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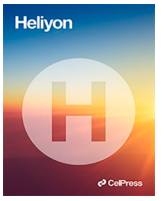

Research article

Mycobacterium tuberculosis and human immunodeficiency virus co-infection and associated variables among presumptive pulmonary tuberculosis patients in Ethiopia; a health institution based cross-sectional study

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ABSTRACT

Background: Co-infection of *Mycobacterium tuberculosis* (MTB) and the Human Immunodeficiency Virus (HIV) is a major global public health issue, particularly in border areas of resource-limited nations, including Ethiopia.
Objective: To explore the prevalence and associated variables of MTB/HIV co-infection among PTB presumptive patients in Northwest Ethiopia.
Methods: From February to August 2021, a cross-sectional institutional investigation was conducted at the Metema and Abrehajira hospitals. Semi-structured questionnaires were used to collect socio-demographic and clinical data. The MTB/RIF Xpert assay was used to process sputum, and 3 ml of veins blood was collected for HIV rapid test (STAT-PAK, ABON, and SD BIOLINE HIV test algorithm) following the Ethiopian National HIV test algorithm. The Gene Xpert assay's sample processing control was checked to ensure data quality. Data entered into Epi-Data were exported to SPSS version 20 for analysis. Statistically significant variables (p-value ≤0.2) from bivariable analysis were included in multivariable analysis. A *p-value* ≤ *0.05* was judged statistically significant.
Results: This study included 314 PTB presumptive patients with a median age of 35.0 years, of which 178 (56.69 %) were males. Among all patients, 40(12.7 %) and 51(16.2 %) were PTB, and HIV seropositivity, respectively. Of the PTB patients, 14/40 (35 %) (95 % CI: 24.4–45.6) were co-infected with HIV/AIDS. Married patients were 70 % less likely than unmarried individuals (AOR = 0.3 CI; 0.07–0.98) to have MTB/HIV co-infection. Patients who had contact history with MDR-TB patients (AOR = 5 CI; 1.37–18.00), and those who had a history of alcohol use (AOR = 12.2 CI; 2.56–57.8) were more likely to have MTB-HIV co-infection than their peers.
Conclusion: Our findings showed that MTB-HIV co-infection is one of the most important community health concerns in the study area. Therefore, MTB/HIV cooperation activities should be fully in place to prevent co-infection and its impact on the population.

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1. Background

Mycobacterium tuberculosis (MTB) and Human Immunodeficiency Virus (HIV) infections are two of the world's most serious issues [1]. This combined burden (MTB and HIV) is regarded as one of the most significant global health issues of the 21st century. Pulmonary tuberculosis is the most common opportunistic disease and cause of death among HIV patients. Similarly, HIV infection is one of the commonest risk factors for the progression of latent TB to active TB. Therefore, MTB and HIV epidemics can fuel one other in a variety of ways [2].

Globally, the pooled prevalence of TB/HIV co-infection was highest in Africa (31 %) and lowest in the USA (15 %) [3]. Another meta-analysis in Sub-Saharan Africa found that the pooled estimate of TB/HIV co-infection was 32 % with 44 % in Southern Africa, 41 % in Central Africa, 31 % in Eastern Africa, and 26 % in Western Africa [4]. A cross-sectional study conducted in South Africa showed that half of the overall MTB/HIV co-infection (50.2 %) were females, and the median age of study participants was 20.0 years [5]. A case-control study was conducted in Khartoum, Sudan where the history of PTB, late clinical stages, non-employment, and no formal education were found to be risk factors associated with PTB/HIV coinfection. However, poor adherence, marital status, age, and gender were not associated with developing PTB among HIV patients [6].

In Ethiopia, the pooled prevalence of TB/HIV from various regions of the country was 23 % [7]. A retrospective study conducted in Gambella, Ethiopia showed that the odd of MTB detection were higher among 15–29 and 30–44-year-old participants. However, significantly lower among females and those study patients with unknown HIV status [8]. A cross-sectional study conducted in a predominantly pastoralist area, Northeast Ethiopia exhibited a higher proportion of bacteriologically confirmed PTB patients (40.4 %) were HIV co-infected compared with patients without bacteriological evidence for PTB (22.3 %) [9]. Another cross-sectional study among 423 presumptive PTB patients at Ataye hospital, Ethiopia revealed that 3/38 (7.89 %) PTB patients were co-infected with HIV [10]. A retrospective study carried out at Metemma, Northwest Ethiopia exhibited the highest (32.4 %) proportion of co-infection among the patients who were in the age group of 25–34 years old [11]. Besides the risk factors mentoind above, the areas where the current study conducted are border areas with Sudan, Ethio-Sudan highway, Eritrea, and Tigray region. Moreover, the study areas have lots of difereent activities such as: market and trading centers, red-light district and bars, and bus station where porters, drivers, food and tea sellers, and most unemployed teenagers (both boys and girls) interact each other and/or with other humans from neighbouring countries, and a lack of health care resources may increase the risk of co-infection [11,12].

This information indicates that MTB/HIV co-infection is still a major global public health issue, particularly in resource-limited nations like Ethiopia. Thus, the purpose of this study was to explore the prevalence and associated variables of MTB/HIV co-infection among presumptive PTB patients in Northwest Ethiopia.

2. Materials and methods

2.1. Study design, period and area

This health facility based planned prospective cross-sectional study was conducted from February to August 2021 at the Metemma and Abrehajira Governmental hospitals, Northwest part of the Amhara National Regional State, Ethiopia. Metemma Hospital is located in the Metemma Woreda/or District in the West Gondar Administrative Zone at a latitude and longitude of 12°58′N 36°12′E with an elevation of 685 m above sea level, and the Abrehajira Hospital is also situated in the Abrehajira Woreda/or District in the same Administrative Zone mentioned above with coordinates of 13°28'3"N 36°29'4"E., 298 and 850 km away from the regional city, Bahir Dar, and the country's capital, Addis Ababa, Ethiopia, respectively. These hospitals provide outpatient, inpatient, TB and ART clinic services for those populations living at the two towns, districts, and from around. The study areas are bordered by Eritrea to the north and Sudan to the west, and the Ethio-Sudan cross-country high way crosses the study towns/districts. These areas are full of human labor-intensive agricultural enterprises (mostly cash crops) or farming in Ethiopia, therefore many people travel here from all over the country for work.

2.2. Operational definition

Presumptive pulmonary TB (PTB): a patient with any of the signs and symptoms suggestive of PTB, including cough > weeks, fever >2 weeks, unexplained significant weight loss, hemoptysis, night sweating and chest pain.

2.3. Source and study population

The source population consisted of all patients who visited the Metemma and Abrehajira Governmental hospitals throughout the study period, whereas the study population consisted of presumptive PTB patients who visited these two hospitals' TB and HIV clinics.

2.4. Pulmonary tuberculosis presumed individual enrollment

Patients who had one or more clinical presentation/symptoms referable to PTB such as cough for > two weeks, night sweating, weight loss, fever >2 weeks, loss of food appetite, and/or chest pain were eligible for enrolment. However, those patients who were on anti-TB drugs, and those who had known HIV status during the study period were non-eligible for this study.

2.5. Sample size determination

The sample size was determined by using a single population proportion formula, taking a 5 % margin of error at a 95 % confidence interval (CI). The target populations for the study would be all PTB presumed patients at the Metemma and Abrehajira hospitals which contain an estimated total number of the population more than 161,000(N value) [11,12]. Prevalence value of PTB-HIVco-infection taken into consideration for sample size calculation was 24.3 % obtained from the previous report from Northeasteren Ethiopia [13].

$$n = Z^2\, p(1-p) = (1.96)^2(0.243)(0.757) = 283$$

$$d^2 \quad 0.0025 \text{ Where}, Z = 95\% \text{ confidence interval } (1.96)$$

p = population proportion (prevalence rate), from previous study
d = Margin of sampling error (5 %)
q = 1-p = 0.5

n=number of sample unit/minimum sample size. Therefore, by considering a 10.7 % non-respondent rate, the total sample size in this study would be 283 + 31 = 314. A convenient sampling technique was used to recruit the study participants.

2.6. Variables

2.6.1. Dependent variables

PTB status and MTB/HIV co-infection.

2.7. Independent variables

Socio-demographic: data such as (age, sex, residence, marital status, occupation, educational status, and family income), **Clinical data**: (night sweating, weight loss, fever, loss of food appetites, chest pain, respiratory disorder, sputum production, history of TB treatment, family history of PTB, and history of contact with MDR-TB patients), and behavioral factors(cigarette smoking, alcohol consumption).

2.8. Data collection methods

2.8.1. Socio-demographic and possible risk factors data collection

The semi-structured closed-ended questionnaires were used to collect data from patients by using a face-to-face interview. A questionnaire that covers the socio-demographic, clinical, and PTB-related associated factors was formulated in English, and then translated into the local (Amharic version) language for data collection, and retranslated into English version for analysis and report.

2.9. Sample collection, handling, and transportation

Spot or morning sputum specimen were collected by using a falcon tube with 4–5 ml from each PTB presumptive patient following the interview, based on the national TB diagnosis guideline [14]. The quality of sputum was checked upon reception. Each specimen was stored at 2–8 °C for a maximum of one week until it gets tested at the Metemma and Abrehajira hospitals by using the GeneXpert assay. The sputum specimens were processed by first checking the label of the sputum cup and the study participants' identification number. Then, detergent reagents NaOH and isopropanol were added into falcon tubes of sample containers in a 2 to 1 ratio, respectively. It was then shaken and kept for 10 min, and repeated shaking was done for more homogenization for 5 min. Two mililitre of the homogenized sample was transferred into cartilage,and the Cepheid machine was operated to perform the test. The results were interpreted following the recommended method [15].

Regarding HIV screening of the study participants, capillary or 3 ml veins blood samples were collected from each PTB presumed patients by trained data collectors for rapid HIV tests (STAT-PAK HIV1/2/kit/20, ABON HIV 1/2/O Tri-Line, and SD BIOLINE HIV-1/2 3.0 test) to know the HIV status of the study patients following the national HIV diagnosis guideline [16].

2.10. Quality control

Quality of the data was assured through a pretested questionnaire in a similar setting that was not included in the study, close supervision and assistance of data collections, checking of filled questionnaires on daily basis for completeness, clarity, and accuracy of the data. All laboratory analysis were done based on the Ethiopian national TB, HIV, and leprosy management guidelines and WHO-approved methods [14]. IQC and EQC were done for gene Xpert assay, and HIV test algorithm. To assure the reliability, and validity of the study test procedures for sample collections, processing, and examination, the pre-analytical, analytical, and post-analytical quality control procedures were applied.

2.11. Data processing and analysis

Data were edited, cleaned, coded, entered Epi-data, and analyzed by SPSS version 20. The mean value, frequency, and proportion were computed. Results were summarized and presented by using words and tables. Bi-variable and multivariable logistic regressions were used to determine the association of independent variables with the dependent variables, and a $p \leq 0.05$ was considered as statistically significant.

3. Results

3.1. Socio-demographic profiles and prevalence of PTB, HIV, and MTB-HIV co-infection

A total of 314 PTB presumptive patients from the two hospitals were included in this study, and their median age was 35.0 year. Majority of the study participants, 178/314 (56.69 %) were males, 170(54.1 %) were married, 121/314(38.5 %) were unable to read and write, almost half, 162/314 (51.6 %) were urban residents, and 165/314(52.5 %) were in the age group of 25–50 years old (Table 1). As it is tried to illustrate in Table 1, among the patients included in this study, 40/314 (12.7 %) (95 % CI: 9.3–16.6) and 51/314 (16.2 %) (95 % CI: 12.7–20.7) were positive for PTB and HIV, respectively, and the MTB/HIV co-infection was accounted for 14/40 (35 %) (95 % CI: 0.2022, 0.4978). Higher PTB was detected among those study participants within the age group of 25 years–50 years old, males, married; primary educational status, private workers, and those who had lower monthly income. In addition, higher HIV positivity, and MTB/HIV co-infection were observed in urban dwellers, and unmarried patients.

4. Predictors of MTB/HIV co-infection among PTB presumptive patients

A higher rate of PTB/HIV co-infection was observed among urban residents 11(6.5 %), than rural residents 3(2.08 %), and males 9 (5.03 %) were more affected than females 5(3.7 %). Married patients were 70 % less likely to develop MTB/HIV coinfection (AOR = 0.3; 95%CI; 0.07–0.98) as compared to their counterparts. Patients that had contact history with MDR-MTB history (AOR = 5; 95 % CI; 1.37–18.00), and those who had a history of alcohol use (AOR = 12.2 CI; 2.56–57.8) were more at risk of acquiring the MTB-HIV co-infection as compared to their counterparts (Table 2).

5. Discussion

It is known that understanding the burden of PTB/HIV co-infection in areas, particularly in resource-constrained nations such as Ethiopia, is critical in filling gaps about the transmission and prevention mechanisms of these chronic diseases, and properly allocating limited resources for prevention, diagnosis, and therapeutics. With this in mind, it was conducted on 314 presumptive PTB patients from the Metemma and Abrehajira hospitals located in northwest Ethiopia to investigate the MTB/HIV co-infection and associated variables. The current study's MTB/HIV co-infection rate was 35 %, which is comparable to numerous studies conducted across the

Table 1
Socio-demographic characteristics, PTB, HIV, and MTB-HIV co-infection among patients at Metemma and Abrehajira hospitals, northwest Ethiopia, 2021 (N = 314).

Variables	Categories of variables	Number (%)	PTB positive N (%)	HIV positive N(%)	MTB/HIV positive N(%)
Age(year)	<25	86 (27.4)	12(13.9)	12(13.9)	5(5.8)
	25–50	165(52.5)	24(14.6)	30(18.2)	8(5.0)
	51–75	58(18.5)	4(10.3)	8(20.5)	1(2.6)
	>75	5(1.6)	0(0)	1(20.0)	0(0)
Sex	Male	(56.69)	25(14)	32(18.0)	8(4.5)
	Female	136(43.31)	15(11)	19(14.0)	6(4.4)
Residence	Urban	162(51.6)	21(13)	31(19.0)	11(6.8)
	Rural	152(48.4)	19(12.5)	20(13.2)	3(2.0)
Marital status	Unmarried	95(45.9)	16(16.8)	23(24.0)	4(4.2)
	Married	170(54.1)	24(14)	28(16.5)	10(5.9)
Educational status	Unable read and write	121(38.5)	15(12.4)	27(22.3)	7(5.8.0)
	primary level	88(28.0)	17(19.3)	12(14.0)	5(5.7)
	Above primary level	105(33.4)	8(7.6)	12(11.4)	2(2.0)
Occupation	Governmental	88(28.0)	3(4.7)	4 (6.0)	0(0)
	Private	64(20.4)	11(26.8)	11(27.0)	2(4.9)
	Housewife	41(13 %)	3(9.4)	7(22.0)	1(3.1)
	Labor worker	32(10.2)	11(11.8)	15(16.0)	5(5.4)
	Farmer	93(29.6)	12 (13.6)	14(16.0)	6(6.8)
Monthly income Ethiopian birr	<1500.00	91(29.0)	15 (16.5)	20(22.0)	4(4.4)
	1500.00–3000.00	93(29.6)	12 (12.9)	14(15.0)	7(7.5)
	3000.00–4700.00	55(17.5)	6 (10.9)	7(13.0)	3(5.5)
	>4700.00	75(23.9)	7(9.3)	10 (13.0)	0(0)

Key: ***Note****-Ethiopian Birr, N = number, PTB-pulmonary tuberculosis, MTB-HIV-*M.tuberculosis*-Human immunodeficiency virus, RR-MTB-rifampicin resistance-*M.tuberculosis,* MDR-MB- multi-drug resistance- *M. tuberculosis*.

Table 2
Predictors of PTB-HIV co-infection among PTB presumptive patients at Metemma and Abrehajira Hospitals, Northwest Ethiopia, 2021 (N = 314).

Variables	Categories	MTB/HIV co-infection		COR (95%CI)	*P*-value	AOR (95%CI)	*P*-value
		Yes, n(%)	No, n (%)				
Sex	Male	9(5.03)	170(94.97)	2.8 (0.8–10.2)	0.119	0.75(0.20–2.77)	0.67
	Female	5(3.7)	130(96.3)	1		1	
Marital status	Married	4(2.35)	166(97.65)	0.32(0.1–1.1)	0.061	0.3 (0.07–0.95)	0.046*
	Unmarried	10(6.9)	134(93.1)	1		1	
Alcohol History	Yes	4(13.33)	26(86.67)	8.39(2.7–26)	<0.001	12.2(2.6–57.8)	0.002*
	No	10(3.5)	274(96.5)	1		1	
Smoking history	Yes	9(14.5)	53(85.5)	4.2 (1.2–14)	0.022	0.81(0.18–3.7)	0.782
	No	5(3.3)	247(96.7)	1		1	
Residence	Urban	11(6.5)	159(93.5)	3.3 (0.9–11.9)	0.075	6(1.41–25.78)	0.015*
	Rural	3(2.08)	141(97.92)			1	
Contact history with MDR-TB patients	Yes	5(17.24)	24(82.76)	6.4(2–20.6)	0.002	4.96(1.37–18)	0.015*
	No	9(3.16)	276(96.84)	1		1	

***Note*:** Only significant values (*P*-value) are indicated by an asterisk indicator (*); 1 = Indicated the reference group.

globe, such as in Felege Hiwot & Debre Tabor hospitals, Ethiopia (41.9 %) [17]; Northeast Ethiopia (40.4 %) [9], Gambella, Southwest Ethiopia (35.5 %) [8], Kenya (41.8 %) [18], Ghana (30 %) [19]; Africa (31%–32 %) with Eastern Africa (31 %), Central Africa (41 %), Southern Africa (41 %), Western Africa (26 %) [3,4]; But, it is higher than the reports from northwest Ethiopia (19.8 %) [20]; (Ataye (7.89 %) [10]; and Addis Ababa, Ethiopia (4.5 %) [21]; Toga (23.7 %) [22]; and China (0.9 %) [23]. In contrast, a higher rate of MTB/HIV co-infection result was reported from PTB confirmed study conducted in South Africa (55.9 %) [24]. Variations of MTB/HIV co-infection prevalence reported across different studies might be relied on the diversity of PTB prevalence, socioeconomic status, geographical variation, and laboratory methods. Furthermore, people living in the current study areas may have a low level of awareness about the transmission mechanisms of - or risk of various activities that can expose individuals to - these infectious diseases, with lower socioeconomic status and daily laborers who are travelled from different parts of the country to the Metemma and Abrehajira areas for work, and probably people temporarily living in border and commercial areas, may display risky contact with individuals having unknown behaviors [25,26]. Existence of high prevalence of PTB cases may also causes for the presence of more MTB/HIV co-infection. On the other hand, The problem of PTB globally is worsened by HIV infection as people with HIV infection have a higher risk of developing active PTB [27]. This may impact for the prevention, early diagnosis and provision of therapy. Thus, serious emphasis should be given for the control and prevention to limit its transmission.

In this study, the MTB/HIV co-infection rate was slightly higher in male patients (5.03 %) than in females (3.7 %) which is in line with a study that showed as males to be more prone to have HIV infection than females [8]. It could be explained by the fact that more males were daily laborers, more mobile, more drugs, including alcohol users, and may demonstrate more risky sexual behaviors than females, particularly in the Metemma and Abrehajira districts [11].

In the current study, there was a high prevalence of MTB/HIV co-infection (20 %) among individuals aged 25–50 years. Individuals in this age bracket are typically sexually activte. This is spported by a study which showed that MTB/HIV co-infection is more likely in the sexually active age range [25]. This finding is also in accorance with the studies that found MTB/HIV co-infection rates to be higher in individuals within this age range [10,11,25,28]. The most likely explanation is that this age range is alao more vulnerable to various activities because it is the productive age at which most individuals are temporarily moving/traveling around for wealth or for outdoor activites, forming temporary friendships with other mobile people, and testing different substances, including alcohol, and having causal sex. These activities may expose individuals to a variety of communicable diseases, including those transmitted sexually and through respiration [29].

In the current study, people who lived in cities were six times more likely to get MTB/HIV co-infection than those who lived in rural. This finding is similar with the recent study conducted in Metemma, which found higher MTB/HIV co-infection rates among urban people [11]. Participants who had contact with MDR-MTB patients were five times more likely to develop MTB/HIV co-infection than those who did not have such a history. This finding is consistent with a prior study that revealed a greater prevalence of MTB/HIV co-infection among MDR-MTB presumptive cases in the country [30]. As a result, present control techniques are unlikely to be effective in reducing disease transmission. Therefore, the results of our study could be an essential signal for the health care system and healthcare providers to design and implement more effective and appropriate preventive and control meaures.

Married patients in the current study were 70 % less likely to have MTB/HIV co-infection than unmarried study participants.This result is in consistent to the studies conducted in Somalia and Turkey where married patients were less exposed to MTB/HIV co-infection than their counterparts [31,32]. This is possible because people who have familial support have a sense of stability that keeps them from engaging in dangerous behavior. Furthermore, the majority of the residents in the current study were unmarried (temporary residents who came from other parts of the country for seasonal work), which may have made this segment of the population more vulnerable to intercourse with commercial sex workers. We found that study patients with a history of alcohol use were 12 times more likely to get MTB/HIV co-infection than those who did not consume alcohol.Similarly, several studies found that alcohol usage is substantially related with MTB/HIV co-infection [24]. The likely explanation for this is that many individuals in the current study's areas work as laborers, which may expose them to such substance usage.

5.1. Strength and limitation

This study's strengths include that it provides insight about PTB/HIV coinfection and associated factors in the border areas which would potentially improve prevention and treatment plans for these diseases. Its limitation; however, is that it used convenient sampling technique which may affect how broadly the results can be applied to the general population.

6. Conclusion

The overall prevalence of PTB and HIV/AIDS among PTB presumed cases was 40 (12.7 %) and 51(16.2 %), respectively. From PTB confirmed cases, 14 (35 %) had PTB/HIV coinfection. Being unmarried, patients that had contact history with MDR-TB patients and those who had a history of alcohol use were variables that had a statistical association with PTB/HIV coinfection. Therefore, the results of the study indicated that PTB/HIV coinfection is still the twin epidemics remained as a major public health problem in Ethiopia, particularity in the study sites, and there is a need for collaborative and intensified prevention and control activities of these infections. Clinicians and laboratory scientists should give attention to the clinical signs and symptoms while they are detecting PTB and treating their patients.

Ethics statement

This study was reviewed and approved by [the research and ethics review committee of the School of Biomedical Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar], with the approval number: [SBMLS/2724/2021]. All participants/patients (or their proxies/legal guardians) provided informed consent to participate in the study.

Consent for publication

Not applicable.

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Nill.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author.

CRediT authorship contribution statement

Birhanu Wubu: Supervision, Investigation, Formal analysis, Data curation, Conceptualization. **Yihenew Million:** Writing – review & editing, Supervision, Investigation, Data curation. **Mucheye Gizachew:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Mucheye Gizachew reports equipment, drugs, or supplies was provided by Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, P. O. Box 196, Gondar, Ethiopia. Mucheye Gizachew reports a relationship with Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, P. O. Box 196, Gondar, Ethiopia that includes: employment. Not applicable has patent pending to Not applicable. Not applicable If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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