ORIGINAL RESEARCH

Characterization of Mycobacterium Tuberculosis (MTB)-Positive Individuals within the Healthcare Catchment Area of Mzuzu Central Hospital, Malawi

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Abstract

Purpose

To investigate the characteristics of the Mycobacterium tuberculosis (MTB)-positive population within the healthcare service area of Mzuzu Central Hospital in Malawi, with the objective of providing a scientific foundation for tuberculosis (TB) prevention and control strategies in the region.

Methods

This retrospective study encompassed 4,711 patients who underwent GeneXpert (GeneXpert MTB/RIF or GeneXpert MTB/RIF Ultra) testing. Data on laboratory results, demographics, HIV status, and residential addresses were analyzed.

Results

Among 4,711 patients, 424 (9%) tested MTB-positive. A strong correlation was observed between MTB and HIV infection, as HIV/TB co-infection accounted for 47.9% of MTB-positive cases (χ^2=46.311, p<0.001). The MTB positivity rate for males, at 12.4% (291/2341), is significantly higher (χ^2=66.858, p<0.001) than that for females, which stands at 5.6% (133/2370), irrespective of HIV status. The age distribution of MTB-positive patients peaked in the 21-55 age bracket, with a median age of 37.0 (29.0, 47.0). The third quarter of each year, particularly September exhibited the highest positivity rate of 13.1%. Within Mzimba District, 87.8% of TB patients resided in Mzuzu city, with Luwinga (21.8%), Mchengautuwa (12.5%), and Zolozolo (9.9%) being the top three townships. Most newly diagnosed cases received treatment (85.1%), but the rifampicin resistance rate (4.7%) exceeded the national average.

Conclusion

Within the healthcare catchment area of Mzuzu Central Hospital, MTB infection is significantly associated with HIV. Males show a higher MTB positivity rate than females. The study identifies high-risk age groups, temporal trends, and geographical TB patterns. Rifampicin resistance is a critical issue needing urgent attention.

Keywords: Mycobacterium tuberculosis, GeneXpert MTB/RIF Ultra, Demographics distribution, HIV/TB co-infection, Rifampicin resistance

Introduction

Tuberculosis (TB), a chronic infectious disease caused by Mycobacterium tuberculosis (MTB), can affect various parts of the body, yet it predominantly manifests in the lungs, hence often categorized into pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB). It stands as the second leading cause of death among infectious diseases, ranking 13th globally in terms of mortality, and serves as a primary cause of death in low- and middle-income countries, particularly those in sub-Sahara Africa[1]. Even as survivors of TB, individuals continue to confront a considerable and persistent disease burden, encompassing respiratory dysfunction[2], psychosocial challenges, and a decline in their quality of life[3]. Over the past two decades, the number of TB cases has declined annually at a rate of 2%, yet the subsequent global COVID-19 pandemic has disrupted this progress significantly. The reduced opportunities for TB diagnosis and treatment have led to a slowdown, disruption, or even reversal of gains made in the fight against tuberculosis, thereby increasing TB-related deaths[4]. In 2021, it was estimated that there were 10.6 million new cases of tuberculosis globally, with an incidence rate of 133 per 100,000 individuals. In 2022, approximately 1.3 million deaths were attributed to TB worldwide, of which 167,000 were cases co-infected with HIV[5].

Africa remains one of the high-burden regions for TB, with statistics indicating that 25% of individuals suffering from the disease in 2019 hailed from the continent. Despite various efforts aimed at controlling tuberculosis, it continues to pose a severe public health challenge in African, many people go undiagnosed or are not treated appropriately[6]. Due to advancements in medical technology and the availability of potent anti-TB medications, Malawi has experienced a notable decline in the threat posed by tuberculosis[7]. Nevertheless, TB remains a critical public health issue and a substantial economic burden for Malawi[8].

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The diagnosis of PTB primarily relies on pathogen-based testing. Compared to traditional pathogen detection methods such as sputum smear microscopy and MTB culture, the rapid molecular diagnostic technology, GeneXpert MTB/RIF, was endorsed by the World Health Organization (WHO) in 2010 for the initial diagnosis of TB and possible multidrug-resistant tuberculosis (MDR-TB) cases in sputum samples[9]. The GeneXpert MTB/RIF Ultra has further enhanced the sensitivity of its predecessor, achieving an overall sensitivity of 87.5% in detecting sputum samples, a sensitivity of 78.9% in smear-negative sputum samples, and a specificity of 98.7%[10]. Additionally, its application in the diagnosis of TB/HIV co-infections and EPTB has been positively recognized[11,12].

Globally, in 2019, approximately 815,000 HIV-positive TB cases were reported, with only 56% accurately documented. In response, the Malawian government has implemented significant initiatives to decrease TB incidence, mortality, and transmission rates. By December 2021, 445 public and Christian Health Association of Malawi (CHAM) health facilities in Malawi were equipped to initiate TB diagnosis and treatment. Notably, the reach of GeneXpert technology expanded from 51 sites in 2016 to 144 sites by 2022[13].

Mzuzu Central Hospital, being the largest public tertiary hospital in the northern region, provides referral services to a vast majority of the northern areas. Its laboratory department boasts the sole level three tuberculosis culture laboratory in the northern region of Malawi that offers specialized diagnostic tests for TB.

The present study aims to retrospectively analyze the epidemiological distribution characteristics and associated factors of TB infection in the healthcare catchment area of Mzuzu Central Hospital in Malawi, by collating relevant laboratory data on tuberculosis. This research aims to provide additional theoretical insights to improve the precision and effectiveness of TB prevention and control strategies tailored to the northern region, complementing existing knowledge.

Methods

Setting

The prevalence of TB in sub-Saharan Africa, remains alarmingly high, exacerbated by concerning rates of rifampicin resistance and mortality. Despite this pressing public health concern, there persists a notable gap in research regarding the epidemiological traits of MTB infection within Malawi. Essential variables such as demographic characteristics (including age, gender, temporal trends, and residential address), HIV co-infection status, anti-TB treatment history, and rifampicin resistance status offer crucial theoretical perspectives. These insights are vital for enhancing the precision and efficacy of TB prevention and control strategies.

Study Design

This is a retrospective cross-sectional study. A total of 4,711 patients from Mzuzu Central Hospital were included in the study. We analyzed the characteristics of gender, age, temporal trends, and geographic distribution of MTB-positive individuals within the healthcare catchment area of Mzuzu Central Hospital. Additionally, HIV co-infection status among MTB-positive patients were explored. Ultimately, we reported the anti-TB treatment status and rifampicin resistance among the MTB-positive patients.

Population

A total of 4,711 patients who underwent testing with GeneXpert (GeneXpert MTB/RIF or GeneXpert MTB/RIF Ultra) at Mzuzu Central Hospital between June 2018 and June 2024 were enrolled in this study. Of these, 424 patients tested positive for MTB, while 4,287 patients tested negative. We focused on 424 patients with MTB-positive and performed statistical analysis on their demographic data and medical records. This study was approved by the Mzuzu University Research Ethics Committee.

Inclusion Criteria

a. Complete test results and demographic data (including age, gender, temporal trends, and residential address) are available.

b. Medical records pertaining to HIV status, screening purpose, screening indications, as well as TB treatment and follow-up information are accessible.

Exclusion Criteria

Patients with incomplete or missing clinical information should be excluded to ensure data integrity and accuracy of the analysis.

Data Collection

We collected GeneXpert test results, demographic, and medical data, including age, gender, temporal trends, HIV status, screening purpose, screening indications of patients from the laboratory information system of laboratory department of Mzuzu Central Hospital. Residential addresses information was obtained from the application form. The medical records of TB treatment and follow-up information comes from TB office of the hospital. The positivity rate was determined as the number of positive test results divided by the total number of tests conducted.

GeneXpert examination were conducted by Cepheid GeneXpert® instrument and its accompanying reagents. The results were derived from conditions characterized by optimal instrument performance, standardized operational procedures.

Statistical Analyses

The figures were generated using GraphPad Prism software, version 8.0. Additionally, statistical analysis was conducted using IBM SPSS Statistics version 25.0. The measurement data were expressed as median (M) with interquartile range (P25, P75). For non-normally distributed data, the Mann-Whitney U test was applied to compare differences between groups. The Pearson correlation coefficient was used to assess the correlation between two continuous variables. Differences in proportions and correlations among categorical variables were analyzed using Pearson's Chi-square test. Statistical significance was determined at a level of $P < 0.05$, and all statistical tests were conducted as two-sided.

Results

General Information

A total of 4,711 patients medical records in Mzuzu Central Hospital were collected. These included 2,341 (49.7%) males and 2,370 (50.3%) females, with ages ranging from 1 to 98, and a median age of 44.0 (32.0, 56.0). The primary specimen type submitted for testing was sputum, accounting for 95.7% (4,509) cases. Regarding HIV status, 54.4% (2,565) patients tested positive for HIV, and 14.6% (690) patients were

Table 1. General Information

specimen	Number of cases (n=4711)	MTB-positive patients(n=424)	HIV-positive patients(n=2565)
sputum	4509(95.7%)	412(97.2%)	2533(98.7%)
faeces	52(1.1%)	2(0.5%)	5(0.2%)
pleural effusion	41(0.9%)	1(0.2%)	9(0.3%)
aspirate	36(0.8%)	2(0.5%)	7(0.3%)
ascites	35(0.7%)	/	2(0.1%)
pus	19(0.4%)	7(1.6%)	5(0.2%)
CSF	12(0.3%)	/	4(0.2%)
tissue	6(0.1%)	/	/
pericardial effusion	1(0.0%)	/	/

Table 2. The Gender Distribution of MTB-Positive individuals

	Male	Female	χ^2	p-value
MTB positive	291(12.4%)	133(5.6%)	66.858	< 0.001
MTB negative	2050(87.6%)	2237(94.4%)		
HIV negative-MTB positive	154(18.7%)	46(7.3%)	39.804	< 0.001
HIV negative-MTB negative	668(81.3%)	588(92.7%)		

Table 3. The Association between MTB and HIV Infection

	HIV positive	HIV negative	χ^2	p-value
MTB positive	184(7.2%)	200(13.7%)	46.311	< 0.001
MTB negative	2381(92.8%)	1256(86.3%)		

Table 4. Gender Difference in MTB Infection among HIV-Positive Individuals

	Male	Female	χ^2	p-value
HIV positive-MTB positive	115(9.9%)	69(4.9%)	23.109	< 0.001
HIV positive-MTB negative	1052(90.1%)	1329(95.1%)		

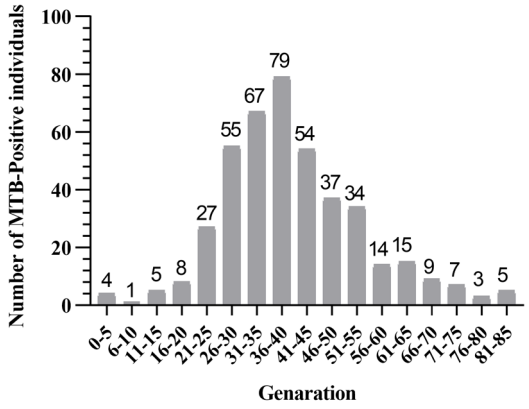

Figure 1. Age Distribution of MTB-positive Individuals

unknown (Table 1).

Nearly half of the total GeneXpert testing, 2565 (54.5%), were conducted on patients with HIV infection as an indication. Testing based on other GeneXpert indications were as follows: 726 (15.4%) patients were screened due to hospitalizations, 214 (4.5%) as presumptive MDR-TB patients, and 1,206 (25.6%) patients were screened due to other reasons such as FAST strategy, and pre-employment physical examinations.

Characteristics of Gender and Age Distribution of MTB-Positive Patients

Among the 4,711 patients subjected to GeneXpert testing, 424 were found to be positive for Mycobacterium tuberculosis (MTB), yielding an overall positivity rate of 9.0%. Notably, a statistically significant gender disparity was observed, with males exhibiting a higher positivity rate of 12.4% (291/2341) compared to females at 5.6% (133/2370) ($\chi^2 = 66.858$, $p < 0.001$). To mitigate potential confounding effects related to HIV status, a subset analysis was conducted focusing on HIV-negative patients who tested positive for MTB. This analysis revealed a consistent trend, with males demonstrating a positivity rate of 18.7% (154/822), which was approximately twice that of females at 7.3% (46/634) ($\chi^2 = 39.804$, $p < 0.001$). (Table 2)

By distributing MTB-positive individuals into 5-year age categories, we observed that more than 80% of MTB-positive patients in the study region were aged between 21 to 55 years (Figure 1), and the median age of MTB-positive patients was 37.0 (29.0,47.0).

Characteristics of Temporal and Geographic Distribution of MTB-Positive Patients

Given that data for 2018 and 2024 are limited to six months, we excluded these years from our analysis of the annual distribution of MTB-positive cases. Since 2019, we observed a continuous decline in MTB-positive cases, which began to gradually increase from 2021 onwards (Figure 2a). To further investigate seasonal patterns among MTB-positive cases, we found that the positivity rate was peaked in the third quarter (10.1%) (Figure 2b). On a monthly basis, the highest MTB positivity rate exhibited in September (13.1%) (Figure 2c). Correlation analyses between the quarterly and monthly MTB positivity rates and their respective screening volumes revealed no significant correlations ($p = 0.074$ and $p = 0.246$, respectively).

Upon removing 52 patients with missing address information from the initial pool of 424 MTB-positive patients, it was found that 92.5% (345/373) of the remaining patients were from the Mzimba district. Notably, a substantial proportion of MTB-positive patients residing in the Mzimba district, specifically 87.8% (303/345), were found to be in Mzuzu city. Upon further segmentation by township within Mzuzu city, the proportions of positive cases in the top 10 townships were shown, especially for Luwinga (21.8%), Mchengautuwa

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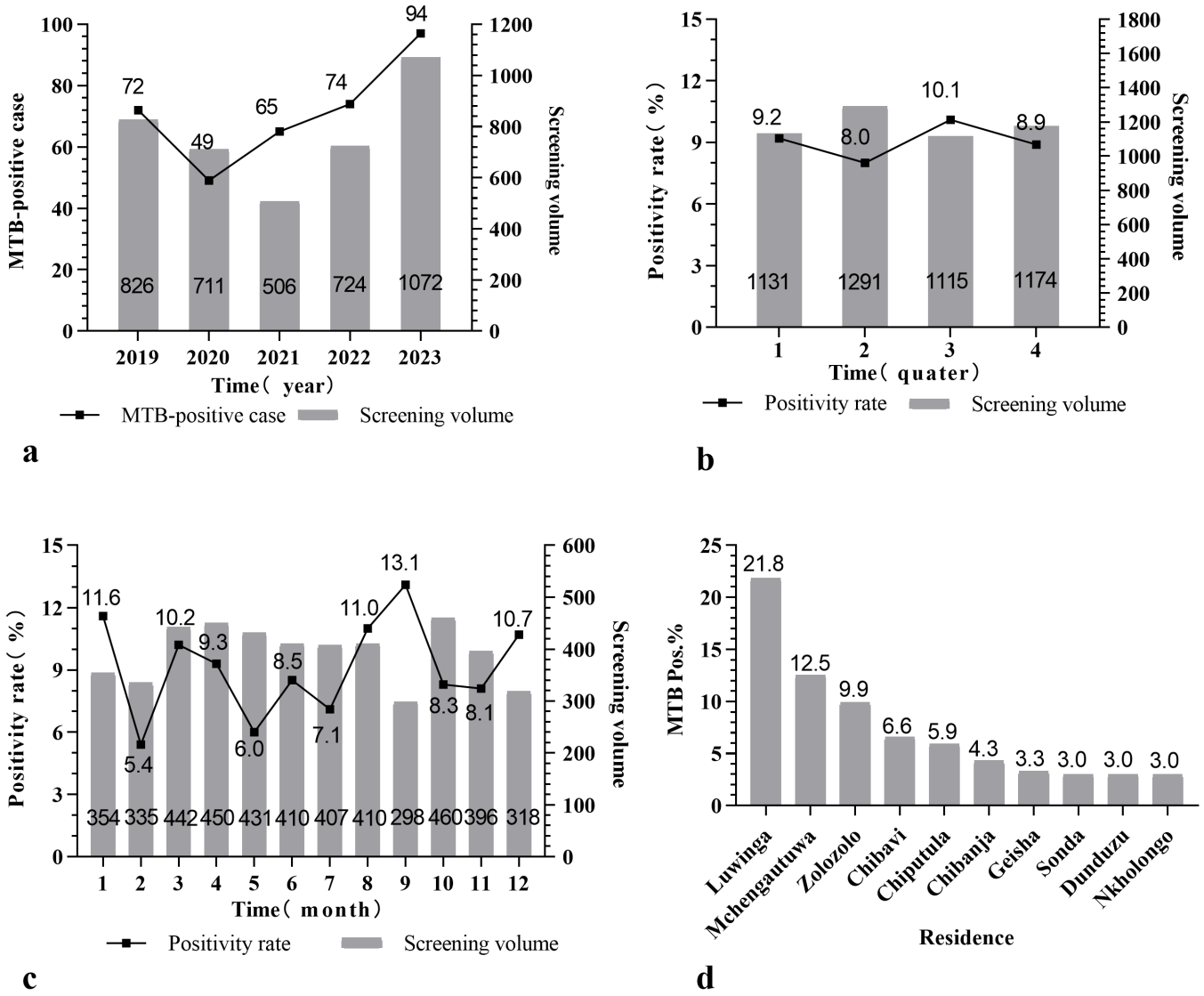

Figure 2. Temporal and Geographic Distribution of MTB-Positive Patients. (a) Annual distribution of MTB-positive Individuals. (b) Quarterly Positivity Rate of MTB. (c) Monthly Positivity Rate of MTB. (d) Geographic Distribution of MTB-positive Individuals in Mzuzu City. MTB Pos.%: The proportion of MTB-positive individuals

(12.5%), and Zolozolo (9.9%), which accounted for the highest proportions (Figure 2d).

HIV Co-Infection Status among MTB-positive Patients

Regarding HIV status, 2,565 of 4,711 patients tested positive for HIV, and 690 patients with unknown HIV status were not included into analysis. One hundred and eighty-four patients presented HIV-positive, indicating an HIV/TB co-infection rate of 47.9%. A significant association was observed between MTB and HIV infection (χ^2=46.311, p<0.001) (Table 3). Furthermore, among HIV-positive individuals, the positivity rate for MTB was significantly higher in males (9.9%, 115/1167) compared to females (4.9%, 69/1398) (χ^2=23.109, p<0.001). (Table 4).

Anti-TB Treatment Status and Rifampicin Resistance among MTB-positive Patients

Out of the 424 MTB-positive patients, 52 had no record of treatment status, 5 did not receive treatment, 3 were lost to follow-up, and 3 died before initiating treatment. The remaining 361 patients (85.1%) received anti-tuberculosis treatment and were regularly followed up. Among the 424 MTB-positive patients, a total of 20 cases were identified with rifampicin resistance, resulting in a resistance rate of 4.7%. Additionally, there were 11 cases where rifampicin resistance was uncertain.

Discussion

TB constitutes the principal cause of hospitalization and mortality among HIV-infected adults and children globally[14]. Our study at Mzuzu Central Hospital reveals a positivity rate of 9% for GeneXpert testing. Notably, we observed a significant correlation between MTB and HIV infection, with HIV/TB co-infection accounting for 47.9% of the MTB-positive cases. Notably, a gender disparity exists, where males in the region demonstrate significant higher positivity rate of MTB compared to females, regardless of HIV status. This finding corroborates similar results obtained from a study conducted in Nigeria[15]. However, contrasting data emerges from the 2021 Global Burden of Disease Study, which reported significantly higher incidence of HIV/TB co-infection among females compared to males[16]. This suggests that the gender distribution of HIV/TB co-infection exhibits geographical variability. Furthermore, studies have indicated a link between HIV and the increase in reported cases of smear-negative and extrapulmonary tuberculosis[17,18], hinting that HIV may be a pivotal factor influencing the tuberculosis

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epidemic pattern in Malawi. Regarding age, the distribution of MTB-positive patients primarily spans the 21-55 age bracket, which is consistent with findings reported in Ghana and Malawi[19,20]. Therefore, gender, age, and HIV infection status should be considered as potential factors that may influence susceptibility to TB.

This study observed a continuous decline in newly diagnosed TB cases since 2019, which began to gradually increase from 2021 onwards. This trend may be attributed to a combination of factors, including the reduction in personnel mobility during the COVID-19 pandemic, the widespread adoption of personal protective equipment, and the general reluctance of both patients and healthcare workers to undergo or conduct TB screenings unless absolutely necessary, due to concerns about acquiring or transmitting COVID-19. The persistent rise in newly diagnosed cases following the easing of pandemic restrictions warrants attention from local governments. Based on the quarterly and monthly distribution patterns of MTB positivity, the third quarter of each year, particularly the transitional period from the dry to rainy season in September, emerges as a pivotal period for TB prevention and control efforts. This may due to the interplay of multiple factors. Rapid climatic changes, characterized by drastic fluctuations in humidity and temperature, favor the survival and dissemination of MTB, while also increasing the incidence of respiratory diseases and weakening individual resistance. Changes in social behaviors, such as increased indoor activities and potential deterioration in nutritional status, further exacerbate the risk of TB transmission.

The study revealed that a higher proportion of MTB-positive patients attending Mzuzu Central Hospital originated from Mzuzu City, particularly Luwinga (21.8%), Mchengautuwa (12.5%), and Zolozolo (9.9%) residential areas. These townships are characterized by high population density coupled with elevated poverty levels[21]. It may be necessary to step up TB control measures in these residential areas based on actual conditions. This includes, but is not limited to, strengthening health education, promoting preventive behaviors such as wearing masks, frequent handwashing, and ensuring adequate ventilation, upgrading infrastructure to provide access to safe drinking water and improved sanitation, reducing overcrowding, and offering economic and medical support to ensure access to basic nutrition, healthcare services, and timely TB screening and treatment.

Rifampicin stands as a potent first-line therapy in TB management, with missed doses posing a risk for the emergence of multidrug-resistant TB (MDR-TB)[22]. The World Health Organization (WHO) documented 450,000 cases of rifampicin-resistant TB (RR-TB) in 2021, with Russia, Eastern Europe, and specific Central Asian countries reporting >50% of MDR-TB or RR-TB cases among previously treated patients[5]. Malawi's Ministry of Health is the sole provider of anti-TB medications and supplies, ensuring treatment quality and rational drug use in both public and private healthcare facilities. Rigorous drug regulation has contributed to Malawi's status as a region with minimal drug-resistant TB (DR-TB) incidence, with a prevalence of 2.3% in newly diagnosed patients[13]. In our study, 4.5% (214/4711) of the patients underwent GeneXpert testing due to presumptive MDR-TB. Among the 424 MTB-positive patients, 85.1% (361/424) received anti-tuberculosis treatment and follow-up care, while 4.7% (20/424) exhibited resistance to rifampicin, a percentage that notably exceeds the national average. This highlights the need for enhanced monitoring and management of anti-TB drug resistance, as well as improved surveillance and evaluation of RR-TB patients in this region. Effective management of these cases is vital to curb transmission and mitigate spread. Moreover, proactive hospitalization and isolation of infectious RR-TB patients should be vigorously promoted.

While this study offers invaluable insights into the epidemiological landscape of tuberculosis in Malawi, it is crucial to acknowledge several limitations that constrain its comprehensive understanding. Notably, the reliability of data sourced from application forms for Xpert testing at Mzuzu Central Hospital is a significant constraint. These data may be impacted by patient recall biases, physician diagnostic accuracy, and potential oversights in form completion. Additionally, the study's geographical scope is limited, and it lacks a comprehensive exploration of the socioeconomic, cultural, and behavioral determinants that influence tuberculosis incidence and prevalence. To further advance our understanding in this area, future research endeavors should prioritize the expanding sample sizes, enhancing data diversity, integrating longitudinal study designs, and thoroughly examining the multifaceted factors influencing tuberculosis and its drug resistance.

Conclusions

Within the healthcare catchment area of Mzuzu Central Hospital in Malawi, a significant correlation is observed between MTB infection and HIV infection. Notably, regardless of HIV status, males exhibit significant higher positivity rate for MTB compared to females. This study points to the high-risk age groups, temporal trends, and geographical distribution patterns of TB infection in the region. Based on these findings, we recommend incorporating potential risk factors such as gender, age, temporal distribution, geographical characteristics, and HIV status into TB prevention and control strategies in this area to achieve more precise interventions. Special emphasis should be placed on the implementation of active screening measures specifically targeted at high-risk populations.

Statements and Declarations

Author Contributions

N.Z. and X.W. contributed to the conception and design of the study. N.Z. and T.S.M. contributed to the statistical analyses and manuscript preparation. N.Z., R.K., D.M.N. and Z.W. participated in data collection. R.K. and J.H. reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Data Availability Statement

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval

All procedures performed in our studies involving human

participants were following the ethical standards of the Research Ethics Committee of the Mzuzu University (approval number: MZUNIREC/DOR/24/166). Due to the retrospective nature of the study, the Research Ethics Committee of the Mzuzu University waived the need of obtaining informed consent.

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