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Article

A High Burden of Infectious Tuberculosis Cases Among Older Children and Young Adolescents of Female Gender in Ethiopia

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Abstract: The study was conducted in all regions of Ethiopia, except Tigray. It describes types of Tuberculosis (TB) based on gender, age, region, HIV, and geographic setting in Ethiopia. It is a cross-sectional study that utilized the Ministry of Health's District Health Information System-based reporting to analyze all types of TB from July 2022 to March 2024. 290,450 TB cases were detected: 42.6% (123,871) were female, 9.4% (27,160) were children (under 15 years of age), and 14.5% (42,228) were adolescents (10–19 years of age). About 48% (20,185) of adolescent TB cases were bacteriologically confirmed, of which 47.5% were females. Compared to children <5 years, male to female ratio is 26% higher among older children (5–9 years of age) (AOR: 1.26, 95% CI: 0.51-2.01) and by 53% among adolescents (AOR: 1.53, 95% CI 0.87-2.18). In short, about half of TB cases are infectious among older children and young adolescents of females' gender in Ethiopia. TB among these age categories may be addressed through integration of TB services with reproductive health services and youth-friendly and pediatric clinics.

Keywords: tuberculosis; adolescent; children and adolescents; TB and gender; ethiopia

1. Introduction

The United Nations High-Level Meeting (UNHLM) declaration on tuberculosis (TB) includes global targets to accelerate action to prevent and treat TB among children and adolescents [1]. However, adolescent TB was a neglected area until a road map of for fighting TB among children (<15 years) and adolescents (10–19 years) globally was release in 20181 and a similar roadmap focusing on Ethiopia specifically was released in 2019 [2]. Yet, adolescents have their own peculiar characteristics that expose them for TB, including homelessness, incarceration, and substance use [3]. Also, the Ethiopian Health Management Information System (HMIS) started capturing routine data disaggregated for children and adolescents in 2021.

As they are transitioning between child and adult health services, adolescents face specific age-related challenges in accessing appropriate care in high burden settings for TB, which could be due to the absence of dedicated adolescent health services that include TB [4,5]. Evidence has also shown that adolescents have a high prevalence of TB [6] and experience a high lost-to-follow-up rate [7]. Adolescents are also a recognized key population in the global human immunodeficiency virus (HIV) epidemic, and having HIV can make them susceptible to developing TB disease [8].

In general, the proportion of males with notified TB cases is higher than females in Ethiopia, which could be due to economic and access factors inherent in the male dominated society, where men have more power than women and some level of privileged access to health care9 and accordingly to diagnostic services. Yet, a simple male-to-female TB disease disaggregation without considering different age categories could be misleading. Disaggregation of gender-based TB in the different age categories accordingly could be important for TB prevention and control, as risks factors could vary depending on both age and gender [10,11]. Specifically, TB among adolescents remains

neglected in that the characteristics of TB among that age group have not been well described or understood and interventions have not been designed to address their specific needs. For instance, routine national data failed to capture the 10–19-years age category based on type of TB [6,7].

Few interventions target TB among adolescents in Ethiopia, and those that do, such as school screening campaigns, tend to be erratic. Yet, school children and teenagers (10–19 years) usually interact with one another and therefore are easily exposed to infection [12–14]. Also, little has been described about the implications of sex and gender for the surveillance and response to TB program in Ethiopia. Therefore, this study is to describe types of TB based on gender, age (including adolescent), and geographic setting in Ethiopia to inform future policy and service delivery improvements to better serve these communities.

2. Materials and Methods

2.1. Settings

Ethiopia is the second most populous country in Africa, and adolescents make up 24% of its general population [15]. The country also has relatively high TB rates, with the respective incidence and mortality estimates of 126 and 17 per 100,000 population in 2022. In Ethiopia 4% of TB cases are also HIV infection⁹ while HIV prevalence in the general population is 0.9% and is higher among women (1.2%) than men (0.6%) [16].

2.2. Interventions

Led by Management Sciences for Health, the USAID Eliminate TB Project has advocated TB prevention and reduction among adolescents since 2021. The project collaborated with the National TB Program to include age disaggregation of adolescents in the TB reporting program. The national TB guidelines and training manual, as well as monitoring and evaluation training materials, were revised to include childhood and adolescent TB. The Eliminate TB Project has also supported the national TB program in building the capacity of health care personnel working in pediatrics and TB clinics on childhood and adolescent TB. Accordingly, the adolescent age category (10-19 years) became part of the TB program reporting system in July 2021.

2.3. Data Source

Ministry of Health District Health Information System 2 (DHIS2)-based reporting was used to collate TB data from July 2022 to March 2024 based on type of TB, age, gender, HIV status, geographic setting, and region.

2.4. Data Quality

Lot quality assurance sampling (LQAS) and quarterly data quality assurance systems were used in health facilities and districts in the country to ensure data quality. Each reporting unit checked the completeness and consistency of data before sending it to the next level.

2.5. Data Analysis

The male-to-female ratio was described among age categories of 5 years interval (up until ≥ 65 years), HIV positive status, types of TB (extra-pulmonary TB [EPTB], clinically diagnosed pulmonary TB [clinical PTB], and bacteriologically confirmed pulmonary TB (BCPTB)), and geographic categories (among agrarian, pastoralist, and city administration of the country) using error bar graphs. In addition, bivariate and multivariable logistics analyses were undertaken for the male-to-female ratio of TB based on age categories (< 5 years, 5–9 years, 10–19 years (adolescent), and ≥ 20 years), types of TB, regions in Ethiopia, and geographic categories using STATA version 17. A two-sample proportion test was applied to compare the BCTB among adolescents and adults.

2.6. Ethical Considerations

The Ethics Review Committee of each Regional Health Bureau (RHB) reviewed and approved the study protocol using the routine DHIS2. As the DHIS2 data are aggregate data, they do not capture any personal identifying information.

3. Results

Sociodemographic and Clinical Characteristics

In July 2022–March 2024, 290,450 TB cases were detected in Ethiopia—42.6% (123,871) among females and 9.4% (27,160) among children under 15 years of age. The range for the proportion of TB among females was 20.7%; 52.5% in the 10–14-years age category and 31.8% in the ≥65-years category. Young female adolescent in the 10–14-years age group have the highest proportion of TB among females at 52.5%.

Of TB patients with HIV infections, 52.5% were among females, 55.3% were among female older children and young adolescent, and 52.9% were among adults above 15 years of age.

Overall, adolescents account for 14.5% (42,228) of all TB cases, and the proportion of BCPTB among them was 47.8% (20,185). Of BCPTB adolescents, 47.3% were among females, even though females account for only 44% of all TB patients. Pastoralist regions (Benishangul Gumuz, Afar, and Gambella) have higher proportions of TB cases among males (>60%) (Table 1).

Table 1. TB cases in Ethiopia by age, region, and HIV status, July 2022–March 2024.

Variables	Total new TB cases	Male	% Male	Female	% Female
New TB cases	282,979	162,197	57.3	123,970	42.7
Relapse TB cases	7,471	4,354	58.3	3,117	41.7
All TB cases (new and relapse TB cases)	290,450	166,479	57.3	127,087	42.7
TB cases with HIV positive and on ART by age category	13,515	6,418	47.5	7,097	52.5
0–4 years	303	205	67.7	98	32.3
5–14 years	588	263	44.7	325	55.3
≥ 15 years	12,624	5,950	47.1	6,674	52.9
TB cases by age group					
0–4 years	7,776	4,411	56.7	3,365	43.3
5–9 years	7,781	3,981	51.2	3,800	48.8
10–14 years	11,603	5,508	47.5	6,095	52.5
15–19 years	30,625	16,808	54.9	13,817	45.1
20–24 years	50,152	28,624	57.1	21,528	42.9
25–34 years	73,498	42,380	57.7	31,118	42.3
35–44 years	45,376	25,886		19,490	43
45–54 years	27,687	16,271	58.8	11,416	41.2
55–64 years	16,489	10,148	61.5	6,341	38.5
≥ 65 years	11,992	8,180	68.2	3,812	31.8
BCPTB	108,671	62,333	57.4	46,339	42.6
Clinical PTB	108,671	32,660	57.5	24,176	42.5
EPTB	63,172	33,068	52.3	30,104	47.7
Relapse	7,471	4,354	58.3	3,117	41.7
TB cases by region					
Sidama	17,041	10,030	58.9	7,011	41.1
Gambella	2,447	1,564	63.9	883	36.1

DD	3,078	1,824	59.3	1,254	40.7
Amhara	36,768	20,653	56.2	16,115	43.8
SWEP	6,544	3,647	55.7	2,897	44.3
HH	1,560	887	56.9	673	43.1
AA	15,374	8,049	52.4	7,325	47.6
Afar	5,215	3,172	60.8	2,043	39.2
Somali	14,654	8,172	55.8	6,482	44.2
CER	10,395	5,723	55.1	4,672	44.9
SER	16,230	9,143	56.3	7,087	43.7
Benishangul Gumuz	1,805	1,130	62.6	675	37.4
Oromia	97,514	54,042	55.4	43,472	44.6

For all forms of TB, the male-to-female ratio (M:F) is greater than one for the age groups older than 55 years. Exceptionally, the M:F is less than one for the 10–14-years age group. Among the BCPTB cases, M:F was less than one in children 10-14 years of age (or young adolescents) but greater than one and steadily increasing in the age categories older than that. For EPTB, M:F ran around one (tending towards females), except in the 0–4-years, 20–34-years, and ≥65-years age categories. Among clinical PTB patients, M:F is more than one categorically in adults and about one in children (Figure 1).

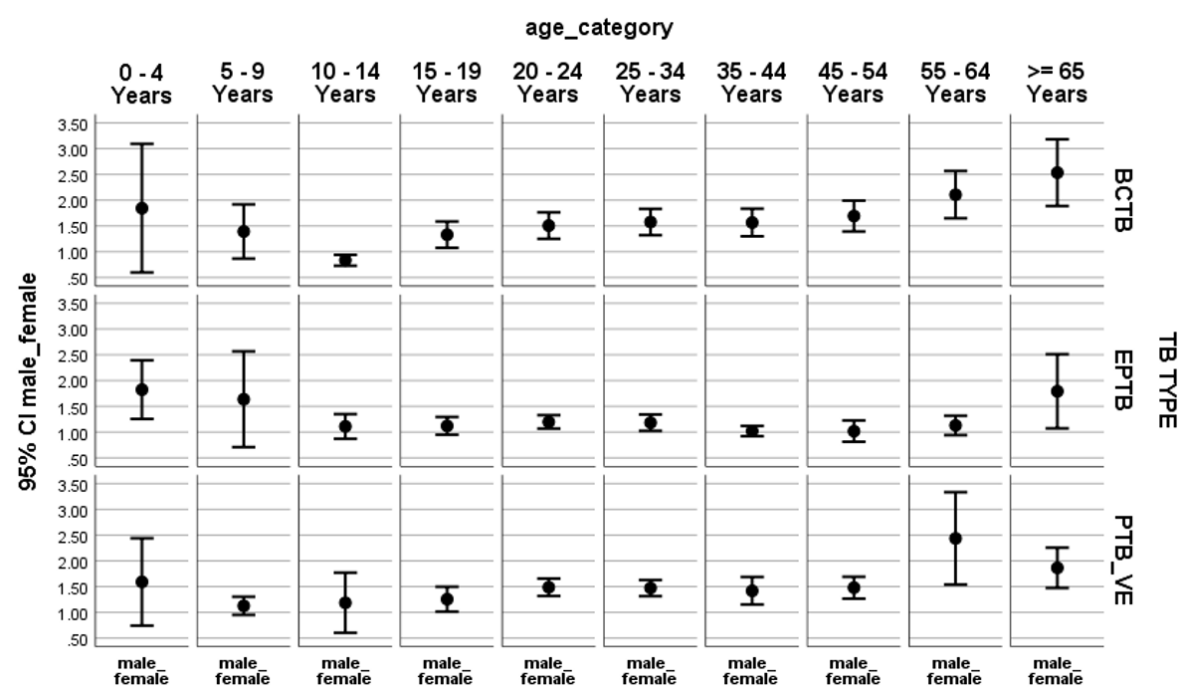


Figure 1. Male-to-female ratio by age and types of TB in Ethiopia, July 2022–March 2024.

In the agrarian regions (regions where 75% of the population makes its living through farming, i.e., Oromia, Amhara, SNNP and Tigray), M:F is greater than one until 5 years of age, drops below one after 5 years of age, drops more drastically after 15 years of age, and then steadily increasing after that until it once again is greater than One over 55 years of age. A similar M:F pattern is noted in the overall national data as well as those from the pastoral regions and cities administrations (Figure 2).

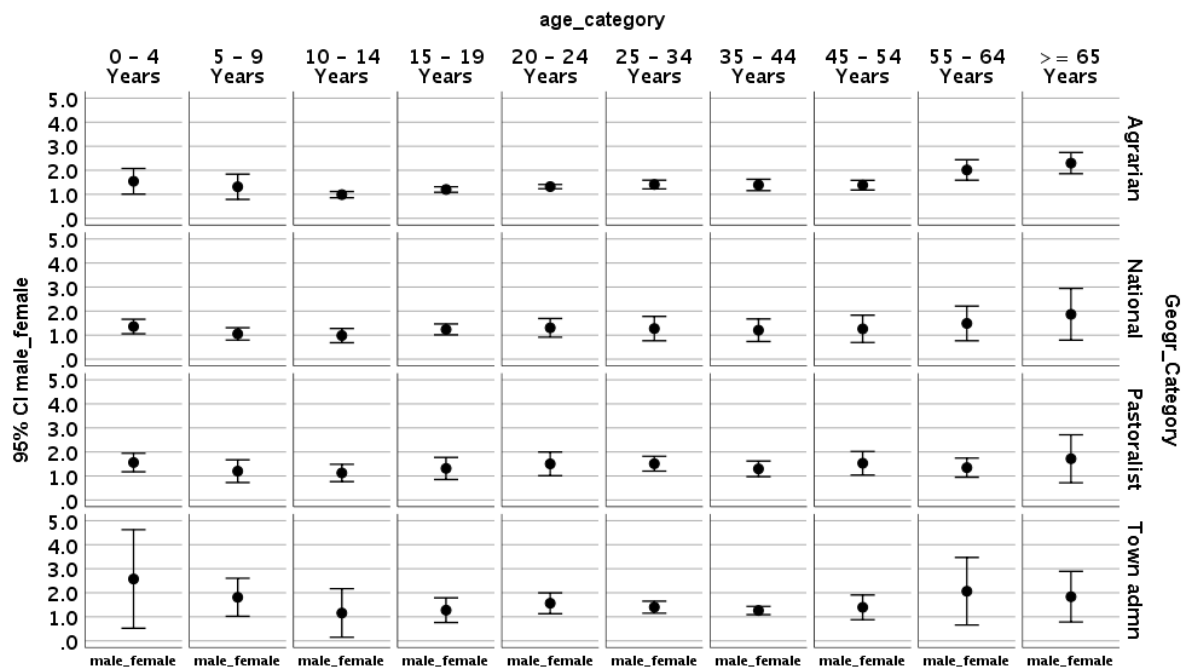


Figure 2. Male-to-female ratio in error chart by age and geographic category in Ethiopia.

Both bivariate and multivariable analyses indicated that M:F is associated with age and types of TB. Compared to children <5 years of age, M:F is 26% greater among children aged 5–9 years (AOR 1.26, 95% CI 0.51-2.01) and 53% greater among 10–19 years (AOR 1.53, 95% CI 0.87-2.18). EPTB cases are higher among males in children <10 years of age, while BCTB cases are higher among female in children 10–14 years of age. Also, EPTB is equally or more prevalent among females 34–54 years of age (p-value<0.001) (Table 2 and Figure 3) than among males in the same age category.

Table 2. COR and AOR of male-to-female ratio in Ethiopia, July 2022–March 2024.

Variables	COR (M:F)	95% CI		p-value	AOR (M:F)	95% CI		p-value
Age Category								
<5 years	1				1			
5–9 years	-1.151	-1.899	-0.403	<u>0.003</u>	-1.258	-2.007	-0.509	<u>0.001</u>
10–19 years	-1.432	-2.087	-0.778	<u>0.000</u>	-1.527	-2.182	-0.872	<u>0.000</u>
Adult >20 years	0.085	-0.481	0.651	0.769	0.013	-0.553	0.579	0.964
Type of TB								
Clinical PTB	1				1			
BCTB	0.201	-0.206	0.608	0.333	0.160	-0.246	0.567	0.439
EPTB	-0.869	-1.283	-0.454	<u>0.000</u>	-0.928	-1.342	-0.513	<u>0.000</u>
Region								
City administration	1							
Amhara	-0.263	-0.979	0.453	0.472				
Benishangul Gumuz	0.274	-0.442	0.990	0.453				
Gambella	-0.103	-0.837	0.632	0.784				
National	-0.182	-0.897	0.534	0.619				

SNNP	-0.370	-0.912	0.172	0.181
Oromia	-0.146	-0.862	0.570	0.689
Pastoralist	0.107	-0.414	0.629	0.687
Sidama	0.208	-0.508	0.924	0.568
Geographic Category				
City administration	1			
Agrarian	-0.102	-0.522	0.319	0.635
National	-0.178	-0.893	0.538	0.627
Pastoralist	0.081	-0.485	0.647	0.779

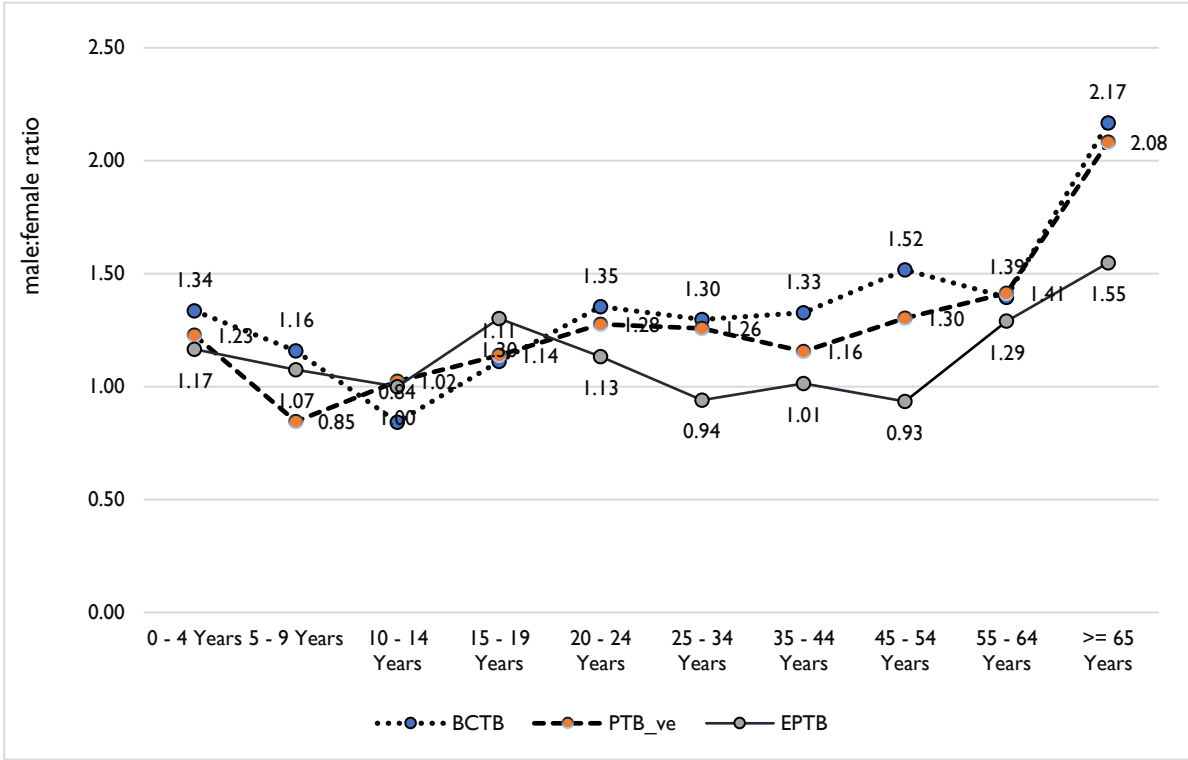


Figure 3. Male-to-female ratio by age category and type of TB, July 2022–March 2024. (BCTB: bacteriologically confirmed TB; PTB_ve: clinical PTB or smear negative PTB; EPTB: Extrapulmonary TB).

The 47.8% proportion of BCPTB cases among adolescents is greater than the 44.7% proportion of BCPTB among all age groups (Z-score = 7.5, p value = 0.0001). Also, the proportion of female BCPTB patients among adolescents (47.3%) is greater than the proportion of female BCPTB patients (44%) among all TB patients (Z-score = 5.0; p value <0.0001). This difference is also statistically significant in the Sidama, Oromia, and South Ethiopia regions (Z-score=4.1-7.8, p-value<0.01).

4. Discussion

Ethiopia is on the World Health Organization’s list of 30 high TB burden countries—third in Africa and eighth in the world—and reports a high proportion of TB cases among males [9]. However, our findings suggest that gender-based TB analysis consider different age categories to allow for a better understanding of age and gender TB epidemiology. Unlike with all forms of TB cases in adults, BCPTB cases are higher among females than males among older children and young adolescents in Ethiopia.

The higher TB burden among adult males, as compared to females in the same age group, could be due to a greater prevalence of TB risk factors among those men, such as silicosis, imprisonment,

alcohol use, deprivation, HIV, cancer, and smoking [11]. A social networking study tried to explain the predominant TB among males, looking at whether distinct mixing patterns by sex and TB disease indicated that TB cases have proportionally more adult male contacts [17]. The higher TB burden among males might also be due to their economic advantage in the Ethiopian culture, which might give them easier access to TB diagnostic services. The gender differences related to health-seeking behavior, stigma, domestic responsibility, access to economy, lack of patient-centered care, and access to health care could also contribute to the TB burden difference between male and females [18].

Moreover, the lower TB burden among females in pastoralist regions (Afar, Gambella, Benishangul, and Somalia) might indicate a weak TB program in these areas, where society is male dominated, and lifestyles tend to be nomadic or mobile [19]. Weak health systems in pastoralist regions could hinder efforts for TB care and control [19,20] as passive TB case finding may miss a relatively high number of TB cases among females who cannot easily visit health facilities for TB diagnosis. This could be due to different socioeconomic and cultural factors that might lead to barriers in accessing health care, leaving behind unnotified TB cases in women [21]. The engagement of girls and women in the health extension program in Ethiopia [22] could be a good opportunity to empower them to address barriers for accessing to TB diagnosis and treatment service.

Like in our study, finding from Zimbabwe explained that EPTB rate was lower among reproductive age males compared to their females' counterparts mainly ascribed to high HIV among females [23]. Studies from Asia also found that while TB of all types was reportedly more prevalent in males, a higher preponderance of EPTB was observed in females [24]. EPTB can lead to pregnancy complications in women, and it warrants surveillance and advocacy for enhancing the development of new diagnostics and new drugs that consider the special needs of women—specifically those living with HIV and those who are pregnant and lactating [25].

The persistent age-related trend in immunologic susceptibility among adolescents and young adults [26] might explain the increasing TB burden among older children, young adolescents, and then adults in our study. That is, puberty is associated with changes in immunity that may contribute to an increased risk of progression to TB disease among these age groups [26–28]. Moreover, our study indicated a shift from the less transmissible TB (EPTB and clinical PTB) among <5 years children to highly transmissible forms of TB (bacteriologically confirmed PTB) among older children and adolescents, which could also be attributable to age-related immunologic susceptibility [3]. Moreover, latent TB infections among children could express themselves as TB disease during adolescence for those affected by malnutrition and HIV [3,29]. Therefore, TB prevention and control activities could consider the age shift for the different types of TB in Ethiopia.

Specifically, older children and adolescents (10–19 years) are highly affected by infectious TB diseases. This could be partly attributable to the fact that adolescents usually spend their time in school and can easily be exposed for TB transmission [13,14]. It could also be due to health challenges associated with pregnancy and childbirth, which may increase the risk of developing TB [20,31]. Hence, older children and adolescents could be a focus area for actively detecting TB cases, which ought to be linked to TB infection control in setting adolescents frequent, such as schools, colleges, and universities.

BCPTB cases not only were higher among adolescents; they also were higher among female adolescents. That is, about half of TB cases among adolescents are infectious cases, as are 47% among females' adolescents in Ethiopia. This might be due to late presentation, higher transmission, and low infection prevention and TB prevention services among these groups. Our study is in line with studies that confirmed adolescent females are more susceptible than males to TB, [32] TB risk for females increases around the time of menarche, and females have a higher risk of disease progression when compared to age-matched male adolescents [10,26,27]. The study has also shown that an increased BCTB risk for females relative to males appears to peak at mid-adolescence (10–14 years), which is similar to the results of a recent pooled analysis from high income countries.¹⁰ These results could be attributable to higher vulnerability to HIV among female adolescents,[3,26,27] but the real reason has yet to be explored in Ethiopia. However, TB screening could be integrated into

reproductive health services in schools to deal with the TB epidemic among younger girls. Also, health extension workers (HEWs) could undertake proactive TB screening among female adolescents in the community at religious gatherings and schools.

The study used aggregate routine DHIS2 data; the lack of patient-level data therefore means risk factors for TB could not be exhaustively analyzed. Data from Tigray was not part of this study as DHIS2 was interrupted in the region due to conflict.

5. Conclusions

The higher proportion of infectious TB cases among school-age older children and young adolescents could necessitate high-quality TB services that are accessible and acceptable to adolescents of both genders to facilitate timely diagnosis and support medication adherence and treatment completion for early control of TB transmission. TB among adolescents may be addressed through its integration into reproductive health and youth friendly clinics and pediatric clinics. In addition, HEWs could consider conducting TB screening of female adolescents at religious and school settings.

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Institutional Review Board Statement: The Ethics Review Committee of each Regional Health Bureau (RHB) reviewed and approved the study protocol using the routine DHIS2.

Informed Consent Statement: As the DHIS2 data are aggregate data, they do not capture any personal identifying information.

Data Availability Statement: All data used here are available in the manuscript.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

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BCPTB Bacteriologically confirmed pulmonary TB

DHIS2 Health District Health Information System 2

EPTB Extra-pulmonary TB

HIV Human immunodeficiency virus

LQAS Lot quality assurance sampling

TB Tuberculosis

UNHLM United Nations High-Level Meeting

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