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Detection of *Mycobacterium tuberculosis* and rifampicin resistance by Xpert® MTB/RIF assay among presumptive tuberculosis patients in Addis Ababa, Ethiopia from 2014 to 2021

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ABSTRACT

Objective: This study aimed to determine the frequencies and trends of *Mycobacterium tuberculosis* and rifampicin resistance among presumptive tuberculosis patients in Ethiopia, who were tested using the Xpert MTB/RIF assay between 2014 and 2021.

Methods: Data were collected retrospectively from patient registries. Laboratory-based data were extracted from the national tuberculosis (TB) referral laboratory database. All patients referred to the National Tuberculosis Reference Laboratory (NTRL) for TB diagnosis from all over the country between March 1, 2014 and September 30, 2021, and tested using the Xpert MTB/RIF assay, were included. The extracted data were entered into a Microsoft Excel sheet and analyzed by Statistical Package for Social Sciences (SPSS) version 23.

Results: Among a total of 13 772 individuals tested using the Xpert MTB/RIF assay, the majority (8223; 59.7%) were males, and 48.5% (6678) of the individuals were aged between 15 and 39 years. *Mycobacterium tuberculosis* (MTB) was detected in 17.0% (2347) of the examined individuals. Of the detected MTB cases, nearly 9.9% (233) were rifampicin resistant (RR-TB), while 24 (1.0%) were RR-intermediate. Among all RR-TB cases, more than half (125; 53.6%) were detected in males, and 105 were new TB cases. Extrapulmonary (EPTB) patients had a greater rate of rifampicin resistance (11.0%) than pulmonary (PTB) patients (9.6%).

Conclusion: The frequency of TB and RR-TB remains high in the study setting. RR-TB was found to have a statistically significant association with previous anti-TB medication treatment. As a result, improving treatment adherence in recognized instances could assist in preventing MTB and RR-TB cases.

Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* complex organisms, also known as tubercle bacilli. The bacillus spreads slowly and widely in the lungs producing hard nodules (tubercles) or cheese-like masses that produce cavities (WHO, 2020). It is a contagious illness that primarily affects the lungs, but can infect any organ in the body (Adhikari et al., 2021). TB has existed for millennia

Abbreviations: EPHI, Ethiopian Public Health Institute; EPTB, extrapulmonary tuberculosis; MDR, multidrug resistance; MTB, *Mycobacterium tuberculosis*; MTBC, *Mycobacterium tuberculosis* complex; NTRL, National Tuberculosis Reference Laboratory; PTB, pulmonary tuberculosis; RIF, rifampicin; RR-TB, rifampicin-resistant tuberculosis; SPSS, Statistical Package for Social Sciences; TB, tuberculosis; WHO, World Health Organization.

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and remains a major global health problem. It causes ill-health for approximately 10 million people each year, and is one of the top ten causes of death worldwide (WHO, 2020).

The prevalence of multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) was estimated to be 3.3% in new cases and 18% in previously treated cases globally in 2020. Overall, an estimated 465 000 incident cases of MDR/RR-TB were reported and the global proportion of RR-TB cases estimated to have MDR-TB was 78% (WHO, 2020). The establishment and spread of MDR-TB has become a major TB control issue, which cannot be addressed with currently available anti-TB medications. Multidrug-resistant tuberculosis treatment involves time-consuming and costly chemotherapy, using second-line medicines that are both toxic and ineffective (El Hamdouni et al., 2019). Drug resistance is mostly a man-made problem that arises through the misuse and mismanagement of medications, either alone or in combination (Demissie et al., 2021).

For timely management of the disease, rapid detection and identification of *Mycobacterium tuberculosis* (MTB) in infected individuals is critical. Rapid molecular tests like Xpert have been approved by WHO and are used as the initial diagnostic test for the detection of TB and rifampicin resistance in adults and children (WHO, 2016). The test simultaneously detects *Mycobacterium tuberculosis* complex (MTBC) and resistance to rifampicin (RIF) in less than 2 hours. Xpert MTB/RIF can detect mutations in the *rpoB* gene and present the results (Boehme, 2010). In the diagnosis of PTB and EPTB, the Xpert MTB/RIF assay is rapid, as well as being highly sensitive and specific (Tessema et al., 2012; Blakemore et al., 2010; Rahman et al., 2018). Rifampicin resistance can be diagnosed quickly, allowing TB patients to begin treatment sooner rather than waiting for results from other classic methods of drug susceptibility testing.

Rapid diagnosis, continuous surveillance, and regular monitoring of drug-resistant TB are critical for disease management and earlier treatment initiation in countries with a high TB prevalence. However, only a few studies have aimed to determine the prevalence of tuberculosis and rifampicin-resistance in presumptive TB cases in Ethiopia (Demissie et al., 2021; Gebretsadik et al., 2020; Derbie et al., 2016; Araya et al., 2020; Mulu et al., 2017; Arega, et al., 2019; Worku et al., 2019). Therefore, our study aimed to determine the frequency of *Mycobacterium tuberculosis* and rifampicin-resistant TB among presumptive TB individuals.

Methods and materials

Study design and study pried

A laboratory-based retrospective cross-sectional study was carried out using presumptive TB patient records that were referred for Xpert MTB/RIF assay testing to the National Tuberculosis Reference Laboratory (NTRL) of the Ethiopian Public Health Institute (EPHI) between March 1, 2014 and September 30, 2021. The NTRL is an accredited national reference laboratory in Addis Ababa, Ethiopia, and provides a range of services: surveillance; technology evaluation; operational research; support for TB laboratory networking; training; mentoring and supervision; external quality assurance; and diagnostic services, such as GeneXpert MTB/RIF testing. The NTRL has one GeneXpert machine that can analyze 16 samples at a time. The laboratory receives samples from variety of healthcare facilities for GeneXpert testing, culture, and drug susceptibility testing; approximately 6000–8500 presumptive TB patients are tested annually. During the study period, 102 public and 175 private health facilities referred samples to the NTRL.

Study population

All presumptive PTB and EPTB patients who were referred to NTRL at the EPHI and tested with the Xpert MTB/RIF assay between March 2014 and September 2021 became the study population.

Data collection

The data were collected using a standardized extraction sheet. Epidemiological, clinical, and laboratory data were collected from the archived database and registration books. The patient's demographics, including age, sex, HIV status, TB treatment history, and MTB and RR results were collected. Microsoft Excel 2016 was used to keep track of all demographic and laboratory test findings.

Laboratory methods

The Cepheid Xpert MTB/RIF system was used to test the specimens. For identification purposes, each sample was given a unique laboratory number. The sputum samples were mixed with the sample reagent in a 2:1 dilution (sample reagent:sputum) using a 50 ml falcon tube. EPTB samples with a volume of < 10 mL were used unconcentrated, whereas samples with a volume > 10 mL were concentrated by centrifugation (3800 × g for 15 min) and decanted to remove the supernatant before resuspension of the sediment in saline. A transfer pipette was used to add a double volume of the sample reagent to a minimum of 0.7 ml of concentrated sample. Next, the falcon tubes were tightly screw-capped and forcefully shaken before being incubated for 10 minutes. After the first incubation, each tube was shaken once more before being incubated at room temperature for 5 minutes. Using of a disposable transfer pipette, 2 mL of liquefied material was transferred to the sample chamber of the Xpert MTB/RIF cartridge. The cartridge was then inserted into one of the Xpert MTB/RIF system's modules, which ran the test automatically. Results were automatically generated within 2 hours and reported as MTB not detected or MTB detected (with semiquantification), and as RIF resistance not detected or RIF resistance detected.

Data analysis

All participants' information and laboratory data were entered onto a Microsoft Excel 2016 spreadsheet, which was then exported and analyzed using the Statistical Package for Social Sciences (SPSS) version 23 (IBM Corp, Armonk, NY). Descriptive analysis was used to describe the demographic and clinical profiles of the study participants. A chi-squared test was performed to describe the presence of association. Statistical significance was determined at a p-value < 0.05, with a 95% confidence interval.

Results

Demographic and clinical characteristics

In total, 13 772 specimens were collected during the study period, including 9762 (70.9%) presumptive PTB cases and 4010 (29.1%) presumptive EPTB cases. The age of the study participants ranged from 2 months to 98 years old, with 48.5% being between the ages of 15 and 39 years. More than half of the study participants were male (8223; 59.7%). Of all the 13 772 study participants, the majority (71.1%) did not have a TB history. The HIV status of the study participants was not recorded for 81.1% of the study participants, while 12.5% were HIV seronegative and 6.5% were HIV seropositive (Table 1).

Frequency of Mycobacterium tuberculosis

Mycobacterium tuberculosis was detected in 17.0% (2343/13 772) of the study participants. The frequency of PTB among presumptive PTB patients was 18.5% (1805/9762), while the frequency of EPTB among presumptive EPTB patients was 13.4% (538/4010). Among the identified EPTB cases, lymph node TB (lymphadenitis) was the most common form, accounting for 57.2% (115/201), followed by abscess TB at 37.9% (61/161). MTB was detected in 18.1% (1486/8223) of male patients and

Table 1
Study participants' demographic and clinical characteristics.

Variables	Category	Frequency	Percentage
Sex	Male	8223	59.7
	Female	5549	40.3
Age in years	< 15	1054	7.6
	15–39	6678	48.5
	40–59	3659	26.6
	> 60	2381	17.3
TB classification	New	9767	71.0
	Relapse	2104	15.3
	Failure	740	5.8
	Defaulter	101	0.7
	Unknown	1060	7.7
HIV status	Positive	889	6.5
	Negative	1716	12.5
	Not recorded	11167	81.1
Type of presumptive TB	PTB	9762	70.9
	EPTB	4010	29.1
Year of GeneXpert test	2014	377	2.7
	2015	1934	14.0
	2016	2703	19.6
	2017	4167	30.3
	2018	2528	18.4
	2019	1497	10.9
	2020	323	2.3
	2021	243	1.8
Total		13772	100

EPTB – extrapulmonary tuberculosis, PTB – pulmonary tuberculosis

15.4% (857/5549) of females. Among HIV-positive patients, TB was detected in 15.0% (133/889), while among HIV-negative patients the frequency was 16.1% (277/1716). TB was detected in 16.1% (1576/9767) of new cases, 20.8% (438/2104) of relapse cases, and 22.6% (167/740) of treatment failure cases (Table 2).

Frequency of rifampicin resistance among Mycobacterium tuberculosis

Among 2343 MTB detected cases, RR-TB was found in 233 individuals (9.9%), while 1.0% (24/2343) of the cases were indeterminate. The proportions of RR-TB among new TB cases and previously treated TB cases were 6.7% (105/1576) and 18% (112/633), respectively. Female patients had a slightly higher rate of RR at 12.6% (108/857) compared with male patients at 8.4% (125/1486). The frequency of RR-TB among children under 15 years confirmed to have TB was 10.9% (8/73). The frequencies of RR-TB among new treatment, relapse, treatment after failure of the initial treatment, and defaulter cases with TB were 6.7% (105/1576), 16.9% (74/438), 19.2% (32/167), and 21.4% (6/28), respectively. The difference in rifampicin resistance between PTB and EPTB cases was not statistically significant ($p = 0.31$) (Table 3).

Trends for Mycobacterium tuberculosis and RR-TB by years

One aim of this study was to assess the frequency of TB and RR-TB based on the year when the specimens are examined. The frequency of MTB was 20.4% (77/377) in 2014, 17.4% (336/1934) in 2015, 15.1% (409/2703) in 2016, 16.4% (684/4167) in 2017, 17.9% (454/2528) in 2018, 20.3% (304/1497) in 2019, 13.3% (43/323) in 2020, and 16.1% (39/243) in 2021. The frequency of RR among these confirmed MTB cases was 35.1% (27/77) in 2014, 14.3% (48/336) in 2015, 11.3% (46/409) in 2016, 8.5% (58/684) in 2017, 4.9% (22/454) in 2018, 6.9% (21/304) in 2019, 16.3% (7/43) in 2020, and 7.6% (3/39) in 2021. Thus, MTB frequency decreased from 20.4% in 2014 to 16.1% in 2021, but increased slightly to 17.9% in 2018 and 20.3% in 2019. The frequency of RR-MTB showed a significant decline from 35.1% in 2014 to 6.9% in 2019 but increased to 16.3 in 2020 before falling back to 7.6% in 2021 (Figure 1).

Discussion

A retrospective study was carried out using the records of presumptive TB patients to determine the frequencies of MTB and RR-TB using the Xpert MTB/RIF diagnostic tool. The overall frequency of MTB (17.0%) among presumptive TB patients was comparable to reports from San Diego County in the USA (17.8%) (Rice et al., 2017), the Republic of Democratic Congo (16.3%) (Lupande et al., 2017), and northwest Ethiopia (14.6%) (Derbie et al., 2016). In contrast, studies conducted in northern parts of Ethiopia (23.2%) (Mulu et al., 2017), northwest Iran (40.5%) (Atashi et al., 2017), Taiwan (33.6%) (Chiang et al., 2018), Dubai in UAE (30.9%) (Habous et al., 2019), Pakistan (28.8%) (Rasool et al., 2019), China (36.6%) (Tang et al., 2017), and Bangui (79.1%) (Farra et al., 2019) showed higher frequencies of MTB than our finding. On the other hand, some studies carried out in north Ethiopia reported lower MTB frequencies — (8.9%) (Gebretsadik et al., 2020), (11.0%) (Wasihun et al., 2021), and (5.7%) (Ayalew et al., 2020), as did studies from southern Ethiopia (11.9%) (Worku et al., 2019), Nepal (13.8%) (Sah et al., 2020), and South Africa (11.4%) (Velen et al., 2021). These differences could be related to variations in the clinical characteristics of study participants, community TB control practices, and localized variations in TB epidemiology and frequencies.

In our study, the 15–39 years age group had the highest frequency of MTB, accounting for (24.4%) of the total. This observation was in agreement with previously reported studies from different countries — (18.7%) (Araya, 2020), (15.6%) (Wasihun et al., 2021), and (14.16 %) (Sah et al., 2020). This could be related to the fact that those in this age group are more likely to be exposed to the external environment, and have a wider range of travelling.

In this study, the rate of MTB detection was highest among patients with EPTB suspected of having TB lymphadenitis (57.2%), followed by abscess tuberculosis (37.9%). This finding was consistent with a previous study conducted in Ethiopia that showed tuberculosis lymphadenitis to be the predominant type of EPTB infection (78.4%), followed by abscess TB (10.7%) (Fanosie et al., 2016). According to recent research from Iran, TB lymphadenitis (36.4%) is the most common form of EPTB, followed by abscess TB (24.7%) (Baghbanbashi et al., 2021). In northeast Ethiopia, investigations revealed that TB lymphadenitis (33.3%) was the most frequent form of EPTB, followed by pleural forms (11.9%) (Metaferia et al., 2018). In contrast, other studies have found genitourinary TB (27.2%) to be the most common type of EPTB, followed by meningeal TB (19.4%) (Gunal et al., 2011). These variations could be attributable to the dynamics of EPTB epidemiology, which are unique to each geographical area, and the genetic variation among the population.

In our study, rifampicin resistance was detected in 9.9% of confirmed TB cases. This was comparable to the results of other studies conducted in Ethiopia — 9.3%, 10.3%, and 11.9% (Derbie et al., 2016; Mulu et al., 2017; Worku et al., 2019), and in Nepal (10.2%) (Sah et al., 2020). However, our figure was lower than that found in a study in the Democratic Republic of Congo (20.8%) (Lupande et al., 2017). On the other hand, it was higher than in studies conducted in northwest Ethiopia (4.3% and 0.5%) (Demissie et al., 2021; Liyew et al., 2020), northeast Ethiopia (5.3%) (Gebretsadik et al., 2020), Nepal (3.36%) (Adhikari et al., 2021), northwest Iran (4.3%) (Atashi et al., 2017), and Nigeria (7.3%) (Ukwamedua et al., 2019). The reasons for these differences may be due to differences in the clinical characteristics of study participants, study periods, and TB control practices.

In our study, the frequencies of RR-TB among previously treated and new TB patients were 18.0%, and 6.7%, respectively. Similar findings were reported in studies in Ethiopia with previously treated TB patients (17.1%) and in treatment-naive patients (6.7%) (Mulu et al., 2017). In contrast, another study in Ethiopia indicated a higher frequency (27.4%) of RR-TB in previously treated TB patients than our finding, while drug resistance among new TB cases (7.6%) was similar to our result (Arega et al., 2019). A high rate of RR-TB in previously treated patients might be due to the development of drug-resistant strains, pos-

Table 2
Prevalence of positive *Mycobacterium tuberculosis* results among the study participants.

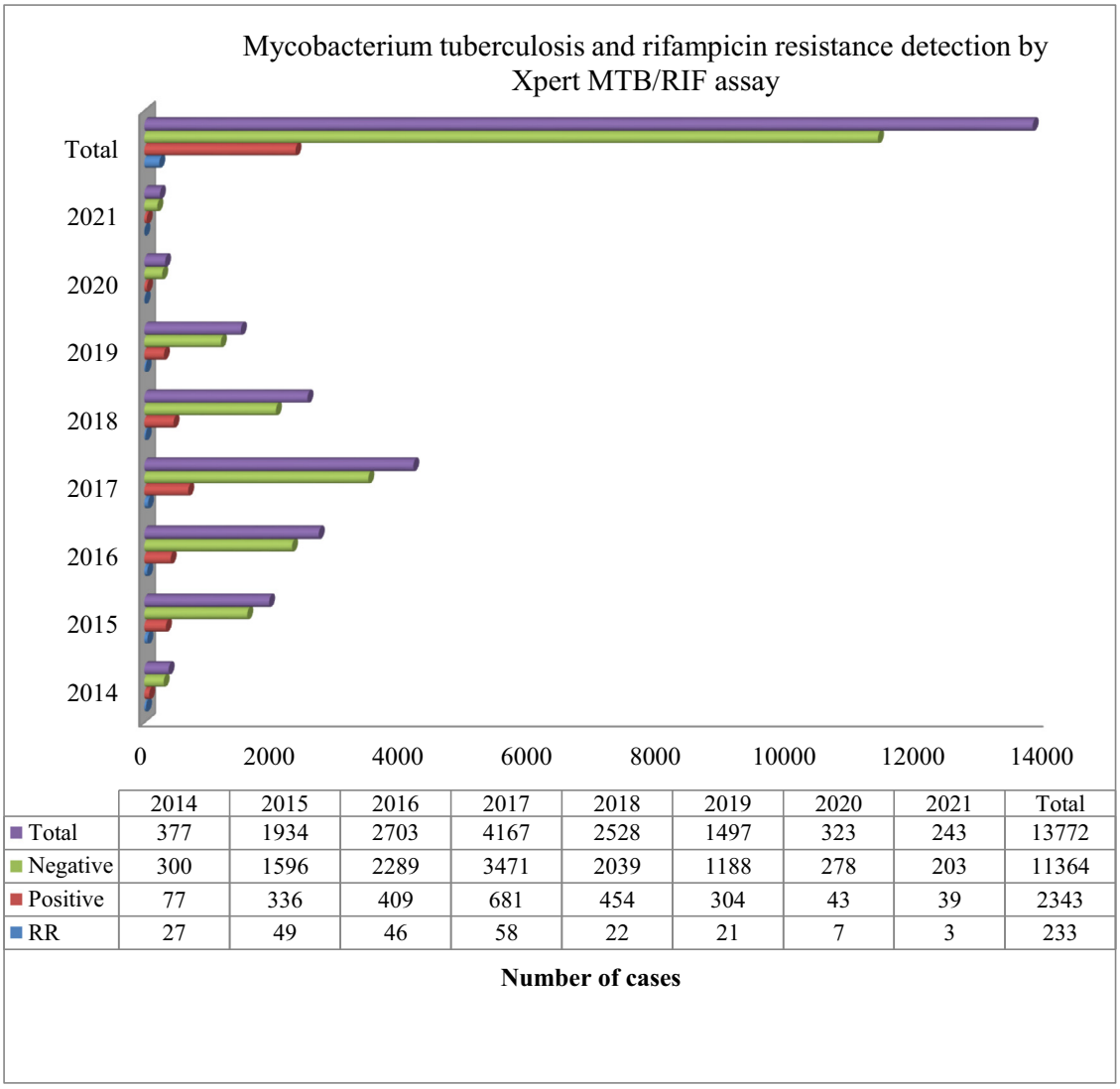
Variables	Category	GeneXpert for *Mycobacterium tuberculosis*			χ^2	*p*-value	Total
		Positive *N* (%)	Negative *N* (%)	Unsuccessful result (error or invalid)*N* (%)			
Sex	Male	1486 (18.1)	6686 (81.3)	51 (0.6)	23.524	< 0.001	8223 (59.7)
	Female	857 (15.4)	4675 (84.5)	17 (0.3)			5549 (40.3)
Age in years	< 15	73 0 (6.9)	971 (92.1)	10 (0.9)	443.232	< 0.001	1054 (7.6)
	15–39	1629 (24.4)	5015 (75.1)	34 (0.5)			6678 (48.5)
	40–59	487 (13.3)	3157 (86.3)	15 (0.4)			3659 (26.6)
	> 60	154 (6.5)	2218 (93.2)	9 (0.4)			2381 (17.3)
TB category	New	1576 (16.1)	8148 (83.4)	41 (0.4)	69.316	< 0.001	9767 (71.0)
	Relapse	438 (20.8)	1652 (78.5)	12 (0.6)			2104 (15.3)
	Failure	167 (22.6)	570 (77.0)	3 (0..4)			740 (5.8)
	Defaulter	28 (27.7)	73 (72.3)	–			101 (0.7)
	Unknown	134 (12.6)	918 (86.6)	8 (0.8)			1060 (7.8)
HIV status	Positive	133 (15.0)	753 (84.5)	3 (0.3)	5.246	0.263	889 (6.5)
	Negative	277 (16.1)	1433 (83.5)	6 (0.4)			1716 (12.)
	Not reported	1933 (17.3)	9175 (82.2)	57 (0.5)			11167 (81.1)
Sample site	PTB	1805 (18.5)	7900 (80.9)	57 (0.6)	58.510	< 0.001	9762 (70.9)
	EPTB	538 (13.4)	3461 (86.3)	11 (0.27)			4010 (29.1)
Specimen type	Sputum	1805 (18.5)	7900 (80.9)	57 (0.6)	497.867	< 0.001	9762 (70.9)
	Pleural fluid	178 (9.1)	1766 (90.6)	5 (0.3)			1949 (14.1)
	Lymph node aspirate	115 (57.2)	85 (42.3)	1 (0.5)			201 (1.5)
	CSF	25 (6.6)	351 (93.4)	–			376 (2.7)
	BAL	56 (13.1)	367 (86.2)	3 (0.7)			426 (3.1)
	Ascitic fluid	15 (5.3)	265 (94.3)	1 (0.4)			281 (2.0)
	Pus	49 (30.5)	111 (68.9)	1 (0.6)			161 (1.2)
	Urine	8 (6.4)	116 (93.6)	–			124 (0.9)
	Abscess	61 (37.9)	100 (62.1)	–			161 (1.2)
	Peritoneal fluid	23 (8.3)	252 (91.7)	–			275 (2.0)
	Other	8 (14.3)	48 (85.7)				56 (0.4)
Total		2343 (17.0)	11361 (82.5)	68 (0.5)			13772 (100)

EPTB – extrapulmonary tuberculosis, PTB – pulmonary tuberculosis, *N* – number, CSF –cerebrospinal fluid, BAL – broncho-alveolar lavage, χ^2 – chi-squared

Table 3
Rifampicin resistance profiles detected among 2343 confirmed *Mycobacterium tuberculosis* patients.

Variables	Category	Rifampicin resistance status			χ^2	*p*-value	Total
		Resistant *N* (%)	Not resistant *N* (%)	Indeterminate *N* (%)			
Sex	Male	125 (8.4)	1346 (90.6)	15 (1.0)	10.698	0.005	1486 (63.4)
	Female	108 (12.6)	740 (86.4)	9 (1.1)			857 (36.6)
Age in years	< 15	8 (10.9)	65 (89.1)	–	8.246	0.221	73 (3.1)
	15–39	175 (10.7)	1438 (88.3)	16 (0.1)			1629 (69.5)
	40–59	38 (7.8)	441 (90.6)	8 (1.6)			487 (20.8)
	> 60	12 (7.8)	142 (92.2)	–			154 (6.6)
TB category	New	105 (6.7)	1458 (92.5)	13 (0.8)	81.582	< 0.001	1576 (67.3)
	Relapse	74 (16.9)	359 (81.9)	5 (1.2)			438 (18.7)
	Failure	32 (19.2)	135 (80.8)	–			167 (7.1)
	Defaulter	6 (21.4)	22 (78.6)	2 (7.1)			28 (1.2)
	Unknown	16 (11.9)	114 (85.1)	4 (3.0)			134 (5.8)
HIV status	Positive	15 (11.3)	118 (88.7)	–	2.101	0.717	133 (5.7)
	Negative	27 (9.7)	246 (88.8)	4 (1.5)			277 (11.8)
	Unknown	191 (9.9)	1722 (89.1)	20 (1.0)			1933 (82.5)
Sample site	PTB	174 (9.6)	1615 (89.5)	16 (0.9)	2.336	0.306	1805 (77.0)
	EPTB	59 (11.0)	471 (87.5)	8 (1.5)			538 (23.0)
Specimen type	Sputum	174 (9.6)	1615 (89.5)	16 (0.9)	31.170	0.093	1805 (77.0)
	Pleural fluid	19 (10.7)	158 (32.6)	2 (1.1)			178 (6.7)
	Lymph node aspirate	20 (17.4)	94 (81.7)	1 (0.9)			115 (4.9)
	CSF	–	25 (100)	–			25 (1.1)
	BAL	2 (3.6)	53 (94.6)	1 (1.8)			56 (2.4)
	Ascitic fluid	1 (6.7)	14 (93.3)	–			15 (0.7)
	Pus	5 (10.2)	43 (87.6)	1 (2.0)			49 (2.1)
	Urine	1 (12.5)	7 (87.5)	–			8 (0.3)
	Abscess	9 (14.7)	50 (81.9)	2 (3.3)			61 (2.6)
	Peritoneal fluid	–	22 (95.7)	1 (4.3)			23 (1.0)
	Other	3 (37.5)	5 (63.5)	–			8 (0.3)
Total		233 (9.9)	2086 (89.1)	24 (1.0)			2343 (100)

EPTB – extrapulmonary tuberculosis, PTB – pulmonary tuberculosis, *N* – number, CSF –cerebrospinal fluid, BAL – broncho-alveolar lavage, χ^2 – chi-squared.



	2014	2015	2016	2017	2018	2019	2020	2021	Total
Total	377	1934	2703	4167	2528	1497	323	243	13772
Negative	300	1596	2289	3471	2039	1188	278	203	11364
Positive	77	336	409	681	454	304	43	39	2343
RR	27	49	46	58	22	21	7	3	233

RR- rifampicin resistance

Figure 1. Graph of Xpert MTB/RIF assay tests, 2014–2021.

sibly exacerbated by poor treatment adherence during the first-line anti-TB treatment.

In our study, the proportion of RR-TB cases among EPTB cases (11.0%) was higher compared with that for PTB cases (9.6%). This was in agreement with a study in Ethiopia that reported an RR-TB frequencies of 9.8% among PTB cases and 11.3% among EPTB cases (Mulu et al., 2017). Increases in RR-EPTB infection may be due to the fact that most EPTB patients are immunocompromised.

The frequency of RR-TB among children under 15 years was 11.3% in our study. This finding was higher than those of previous studies carried out in Ethiopia (7.9%) and China (0.52%) (Arega et al., 2019; Liyew et al., 2020). On the other hand, our result was lower than figures reported in South Africa (22%) (Dodd et al., 2014) and China (30%) (Jiao et al., 2015). An explanation for these differences could be related to differences in tuberculosis frequency in the general population, sputum sample collecting methods, the study environment, sociocultural practices, and diagnosis.

In our study, the frequency of RR-TB was higher in females compared with males. This finding was comparable with that of previous studies in Addis Ababa and Bangui, where rifampicin resistance was higher in females than in males (Araya et al., 2020; Farra et al., 2019). In contrast, other studies have found the proportion of RR-TB to be higher among male patients, for example in northwest Ethiopia (Demissie et al., 2021; Mulu et al., 2017; Wasihun et al., 2020) and southern Nigeria (Ukwamedua et al., 2019). This disparity in RR-TB incidence between genders could be attributed to differences in social roles, risk behaviors, and activities.

Our research also assessed the frequencies of MTB and RR-MTB by year across the study period. The frequency of MTB was shown to have decreased from 20.4% in 2014 to 16.1% in 2021, following a slight rise to 20.3% in 2021. RR-MTB frequency also decreased significantly — from 35.1% in 2014 to 6.9% in 2019, increasing again to 16.3% in 2020 before falling to 7.6% in 2021. Other investigations in central Ethiopia (Araya et al., 2020), northwest Ethiopia (Demissie et al., 2021), and northern Ethiopia (Wasihun et al., 2020) all showed generally decreasing MTB/RR patterns, in agreement with our findings.

The decreasing MTB/RR patterns from 2014 to 2019 due to previous GeneXpert diagnoses in the country were for selective patients, such as HIV-positive patients, children, and suspected RR cases, and not for all presumptive TB cases. The increasing MTB and RR-TB prevalences in 2020 and 2021 in our study might have been due to the unprecedented COVID-19 pandemic, which could have had a variety of conse-

quences for TB prevention and control systems. Staying at home to avoid the spread of COVID-19 may have made TB transmission easier within households. In addition, the interruptions to healthcare services caused by the COVID-19 workload and resource transfer could have affected TB treatment and diagnosis. Furthermore, the pandemic's considerable economic damage will have a long-term influence on TB prevention and control systems, particularly in resource-scarce, high-TB-burden developing countries such as Ethiopia.

There were a few limitations to this research. First, retrospective data were used for this research, with inherent drawbacks such as incomplete clinical data. Second, no alternative diagnostic approach was used as a comparison in this study, such as culture or phenotypic DST —for eligible cases, the Xpert MTB/RIF test was the only technique used to diagnose TB and RIF resistance. Despite these limitations, this study provides relevant information on the use of the Xpert MTB/RIF assay for detecting MTB and RR-TB cases in the studied area.

Conclusions

Our study showed that there was a significant frequency of tuberculosis and RR-TB in Ethiopia, with RR-MTB prevalence high in both PTB and EPTB patients. Previous anti-TB treatment had resulted in a high RR-TB prevalence. Therefore, efforts to prevent DR/RR-TB should focus on effective drug resistance surveillance, preventing the emergence of new cases of DR/RR-TB, and treating existing patients. Strengthening TB infection control activities should be the focus of future interventions.

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Ethical approval and consent to participate

Permission for this study was obtained from the National Tuberculosis Reference Laboratory of the Ethiopian Public Health Institute. Participants were not approached for consent forms because the study was based on a retrospective record review. Throughout the process, no patient names or identifiers were used.

Author contributions

GD: study concept, data analysis, and writing of the manuscript. GD, AA, KE, AK, and HHT: study design, manuscript drafting. AM, AK, AA, BY, BZ, BD, MG, GS, HMJ, MT, MA, SM, WS, DFG, YA, AW, MH, BB, MG, and ZT: data analysis, interpretation, and quality control. The final paper was read, evaluated, and approved by all authors.

Availability of data and material

The data sets used or analyzed during this study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable, because details such as videos or images relating to study subjects were not recorded for this study.

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Competing interests

There are no competing interests stated by the authors.

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