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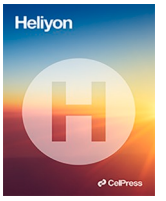

Research article

Mycobacterium tuberculosis and rifampicin-resistant tuberculosis among tuberculosis presumptive patients in selected zones of Tigray, Northern Ethiopia, 2016–2019

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ABSTRACT

Introduction: Tuberculosis (TB) is the second leading cause of mortality from an infectious disease worldwide. Multidrug-resistant tuberculosis (MDR-TB), where rifampicin-resistant TB is the biggest contributor, remains a global health threat. There is scant data on MTB and rifampicin resistance (RR-MTB) using Gene Xpert MTB/RIF assay in Ethiopia. This study aimed to determine the prevalence of MTB and RR-MTB among presumptive TB patients in Tigray, Northern Ethiopia.
Methods: A multi-center retrospective cross-sectional study was conducted from October 2019 to December 2019 among presumptive MTB patients from four hospitals in Tigray. Records of sputum sample results of presumptive MTB patients analyzed with Gene Xpert MTB/RIF assay from January 2016 to December 2019 were investigated. Data were extracted using a data-extraction tool from registration books and analyzed using SPSS ver.21. Statistically significant was set at p-value $\leq$0.05.
Results: From 17,329 presumptive adult MTB patients who had submitted sputum samples for TB diagnosis, 16,437 (94.9 %) had complete records and were included in the study. More than half (60.2 %) of them were males and ages ranged from 18 to 98 years. Majority of the participants: 15,047(91.5 %) were new cases and 11,750 (71.5 %) were with unknown HIV status. Prevalence of MTB was 9.7 % (95 % CI: 9.2–10.2 %) of these, rifampicin resistant-MTB was 8.7 % (95 % CI: 7.32–10.09 %). Age (being >29 years) [$p < 0.001$] and new cases [AOR = 0.46; 95%CI = 0.39, 0.53, $p < 0.001$] were associated with low TB infection. Age groups of 18–29 years were associated with higher RR-MTB [AOR = 3.08; 95 % CI = 1.07, 8.72, $p = 0.036$].
Conclusion: Nearly one-tenth of the presumptive tuberculosis patients tested positive for MTB; out of these, 8.7 % were RR-MTB. The high prevalence of TB and RR-MTB at a young age and previously treated cases calls for a concerted effort to improve and monitor TB treatment to reduce the problem.

1. Introduction

Tuberculosis (TB) and multidrug-resistant (MDR-TB) is a major global health problem. According to the 2023 WHO report, TB was

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the world's second leading cause of death from a single infectious agent, after coronavirus disease (COVID-19), and caused almost twice as many deaths as HIV/AIDS. More than 10 million people continue to fall ill with TB every year. WHO has also reported about 1.3 million deaths from TB globally and an estimated 410,000 people developed multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) in 2022 [1]. Delays in early diagnosis and appropriate treatment initiation, and the high prevalence of HIV in resource-limited settings made TB and MDR-TB-associated morbidity and mortality to be quite high [2].

A key element in the management of TB and MDR-TB is early diagnosis and immediate initiation of appropriate treatment [3]. Conventionally, the diagnosis has relied upon culture and sensitivity testing, a process that needs a longer time, expensive laboratory infrastructure, extensive bio-safety precautions, and specialized laboratory personnel which are not feasible in resource-limited settings [4]. To overcome this problem, the WHO endorsed Xpert MTB/RIF assay in 2010, a rapid and automated molecular system to detect the DNA of MTB and rifampicin resistance concurrently [5]. Rifampicin resistance (RR) is a surrogate marker for MDR-TB in more than 90 % of the cases [6]. Initially, this method was indicated for patients with TB/HIV co-infection, presumptive MDR-TB, and pediatric TB patients [7]. Three years after its implementation, however, it was recommended for all patients suspected of TB infection [8]. In Ethiopia, Xpert MTB/RIF assay has been implemented in all general and referral hospitals since 2014 [9].

Ethiopia was among the high TB burden countries ranking 10th from the high-TB-pandemic and 15th from the 27 high-MDR-TB countries [10]. According to the 2023 WHO report, Ethiopia is still among the list of high TB burden countries but was transitioned out of the list of the 30 high MDR/RR-TB burden countries [1].

A systematic review and meta-analysis of the epidemiology of MDR-TB in Ethiopia showed that 2.18 % of newly diagnosed and 21.07 % of previously treated cases had MDR-TB [11]. The review was on articles published using culture and drug sensitivity test methods to detect TB and MDR-TB.

Since implementing the Xpert assay, there has been limited data on MTB and RR-MTB in Ethiopia. Few studies exist from Addis Ababa [12], Amhara Regional state [5], and southern Ethiopia [13] on the prevalence of RR-MTB and have reported a prevalence of 15.11 %–19.4 % using Xpert MTB/RIF assay. The studies in Amhara Regional State and South Ethiopia collected data from a single hospital each; they used one-year data. Similarly, the report conducted in Addis Ababa collected 12,414 samples from four health facilities, but it may not represent the national picture of the prevalence. Thus, more data from regions with a representative sample from many health facilities will give a reasonable power to help policymakers and implementers plan and design intervention strategies to prevent and control TB-associated morbidities and mortalities.

There are studies on MDR-TB from Tigray Regional State [14,15]. In the region, there are two studies on MDR-TB [15,16]. These studies, however, were on MDR-TB suspected patients [failure, who have contact with MDR-TB patients and relapsed] which cannot show the magnitude of TB and MDR-TB among the presumptive TB patients in the region. Besides, the results were from culture and drug susceptibility testing methods on a small sample size. Recent work by Wasihun et al. has reported a prevalence of 7.9 % and 9 %

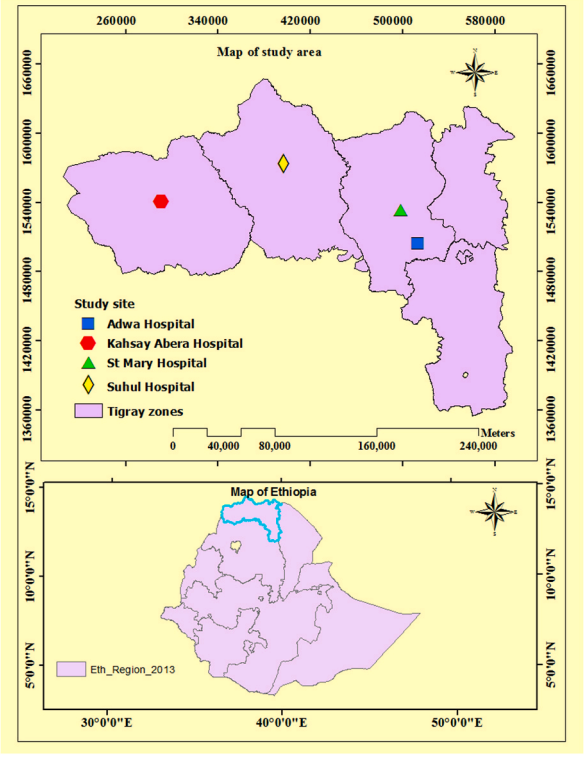

Fig. 1. Map of the study area.

for MTB and RR-MTB, respectively in five general hospitals and one comprehensive specialized teaching hospital from three zones (Southern, Mekelle City, and Eastern zones) of Tigray [17]. However, the report covers only three zones and cannot represent the whole regional state.

Therefore, this study aimed to determine the prevalence and associated factors of MTB and RR-MTB among presumptive adult TB patients in Central, North West, and Western Tigray using Xpert MTB/RIF assay. The data generated in this study will complement the report by Wasihun et al. [17] in Tigray.

2. Materials and methods

2.1. Study design and study population

2.1.1. Study setting

Tigray Regional State, one of the nine National Regional states of Ethiopia, is the northernmost of the Federal Democratic Republic of Ethiopia. According to the population and housing census of 2007, the region has a population size of 6,960,003 within an area of 54,572.6 km^2. The capital city of the state of Tigray, Mekelle, is located 783 km north of Addis Ababa, the capital of Ethiopia. The region is administratively divided into seven Zones and 52 districts (rural = 34; urban = 18). One teaching and specialized hospital, 15 general hospitals, 20 primary hospitals, 204 health centers, 712 health posts [village clinic], and 500 private health facilities provide health services in Tigray. A multi-center health facility-based retrospective cross-sectional study design was used to collect data from October 2019 to December 2019 from four public hospitals. The hospitals were: Adwa, St. Mary, Sihul, and Kahsay Abera hospitals located in the three zones of Tigray region (Central, Northwest, and Western zones) (Fig. 1).

There were three primary hospitals in addition to the list of general hospitals in the three study zones but were not included in the study because their data record on Xpert assay was limited. Hence, we purposively selected the four general hospitals that started Gene Xpert for the diagnosis of TB in 2016 to assess the trend of MTB and RR-MTB. All health facilities use Directly Observed Treatment, Short-Course (DOTS) TB treatment protocol. The region has three MDR-TB treatment initiation centers and 52 treatment follow-up centers [16].

The source population was all patients (N = 17,329) with clinical signs and symptoms suggestive of TB and visited the hospitals between January 2016 and December 2019, and gave sputum samples for Xpert MTB/RIF assay. Our study participants were all adult patients (≥18 years) (N = 16, 437) having data on age, gender, Xpert MTB/RIF results, HIV status (positive, negative or unknown), and TB treatment history. Whereas, those patients with any missing information in age, gender, Xpert MTB/RIF results, invalid, indeterminate Xpert MTB/RIF results, HIV status, and TB treatment history were excluded from the study (Fig. 2).

2.2. Variables

Outcome Variable: Prevalence of MTB and RR-MTB among presumptive adult TB patients.
Independent variables: Age, gender, HIV status and TB treatment history.

2.3. Operational definitions [18]

Failure case: a TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Relapse case: a TB patient who has become (and remained) culture-negative while receiving therapy but after completion of therapy become culture positive again.
Lost to follow up: a TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
New cases: Patients have never been treated for TB before.
MDR-TB: Isolate of M. tuberculosis showed resistance to at least two of the most important first-line anti-TB drugs, rifampicin and isoniazid.
Rifampicin-resistant TB (RR-MTB): resistance to rifampicin detected using genotypic or phenotypic methods with or without

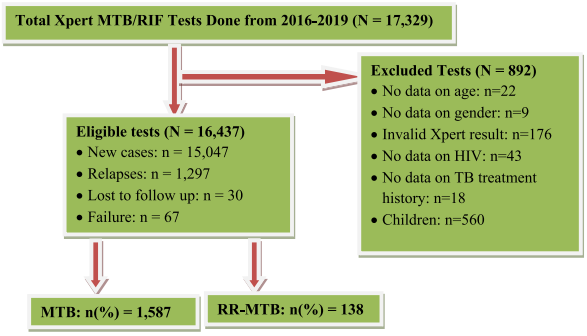

Fig. 2. Flow charts for inclusion and exclusion criteria.

resistance to other first-line anti-TB drugs.

2.4. Data collection

Patients' socio-demographic characteristics (such as age and gender) and clinical-related data (such as Xpert MTB/RIF results, HIV status, and MTB treatment history) were collected using a structured data extraction sheet from Xpert MTB/RIF registration books in each health facility.

2.5. Laboratory processing

During data extraction, Standard Operating Procedures (SOP) were checked for consistency and proper collection and testing of sputum specimens from patients in each health service facility included in this study. This was important to make sure that the results in the registry books were obtained following similar procedures in all study health facilities. All health facilities used the working protocols presented hereafter.

A single sputum sample per patient was used for the diagnosis of MTB using Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, USA). Samples were collected before the start of anti-TB treatment and processed using Gene Xpert MTB/RIF assay using the standard protocol. Briefly, after sputum was collected, it was mixed with a sample reagent buffer in 1:2 (sample: sample reagent buffer) volume ratio. Then, closing it tightly, vortexed for 15 s and allowed to stand at room temperature for 10 min. It was again vortexed after 10 min and allowed to stand for 5 min. Using the Pasteur pipette provided with the kit >2 mL of the (just above 2 ml mark on pipette) processed sample was put into the Xpert MTB/RIF cartridge. Then the cartridge with the specimen was loaded to the Gene Xpert machine. Eventually, results were collected from the Gene Xpert computer after 2h [18].

2.6. HIV testing

Testing for HIV was done according to the national algorithm recommended by the Federal Ministry of Health of Ethiopia. The test uses HIV (1 + 2) Antibody Colloidal Gold (KHB, Shanghai Kehua Bio-engineering Co Ltd, China) as a screening test, followed by HIV 1/2 STAT-PAK® (Chembio Diagnostics, USA) if KHB positive. Where the result of STAT-PAK® is discordant with KHB, a third test, Unigold™ HIV (Trinity Biotech, Ireland), is used as a tiebreaker to determine the result.

2.7. Source of kits and reagents

The kits and reagents for the Gene Xpert MTB/RIF assay and HIV test were provided by the Federal Ministry of Health of Ethiopia free of cost to all hospitals.

Table 1
Socio-demographic, clinical characteristics and MTB result of MTB presumptive adult patients in Central, Northwest and Western Tigray, Ethiopia, 2016–2019 (N = 16437).

Variables	Frequency	%
Gender		
Male	9894	60.2
Female	6543	39.8
Age		
18–29	3499	21.3
30–39	3727	22.7
40–49	2971	18.1
50–59	2493	15.2
60–69	2242	13.6
70–98	1505	9.2
HIV Status		
Positive	1701	10.3
Negative	2986	18.2
Unknown	11750	71.5
TB Treatment History		
New cases	15047	91.5
Relapse	1297	7.9
Lost to follow up	30	0.2
Failure	63	0.4
MTB Result		
Positive	1587	9.7
Negative	14850	90.3
RR-MTB Result (N = 1587)		
RR-MTB Positive	138	8.7
RR-MTB Negative	1449	91.3

2.8. Quality control and data analysis

Gene Xpert MTB/RIF assay was done using the standard operating method. After data completeness was checked, it was entered and analyzed using SPSS Version 21. Frequency, mean, range, and standard deviation were computed. Besides, Chi-square and logistic regression analysis were computed to identify the associated factors with MTB and RR-MTB. Variables that showed significant association ($p < 0.05$) with the outcome variables in the binary logistic regression were further analyzed using multiple logistic regressions to identify if they have a real association with MTB and RR-MTB at a p-value less or equal to 0.05.

3. Results

3.1. Socio-demographic, clinical characteristics and TB results of the participants

Of the total 17,329 presumptive adult TB patients who submitted sputum samples for TB diagnosis, 16,437 (94.9 %) had complete data and were, therefore, included in the study. Males (i.e., 9894 or 60.2 %) dominate females, and the age of the patients ranged from 18 to 98 years, with a mean age of 44.2 (±16.4 SD). Of the total participants of the study, the majority (15,047, i.e., 91.5 %) were new cases, and 11,750 (71.5 %) of them were with unknown HIV status. The overall prevalence of MTB was 9.7 % among suspected patients, out of which the prevalence of RR-MTB was 8.7 % **[Table 1]**.

4. Factors associated with MTB infection

Adjusting for age, HIV status, and previous TB treatment history, the odds of having TB showed a decreasing trend by age. Patients whose age was greater than 29 years were less likely to have TB compared to 18–29 years ($p < 0.001$). Likewise, new cases were 54 % times [AOR = 0.46; 95%CI = 0.39, 0.53, $p < 0.001$] less likely to have TB compared to the previously treated cases [Table 2].

4.1. Factors associated with RR-MTB infections

Of the total 1,587, TB confirmed patients, 138 (8.7 %) tested positive for RR-MTB. As shown in Table 3, adjusted for gender, age, and TB treatment history, males were 32 % [AOR = 0.68; 95 % CI = 0.47, 0.96, $p = 0.032$] less likely to be infected by RR-MTB compared to females. Similarly, TB presumptive patients who had no history of previous treatment were 71 % less likely to be infected by RR-MTB [AOR; 0.29, 95 % CI = 0.202, 0.44, $p < 0.001$] compared to previously treated cases. Whereas, the age group of 18–29 years was 3.08 times [AOR = 3.08; 95 % CI = 1.07, 8.72, $p = 0.036$] more likely to acquire RR-MTB compared to the age group of 70–98 years **[Table 3]**.

Fig. 3 compares the percentage prevalence of MTB and RR-MTB by study years. Accordingly, our study revealed that MTB prevalence significantly decreased from 16.9 % in 2016 to 8.1%in 2019 ($p < 0.001$, data not shown). Likewise, the trend of RR-MTB has shown a decline from 14.3 % in 2016 to 5.8 % in 2019 ($p < 0.001$) [Fig. 3]. The number of MTB increased from 314 in 2019 to 531 in 2019, while RR-MTB decreased from 45 in 2016 to 31 in 2019 (Fig. 4). This increasing number of MTBs was owing to the increasing number of TB-suspected patients from 2016 to 2019.

Table 2
Prevalence of MTB among adult TB patients by gender, age, treatment history, and HIV status in Central, Northwest and Western Tigray, 2016–2019 (N = 16437).

Variables	MTB Pos. N (%)	MTB Neg. N (%)	COR (95 % CI)	P value	AOR(95%CI)	P -value
Gender						
Male	983(9.9)	8911(90.1)	Ref			
Female	604(9.2)	5939(90.8)	0.92(0.83–1.03)			
Age						
18–29	468(13.4)	3031(86.6)	Ref		Ref	
30–39	401(10.8)	3326(89.2)	0.78 (0.68–0.90)	<0.001*	0.78 (0.67–0.88)	<0.001[a]
40–49	275(9.3)	2696(90.7)	0.66 (0.56–0.77)	<0.001*	0.62 (0.53–0.73)	<0.001[a]
50–59	181(7.3)	2312(92.7)	0.51 (0.42–0.61)	<0.001*	0.49 (0.41–0.59)	<0.001[a]
60–69	163(7.3)	2079(92.7)	0.51 (0.42–0.61)	<0.001*	0.49 (0.41–0.59)	<0.001[a]
70–98	99(6.6)	1406(93.4)	0.46 (0.36–0.57)	<0.001*	0.44 (0.35–0.56)	<0.001[a]
HIV status (n = 4687)						
Positive	181(10.6)	1520(89.4)	1.08(0.89–1.31)	0.42		
Negative	341(11.4)	2645(88.6)	Ref			
TB treatment history						
New cases	1332(8.9)	13715(91.1)	0.46 (0.40–0.54)	<0.001[a]	O.46 (0.39–0.53)	<0.001[a]
Previously treated cases	255 (18.3)	1135(81.7)	Ref		Ref	

[a] Statistically significant ($p < 0.05$).

Table 3
Prevalence of RR- MTB among adult TB patients by gender, age, treatment history, and HIV status in Central, Northwest and Western Tigray, 2016–2019 (N = 1589).

Variables	RR-MTB N (%)	Not RR-MTB N (%)	COR (95 % CI)	P value	AOR (95%CI)	P- value
Gender						
Male	74 (7.5)	911(92.5)	0.69 (0.48–0.97)	**0.035**	**0.68(0.47–0.96)**	**0.032**
Female	64 (10.6)	540(89.4)	Ref		Ref	
Age						
18–29	57 (12.2)	412(87.8)	3.22(1.14–9.09)	0.027	3.08 (1.07–8.72)	0.036[a]
30–39	36 [9]	366(91)	(2.290.80–6.59)	0.13	2.20(0.76–6.42)	0.15
40–49	14(5.1)	261(94.9)	1.25(0.4–3.89)	0.70	1.09 (0.35–3.47)	0.88
50–59	13(7.1)	170(92.9)	1.8(0.56–5.61)	0.33	1.47(0.46–6.77)	0.51
60–69	14(8.6)	149(91.4)	2.2(0.70–6.84)	0.18	2.16 (0.68–0.97)	0.19
70–98	9(9.3)	93(90.7)	Ref		Ref	
HIV Status (n = 524)						
Positive	18(9.9)	163(89.1)	1.11(0.60–2.05)	0.74		
Negative	31(9)	312(91)	Ref			
TB Treatment History						
New cases	91(6.8)	1242(93.2)	0.33(0.22–0.48)	<0.001	0.29 (0.202–0.44)	<0.001[a]
Previously treated cases	46(18.4)	209(81.6)	Ref		Ref	

[a] Statistically significant ($p < 0.05$).

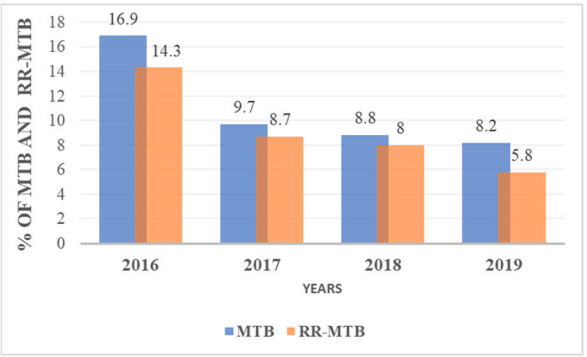

Fig. 3. Percentage of MTB and RR-MTB by study years (2016–2019).

5. Discussion

The availability of local epidemiological data on MTB and RR-MTB prevalence and the identification of potentially modifiable predisposing factors are essential to designing appropriate intervention strategies. The overall prevalence of MTB among suspected patients is 9.7 %, out of which RR-MTB prevalence was 8.7 %. The MTB and RR-MTB prevalence is comparable with a similar study carried out in the same period in Tigray region but in different zones (and hospitals) [17]. Therefore, this study will complement the previous study to give a complete picture of the problem in the Tigray regional state.

The MTB prevalence (9.7 %) in the present study was comparable with previous reports from Tigray, 7.9 % [17], Addis Ababa, 6.5 % [19], the Amhara region, 8 % [20], South Africa, 13 % [21] and Korea, 13.8 % [22]. The prevalence in this study is lower than those

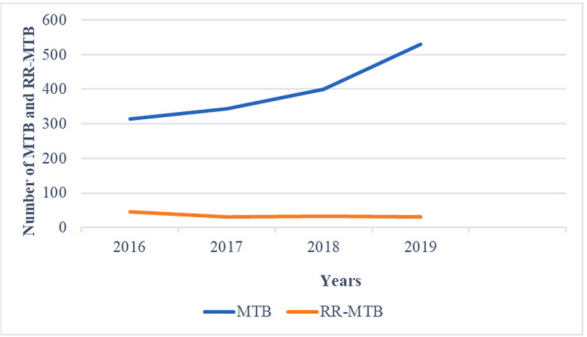

Fig. 4. Trends in the number of MTB and RR-MTB by study years (2016–2019).

conducted in South Ethiopia,16.5 % [13], Addis Ababa,15.11 % [12], Eastern Ethiopia,19.4 % [4], the Oromia region,60.4 % [23], 23.2 % [4], Uganda, 20.9 % [24], Bangui,79.1 % [25], Togo, 57 % [26], Nigeria, 22.9 % [27], 19.1 % [28], Pakistan, 59 % [29], India, 60 % [30], 63.6 % [31], 20.3 % [28], 81.1 % [32], and China, 51.4 % [33]. However, the prevalence in this study is higher than previous ones from Addis Ababa, 6 % [19].

Possible reasons for the variations in MTB prevalence could be due to differences in methodological techniques, study participants, study period, geographical and TB control, and prevention policies. The high TB prevalence reported in other studies [19,26,28,29,31,32] could also be attributed to their study participants who were MDR presumptive patients (relapse, defaulter, lost to follow-up and failure). By contrast, TB-suspected patients were enrolled in this study. Another possible reason could be the small sample size that they used. In other words, small sampling could generate a higher prevalence rate.

The high prevalence of MTB in other reports [4,27,27,31,34] compared to the result of this study could be attributed to the difference in the study period (2011–2014) during which GeneXpert was indicated only for patients with TB/HIV coinfection and presumptive MDR-TB patients. In this study, data were collected from 2016 to 2019, when GeneXpert was adopted for all presumptive TB patients. The ages of the study participants ranged from 18 to 98 years. Of these, patients aged 18–29 years were less infected by TB compared to the other age groups ($p = 0.037$). Though there is no clear-cut for the age group, other studies reported that age groups of 16–30 years [13] are to be less likely to be infected by TB. On the other hand, no association was reported between age and TB infection elsewhere [2,12,23,28]. A study by Mulu et al. [5] from Amhara region has reported that males were more infected by TB than females, which contradicts this study where there was no association between gender and TB infection. The high MTB prevalence among previously TB-treated cases in this study could indicate the presence of high TB transmission in the community. This again calls for coordinated action to combat the problem in the study region.

As can be seen from Table 4, the prevalence of RR-MTB (8.7 %) among the MTB confirmed cases was similar with previous reports from Tigray [17], Addis Ababa [12,19], Amhara region [5], Nigeria [28,34], India [29,31,32] and Seoul [22]. However, this prevalence was lower than those found in previous studies in Oromia region [23], Tigray [15], Bangui [25], Togo [26], Nigeria [27], Russia [35], India [32], Bangladesh [36], Pakistan [29] and China [33]. Others have reported lower RR-MTB prevalence in south Ethiopia [13], Oromia region [2], and Zambia [37] [Table 4].

There are many possible reasons for the variation in RR-MTB reports. For example, geographical differences, methodology (sample size, method of diagnosis, study participants), study setting, study period, and TB control practice could be among the reasons. The high RR-MTB prevalence reported by Refs. [5,24,26] could be because their study participants were previously TB positive (i.e., relapse, defaulter, lost to follow-up, or failure) and had a history of MDR contacts which put them at a higher risk to develop MDR-MTB whereas this study included presumptive TB patients.

The high RR-MTB in studies conducted in the Somali region [14], Pakistan [29], Bangladesh [36], India [28], and Togo [26] compared to our results might be due to the temporal difference. Their studies were from 2011 to 2014 when Gene Xpert assay was used for patients with presumptive MDR-TB patients. By contrast, in this study, data were collected from records of patients who visited the hospitals from 2016 to 2019, and the method was used for all TB-suspected patients.

Age groups of 18–29 years were more likely to acquire RR-MTB. Others reported 0–20 years and 61–80 years [34]. The high prevalence of RR-MTB among confirmed TB cases in the productive age group (18–29 years) aligns with the WHO reports, where TB primarily affects people in economically productive age groups [38]. This could be related to their wide range mobility which increases

Table 4
Comparison of RR-MTB prevalence with other studies.

Study area	Authors	RR-MTB prevalence (%)
Tigray	Wasihun et al. [17]	9.0
Addis Ababa, Ethiopia	Balew et al. [12]	9.9
	Sinshaw et al. [19]	11
Amhara region, Ethiopia	Mulu et al. [5]	10.3
South Ethiopia, Ethiopia	Hordofa & Adela [13]	3.4
Oromia region, Ethiopia	Mulisa et al. [23]	33
	Abebe et al. [2]	2.2
Tigray region, Ethiopia	Tesfay et al. [15]	54.6
Nigeria	Denue et al. [28]	6.1
	Ukwamedua [36]	7.3
	Ikuabe1 & Ebuuenyi [27]	14.7
India	Ramandeep et al. [32]	I9.9
	Reddy & Alvarez-uria [30]	9.2
	Ingole et al. [31]	9.43
Seoul	Kim et al. [22]	8.9
Uganda	Mboowa et al. [24]	3.8
Bangui,	Farra et al. [25]	42.2
Togo	Dagnra et al. [26]	24
Russia,	Toungoussova et al. [35]	25.2
Bangladesh	Rahman et al. [36]	35
Pakistan	Ullah et al. [29]	29
China,	Hai et al. [33]	15.3
Tigray, Ethiopia	This study	8.7

their exposure to TB [39].

Regarding the association between RR-MTB and gender, females were significantly infected by RR-MTB compared to males ($p = 0.032$). These results are consistent with other reports ([12,35]). Other studies reported more RR-MTB infections among males than females [15,28,34]. The higher prevalence of RR-MTB in females reported in this study could be due to the poor knowledge of females about TB transmission and control, poor health-seeking behavior, and hence delay in detection in females [3,12,40]. These may help the bacteria to disseminate to the household members (such as children) as mothers are more responsible for giving care to the children and have more close contacts.

The other independent predictor for RR-MTB was found to be previous TB treatment, which was supported by many similar studies [12,23,27,28]. The high prevalence of rifampicin resistance-MTB among previously treated patients highlights for more concerted effort of the regional government and stakeholders to improve the monitoring of TB treatment and thereby reduce the emergence of circulating drug-resistant TB strains in the community.

The prevalence of TB and RR-MTB were compared by the study years. Accordingly, it was revealed that TB prevalence among TB presumptive patients significantly decreased from 16.9 % in 2016 to 8.1 % in 2019. Similarly, the RR-MTB among the TB-confirmed cases indicated a significant decrease in trend (from 14.3 % in 2016 to 5.8 % in 2019). The overall declining trend of MTB and RR-MTB in the region might indicate that the implementation of the policies on TB diagnosis and treatment by the regional government and stakeholders is in the right direction. The significant increase in tests done per year could also be a factor in decreasing the prevalence.

Despite this decreasing trend of TB among TB presumptive patients, the prevalence still calls for more efforts to be exerted to reduce the morbidities and mortalities associated with MTB. The strong association of rifampicin resistance-MTB with patients having a history of previous treatment (relapse, failure, and lost to follow-up) implies the need for evaluating and monitoring the existing directly observed treatment, short-course TB treatment services of the health of the health facilities. This, in turn, helps to intervene and minimize the magnitude of further emergence of drug-resistant MTB strains in the community.

The strength of this study was that it is a multi-center health facility-based study in the region with a large sample size that can complement and give the latest data on the prevalence of TB and RR-MTB for the regional and national governments. However, the study was not devoid of limitations. First, as we examined a single region in Ethiopia, the economic and regional disparities limited the generalizability of the results to a national level. Second, we were not able to do microbiological confirmation of tuberculosis, phenotypic rifampicin resistance, and resistance to other anti-TB drugs because of the retrospective nature of the study. Third, retrospective data provided little information on the contact history of MDR-TB and TB, education, and living conditions of patients. Fourth, given the data were only from four hospitals, results may not be generalizable to the region. Fifth, the higher number of patients with unknown HIV status did not allow us to see the association of MTB and RR-MTB with HIV.

6. Conclusion

Overall, the prevalence of TB and RR-MTB during the study period showed a decline over the years. However, RR-MTB is still prevalent in the productive age groups and females, which needs coordinated efforts to address the problem in these groups. Besides, as patients having a history of previous treatment were infected with rifampicin resistant-MTB, evaluation, and monitoring of the directly observed treatment, short TB treatment services in the region need more attention.

Ethical consideration

Ethical clearance was obtained from Aksum University; College of Health Sciences, Institutional Review Board (IRB's approval number is 152/2019). Besides, a letter of cooperation was written from the Tigray Regional Health Bureau (THRB) to each study hospital, and permission was obtained accordingly. As the study was a retrospective type, we did not get informed consent and assent from the study participants.

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Additional information

No additional information is available for this paper.

Data availability statement

All relevant data are within the manuscript.

CRediT authorship contribution statement

Tsehaye Asmelash Dejene: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Conceptualization. **Genet Gebrehiwet Hailu:** Writing – review & editing, Writing – original draft, Conceptualization. **Atsebaha Gebrekidan Kahsay:** Writing – review & editing, Writing – original draft, Conceptualization. **Araya Gebreyesus Wasihun:** Writing –

review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper:Tsehaye Asmelash Dejene.

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