# Original Article

# Prevalence and Associated Factors of Multidrug-Resistant Tuberculosis among Tuberculosis Patients at Yirgalem General Hospital, Sidama Regional State, Ethiopia: A Cross-Sectional Study Based on Five Years of Secondary Data.

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**Abstract**

**Background:** Drug-resistant tuberculosis (DR-TB) presents new barriers to the control of TB worldwide. It is a man-made problem, largely as a consequence of human error in the quality of anti-TB drugs and patient treatment. Despite its importance, information is scarce about MDR-TB to design effective and efficient recommendations for prevention and treatment strategies and policies in the study area.

**Objective:** This study aimed to assess the magnitude of MDR-TB and associated factors among tuberculosis patients at Yirgalem General Hospital, Sidama Regional State, Ethiopia, from 2016 to 2020

**Methods:** A hospital-based retrospective document review was conducted at Yirgalem General Hospital. Data abstraction was done by trained data collectors using a standard abstract sheet. Bi-variable and multi-variable logistic regressions were done to identify factors associated with the occurrence of MDR-MTB. Variables with a p-value less than 0.25 in binary logistic regression were further fitted into multi-variable logistic regressions to control cofounders. In the final model, variables with a P-value <0.05 were considered statistically significant. The results were presented as Odds ratio with 95% CI.

**Results:** The prevalence of MDR-TB among TB-positive cases was 5.3% (95%CI, 3.8%, and 7.1%). Among MDR-TB cases, 2.2% were newly treated cases, while 12.9% were previously treated cases**.** The trend of tuberculosis across the five years showed a high proportion of MDR-TB cases in 2016 and 2017, with a declining trend in the last three consecutive years. Study participants who had previous history of anti-TB treatment, 20-40 years and 41-60 year age groups, and patients who came from rural areas were more likely to develop multi-drug resistant *Mycobacterium tuberculosis*.

**Conclusions:** The prevalence of MDR-TB among TB-positive clients was high. In addition, the trend of MDR-TB declined from 2016 to 2020. Factors like having a TB treatment history, advanced age, and living in a rural area were factors linked with MDR-TB. Hence, monitoring and controlling mechanisms for correct and complete drug treatment should be enhanced. Stakeholders should provide special attention to the diagnosis, treatment, and prevention of MDR-TB among rural and older TB patients. [*Ethiop. J. Health Dev.* 2024; 38(2): 00-00]

**Keywords:** Multi-drug Resistant, Tuberculosis, prevalence, Trend, Yirgalem, Institution.

## Background

Tuberculosis (TB) is a chronic airborne infectious disease caused by Mycobacterium tuberculosis and primarily affects the lungs, although extra-pulmonary manifestations are also observed. Tuberculosis (TB) remains a significant global health challenge, contributing to millions of cases and deaths annually. Approximately 10.4 million individuals worldwide are affected by TB each year, leading to around 1.8 million TB-related deaths. Alarmingly, 95% of these deaths occur in resource-limited countries(1). In Sub-Saharan regions, particularly among previously treated TB cases, the prevalence of multidrug-resistant TB (MDR-TB) is notably high compared to new TB cases(2). Research indicates that approximately 500,000 cases of MDR-TB emerge annually(3), with a plain reality that only about 3% of these cases receive treatment, resulting in over 100,000 deaths each year. Moreover, up to 10% of MDR-TB cases progress to extensively drug-resistant TB (XDR-TB)(4). MDR-TB is characterized by resistance to both Rifampicin and isoniazid, while XDR-TB entails additional resistance to fluoroquinolones and certain second-line injectable drugs(5).

In Sub-Saharan Africa, the prevalence of any drug-resistant TB is estimated to be 12.6% among new cases and 27.2% among previously treated patients(6). The burden of Multidrug-Resistant Tuberculosis (MDR-TB) is notably severe in resource-limited countries, where constraints such as insufficient health resources, financial limitations, and a scarcity of skilled personnel impede effective diagnosis and management, posing challenges for containment and prevention of further spread (7). In Ethiopia, factors such as low socio-economic status, a high prevalence of infectious diseases, poor treatment outcomes, a lengthy treatment duration (approximately two years), high treatment costs, and various complications exacerbate the complexity of MDR-TB compared to TB(8).

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In Ethiopia, tuberculosis (TB) has been recognized as a major public health threat for over half a century. The national TB control program has adopted a standardized prevention and control program known as directly observed treatment, short course (DOTS). Ethiopia continues to be one of the countries with a high burden of TB and MDR-TB, with TB remaining a significant cause of morbidity and mortality(9). According to a WHO report, Ethiopia ranks 15th among 27 countries with a high burden of drug-resistant TB, with an estimated 5,200 cases occurring annually (10).

A study conducted across various regions of Ethiopia revealed varying magnitudes of Multidrug-Resistant Tuberculosis (MDR-TB): 15.3% in the Amhara region (11). 18.5% from the Tigray region (12). 5.7% from Metema and west Armachiho(13), and 23% eastern Ethiopia(14). These discrepancies in findings could be attributed to differences in sample sizes, variations in study populations, access to healthcare facilities, and disparities in the effectiveness of TB control programs.

Despite existing research on Multidrug-Resistant Tuberculosis in Ethiopia, there is a paucity of information from specific regions. Therefore, the objective of this study was to evaluate the prevalence and determinants of MDR-TB among tuberculosis patients at Yirgalem General Hospital, Sidama Regional State, Ethiopia, in 2020.

## Methods and materials

### *Study setting and design*

The study was conducted at Yirgalem General Hospital, Sidama Regional State, which is about 315 km from Addis Ababa, the capital city of Ethiopia. The hospital serves more than 4.3 million populations in the catchment area and nearby zones of the Oromia Region and Gedeo Zone. The hospital has the following departments: Medical, Surgical, Pediatrics, and Gynecology/Obstetric/ wards. Besides, the hospital has special care units like the Medical Intensive Care Unit, Neonatal Intensive Care Unit, and surgical recovery room, and clinics like eye, antiretroviral therapy, dental, TB, and MDR-TB clinics. It provides health services at both inpatient and outpatient levels.

This study aimed to assess the prevalence level, and associated factors of MDR-TB among TB cases treated at Yirgalem General Hospital from January 2016 to December 2020.

### Population

### Source Population

All TB cases that were registered and treated for MD-TB from January 2016 to December 2020 were considered as the source population. Client cards, whose cards were filledcompletely, were included in this study. However, clients whose cards were filled incompletely were excluded from this study. The study populations were MDR-TB confirmed cases and booked to be treated from January 2016 to December 2020.

### Sample size and sampling

The study aimed to include all tuberculosis cases admitted to the hospital between 2016 and 2020, irrespective of their age or gender. During this period, a total of 770 TB patients were recorded, and all of them were enrolled in the study. Given the limited number of patients, there was no need for patient sampling, and therefore, all patients were recruited for the study.

### Variables of the Study

**Dependent Variable:** . This study's dependent variable was Multi-Drug-Resistant Tuberculosis status. It was a binary variable. Cases that satisfied the standard definition of MDR tuberculosis were coded as ‘yes’ and labelled as ‘1’; otherwise, ‘0’.

**Independent Variables:** The explanatory variables were classified as socio-demographic and individual behavioral factors. The socio-demographic factors include gender, age, residence, and duration of stay from diagnosis. The individual factors consist of the following variables: types of TB, category of TB, previous treatment, and HIV status.

### Operational definitions

**Tuberculosis case:** A case of TB was one with bacteriological confirmation (sputum smear positive or culture) or where a clinician decided to treat for TB. Each TB case is reported as pulmonary TB (smear-positive, smear smear-negative, or smear not done) or extrapulmonary TB.

MDR-TB: It was defined as patients with TB cases who had bacteriologically proven resistance to Rifampicin and isoniazid or had clinically evident MDR-TB based on a history of treatment failure or MDR-TB contact defined according to WHO guidance.

### Data Source

The MDR-TB register and treatment card data were gathered using a pretested and standardized record review checklist. When necessary, the MDR-TB register's missing data for HIV-positive patients enrolled in long-term HIV/ART care was filled in by reviewing the ART registration. Following the clinician’s diagnosis, unit TB focal person or TB staff record patient data in paper based unit TB registers. We used the national guideline definitions as adapted from the WHO TB guidance of 2006 for case classification during the review period(15).

Two teams, each with one supervisor and two data collectors, collected the data. The supervisors were trained MSC public health graduates, while the data collectors were trained laboratory technologists.

### Data analysis and quality check

Data were entered and analyzed by using IBM SPSS Statistics version 20. Data were summarized using descriptive measures and presented in tables. A chi-square test was conducted for categorical variables.

Variables with p<0.05 were exported to the binary logistic regression analysis model.

Bi-variable and multivariable logistic regressions were used to determine factors associated with the prevalence of MDR-TB. -Multivariable logistic regressions further analyzed variables from bi-variable logistic regression with a p-value less than 0.25. A P-value <0.05 was considered statistically significant. A multicollinearity test was conducted.

The necessary assumption of logistic regression analysis was checked by using the Hosmer-Lemeshow test of goodness of fit which has a chi-square distribution. As there were multiple potential predictor variables of interest for each of the variables of outcomes, backward selection logistic regression modeling was fitted with a probability of removal of a variable set at 0.2. Multicollinearity and interaction effect checks were also done by measuring Variance Inflation Factors (VIF), labeling of outliers, and running cross-products. Multicollinearity and interaction effects were not observed among the variables included in the models. In order to ensure the quality of the data, the supervisors received the collected data every day and verified it, providing feedback the next morning.

## Results

### *Socio-demographic characteristics*

A total of 770 positive TB patients were found in the record at Yirgalem General Hospital from January 2016 to December 2020. All medical records were filled and completed making a response rate of 100%.

The mean (± standard deviation) age of study participants was 24±4.7years. Of these, 496(64.4%) cases were males. Among the total study participants, 472(61.3%) of them were from rural areas.

Table 1. **Socio-demographic characteristics of TB confirmed patients at Yirgalem General Hospital, Sidama Regional State, Ethiopia, January 2016 and December 2020 (n=770).**

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Gender | Male | 496 | 64.4 |
| | Female | 274 | 35.6 |
| Age in years | ≤20 | 289 | 37.5 |
| | 21-40 | 376 | 48.8 |
| | 41-60 | 56 | 7.3 |
| | ≥61 | 49 | 6.4 |
| Residence | Urban | 298 | 38.7 |
| | Rural | 472 | 61.3 |
| Year of Diagnosis | 2016 | 203 | 22.7 |
| | 2017 | 194 | 18 |
| | 2018 | 169 | 16.8 |
| | 2019 | 120 | 14.5 |
| | 2020 | 84 | 9.2 |

### The burden of MDR-TB among tuberculosis

Out of 770 confirmed TB patients 728(94.6%) were confirmed for MTB, 41(5.3%) were MDR-TB, and 1(0.1%) had XDR-TB. Based on the collected data, there has been a significant reduction observed in the prevalence rates of Mycobacterium tuberculosis (MTB) and Multidrug-Resistant Tuberculosis (MDR-TB) over five years (figure 1)

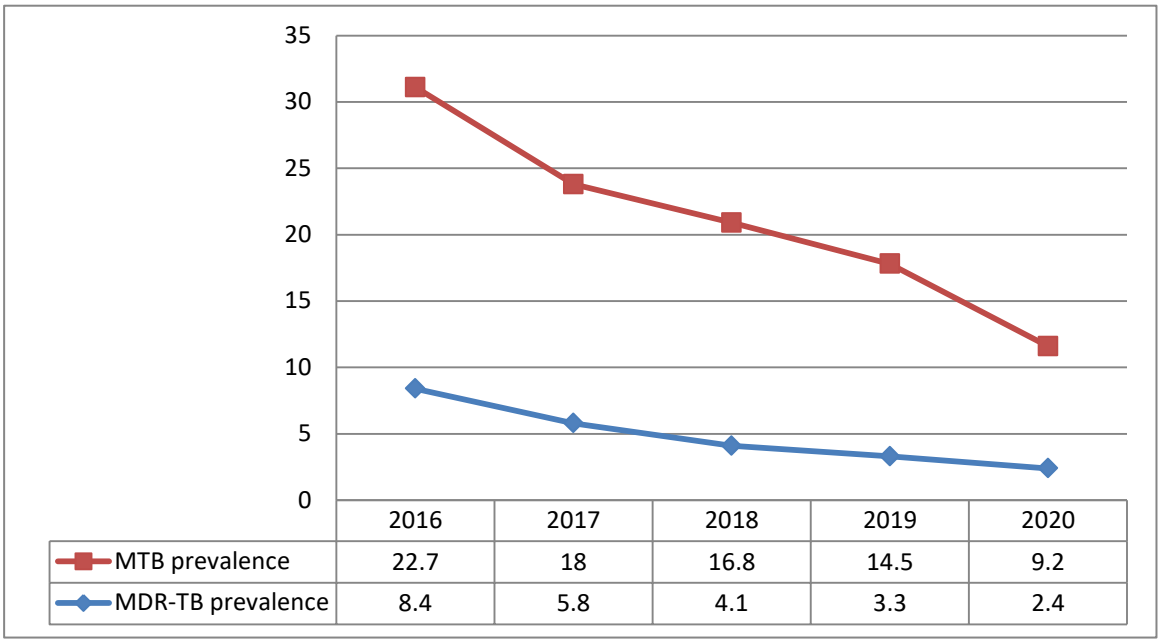


Figure 1. **The tend of MDR-TB among TB-confirmed patients at yirgalem General Hospital, Sidama Regional State, in Ethiopia from 2016 to 2020.**

**Individual characteristics of study participants**

A majority (79.2%) of the participants had pulmonary tuberculosis. Two hundred twenty-three (30.1%) had a previous TB treatment history with first-line drugs, while 224 (29.1%) had a previous TB disease history. Of the 770 participants, most (70.9%) were new cases, one–third (28.1%) were relapses, and after failure to treatment with first-line drugs, second-line drugs. Moreover, only 7(0.9%) were due to drug adherence. 1(0.1%), and 8(1.0), considering their HIV status 118(15.3%) had HIV positive results, 505(65.5) were HIV negative, and 147(19.1) were unknown HIV serostatus (not available in the record).

Table 2. **Individual characteristics of TB confirmed patients and burden of MDR-TB at Yirgalem Hospital, Sidama Region, Ethiopia, from January 2016 to December 2020 (n=770).**

| Variables | Category | frequency | Percentage |
|---|---|---|---|
| Classification of TB type | Pulmonary | 610 | 79.2 |
| | Extra pulmonary | 160 | 20.8 |
| Resistant type | M-TB | 728 | 94.6 |
| | MDR/RR-TB | 41 | 5.3 |
| | XDR-TB | 1 | 0.1 |
| TB Category | New | 546 | 70.9 |
| | Relapse | 216 | 28.1 |
| | Failed with FLD | 7 | 0.9 |
| | Failed SLD | 1 | 0.1 |
| Previous TB disease | Yes | 224 | 29.1 |
| | No | 546 | 70.9 |
| Previous TB treatment | With FLD | 223 | 29.0 |
| | With SLD | 1 | 0.1 |
| | No | 546 | 70.9 |
| HIV Status | Positive | 118 | 15.3 |
| | Negative | 505 | 65.5 |
| | Unknown | 147 | 19.1 |

**Factors associated with MDR-TB**

In the bivariable logistic regression analysis model, five variables were found to be associated with MDR-TB: the patient's age, type of residence, tuberculosis type, tuberculosis category, and previous tuberculosis treatment. In the multivariable analysis model, only 4 variables were statistically associated with MDR-TB. Specifically, patients whose ages ranged from 20 to 40 were 84% less likely to develop MDR-TB than cases

whose age was less than 20 (AOR=0.16,95%CI,0.06,0.42). Besides, the chance of getting MDR-TB was decreased by 79% among patients whose age was from 41 to 60 years compared to younger cases (AOR=0.21,95%CI,0.5,0.8). The odds of patients who had been treated with first-line drug previously were 3.6 times more than their counterparts (AOR=3.6, 95%CI, 2.3, 5.6). Compared with urban patients, rural patients had a 2.7-fold higher chance of getting MDR-TB (AOR=2.7, 95%CI, 1.4, 5.6). Compared with urban patients, rural patients had a 2.7-fold higher chance of getting MDR-TB (AOR=2.7, 95%CI, 1.4, 5.6). Patients who had a history of relapse were 3.6 times more likely to acquire MDR-TB than their counterparts (AOR=3.6, 95%CI, 2.3, 5.6).

Table 3. **Result of logistic regression analysis MDR-TB Among Tuberculosis patients at Yirgalem Hospital, Sidama, Ethiopia, from January 2016 to December 2020 (N=770).**

| Variables | | MDR Status | | COR(95%CI) | AOR(95%CI) | P value |
|---|---|---|---|---|---|---|
| | Category | Positive | Negative | | | |
| Age in years | More than 61 | 5 (1.7) | 284 (98.3) | Ref | Ref | 1 |
| | 41-60 years | 30 (8) | 346 (92) | 0.22(0.08,0.5)* | 0.16(0.06,0.42)** | **0.021** |
| | 21-40 years | 4 (7.1) | 52 (92.9) | 0.23 (0.06,0.9)* | 0.21(0.5,0.8)** | **0.032** |
| | Less than 20 | 2 (4.1) | 47 (95.9) | 0.4(0.08,2.2) | 0.16(0.03,1.1) | 0.053 |
| Residence | Rural | 18 (3.8) | 454 (96.2) | 2.1(1.12,3.9)* | 2.8(1.4,5.5)** | **0.004** |
| | Urban | 23 (7.7) | 275 (92.3) | Ref | Ref | 1 |
| Classification of TB type | Pulmonary | 40 (6.6) | 569 (93.4) | Ref | Ref | 1 |
| | Extra-Pulmonary | 1 (0.6) | 160 (99.4) | 11.2 (1.5,2.5)** | 2.7(0.5,14.9) | 0.26 |
| TB Category | New | 12 (2.2) | 534 (97.8) | Ref | Ref | 1 |
| | Relapse | 29 (12.9) | 195 (87.1) | 0.15 (0.08,0.3)** | 3.6(2.3,5.6)** | **0.001** |
| Previous TB Treatment | With FLD | 29 (12.9) | 195 (87.1) | 0.15 (0.08,0.3)** | 3.6(2.3,5.6)** | **0.001** |
| | No | 12 (2.2) | 534 (97.8) | Ref | Ref | 1 |

Key: *-p-value <0.25, *-p-value >0.05, Ref-Reference category, FDL-

**Discussion**

We have tried to assess the prevalence, trend, and predictors of MDR-TB among TB patients treated for TB in Yirgalem Hospital, Sidama region, Ethiopia, from 2016-2020.

This study revealed that the overall prevalence of MDR-TB among TB-confirmed cases was 5.3 %( 95%CI, 2.9, 13.6%) in Yirgalem Hospital, Sidama, Ethiopia. This finding is in line with national prevalence (7.2%)(15).

This finding is lower than the finding of previous studies like a study done in Gambela, Southwest Ethiopia (20%)(16), Bahirdar, Northwest Ethiopia (24.3%) (17), Kathmandu, Nepal (21.32%) (18), in Northern Nigeria (23%) (19), South Africa (26%) (20) and Lagos, Nigeria (37.7%) (21). The probable reason might be associated with geographical and demographical variation and the laboratory method used.

Regarding of trend of the prevalence of MTB, there was a slight decline from 22.7% in 2016 to 9.2% in 2020. Similarly, MDR-TB was dropped from 8.4% to 2.4% between 2016 and 2020. These trend findings are similar to the study done in North-western Tigray, Ethiopia(22), and the Eastern zone of Tigray reported an increasing trend of TB (23). The possible justification might be due to the recent unprecedented COVID-19 crisis may have an impact on TB prevention and control systems in a number of ways. The stay-at-home strategy implemented to stop the virus's spread may make it easier for TB to spread

within households. The disruption of healthcare settings brought on by COVID-19's workload and service shift may jeopardize TB treatment and diagnostic services. On the other hand, these findings are contrary to the studies done in Zambia (24), Zimbabwe(25), Thailand (26), and Saudi Arabia(27). This clearly shows the effect of COVID-19 on the prevention of pulmonary tuberculosis and the reduction of TB diagnosis services in the current study.

This finding is higher than the nationally reported prevalence of Rifampicin-resistant TB, which was less than 2% (28). It was also higher than the globally reported prevalence of RR-TB, which was less than less than 1% (29, 30). However, it is comparable to a study done in Northwest Ethiopia (5.7%) (31), Saudi (5.3%) (31), and the Afar region of Ethiopia (4.1). On the other hand, it was lower (7.5%) than the study in central Ethiopia and Bahir Dar (32). This variation might be due to the method variation used to diagnose MDR-TB. Moreover, our result was much lower than the study reported from Sudan (22.5%) (33). These differences from place to place could be due to differences in patient selection, TB case management, and diagnosis and treatment compliance. Additionally, Rifampicin has several adverse effects that could result in patient non-adherence and, hence, may lead to an increase in resistant strains.

In the present study, MDR-TB was significantly higher among previously treated patients compared to treatment naïve (newly diagnosed) patients. In Ethiopia, the prevalence of MDR-TB among previously treated cases (11.8%) is higher than among new cases (1.6%) (34). This is in agreement with other studies in Ethiopia. The high prevalence of MDR-TB among new TB cases in the current study suggests the existence of active person-to-person transmission or the existence of undiagnosed new MDR-TB cases. This is due to the fact that prior anti-TB exposure only suppresses the growth of susceptible bacilli. However, on the other side, it could permit suitable circumstances for the multiplication of pre-existing drug-resistant mutants.

In addition, drug resistance among previously untreated cases indicates the performance of TB control programs in the past. The strict practice of Directly Observed Therapy (DOTS) and the DOTS-plus program currently run through in Ethiopia is questionable. As in other high TB-incidence settings, most MDR-TB patients initially undergo first-line TB treatment till they are considered treatment failures and have access to MDR-TB diagnostic services.

According to this study, TB patients with a previous history of relapse after the first course of anti-TB treatment had an increased risk of developing MDR-TB. Studies from Addis Ababa and Jimma, Ethiopia, showed similar results (10, 35). This may be related to an inappropriate combination of medications for the specific treatment regimen and re-infection. Thus, strictly applying the WHO-recommended treatment regimens for the specific treatment category and applying the TB infection control measures may reduce the risk of MDR-TB.

Patients of advanced age, less than 20 years, are less likely to develop MDR-TB than those aged 60 years and above. This finding is consistent with meta-analysis studies conducted in Ethiopia. Rural MDR-TB cases had more chance of developing MDR-TB than their counterparts. This was comparable to the findings of a study done in Ethiopia (32). The most likely reason could be low socio-economic status and long distance from health facilities for women who live in rural areas, which may, in turn, affect treatment adherence.

**Limitations**

This study was done on a single institution, which limits its generalizability. Furthermore, the nature of secondary data limits variables only recorded on the chart. Future studies should focus on multicentre health facilities and primary data.

**Conclusions**

In conclusion, the prevalence of MDR-TB among TB-positive cases remains similar compared with the national prevalence. Previous TB treatment failure, advanced age, and rural patients were factors associated positively with MDR-TB.

**Recommendation**

Adherence to WHO treatment regimens and infection control measures is essential for preventing the development and transmission of MDR-TB. Ensuring healthcare providers are trained in evidence-based practices and monitoring adherence to treatment protocols can improve patient outcomes and reduce the spread of drug-resistant TB strains.

**Abbreviation**

MDR-TB-Multi-Drug Resistance Tuberculosis, MTB-Mono-resistance Tuberculosis, HIV-Human Immune Virus, MDR-Multi Drug Resistance, WHO-World Health Organization, FLD –First Line Drug, RR-MTB-Rifampicin Resistant Tuberculosis.

**Ethical declarations**

Ethical clearance was obtained from the Institutional Review Board (IRB) of the College of Medicine and Health Science of Hawassa University. Consent was obtained from Yirgalem General Hospital.

**Consent for publications**

Not applicable

**Availability of data and materials**

The data sets used and analyzed in the current study are available from the corresponding author on reasonable request.

**Competency interest**

The authors of this study declare that they have no competing interest to disclose. They have no financial or personal relationships that could potentially influence the research findings or bias the interpretation of the results. The study was conducted with the sole purpose of advancing knowledge and

understanding in the field, without any external influences or conflicts of interest. This declaration ensures transparency and upholds the integrity of the research process.

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**Author's contributions**
MMM was involved in the initiation of the research question, prepared the research proposal, carried out the research, entered and analyzed data and wrote the manuscript. MMA conducted an edition, advising, cooperatively prepared research tools and revised the manuscript. BTN conceived, entered, and analyzed data, interpreted data, and drafted the final report. He wrote up and prepared the manuscript. All authors read and approved the final manuscript.

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