employment, income, education status, HIV status, multiple sex partners, having a caregiver, and place of residence in Lesotho. The data collected were cleaned and used for the study analysis.

Data Development and Management

Following the collection of data for this study, a database was constructed to contain the dependent and independent variables under consideration. Subjects' information in the database was identified by their assigned identifier during the data collection stage. Information about respondents that was missing more than three data or inconsistent answers was not included in the development of the database. The questions for the questionnaire were precoded, and how information about the outcome variable from the sampling frame was organized to facilitate the development of the database and statistical analysis is shown in Table 1. Quality control checks were carried out at every stage of data entry through verification and cross-matching of the response entry of the respondents, linkage of study participants’ assigned code to the entered data, and correct classification of the respondents. Data were reviewed and verified for accuracy before analysis.

Protection of Data and Human Subjects

Approval to conduct the study was obtained from the Walden University Institutional Review Board. Ethical issues required by the IRB was strictly observed during the process of the research. Upon approval from the Lesotho Health Services to collect data for the study, subjects were contacted and informed about the study. During the primary data collection process, information about the study and participation consent was translated into Sesotho (the official language of Lesotho) and offered to potential study subjects for recruitment. Potential subjects were then asked for their informed consent to participate in the study. Once they acknowledge on the phone that they would participate in the study, it was proceeded with a survey interview. Individuals who participated in the study were provided the opportunity to ask questions for clarification about the study and their participation. It was made clear to participants that they can exit the study if they so wish. The confidentially of study subjects' identity and their data were ensured through the following:

1. Participation in the study was voluntary.
2. Respondent's consents were obtained through an informed consent process and agreeing to the study on the telephone was carried out in either English or Sesotho language.
3. Subjects who volunteered to participate in the study were given special study identification (ID) numbers. The identification numbering system was started with the subject's ID number from the TB register. Study participants were identified on the survey instrument by using the study ID.

4. Trained data collectors contacted participants on phone and administered the survey instruments.
5. The data were then cleaned, ensured it was completed, transferred to an SPSS software, and analysed.
6. All data that were collected and used for the study were maintained in a secured Excel central database with a secure password that is accessible to me alone.
7. Any presentation or publication that will be based on this study will not reveal the names of the human subjects.
8. All data were reported in aggregate form in the results so that subjects cannot be identified based on demographic or descriptive characteristics. This ensured that respondent's identity and information were protected.
9. Records from this study and files have been stored in a secured place until after 5-years before they will be destroyed.
10. Written permissions were obtained from the appropriate authorities prior to data collection for the study.
11. A two-page summary report of the results were provided to the Lesotho Health Services and shared with WHO offices in Lesotho. Whenever invited to make a presentation on the study, a PowerPoint presentation will be utilized.
12. All the rules required by the Lesotho Health services and Walden University IRB were strictly followed.

13. The study was commenced based on approval from the Walden University IRB.

Instrumentation

The development of an instrument for this study was based on the methodological procedures of the Demographic and Health Survey (DSH) program that assisted countries to undertake population and health surveys worldwide. To collect the primary data in the field, the DHS standard questionnaire were adapted to reflect the population and health issues relevant to Lesotho (See Appendix B). The Lesotho Demographic Surveys (LDHS) survey instrument was developed in consultation with stakeholders in Lesotho under the supervision of the Ministry of Health of Lesotho. The tool was pretested to rectify all inconsistencies and to ensure that it was reliable prior to its use. Moreover, the survey takers were familiar with the survey since they previously used it to collect data on previous studies. Nonetheless, there were retrained and had supervisors who called subsamples of the respondents to verify selected pieces of information. The tool was used to collect data on sociodemographic characteristics and other health variables in the past such as knowledge on HIV/AIDS and TB. The instrument was used in 2004, 2009, and 2014, hence, the questions were familiar to some of the respondents. The 2014 LDHS yielded a response rate of 99% which compared favorably with the 2009 LDHS response rate of 98%. By using an established measure that was used consistently in previous studies like in the 2004, 2009, and 2014 surveys, the instrument served as a good guide and ensured the reliability of the information from the respondents.

A study by Luba and colleagues (2019) used data from the 2014 LDHS to assess the knowledge, attitude, and associated factors towards TB in the general population in Lesotho. The authors accessed variables such as age, sex, religion, place of residence, level of education, marital status, occupation, and wealth index from the survey as predictors of respondent's knowledge and attitude towards TB. The study predicted that sex ($aOR = 2.45$, 95% CI [3.90, 2.86] $P < 0.001$), educational level ($aOR = 6.26$, 95% CI [3.90, 10.06], $p < 0.001$), age ($aOR = 1.76$, 95% CI [1.29, 2.41], $p < 0.001$), occupation ($aOR = 1.20$, 95% CI [1.00, 1.44], $p < 0.049$) were associated with respondents' knowledge of TB. It was clear from this result, that the datasets from the survey established relationships and predicted outcomes, hence, the tested validity of measures of the survey in a way was guaranteed.

The instrument was adopted and dovetailed to fit the needs of the current study (Appendix A). The survey instrument was redeveloped, pretested, and a debriefing session was held with the pretest staff which ensured all inconsistencies were rectified. In summary, whereas the reliability of measures was improved using established measures, and examination of the work of research field workers, the yardstick for assessing measures validity was based on criterion-related or predictive validity. The survey tool was used to elicit relevant sociodemographic and economic data from the study subjects including their age, sex, income levels, employment status, educational levels, HIV status, have a caregiver, and have multiple sex partners. Any information that enabled the easy identification of study subjects was not included on the instrument.

Operationalization of Study Variables

There are many caveats to coding variables into categories. However, Song and colleagues (2013) cautioned that there are consequences of combining related variables into a campsite variable. The authors explained that combining variables into composites might alternate the relationship of the strength with the dependent variable, affect the statistical power, and over-reduce or lead to loss of information. In cognizance of this fact, the coding of some of the variables into many categories is to ensure that basic information and details are not lost to oversimplification of the data into a few categories.

In this study, age was a nominal variable and was used as a covariate. The age variable was grouped into five categories as follows: 0 = 18-29, 1 = 30-39, 2 = 40-49, 3 = 50-59, and 4 = 60+. The sex of respondents was validated during data collection. The variable was a covariate and measured whether a person is female or male. Therefore, the variable was coded into 0 = male and 1 = female.

The level of education variable measured the highest level of education obtained by participants. It was treated as a predictor variable and grouped into the following five categories: 0 = Never attended school or only attended kindergarten, 1 = Elementary (Grades 1 through 8), 2 = High School (Grades 12 or GED), 3 = college education (4 years of college or technical school), 5 = Higher Education (professional or postgraduate). For the purposes of this study, the United States Census Bureau definition of rurality as a community of a population of fewer than 2500 people with substantial commuting (Hart et al., 2005) was used. Therefore, the place of residence solicited information from subjects on whether they live in a rural or urban area. This variable was put into categories of 0 = rural and 1 = urban 2 = unknown.

Furthermore, the employment variable sought to know if respondents were employed or not employed. It was treated as a nominal and categorical variable. So, respondents had a close option of choosing from four coded responses namely 0=Employed, and 1 = Not employed, 2 = retired, and 3 = not answered. Income level, on the other hand, was an ordinal independent variable and was used to measure the average income levels of participants. Using the World Bank (2018) GNI per capita definition, incomes were defined by 4 categories. Here, respondents had a closed-ended question with four responses. The categories will be ordered as follows 0 = below $1, 026 (low income), 1 = $1, 026 and 3, 995 (lower middle-income), 2 = $3, 0996 and $12, 375 (Upper middle-income), and 3 = $12, 376 or more (high-income).

For HIV status, all TB patients are required to test for HIV, so it was assumed that they knew their status. The measurement level was categorical, and it assessed whether respondents have HIV positive results or not. So, HIV status was coded as 0 = Positive 1= Negative. Finally, MDR-TB was the dependent variable for the study and the measurement level was nominal. The variable assessed whether participants were resistant to two or more TB treatment drugs or not. Thus, it measures whether a TB patient has MDR TB or Do not have MDR-TB. It was treated as a dichotomous variable and grouped into two categories of 0 = Has MDR-TB and 1 = Do not have MDR-TB. Table 1 gives the coding and the measurement levels of the study variables.

Table 1

Measurement Levels and Coding for Study Variables

Variables	Information source	Variable type	Measurement level and coding
Age	Primary	Independent	Categorical 0 = 18-29 1 = 30-39 2 = 40-49 3 = 50-59 4 = 60+.
Sex	Primary	Independent	Categorical 0 = Male 1 = Female
Education level	Primary	Independent	Categorical 0 = Never attended school or only attended kindergarten 1 = Elementary (Grades 1 through 8) 2 = High school (Grade 12 or GED) 3 = College education (4 years of college or technical school) 4 = Higher education (professional or postgraduate)
Place of residence	Primary	Independent	Categorical 0 = Urban 1 = Rural 3 = Other
Employment status	Primary	Independent	Categorical 0 = Employed 1 = Not employed 2 = Retired 3= Not answered
Income levels	Primary	Independent	Categorically ordered 0 = below $1,026 (low income) 1 = $1,026 to $3,995 (lower middle income) 2 = $3,0996 to $12,375 (upper middle-income) 3 = $12,376 or more (high income).
HIV status	Primary	Independent	Categorical 0 = Positive 1 = Negative 2 = Unknown
MDR-TB	Secondary	Dependent	Categorical 0 = Present 1 = Absent

Data Analysis Plan

The research question formulated to guide the study was as follows: What socioeconomic and demographic factors were associated with MDR-TB outcomes in Lesotho? The specific research questions and associated hypotheses that were set for the study are listed below. The hypotheses tested to falsify or agree to the statements based on the observations from the data:

Research Question 1: Do sociodemographic factors (sex, age, income, educational status, place of residence, and employment status of participants) have an influence on MDR-TB status among TB patients in Lesotho?

Null Hypothesis (H_0) 1: Sociodemographic factors (sex, age, income, educational status, place of residence, and employment status of participants) do not have influence on MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 1: Sociodemographic factors (sex, age, income, educational status, place of residence, and employment status of participants) do contribute to the MDR-TB status among TB patients in Lesotho.

Research Question 2: Is the HIV status of participants associated with MDR-TB status among TB patients?

Null Hypothesis (H_0) 2A: The HIV status of participants is not associated with MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 2: The HIV status of participants is associated with MDR-TB among TB patients in Lesotho.

Given the research questions and the hypotheses, a structured survey questionnaire was used to collect primary data on independent variables in the study. The data captured from the survey questionnaire was grouped and examined for errors and inconsistencies in a spreadsheet. Subsequently, the data were cleaned and transferred into a stata format for further analysis. An initial descriptive analysis was conducted to summarize the data in a cross-tabulation form for the demographic characteristics of the study population. The descriptive statistics were then used to obtain measures of central tendencies (such as the mean, medians, and mode) and dispersion (such as range, variance, and standard deviation) for continuous variables, and frequency distribution for categorical variables.

With MDR-TB as the outcome variable, exposure to putative risk factors was assessed retrospectively in a bivariate analysis for each variable to examine the possible association with MDR-TB. A chi-square test was used for the bivariate analysis with a *p*-value < 0.05 considered as statistically significant, variables with $P < 0.25$ were entered into a multivariate logistic regression model. An adjusted ratio (*aOR*) with 95% CI was calculated to determine the independent association between the independent and dependent variables. That is, *aORs* was used to quantify the strength of the association between the potential risk factors and MDR-TB (a binomial variable). The multivariate logistic regression models were used to determine the risk factors or exposure histories that contribute to the outcome (MDR-TB).

Table 2 depicts the hypotheses and statistical test that was used to conduct each study variable. Seven blocks of independent and moderating variables were tested to assess their individual and combined relationship to MDR-TB, the dependent variable. Results was reported in odd ratios and 95% confidence interval (*CI*).

Table 2

Statistical Test for Research Questions

Research question	Variables	Statistics
1. Do demographic factors contribute to MDR-TB status among TB patients in Lesotho?	Age Sex	Chi-square test of independence Chi-square 2x2 contingency table analysis
2. Are socioeconomic factors of participants associated with MDR-TB status?	Income, educational status, place of residence, employment status Place of residence	Chi-square test of independence Chi-square 2x2 contingency table analysis Logistic regression analysis to examine the interactions of the variables and determine the relative importance of the predictor variables concerning the presence or absence of MDR-TB.

Through the application of a chi-square, the independent categorical variables were tested to assess their statistical significance of association with the dependent variable. To analyze the demographic and socioeconomic factors, multivariable logistic regression models were constructed to adjust for confounders *a priori* namely have multiple sex partner and a caregiver. Moreover, age and sex were adjusted in a multivariable model for factors related to the patient's health and behavior. Furthermore, adjustment for models for socioeconomic and demographic variables that will show a significant statistical association with MDR-TB in the bivariate analysis ($p<0.025$) were carried out. Models were also constructed for the patient's place of residence to examine the difference between patients who live in rural or urban areas. In the end, the crude ORs from the univariable analysis and adjusted ORs from the multivariable analysis with their corresponding confidence intervals and two-tailed *t*-test for Wald test were presented. Regression coefficients were presented with their confidence intervals and associated *p*-values for the simple and Omnibus hypothesis.

Threats to Validity

A potential threat to validity was that it was not practical to obtain a truly random sample since some of the participants refused to participate. Additionally, the sample was a select group with their idiosyncrasies with a limitation on the ability to generalize findings to the general population under study. There was also the risk of participants who did not want to disclose sensitive or personal behavior information. Moreover, interviewer bias could affect the quality of the data and subsequently the generalization of the findings of the study. Potential internal validity could result from data integrity during the data capture process. On the other hand, there could be a possible threat to statistical conclusion validity for an unmeasured covariate with a greater explanatory value of the independent variables.

Ethical Procedures

Ethical conduct was fundamental to this study. Bearing in mind that TB is still associated with a great deal of stigma, action was taken to protect study subjects to minimize risk and maximize benefits. Therefore, ethical approval for this study was sought from the Walden University Institutional Review Board (IRB). Thereafter, clearance was sought from the Lesotho Health Services Ethics Review Committee. The researcher wrote to the Lesotho NTP manager, who forwarded the request to the Ethics Review Committee. In their response to the request, they requested that I send them an approval letter from Walden University or forward to them the tracking number (or ID) for the study. Once approval was given, the study commenced with verbal informed consent obtained from all participants for the study. Full disclosure about the study, confidentiality of responses, the intended use of the results, who will access the data, and the individual rights of each participant was discussed with them in either Sesotho or English by a trained interviewer. The identity, privacy, and confidentiality of the information of subjects was protected by ensuring that their information was coded and kept confidential in a special folder on the researcher's laptop with a password that can be accessed by me alone. Materials and all datafiles about the study subjects will be destroyed after five years of the study. The questioning of participants did not induce fear or guilt. Participants were duly informed of their rights to withdraw from the study at any time and it will not affect their treatment and care provided for them at TB clinics.

Summary

The purpose of the study is to assess the association between socio-demographic and economic variables to MDR-TB among TB patients in Lesotho. Given the objectives and subsequent research questions of the study, an observational case-control design and a quantitative methodology were utilized. The research design and methodology selected for the study is deemed appropriate given that it allowed for a broader study of the problem involving a greater number of the subjects and the empirical relationship it presented among the variables that can be generalized to the larger population. In other words, the analysis adopted allowed for the measurement of the association between the predictive and the outcome variable. The quantitative method ensured that data summaries were provided that support the generalization of the conclusions of the study. Chapter 4 of this study was devoted to presenting the results. The chapter also characterizes the study sample and discussed methodological issues that arose during the research process.

Chapter 4: Results

Introduction

The purpose of this retrospective, quantitative cross-sectional study was to assess the association of selected sociodemographic factors to MDR-TB in Lesotho. The social determinants selected for the study included age, gender, level of education, employment status, income level, HIV status, and the place of residence of study participants. Having a caregiver and having multiple sex partners were used as cofounders in the study. The MDR-TB status of participants (a binary variable: the presence or absence of MDR-TB) served as the outcome variable for the study. The social determinants selected for the study were considered relative to their predictive nature in previous studies that had similar geographic settings as the current study area. The study was designed to answer the following overarching research question: What is the association between MDR-TB to age, gender, employment status, education status, income, and place of residence? The specific underlisted research questions and their corresponding hypotheses were formulated to guide the study.

Research Question 1: Do sociodemographic factors (age, employment status, education status, income, place of residence, and sex) contribute to MDR-TB status among TB patients in Lesotho?

Null Hypothesis (H_0) 1: Sociodemographic factors (age, employment status, education status, income, place of residence, and sex) do not contribute to MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 1: Sociodemographic factors (age, employment status, education status, income, place of residence, and sex) contribute to the MDR-TB status among TB patients in Lesotho.

Research Question 2: Is the HIV status of participants associated with a high risk of MDR-TB status among TB patients?

Null Hypothesis (H_0) 2A: HIV status of participants is not associated with MDR-TB status among TB patients in Lesotho.

Alternate hypothesis (H_A) 2: HIV status of participants is associated with MDR-TB status among TB patients in Lesotho.

Chapter 4 contains a summary of how the data were collected and presents the results of the survey data and how they were organised. Specifically, the chapter begins with an introduction of the chapter and recaps the research questions with their associated hypotheses. This is followed by a description of the data collection process, a presentation of the characteristics of the study sample, and the results of the univariate analysis. Next, I present a description of the research results that begins with the descriptive statistics results, assumptions, and the statistical analysis of the findings relative to the research questions and hypothesis tests of the study. The chapter concludes with a summary of the results.

Data Collection

Two research assistants were recruited in the field and trained for the purpose of the data collection. The data collection was carried out by phone and in a few cases, participants were contacted face to face in the field on their TB clinic visit days. The data were collected from 12 sampled health facilities that provided TB services across the 10 districts in the country. To increase the representativeness of the sample, a stratified random sampling was used to select subjects for the study. Cases for the study were subjects with MDR-TB, while controls were subjects diagnosed with active TB. Following the inclusion criteria, all patients who were 18 years or above, who were diagnosed with TB, who attended TB clinics, and who could be contacted were eligible and included in the sample. However, those who were under the age of 18 years, who could not be reached, who were in state institutions (prison settings), or who did not attend TB clinics were excluded from the study. The TB clinic attendance register served as the sampling frame for the study. From the TB register, patients' names and contact data were extracted into a spreadsheet. The participants were randomly selected based on stratified sampling from each of the 10 districts of the study country. The data were collected from November 2021 to February 2022.

The study relied on a set of questions that were asked through a survey to collect data to accomplish the purpose of the study. Data analysis was done using Stata software (StataCorp, 2015). All 312 persons invited for the interviews responded, but six (2.2%) were excluded from the final analysis due to their low age, which were below 18 years. To this end, the internal and external validity of the final data were consistent relative to similar and previous studies. Indeed, the frequencies and means of the data collected on the study variables were within expected limits. Following approval from the Walden University Ethics Review Committee and the Lesotho Health Services Research and Ethics committee, I encountered some difficulties in obtaining access to the TB patient clinic register when some of the managers of the TB clinics asked that I formally write to their facilities to get approval before access was given to patients' data. After following this directive, I was finally allowed access to patients' data.

Results

Descriptive statistics were performed on the data. Additionally, a series of chi-square tests of association and a simple logistics regression test were performed to address the hypotheses and research questions. Next, a multiple regression analysis was conducted that included all the independent variables to determine the effect of each of the significant variables while holding the value of the other independent variables fixed.

Basic Characteristics of the Study Participants

A total of 312 participants were sampled for the study. However, six (2.2%) persons were excluded from the final analysis due to their low age, which was below 18 years. Therefore, a total of 306 were included in the final study, comprising 200 (65.4%) females and 106 (34.6%) males. This was consistent with a previous study conducted by Luba and colleagues (2019), who used data from Lesotho Demographic and Health Survey (LDHS, 2014) and reported that most of the respondents who had TB in the survey were females (71.6 %). Further, data from this study demonstrated that the minimum age for the sample was 18 years while the maximum age was 98 years, with an average age of 47.8 years (*SD* =16.2). Table 1 also shows that 26.5% of the respondents were 65+ but a majority of the respondents (26.8%) were between 30 and 39 years of age, which was slightly different from the data in the 2014 LDHS, in which a majority of the respondents were between the ages of 15 and 24 years (44%). Among the 306 participants included in the study, 224 (73.2%) resided in rural areas, and 82 (26.8%) resided in urban areas, similar to the LDHS (2014), in which a majority (67.3%) of the population resided in rural areas (Luba et al., 2019). It was observed that twice the respondents (62.4%) interviewed had pulmonary TB compared to respondents who had MDR-TB (37.6%), as shown in Figure 4.

Figure 4

Tuberculosis Status of Respondents

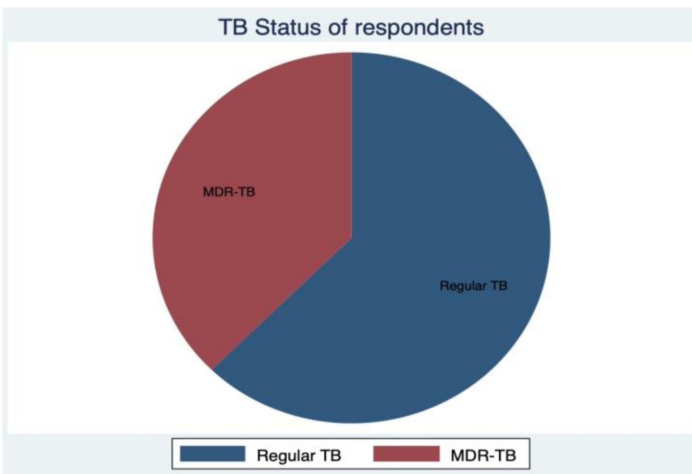


Table 3 presents a summary description of the sociodemographic characteristics of the study sample and reports frequencies and percentages for the study variables. In terms of education, over half of the study population had an elementary education (55.6%), but those with a higher education constituted only 1% of the population. Again, this result differs from the 2014 LDHS data, in which majority of the TB respondents had a high school education at 46.8%.

Table 3

Sociodemographic Characteristics of Study Participants

Characteristic		Number	Percent
Age group			
	18–29 years	36	11.8
	30–39 years	82	26.8
	40–49 years	51	16.7
	50–59 years	56	18.3
	65+ years	81	26.5
Gender			
	Male	106	34.6
	Female	200	65.4
Setting			
	Urban	82	26.8
	Rural	224	73.2
Education			
	Never attended school	19	6.2
	Elementary school	170	55.6
	High school	96	31.4
	College	18	5.9
	Higher education or tertiary	3	1.0
Employment status			
	Not employed	228	74.5
	Employed	51	16.7
	Retired	26	8.5
	Not answered	1	0.3
Income status			
	Below $1.026 (low income)	262	85.6
	$1.026 to $3.995 (lower middle income)	37	12.1
	$3.995 to $12.375 (upper middle income)	3	1.0
	$12.376 or more (high income)	4	1.3
HIV status			
	Negative	177	57.8
	Positive	129	42.2
Multiple sex partners			
	No partner	25	8.2
	One partner	127	41.5

Characteristic		Number	Percent
	More than 1 partner	154	50.3
Distance to health facility			
	Less than 2km	113	36.9
	Between 2km and 5km	77	25.2
	Between 6km and 10km	69	22.6
	More than 10km	47	15.4
Have caregiver			
	No	223	72.9
	Yes	83	27.1
MDR-TB status			
	No	191	62.4
	Yes	115	37.6

Three-quarters of the study sample were unemployed (74.5%). Also reported in Table 3 are frequencies and percentages for sex partner, distance to health facility, and caregivers of TB patients. Half of the population was reported to have more than one sex partner (50.3%); few did not have any sex partner (8.2%). The data on distance to health facility showed that the largest percentage (36.9%) of the participants traveled less than 2 km to the nearest health facility to access health. It also revealed that about 15.4% of the participants traveled more than 10 km to the nearest TB clinic to access healthcare. Furthermore, the sample indicated that three quarters (72.9%) of the respondents did not have caregivers who assisted them at home.

Relationship With Other Variables

To understand the relationship between the dependent variable (TB status) and the independent variables, chi square of proportions was used to estimate the relationship. Though most of the independent variables were statistically insignificant, having a caregiver was significantly associated with TB status ($p = 0.031$). Respondents with

MDR-TB had a wider age range compared to those with regular TB, as shown in Figure 5.

Figure 5

Boxplot of Age and Tuberculosis Status

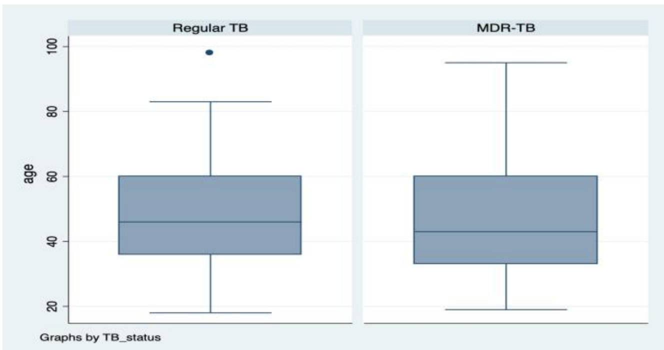


Table 4 reports the associations between TB status and all independent variables.

Table 4

Association Between Independent Variables and Multidrug-Resistant Tuberculosis

Characteristic	Active TB *n* (%)	MDR-TB *n* (%)	Chi2 *p*-value
Age group			
18–29 years	17(8.9)	19(16.5)	0.174
30–39 years	49(25.7)	33(28.7)	
40–49 years	37(19.4)	14(12.2)	
50–59 years	37(19.7)	19(16.5)	
65+ years	51(26.7)	30(26.1)	
Gender			
Male	70(36.7)	36(31.3)	0.341
Female	121(63.3)	79(68.7)	
Setting			
Urban	48(25.1)	34(29.6)	0.396
Rural	143(74.9)	81(70.4)	
Education			
Never attended school	12(6.3)	7(6.1)	0.762
Elementary school	105(55.0)	65(56.5)	
High school	60(31.4)	36(31.3)	
College	11(5.6)	7(6.1)	
Higher education or tertiary	3(1.6)	0(0.0)	
Employment status			
Not employed	139(72.8)	89(77.4)	0.278
Employed	37(19.4)	14(12.2)	
Retired	14(7.3)	12(10.4)	
Not answered	1(0.5)	0(0.0)	
Income status			
Below $1,026 (low income)	159(83.3)	103(89.6)	0.291
$1,026 to $3,995 (lower middle income)	26(13.6)	11(5.6)	
$3,995 to $12,375 (upper middle income)	2(1.0)	1(0.9)	
$12,376 or more (high income)	4(2.1)	0(0.0)	

Characteristic	Active TB *n* (%)	MDR-TB *n* (%)	Chi2 *p*-value
HIV status			
Negative	112(58.6)	65(56.5)	0.716
Positive	79(41.4)	50(43.5)	
Multiple sex partners			
No partner	15(7.9)	9(8.3)	0.933
One partner	78(40.8)	46(42.6)	
More than 1 partner	98(51.3)	53(49.1)	
Distance to health facility			
Less than 2 km	70(36.7)	41(38.0)	0.601
Between 2 km and 5 km	53(27.8)	24(22.2)	
Between 6 km and 10 km	39(20.4)	28(25.9)	
More than 10 km	29(15.2)	15(13.1)	
Have caregiver			
No	146(76.4)	70(64.8)	0.031
Yes	45(23.6)	38(35.2)	

Statistical Assumptions

The analysis in this study was characterized by a multiple logistic regression on a binary outcome variable (MDR-TB status) and eight independent variables (age, level of education, income levels, place of residence, multiple sex partners, HIV status, having a caregiver, and employment status). Logistic regression does not involve many of the key assumptions in linear models that places emphases on ordinary least squares algorithms like linearity, normality, homoscedasticity, and measurement levels (Schober & Vetter, 2020). The logistic regression model is a construction between *P*, that is, the probability of an event of interest occurring $p(Y = 1)$, and a linear combination of independent variables with a logit link function (Srimaneekarn et al., 2022). The logit link function is used here to mean the natural log of the odds ratio, that is, the ratio of the probability that an event will occur or not (Faraway, 2016; Kirkwood, 2020). The logit link function is less complicated and was used to interpret the model. The basic assumption for the use of a logistic regression analysis is that it must have a dichotomous dependent variable. Therefore, the dependent variable was coded accordingly as a binary factor such that the factor level of 1 represented the desired outcome. The dependent and independent variables do not need to be linearly related. However, to ensure that the model was robust, the assumptions for linearity of the continuous variables to the logit of the dependent variable and multicollinearity were examined. The variance inflation factor (VIF) was used to test for multicollinearity, and the Box-Tidwell test was used to verify for linearity of the logit of the DV. The results indicated that all the VIFs were less than 10; hence, there was no multicollinearity.

As part of the Box-Tidwell test, the dataset was filtered to keep only the continuous independent variables. Thereafter, the log transformed interaction terms between the continuous independent variables and the corresponding natural log were added to the model. The output showed that all the continuous independent variables were not statistically significant, therefore, we fail to reject the null hypothesis. Specifically, the interaction term for age has a p-values of 0.132, distance p<1.00, and income p< 0.652 which are above the required threshold of p>0.5 and not statistically significant. This implies that the independent variables age, distance, and income are linearly related to the logit of the dependent variable (MDR-TB), hence, the assumption of linearity of the logit is met. To satisfy the sample size requirement for a logistic requirement, the study complied with a minimum of 10 cases of each variable (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996).

Determinants of Multidrug-Resistant Tuberculosis

A logistic regression model was used to estimate the odds of MDR-TB based on a combination of the predictor variables. The outcome variable (MTB-TB status) was coded as a dummy, while the rest of the predictor variables were coded into various categories. The results from the model are reported in Table 3 below. The results are reported in odd ratios and 95% confidence interval. As part of the model selection, the model with the lowest AIC (397.37) was selected for the final result. The *Pseudo* R^2 was used to measure the predictive power of the model, while the Hosmer–Lemeshow statistic calculated the goodness of fit of the model. The *Pseudo* R^2 was reported at 0.04, indicating that 4% of the variation in the dependent variable was explained by the model. The Hosmer–Lemeshow goodness of fit test statistic on the other hand, was found to be insignificant with the statistic result = 6.24 (p = 0 .6205). This suggest that the model is a good fit for analyzing the data. As detailed in Table 5 the model predicted age group to be associated with MDR_TB. Income status of the study participants were found to be statistically associated with MDR-TB. Further having care giver was significantly associated with MDR-TB.

Table 5

Logistic Regression Analysis of Tuberculosis Status Against the Independent Variables

	Tuberculosis status							
	Unadjusted				Adjusted			
	Odds ratio	*p*-value	95% confidence interval		Odds ratio	*p*-value	95% confidence interval	
Age group	0.9	0.174	0.750	1.050	0.8	0.040	0.67	0.99
Gender	1.3	0.342	0.780	2.080	1.4	0.205	0.83	2.42
Setting	0.8	0.397	0.480	1.340	0.7	0.238	0.40	1.25
Education	0.9	0.647	0.680	1.270	1.1	0.685	0.73	1.61
Employment status	0.9	0.737	0.650	1.350	1.2	0.379	0.79	1.87
Income status	0.6	0.076	0.340	1.060	0.5	0.034	0.22	0.94
HIV status	1.1	0.716	0.680	1.740	1.1	0.720	0.65	1.85
Multiple sex partners	0.9	0.723	0.650	1.350	0.8	0.355	0.56	1.23
Have caregiver	1.8	0.032	1.050	2.950	1.8	0.036	1.04	3.11
Distance from health facility	1.0	0.902	0.810	1.260	1.0	0.983	0.80	1.26
Pseudo R^2					0.04			
AIC					397.37			
BIC					438.07			

Note. The Hosmer–Lemeshow goodness-of-fit test statistic was 6.24 (*p* =0 .6205).

The model above demonstrates that, holding everything at a fixed value, a unit increase from the lower age groups (18 – 29 years) to the upper age groups (65+ years) is significantly associated with a 20% decrease in the odds of the risk of MDR-TB (*OR* = 0.8, 95% *CI* [0.673, 0.991], *p* = 0.040). Similarly, a unit increase in income is associated with a 50% decrease in the odds of the risk of MDR-TB. That is, moving from a low-income status (below $1.026) category to a higher income ($12.376 or more) category is significantly associated with a 50% decrease in the odds of getting MDR-TB (*OR*: 0.5, 95% *CI* [0.222, 0.943] *p* = 0.034) holding everything constant.

Furthermore, the model demonstrates that, not having a caregiver is significantly associated with the odds of an 80% increase in the adverse effects of TB (*OR* = 1.8, 95%

CI [1.039, 3.110], *p* = 0.036) holding everything at a fixed value. Therefore, the null hypothesis was rejected for age, income levels, and having a care giver. Invariably, education, employment, setting, gender, multiple sex partners, HIV status, and distance to health facility did not meet the *p*-value acceptance threshold. The results for HIV status for instance demonstrate that there is no statistically significant association between HIV and MDR-TB in Lesotho (a*OR* = 1.1, 95% *CI* [0.720, 0.65], *p* = 1.85). Hence, the null hypothesis is accepted and conclude that respondent's level of education, employment status, gender, having multiple partners, place of residence, distance to the nearest health facility, and HIV status did not predict MDR-TB in Lesotho.

Summary

The key findings of this study are that age, income levels, and having a care giver moderates the association between TB status and socio-demographic factors. Age and income levels were found to significantly decrease the odds of getting MDR-TB by 20% and 50% respectively. Conversely, not having a caregiver was strongly associated with the increased odds of MDR-TB status by 80%. The concluding part of this study is the Chapter 5. The chapter includes a discussion on the findings how this study relates to previous research. It also provides concluding remarks and recommendation for future research on the social determinates that moderate the odds of MDR-TB in Lesotho.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this quantitative retrospective case-control study was to examine the social determinants of MDR-TB in Lesotho. There is evidence that MDR-TB status can be mediated by a single significant risk factor or multiple significant risk factors (Raazi et al., 2017; Sharma, 2019; Stosic, 2018). This study tested the association between some selected sociodemographic variables such as age, gender, level of education, employment status, income level, place of residence, marital status, multiple sex partners, having a caregiver, and HIV status and the influence MDR-TB status in Lesotho. The data for the study were collected directly from TB patients from noninstitutionalised facilities between 2021 and 2022. In the results section, I presented and described the different sociodemographic risk factors that mediate MDR-TB status. The key findings of this study are based on the individual research questions. The results of this study indicated that age, income, and not having a caregiver are independent predictors of MDR-TB status in Lesotho.

Interpretation of the Findings

This study assessed selected sociodemographic variables that facilitated the risk of MDR-TB. The findings are first presented with a discussion of how age mediates MDR-TB. This is followed by a discussion of how income influences MDR-TB. Further, the findings provide an analysis of how the risk of MDR-TB is influenced by having a caregiver. Finally, the findings address the relationship between HIV status and MDR-TB.

Significant Association Between Sociodemographic Variables and Multidrug-Resistant Tuberculosis

The study analysis showed that age was significantly associated with the risk of MDR-TB. The findings specifically demonstrated that a unit increase in age was associated with a 20% decrease in the risk of MDR-TB status. This means that younger TB patients have a high risk of MDR-TB relative to older TB patients. This supports an earlier study conducted by the National TB Programme of Lesotho (2017), in which researchers discovered that TB patients within the age bracket of 0–14 were significantly associated with MDR-TB (OR = 5.8; 95% CI [1.2, 28.5]; p = 0.03). This suggests that young people were 6 times more likely to develop MDR-TB than older people. Another study also found a statistically significant association between DR-TB and ages between 10 and 25 compared to those in higher age brackets (Ullah et al., 2016). Similar results were found by Raazi et. al., (2017), who established that younger TB patients had a high risk to MDR-TB (x^2 = 19.956 df = 2, p = 0.05). The possible reason that accounts for this association might be that TB patients within the young age bracket of 18–25 years have active lifestyles and do not comply with their medication intake compared to those with higher ages (Law et al., 2008). Thus, age-related differences in medication compliance and lifestyles could contribute to the difference in the increased risk of the MDR-TB among different age groups. There were other studies that found a relationship between and age and MDR-TB, but they moved in the opposite direction. These studies reported that older people have a higher risk of developing of MDR-TB compared to younger TB patients (Elduma et al., 2019; Lui et al., 2013; Workicho, 2017). The study by Workicho, for instance, demonstrated that TB patients at 30 years and above were 7 times more likely to develop MDR-TB compared to those below the age of 30 years. This might have been due to their weakened immune system (Thrupp et al., 2004), which could predispose them to progress from pulmonary TB to MDR-TB. Further, there are studies that did not find any association between age and MDR-TB (Demile et al., 2018; Maharjan et al., 2017; Stosic et al., 2018). It should be noted that the study settings, sample sizes, sampling methods, and study designs differed from one study to another, and this might account for the difference in study findings. Therefore, although age might be a risk factor to MDR-TB in Lesotho, it is not the same for every setting.

The study also examined the relationship between income and MDR-TB and indicated that income was a statistically significant risk factor associated with MDR-TB. A unit increase in annual incomes from $1,026 (low income) was associated with a 50% decrease in the odds of the risk of MDR-TB (a*OR*: 0.5, 95% *CI* [0.222, 0.943] $p = 0.034$). This suggest that higher per capita income is a protective exposure, hence, TB patients who had relatively high incomes had a decreased risk to develop MDR-TB. Of all the MDR-TB cases sampled for this study, 89.6% were in the low-income bracket. The low-income level is further worsened by the general prevalence of poverty and persistent economic vulnerability in Lesotho, where over 75% of the population are either poor or vulnerable to poverty (Sulla et al., 2019). The findings align with earlier studies that identified income to be associated with both TB (De Castro et al., 2018; Harling & Castro, 2014) and MDR-TB (Sharma, 2019; Stosic, 2018). In Serbia, for instance, Stosic and colleagues (2018) observed that TB patients from low-income families were 4 times more likely to develop MDR-TB compared to patients from high-income families (*OR* = 3.71, 95% *CI* [1.22, 11.28], $p = 0.021$). Sharma and colleagues also found that low per capita income groups had 2 times the odds of developing MDR-TB compared to those with higher per capita income (*aOR* = 1.82, 95% *CI* [1.21, 2.59], $p = 0.41$).

These findings support the longstanding contention that income inequality affects the health of individuals (Fletcher & Wolfe, 2014; Truesdale & Jencks, 2016). In developing countries, for instance, higher levels of income inequality are linked with lowered average lifespan of individuals (Wilkinson, 1992). The findings showed that, though MDR-TB diagnosis and treatment services are free, patients suffer some direct and indirect costs such as those associated with travel, food, nutritional supplements, and income losses due to inability to work (Fuady et al., 2018: Van den Hof et al., 2016). The economic hardship and associated cost of TB treatment create access and medication adherence barriers (Fuady et al., 2018; Van den Hof et al., 2016).

These findings are alarming, given the situation that this group of patients do not have any social welfare payment arrangements to improve their condition and ultimately their health. The association between spending on social protections and TB outcomes such as prevalence, incidence, and mortality has long been established by Siroka and colleagues (2016). They found that, social protection spending was associated with a reduction in TB prevalence, incidence, and mortality. Moreover, Nery and colleagues (2017) found a statistically significant association between increase in cash transfer program coverage and reduction in the TB incidence rate in Brazil. This strongly suggests the importance of including TB patients in social protection programs during TB treatment. General low socioeconomic status has been found to be associated with TB treatment abandonment (Harling et al., 2017); this affects the overall effectiveness of WHO STOP TB strategy, despite the fact that TB treatment is free.

However, this finding differs from those of Khan and colleagues (2017) and Rifat and colleagues (2014). Khan and colleagues did not find any association between low income (*aOR* = 1.05, 95% *CI* [0.61, 1.81], $p = 0.0866$) or high income (*aOR* = 1.01, 95% *CI* [0.57, 1.78], $p = 0.0966$) to MDR-TB in Myanmar. Similarly, Rifat and colleagues did not find any association between low-income status and MDR-TB in Bangladesh (95% *CI* [-0.001, 0.002], $p = 0.71$). Differences in study settings, sample sizes, sampling methods employed, and study designs could the study findings. This suggests that the application of the findings to other regions should be done with caution because one shoe does not fit all. Despite the difference in results from different studies, there is a common level of agreement on how income heterogeneity explains the risk of MDR-TB. It is obvious that the probability of contracting MDR-TB is significantly high among socially disadvantaged and economically vulnerable populations (De Castro et al., 2018; Sharma et al., 2019; Stosic et al., 2018).

Furthermore, the study demonstrated that MDR-TB cases are almost 2 times more frequently experienced by TB patients who do not have caregivers at home. In other words, TB patients without homebased caregivers have 80% odds of MDR-TB (*OR* = 1.8, 95% *CI* [1.039, 3.110], $p = 0.036$). This is consistent with a study in eastern Delhi, India where homebased care treatment success was statistically significant ($p<0.03$) and 40% higher than no homebased care treatment (Taneja, 2017). MDR-TB treatments are long, given that there are 3 to 4 times longer treatment periods than for active TB, and this has a high-cost implication (Van den Hof et al., 2016). To reduce cost, patients are allowed to use community-based care. Consequently, family members take the burden of caregiving and become an extension of the health system (Fana & Sotana, 2021). The knowledge and awareness levels of caregivers on the causes, transmission, prevention, and management (Tshililo et al., 2009) when improved can lead to reduced cases of MDR-TB infections.

Finally, the results from this study demonstrated that HIV status did not mediate MDR-TB status in Lesotho (*aOR* = 1.1, 95% *CI* [0.720, 0.65], *p* = 1.85). This is similar to a previous case-control study conducted in Southeast Korea, where Lee and colleagues (2016) did not find HIV as an independent predictor of DR-TB (*OR* = 1.40, 95% *CI* [0.54, 3.61] *p* = 0.42). Baya and colleagues (2019) did not also find any statistically significant association between HIV status and MDR-TB (*OR* = 0.82, 95% *CI* [0.34, 1.94], *p* = 0.65). There were other similar studies conducted in Thailand, Malesia, and Uganda that did not find any significant association between HIV and MDR-TB status (Chuchottaworn et al., 2015; Elmi et al., 2016; Lukoye et al., 2013). However, different findings were observed by Workicho and colleagues (2017) in their case-control study. They observed that HIV-positive patients were at 3 times greater risk of MDR-TB compared to TB patients without HIV (*aOR* = 3.1, 95% *CI* [1.02, 9.40], *p* = 0.046). Similar results were observed by Mulisa et al. (2015), who reported a strong association between HIV and MDR-TB status (*OR* = 2.7, 95% *CI* [1.43, 5.06], *p* = 0.01). Sharma and colleagues (2019) and Assefa and colleagues (2017) both reported significant associations between HIV and MDR-TB (*aOR* = 9.45, 95% *CI* [6.8, 15.9], *p* = 0.008; *aOR* = 1.95, 95% *CI* [1.13, 3.35], *p* = 0.001). The different findings might be a result of the different settings in which the studies were conducted. Moreover, the sample sizes and sampling methods used differed, and this could account for the different findings.

Limitations

The study was limited to the TB population in Lesotho, a resource-constrained country, and it focused on the sociodemographic risk factors that mediate MDR-TB. Given that the study was limited to Lesotho, the findings may not be generalized to other populations within a setting or country. There is a possible recall and social desirability bias in this study, given that the data on all the variables were self-reported. While some of the respondents might not recall some events properly, others might be reluctant to give responses that they see as negative. There was also a fundamental psychosocial risk to the study due to the negative consequences that might have occurred if a patient's diagnosis became public. This situation was mitigated by ensuring that the survey administrators were trained to ask questions in a standardized manner. I also ensured that there was confidentiality for respondents and that survey administrators spoke to them alone and in environments in which they felt comfortable. Additionally, other unmeasured potential covariates excluded in the analysis could be a limitation.

Furthermore, the study was a case-control, which can basically be used for assessing association but cannot infer any causality. Nonetheless, the findings of this study can be generalized to the TB population in Lesotho, given that it was randomized. Moreover, the study provided valuable information on the risk factors associated with

MDR-TB for health policy and planning that can target interventions for future MDR-TB prevention and control in Lesotho. To the best of my knowledge, the present case-control study is the first to investigate the sociodemographic risk factors that mediate MDR-TB in Lesotho.

Recommendations

This quantitative case-control study provides valuable insights into the sociodemographic risk factors that mediate MDR-TB in Lesotho. Based on the results of this study, targeted measures are recommended to improve access to health care and reduce the risk of drug resistance among younger age groups within the population. This can be done by educating young TB patients on the importance of seeking treatment and completing their treatment. The findings highlight the need to reduce poverty and income security among TB patients and their families. In recognition of the cost burden, policy goals around financial protection of patients are imperative. To reduce the burden of the cost among patients and their families, policy goals should target establishing social protection programs in the form of cash-transfer programs to eliminate catastrophic cost associated with TB treatment, care, and management among communities and families affected by TB. Furthermore, there is a need for increased knowledge and awareness about the causes, transmission, prevention, and management of TB. Therefore, a public health campaign and initiative are imperative to enhance caregivers' knowledge on infection control of MDR-TB. The use of protective equipment needs to be enhanced and evaluated, and if acceptable, it should be scaled up for communities affected by TB.

Similarly, personal hygiene and regular washing of hands are an ideal MDR-TB prevention strategy.

The NTP is expected to build on the findings from this study and take appropriate action to prevent further development of MDR-TB. This calls for an increase in the number of MDR-TB prevention and treatment initiatives because Lesotho is a high-burden MDR-TB country. This calls for the promotion of greater coordination of Lesotho government TB resources, including domestic, bilateral, and multilateral funding to reduce the risk of MDR-TB. Equally important is to increase public awareness of the threats posed by MDR-TB and serve as a call to action to encourage donors, the private sector, and affected communities to increase investments in MDR-TB prevention and control initiatives. Finally, investments in research and development should be broadened to include preventive interventions of identified MDR-TB risk factors to contribute to improved TB treatment outcomes through the discovery of new tools that are easy to implement in the existing health system. These actions, when properly implemented, are expected to prevent the emergence of further resistance to TB medication and significantly reduce the spread of MDR-TB.

The study did not measure many social variables that could possibly predict MDR-TB. It is recommended that dedicated database personnel are stationed at each TB clinic to capture data related to socioeconomic variables that go beyond the clinical monitoring and management of TB patients. This will make it easy for captured data to be analyzed and used for decisions that will improve patients’ progress. Similarly, follow-up studies are recommended to measure all the social and economic factors that contribute to MDR-TB so that they can be addressed adequately. Predictor variables such as treatment adherence, stigma, alcohol use, and tobacco use should be included in future studies to increase the generalization of the findings. This will increase efforts to identify the social mechanisms or the exact factors that influence the risk of developing MDR-TB for individuals within a population.

Implications

As the first study that investigated the social determinants that influence MDR-TB in Lesotho, the study contributed to the understanding of the sociodemographic factors that influence the risk of MDR-TB in Lesotho and identified appropriate measures to prevent and control the problem. Specifically, the study has contributed to generate knowledge that age, income status, and having a caregiver influence MDR-TB in Lesotho. The study has social change implications through the findings, which elicited some recommendations on how to mobilize and engage relevant stakeholders to develop and implement initiatives that will lead to prevention and control of MDR-TB.

Through this study, there is evidence to support the understanding that age, income, and having a caregiver are the risk factors that mediate MDR-TB in a resource-constrained setting such as Lesotho. The findings are significant for developing public health interventions such as having public health campaigns for TB prevention and control activities aimed at the identified risk factors. The findings on the determinants of MDR-TB in this study will also serve as a guide to the National TB program in designing evidence-based algorithms to prioritize access to MDR-TB services and tailor prevention and control strategies. For instance, the knowledge gained from the findings of this study can be applied during decision making for appropriate interventions targeted at high-risk populations such as those with low incomes, younger populations, and TB patients who do not have caregivers.

Ultimately, the study is valuable for ensuring that resources on specific programs and interventions are allocated efficiently for the benefit of affected populations especially in the face of the competition for public health resources. The findings will serve as guidance for policy makers, health managers, and other health partners of the Government of Lesotho to allocate resources to vulnerable and affected populations. For instance, the recommendation that TB patients should be given some social welfare payments in a cash payment campaign will go a long way to assist TB patients to address feeding and transportation cost issues. This benefit will help patients to have access to healthcare and to eat nutritious food needed to improve their health.

The study is valuable by recommending that resources on specific campaigns and initiatives should be allocated efficiently. In the face of the competition for public health resources, affected populations will benefit more from implemented campaigns and interventions. The findings, if appropriately applied could guide the design of public health interventions aimed at addressing the factors that affect MDR-TB in a poor resource setting like Lesotho, to reduce the cases of MDR-TB. The moderating effect of having a caregiver on MDR-TB for instance has implications for the training and education of caregivers on basic hygiene and the need to wear protective gear when assisting MDR-TB patients. The development of a standard protocol in the form of comic strips can be shared among caregivers and communities affected by TB to improve their knowledge on how to manage, prevent and control MDR-TB infection. To this end, the study findings will be disseminated to the Lesotho health Service, the Ministry of Health, and their partners. Moreover, the study will be published in a peer-reviewed journal to make the findings accessible to the wider international public health community.

Conclusion

The literature on the social determinants of MDR-TB has not been properly elucidated for many regions. But to halt MDR-TB, it is important to have effective preventive and control measures. This requires the proper understanding of the problem to optimize the findings of this study to ensure an efficient and sustainable investment is carried out to counter the problem. As the first survey that used a case-control design to examine the sociodemographic risk factors associated with MDR-TB in Lesotho, the study has provided compelling evidence that can be used as baseline data to formulate policies for MDR-TB prevention, management, and control. The findings of this study advanced knowledge that highlights the need for policy makers to find ways of mobilising resources, both human and fiscal towards the prevention and control of MDR-TB by emphasizing on the recommendations. There is the need to expand MDR-TB prevention services, particularly for young people of 26 years and below, low-income earners, and caregivers who provide support for TB patients at home. Similarly, government through the MoH and its partners, should engage civil society organisations (CSO), faith-based organisations (FBOs), and the private sector to accelerate and improve efforts towards the elimination of the socioeconomic and demographic barriers that increases the risk of MDR-TB. In particular, it is important to improve the socioeconomic drivers of MDR-TB among TB patients by targeting those that are poor and vulnerable. Pivotal to the success of an intervention to reduce MDR-TB cases is to prioritise and intensify the education of family members and communities affected by TB on the need to support patients with homebased treatment and care.

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Appendix A: Survey Instrument

Informed Consent

Read to respondents: This questionnaire is for a study that is being conducted by a Ph.D. student from Walden University in the United States of America. We wish to learn about the risk factors associated with MDR TB in Lesotho. We hope to understand your needs and the best way that you can be supported through policy interventions. The information you will provide will be used to improve TB control and prevention initiatives. Your answers will not be released to anyone and will remain anonymous. Your name will not be written on the questionnaire or be kept in any records. Your participation is voluntary, and you may choose to stop the interview at any time.

Thank you for your assistance.

Note to Interviewer: Place an X on the selected answer. Do not read responses unless the directions indicate.

Age

1. Are you 18 years and over?

   0=Yes

   1=No

   If yes, continue.

   If no terminate the interview by saying thank you very much but we are only interviewing persons aged 18 years or older.

2. What is your age?

   0= 18-24 years

1 = 25-34 years

2 = 35-44 years

3 = 45-54 years

4 = 55-64 years

5 = 65 and above

Sex

1. Are you male or Female?

0=Male

1=Female

3= Did not respond

Education

1. What is your highest grade or level of education?

0= Never attended school or only attended kindergarten

1 = Elementary (Grades 1 through 8)

2 = High School (Grades 12 or GED)

3 = College Education (4 years of college or technical school)

4 = Higher Education (professional or postgraduate)

Place of Residence

1. In what district do you currently live?
2. In what community do you currently reside?

Employment

1. Do you currently have paid employment?

0 = Yes

1 = No

2 = Retired

3 = No response

Income

1. What is your average income per year? (Place in the right category)

0 = below $ 1, 026 (low income)

1 = $ 1, 026 and 3. 995 (lower middle-income)

2 = $ 3, 0996 and $ 12, 375 (Upper middle-income)

3 = $ 12, 376 or more (high-income).

Multiple Sex Partners

1. Do you have two or more sex partners?

0 = Yes

1 = No

Care Giver

1. Do you have a care giver at home?

0 = Yes

1 = No

Appendix B: Budget

Budget Item	Amount	Total $
Personnel		
Stipend for the research assistant/home country data collector for administrative assistance, data coding, language translation, and analysis support.@ average of approx. $2/interview	$2	476
Project Participants		
Participant Incentives @3*238	$3	714
Materials and Supplies		
• Copying, Paper, printing, binding, envelopes, Misc. supplies • Postage • Communication	$50 $50 $100	200
Fees for registration and review of the project	$100	100
Total		**1,490**
Overhead: @ 10%		**149**
Grand total		**1,539**

Note: The study is financed by Principal Investigator (PI).