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Original Article

Determinants of multi-drug resistant tuberculosis at Yirgalem General Hospital, Sidama region, Southern Ethiopia

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Abstract

Background: The emergence of multi-drug-resistant tuberculosis (MDR-TB) is a challenge for the global prevention and control of the disease. Ethiopia is one of the 30 multi-drug-resistant tuberculosis burden countries. Addressing underlying risk factors is one of the principal ways to prevent drug resistant tuberculosis. However, there is limited evidence of determinants of multi-drug-resistant tuberculosis in the study area. The primary aim of this study was to identify the determinants of MDR-TB among patients attending anti-tuberculosis treatment at Yirgalem General Hospital, Sidama region, Southern Ethiopia, 2022.

Methods: Institution-based unmatched case control study conducted from July to August 2022 in Sidama Ethiopia. Cases were confirmed MDR-TB patients, while controls were those who declared cured or completed first line anti-TB treatment. Simple random sampling technique used to select 245 participants. The data entered into Epi data version 3.1, cleaned and analyzed by SPSS 25. Bivariable and multivariable analyses used to identify determinants of MDR-TB. Determinants with P-value <0.05 were declared as having significant association with MDR-TB and OR with 95% CI used to measure a degree of association.

Results: Having no formal education [AOR=5.01, 95% CI: (1.48, 17.04)], primary education [AOR=2.99, 95% CI: (1.12, 7.94)] having separate room [AOR=0.43, 95% CI: (0.22, 0.83)], ever alcohol drinking [AOR=3.27, 95% CI: (1.40, 7.62)], known TB contact history AOR=3.13, 95% CI: (1.38, 7.09)], and previous tuberculosis treatment history [AOR=6.22, 95% CI: (1.35, 28.75)] were the determinants for the development of multi-drug resistant tuberculosis.

Conclusion: This study identified lower educational status, lack of a separate room, alcohol use, contact with tuberculosis patients, and prior tuberculosis treatment as key determinants of MDR-TB. A community level education to enhance public awareness about MDR-TB, strengthening contact tracing strategies and DOT strategies with treatment adherence interventions are recommended.

Keywords: Multi-drug, resistant, tuberculosis, determinants, Yirgalem, Sidama Region

Introduction

Tuberculosis (TB) is a communicable disease caused by *Mycobacterium tuberculosis* and transmitted through airborne droplets expelled by individuals with pulmonary TB. Despite being a preventable and curable disease, TB remains one of the leading causes of morbidity and mortality worldwide (1). MDR-TB is defined as TB resistant to at least rifampicin (RIF) and isoniazid (INH), poses a major threat to global TB prevention and control efforts. MDR-TB may result from primary transmission of resistant strains or may develop during treatment because of inadequate or incomplete therapy (2).

Globally, the burden of TB and MDR-TB remains disproportionately concentrated in low- and middle-income countries. In 2020, WHO reported the highest numbers of TB cases from South-East Asia (43%), African (25%), and Western Pacific (18%) regions (2). Ethiopia is among the 30 high MDR-TB burden countries. A systematic review and meta-analysis conducted in Ethiopia estimated the prevalence of MDR-TB to be 2.18% among newly diagnosed TB patients and 21.07% among previously treated patients, with an overall prevalence of 7.24% (3-5).

The emergence and transmission of MDR-TB are driven by multiple interacting demographic,

socioeconomic, behavioral, clinical, and health system factors. Previous studies have identified low educational and socioeconomic status, HIV infection, malnutrition, smoking, alcohol and substance use, delayed diagnosis, poor access to quality health services, and inadequate treatment adherence as important determinants of MDR-TB (6,7). Among these, poor adherence to first-line anti-TB treatment remains one of the strongest modifiable determinants, as it promotes the selection and amplification of drug-resistant *Mycobacterium tuberculosis* strains (7).

Evidence from Ethiopia has identified additional factors associated with MDR-TB, including previous TB treatment, contact with known TB patients, malnutrition, HIV co-infection, smoking, alcohol consumption, smear positivity, prior hospitalization, comorbidities, and TB-related stigma (4,8-11). However, the magnitude and relative importance of these determinants vary across geographical settings because of differences in socioeconomic conditions, healthcare access, patient behaviors, and local TB control practices (4,8-11).

Addressing modifiable determinants is one of the key strategies for preventing MDR-TB and achieving the targets of the WHO End TB Strategy (1,5,7). Although several studies have examined determinants of MDR-TB in different parts of Ethiopia (4,8-11), evidence from the

Sidama Region, particularly Yirgalem General Hospital, remains scarce. No previous study has specifically assessed the determinants of MDR-TB among patients receiving anti-TB treatment at Yirgalem General Hospital. Generating local evidence is essential because determinants of MDR-TB may differ across settings and context-specific findings are needed to guide targeted prevention and control interventions. Therefore, this study was aimed to identify the determinants of MDR-TB among patients undergoing anti-tuberculosis treatment at Yirgalem General Hospital, Sidama Region, Southern Ethiopia.

Materials and Methods

Study setting, design and period

A hospital-based unmatched case control study was conducted from July to August 2022 at Yirgalem hospital, Sidama National Regional State. Administratively, the region divided into thirty rural districts, six town administrations, and one city administration. According to the 2007 report of the Ethiopia Central Statistical Agency (CSA), the region's population was estimated to at 4.37 million (12).

The health infrastructure includes 1 tertiary hospital, 4 general hospitals, 12 primary hospitals, 137 health centers, 553 health posts, and 173 private health facilities. Yirgalem General Hospital, one of the oldest hospitals in

Ethiopia, is located about 320 kilometers south of Addis Ababa and 45 kilometers from Hawassa, the regional capital. The hospital currently serves an estimated population of 5.2 million, covering both the Southern and Oromia regions.

Yirgalem General Hospital has served as the regional MDR-TB Treatment Initiation Center (TIC) since 2013. The hospital provides comprehensive TB and MDR-TB services, including TB diagnosis, initiation and follow-up of MDR-TB treatment, directly observed treatment (DOT), TB/HIV collaborative services, and coordination of several MDR-TB treatment follow-up centers within the region. During the study period, it was the only MDR-TB treatment initiation center serving the Sidama Region, where patients diagnosed with MDR-TB from referring hospitals and health centers were enrolled for treatment initiation and subsequent follow-up.

Population, eligibility, sample size determination and sampling procedure

The source population included all confirmed MDR-TB patients (cases) and Non-MDR-TB patients at the end first line anti-TB treatment (controls) at Yirgalem General Hospital whereas all confirmed MDR-TB patients (cases) and Non-MDR-TB patients at the end first line anti-TB treatment (controls) at

Yirgalem General Hospital during data collection period were the study population.

Patients with MDR-TB confirmed by culture and drug susceptibility testing, and who were undergoing treatment during the data collection period, were included as cases. Drug-susceptible TB patients who were declared cured, had completed treatment, or were smear-negative at the end of treatment during the study period were included as controls. Patients who were seriously ill or unable to communicate were excluded from the study.

The sample size was calculated using a double population proportion formula with Epi-Info version 7.2. The calculation was based on a previous study conducted in the Oromia region of Ethiopia (12) using the following assumptions: 95% confidence level, 80% power, a 1:2 case-to-control ratio, an odds ratio of 2.6, and 65.5% of controls exposed. A 1:2 case-to-control ratio was selected because it provides greater statistical power and improves the precision of the estimated odds ratios compared with a 1:1 ratio, while remaining feasible given the available number of confirmed MDR-TB cases. Based on these parameters, the final sample size was determined to be 245 participants, comprising 82 cases and 163 controls.

A total of 153 MDR-TB patients were on follow-up at Yirgalem General Hospital. From these, 82 cases were selected using a simple random sampling technique. For the control group, 163 patients who had completed first-line anti-TB treatment and were registered as cured or treatment completed were selected. Prior to selecting controls, five health facilities were identified based on the number of MDR-TB cases they referred to Yirgalem General Hospital, and an equal number of controls were drawn from each facility.

The required sample of controls was selected using simple random sampling from the sampling frame. Contact information for both cases and controls was obtained from the TB clinic patient registration books. Selected individuals were contacted by telephone, provided with information about the study, and those willing to participate and give written informed consent were scheduled for an interview at the health facility.

Data collection tools and quality assurance

A structured interviewer-administered questionnaire was used to collect data from the study participants. The questionnaire was adapted from previously published Ethiopian studies on the determinants of MDR-TB (12), the National Guidelines for TB, DR-TB and

Leprosy in Ethiopia (13), the National Guidelines for Comprehensive HIV Prevention, Care and Treatment (14), and the National Guidelines for the Programmatic Management of DR-TB (15). The adapted questionnaire was reviewed for content validity by experts in tuberculosis care and epidemiology and modified to fit the objectives of the present study. Clinical and treatment-related data were extracted from TB and MDR-TB registers and patients' medical records using a standardized data extraction checklist. Patient charts were reviewed to verify and document the initial tuberculosis episode, treatment history, and other relevant clinical information.

A structured interviewer administered questionnaire was used to collect data from the study participants. Data collection tool was adopted from previously locally conducted studies, national TB, HIV/AIDS guidelines and MDR-TB manual. Secondary data was collected from TB and MDR-TB registers. Patient charts and the data collection format was used to determine and record their initial TB episode.

Cases were interviewed during their follow-up visit to the hospital or during hospital admission, and controls at completion of their treatment (when declared as treatment completed or cured). After completing the interview section, additional data was collected

from the MDR-TB registers and Drug Susceptible Tuberculosis (DS-TB) registers as per the protocol.

Data quality was ensured through careful questionnaire design, pre-testing, and proper coding. The questionnaire, prepared in English was translated into Amharic and back-translated to English to ensure consistency. Data collectors and supervisors received training for two days on participant approach, study objectives, and the importance of accurate responses. Supervisors were also trained to check the completeness and consistency of questionnaires. A pretest was conducted in Adare General Hospital on 5% of the sample one week before data collection to assess clarity, understandability, and uniformity, and necessary amendments were made based on the results to maintain a logical flow of ideas.

Variables of the study and operational definitions

The dependent variable of the study was multi-drug resistant tuberculosis.

The independent variables were:

Socio-demographic characteristics: Age, sex, ethnicity, religion, marital status, educational status, occupation, monthly income, residence, living condition and separate living and sleeping room.

Behavioral characteristics: Alcohol drinking, cigarette smoking, chewing Khat, shisha use, Imprisonment, consumption of raw meat and consumption of raw milk.

Clinical characteristics: Comorbidity, previous treatment, contact history, nutritional status, type of TB, smear status, treatment outcome, hospitalization for TB, and disclosure of TB status.

Multidrug-resistant tuberculosis (MDR-TB): Tuberculosis caused by *Mycobacterium tuberculosis* that is resistant to at least both rifampicin and isoniazid, confirmed by drug susceptibility testing (DST) or molecular diagnostic methods in accordance with the national tuberculosis guidelines (2,13).

Separate room: A household condition in which the participant had a separate room exclusively used for sleeping during the period of tuberculosis treatment. This variable was categorized as “Yes” if the participant had a separate sleeping room and No otherwise.

Known TB contact history: A history of close contact with a person diagnosed with active tuberculosis before the participant's current TB diagnosis. Close contact refers to living in the same household or sharing an enclosed space (e.g., workplace, school, or other social setting) with an infectious TB

patient for a prolonged period, as defined by the national TB guidelines (2,13).

Body Mass Index (BMI): Nutritional indices that is used to assess and classify malnutrition. A normal if $BMI \geq 18.5$ and $< 25.0 (Kg/m^2)$ and malnutrition (underweight) if $BMI < 18.5 kg/m^2$ (8).

Cured: A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture-negative in the last month of treatment and on at least one previous occasion (8).

Treatment completed: A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable (8).

Drug susceptible TB: A tuberculosis that is susceptible to Rifampicin and Isoniazid (2).

Close contact: A person who is not in the household but who shared an enclosed space (social gathering place, workplace, facility) with the index case for extended daytime periods during the 3 months before the start of the current treatment episode (2).

Data processing and analysis

Data were coded and entered twice using Epi Data version 3.1 to ensure accuracy. Any inconsistencies identified during verification were corrected using the original questionnaires. The cleaned data were then exported to SPSS version 25 for analysis. Descriptive statistics were performed for cases and controls, and frequencies and percentages were presented using text, tables, and graphs. Binary logistic regression was conducted, with results presented as Crude Odds Ratios (COR) and p-values.

Variables with p-values <0.25 in the bivariate analysis were included as candidates for the multivariable logistic regression model. A backward stepwise approach was used to build the multivariable model. Model fitness was assessed using the Hosmer-Lemeshow test, and multicollinearity was checked with the variance inflation factor (VIF). Variables with p-values

<0.05 were considered statistically significant, and Adjusted Odds Ratios (AOR) with 95% confidence intervals were reported to indicate the strength of association.

Results

Socio-demographic characteristics of the participants

A total of 245 patients (82 cases and 163 controls) were participated in this study, and with a response rate of 100%. The median (IQR) age of the patients were 25 (10) and 29 (18) years for cases and controls, respectively. More than half, 68.3% of cases and 58.3% of controls were between the age group of 16-30 years. The male-to-female ratio has nearly equally represented for both the cases (1.4) and controls (1.3) groups. The majority of cases and controls were Sidama ethnic group and Protestant religion followers. About 74.4% of cases and 51% of the controls did not have separate living room, respectively (Table 1).

Table 1:The socio-demographic characteristics of study participants at Yirgalem Hospital, Ethiopia, 2022.

Variable	Case (N=82)		Control (N=163)		Total (N=245)	
	No	(%)	No	(%)	No	(%)
Age (year)						
• ≤15	10	12.2	2	1.2	12	4.9
• 16-30	56	68.3	95	58.3	151	61.6
• 31-45	13	15.9	32	19.6	45	18.4
• ≥46	3	3.7	34	20.9	37	15.1
Sex						
▪ Male	48	58.5	91	55.8	139	56.7
▪ Female	34	41.5	72	44.2	106	43.3

Marital status						
○ Single	42	51.2	46	28.2	88	35.9
○ Married	37	45.1	106	65	143	58.4
○ Divorced/widowed	3	3.7	11	6.7	14	5.7
Educational status						
● No formal education	16	19.5	10	6.1	26	10.6
● Primary	28	34.1	41	25.2	69	28.2
● Secondary	29	35.4	76	46.6	105	42.9
● College & above	9	11.0	36	22.1	45	18.4
Occupation						
○ House wife	15	18.3	37	22.7	52	21.2
○ Farmer	8	9.8	51	31.3	59	24.1
○ Student	37	45.1	33	20.2	70	28.6
○ Merchant	4	4.9	28	17.2	32	13.1
○ Government employee	17	20.7	6	3.7	23	9.4
○ Unemployed	1	1.2	8	4.9	9	3.7
Income						
● ≤2000	52	63.4	86	52.8	138	56.3
● 2001-4000	9	11.0	29	17.8	38	15.5
● 4001-6000	11	13.4	32	19.6	43	17.6
● ≥6001	10	12.2	16	9.8	26	10.6
Residence						
● Urban	38	46.3	47	28.8	85	34.7
● Rural	44	53.7	116	71.2	160	65.3
Living condition						
○ With family	73	89.0	132	81	205	83.7
○ With relative/friends	6	7.3	23	14.1	29	11.8
○ Alone	3	3.7	8	4.9	11	4.5
Have separate room						
● Yes	21	25.6	80	49.1	101	41.2
● No	61	74.4	83	50.9	144	58.8

*Catholic, Traditional

Behavioral characteristics of MDR-TB

Among the total study participants, 22(26.8%) of cases and 26(16%) controls chewed khat at least once in their lifetime. Twelve (14.6%) of cases and 16 (9.8%) of the controls smoked

cigarette at least once in their life, whereas five (6.1%) of cases and 15 (9.2%) of controls currently smoked cigarette. About 11% of cases and 14.1% of controls had imprisonment history and 9.8% of cases and 8% of controls has refugee camp stay history (Table 2).

Table 2: The behavioral characteristics of study participants in Yirgalem Hospital, Ethiopia, 2022.

Variable	Case (N=82) No. (%)	Control (N=163) No. (%)	Total (N=245) No. (%)
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Ever chewed khat			
○ Yes	22 (26.8)	26 (16.0)	48 (19.6)
○ No	60 (73.2)	137 (84.0)	197 (80.4)
Currently chewing khat			
● Yes	8 (9.8)	16 (9.8)	24 (9.8)
● No	74 (90.2)	147 (90.2)	221 (90.2)
Ever smoked cigarette			
● Yes	12 (14.6)	16 (9.8)	28 (11.4)
● No	70 (85.4)	147 (90.2)	217 (88.6)
Currently smoked cigarette			
○ Yes	5 (6.1)	15 (9.2)	20 (8.2)
○ No	77 (93.9)	148 (90.8)	225 (91.8)
Ever drunk alcohol			
● Yes	22 (26.8)	12 (7.4)	34 (13.9)
● No	60 (73.2)	151 (92.6)	211 (86.1)
Currently drink alcohol			
● Yes	3 (3.7)	12 (7.4)	15 (6.1)
● No	79 (96.3)	151 (92.6)	230 (93.9)
Ever used shisha			
○ Yes	2 (2.4)	7 (4.3)	9 (3.7)
○ No	80 (97.6)	156 (95.7)	236 (96.3)
Currently using shisha			
● Yes	1 (1.2)	1 (0.6)	2 (0.8)
● No	81 (98.8)	162 (99.4)	243 (99.2)
History of imprisonment			
○ Yes	9 (11.0)	23 (14.1)	32 (13.1)
○ No	73 (89.0)	140 (85.9)	213 (86.9)
History of refugee camp stay			
● Yes	8 (9.8)	13 (8.0)	21 (8.6)
● No	74 (90.2)	150 (92.0)	224 (91.4)
Drink raw milk			
○ Yes	67 (81.7)	144 (88.3)	211 (86.1)
○ No	15 (18.3)	19 (11.7)	34 (13.9)

Clinical and nutritional characteristics of MDR-TB

One-fourth (25.6%) of the cases and 30 (18.4%) of the controls had chronic medical illness. Twelve (14.6%) of the cases had BMI less than 18.0 kg/m² whereas nearly one fifth (22.7%) of the control had BMI less than 18.5 kg/m².

About 75(91.5%) of the cases and 137(84%) of controls had pulmonary TB. From the cases, 47(52.2%) had contact history with known TB patients as compared to control only one-fourth 23(25.6%) had a contact history. The prevalence of HIV was 12.2% among cases and 7.4% among controls (Table 3).

Table 3:The distribution of clinical characteristics of study participants at Yirgalem Hospitals, Ethiopia, 2022.

Variable	Case (N = 82) No. (%)	Control (N = 163) No. (%)	Total (N = 245) No. (%)
Chronic medical illness			
○ Yes	21 (25.6)	30 (18.4)	51 (20.8)
○ No	61 (74.4)	133 (81.6)	194 (79.2)
Body mass index (kg/m²)			
• <18.5	12 (14.6)	37 (22.7)	49 (20.0)
• 18.5-24.9	70 (85.4)	126 (77.3)	196 (80.0)
Site of TB			
○ Pulmonary TB	75 (91.5)	137 (84.0)	212 (86.5)
○ Extrapulmonary TB	7 (8.5)	26 (16.0)	33 (13.5)
Sputum smear result			
○ Positive	79 (96.3)	158 (96.9)	237 (96.7)
○ Negative	3 (3.7)	5 (3.1)	8 (3.3)
Known TB contact			
○ Yes	71 (86.6)	108 (66.3)	179 (73.1)
○ No	11 (13.4)	55 (33.7)	66 (26.9)
Previous TB treatment history			
• Yes	49 (59.8)	39 (23.9)	88 (35.9)
• No	33 (40.2)	124 (76.1)	157 (64.1)
Treatment outcome[†]			
○ Cured	11 (22.5)	30 (76.9)	41 (46.1)
○ Treatment completed	4 (8.2)	7 (17.9)	11 (12.4)
○ Treatment failure	3 (6.1)	1 (2.6)	4 (4.5)
○ Loss to follow-up	31 (63.2)	1 (2.6)	32 (36.0)
TB status disclosure[*]			
• Yes	70 (85.4)	139 (85.3)	209 (87.8)
• No	12 (14.6)	24 (14.7)	36 (12.2)
HIV test result			
• Positive	10 (12.2)	12 (7.4)	22 (9.0)
• Negative	72 (87.8)	151 (92.6)	223 (91.0)

Determinants of MDR TB

In the bivariable logistic regression analysis age, marital status, education status, residence, living/sleeping in separate room, ever chewed

khat, ever drunk alcohol, smear result, known TB contact history, previous TB treatment history, and previous hospitalization history were the variables that were taken to the final

model. After adjusting for potential confounding variables in multivariable logistic regression, educational status, living/sleeping in separate room, ever drunk alcohol, known TB contact history, and previous TB treatment history found to be independent determinants of MDR-TB.

The odds of MDR-TB were 5 times higher among patients with no formal education as compared to patients with a College or above educational status [AOR=5.01, 95% CI: (1.48, 17.04)]. Similarly, the odds of MDR-TB were 2.9 times higher among patients with a primary education as compared to patients with college or above education [AOR=2.99, 95% CI: (1.12, 7.94)]. The odds of MDR-TB were 57% lower

among patients who had a separate room for living/sleeping as compared to those who do not have a separate room [AOR=0.43, 95% CI: (0.22, 0.83)].

Patients who ever drunk alcohol had 3.27 times higher odds of developing MDR-TB as compared to their counterparts [AOR=3.27, 95% CI: (1.40, 7.62)]. The odds of MDR-TB were 3.13 times higher among patients who had known TB contact history compared to those who did not [AOR=3.13, 95% CI: (1.38, 7.09)]. Moreover, the odds of MDR-TB were 6.2 times higher among patients who had previous TB treatment history compared to those who did not had previous TB treatment history [AOR=6.22, 95% CI: (1.35, 28.75)].

Table 4: Multivariable Logistics Regression Analysis of Determinants for MDR-TB in Yirgalem Hospital, Ethiopia, 2022.

Variables	MDR-TB			
	Cases (%)	Controls (%)	COR(95% CI)	AOR(95% CI)
Educational status				
○ No formal education	16(61.5)	10(38.5)	6.40 (2.18, 18.77)	5.01 (1.48, 17.04)*
○ Primary education	28(40.6)	41(59.4)	2.73 (1.14, 6.55)	2.99 (1.12, 7.94)*
○ Secondary education	29(27.6)	76(72.4)	1.53 (0.65, 3.56)	1.33 (0.505, 3.49)
○ College or above	9(20.0)	36(80.0)	1	1
Residence				
● Urban	38 (44.7)	47(55.3)	2.13(1.23, 3.69)	1.29 (0.67, 2.51)
● Rural	44 (27.5)	116 (72.5)	1	1
Live & sleep in separate room				
○ Yes	21 (20.8)	80 (79.2)	0.36(0.19, 0.64)	0.43 (0.22, 0.83)*
○ No	61 (42.4)	83 (57.6)	1	1
Ever chewed khat				
● Yes	22 (45.8)	26 (54.2)	1.92(1.01, 3.65)	1.43 (0.60, 3.40)
● No	60 (30.6)	136 (69.4)	1	1
Ever drunk alcohol				
○ Yes	22 (64.7)	12 (35.3)	4.61(2.15, 9.90)	3.27 (1.40, 7.62)*
○ No	60 (28.4)	151 (71.6)	1	1
Drink raw milk				
● Yes	67 (31.8)	144 (68.2)	0.59(0.28, 1.23)	0.48 (0.19, 1.18)*
● No	15 (44.1)	19 (55.9)	1	1

Comorbidity				
○ Yes	21 (41.2)	30 (58.8)	1.53(0.81, 2.88)	1.92 (0.86, 4.28)
○ No	61 (31.4)	133 (68.6)	1	1
BMI				
● < 18.5 kg/m ²	12 (24.5)	37 (75.5)	0.58(0.29, 1.19)	0.98 (0.39, 2.45)
● 18.5-24.9 kg/m ²	70 (35.7)	126 (64.3)	1	1
Site of TB				
○ Pulmonary TB	75 (35.4)	137 (64.6)	2.03(0.84, 4.91)	1.69 (0.61, 4.64)
○ Extra-pulmonary TB	7 (21.2)	26 (78.8)	1	1
Known TB contact history				
● Yes	71 (39.7)	108 (60.3)	3.29(1.6, 6.71)	3.13 (1.38, 7.09)*
● No	11 (16.7)	55 (83.3)	1	1
Previous TB treatment history				
○ Yes	78 (37.3)	131 (62.7)	4.76(1.62, 13.97)	6.22 (1.35, 28.75)*
○ No	4 (11.1)	32 (88.9)	1	1
Hospitalization history				
● Yes	72 (37.3)	121 (62.7)	3.67(1.48, 9.12)	1.92 0.68, 5.42)
● No	10 (86.0)	42 (14.0)	0.36(0.08, 1.64)	1
HIV status				
○ Reactive	10 (45.5)	12 (54.5)	1.78(0.74, 4.36)	0.77 (0.28, 2.64)
○ Non-reactive	70 (31.7)	151 (68.3)	1	1

*p<0.05,

Discussion

This unmatched case-control study aimed to identify determinants of MDR-TB. Educational status, having a separate living/sleeping room, alcohol consumption, known TB contact history, and previous TB treatment history were identified as independent determinants of MDR-TB. The odds of MDR-TB were five and three times higher among patients with no formal education and those who completed only primary education, respectively, compared to patients with college-level education or higher. Similar findings were reported in studies from China (17), Bangladesh (18), Pakistan (19), India (20), Addis Ababa (21), Northwest Ethiopia (22), and Southern Ethiopia (23). This

may be because patients with little or no education are less likely to understand the importance of treatment adherence, leading to premature discontinuation of therapy when symptoms improve or side effects occur, thereby facilitating the development of MDR-TB. Additionally, in this study, patients with low education were predominantly from rural areas and had higher rates of previous TB treatment, both of which are strong predictors of MDR-TB.

Having a separate living/sleeping room was another important determinant. Patients with a separate room had 57% lower odds of developing MDR-TB compared to those without one. This finding is consistent with

studies conducted in developed countries (24), Pakistan (25), India (26), Addis Ababa (27), and Southern Ethiopia (28). Separate rooms likely reduce household contact, limiting exposure to index cases, while increased space and better ventilation decrease the concentration of *Mycobacterium tuberculosis* in the air. Overcrowding, in contrast, increases the risk of transmission of drug-resistant strains.

Alcohol consumption was also identified as an independent predictor of MDR-TB. Patients who drank alcohol had three times higher odds of developing MDR-TB than non-drinkers. Similar findings were reported in Sudan (29), Northern Ethiopia (30), East Shoa (10), and Jimma, Southwestern Ethiopia (11). Alcohol may contribute to MDR-TB by increasing non-compliance with treatment, impairing immune responses, and exacerbating negative drug effects. The WHO has also recognized alcohol consumption as a significant population-level risk factor for MDR-TB.

Known TB contact history was associated with MDR-TB, with patients reporting such contact having three times higher odds of developing MDR-TB compared to those without contact. This aligns with studies from Bangladesh (18), India (20), Sudan (29), Oromia Region (16), Addis Ababa (31), Southern Ethiopia (23), and a meta-analysis in Ethiopia (32). Delays in diagnosis and treatment, coupled with

inadequate infection prevention measures at both home and healthcare facility levels, may prolong exposure and increase the likelihood of developing MDR-TB.

Globally, the WHO reported that in 2020, 3-4% of new TB cases and 18–21% of previously treated cases had MDR/RR-TB (1). This study supports these estimates: patients with a history of previous TB treatment had seven times higher odds of developing MDR-TB compared to treatment-naïve patients. Corresponding evidence comes from studies in India (33), Nepal (34), Tanzania (35), Addis Ababa (9, 31), Oromia (16), SNNPR (23), and East Shoa in Ethiopia (10). A systematic review and meta-analysis in Ethiopia also highlighted previous TB treatment as a strong determinant of MDR-TB (32). Repeated exposure to first-line anti-TB medications and improper treatment regimens may promote bacterial mutation and drug resistance (1,9). Nevertheless, individuals without prior TB treatment remain at risk due to the increasing spread of resistant strains in the community (32).

Limitations of the study

The study has several limitations that should be considered when interpreting its findings. First, because of the sensitive nature of some variables, participants may have underreported or over reported certain behaviors, resulting in social desirability bias. In addition, information

on past exposures relied on participants' recall, which may have introduced recall bias. As a case-control study, the selection of controls may also have introduced selection bias if they were not fully representative of the population that gave rise to the cases. Furthermore, survivor bias may have occurred because only individuals who survived long enough to be included in the study were enrolled, potentially excluding those with more severe disease or poorer outcomes. Differences in exposure opportunities between cases and controls may also have affected the observed associations. Although multivariable analysis was performed to adjust for potential confounders, residual confounding from unmeasured or imperfectly measured variables cannot be ruled out. Finally, the relatively small sample size may have reduced the statistical power to detect modest associations and limited the precision of some estimates.

Conclusions

The study revealed that no formal education, primary education, having separate living/sleeping room, ever alcohol drinking, known TB contact history and previous history of TB treatment identified as independent determinants of developing MDR-TB.

Based on the main findings of this study, MDR-TB requires urgent and coordinated attention from government bodies and stakeholders,

including strengthened community engagement by health extension workers, religious leaders, and community leaders to raise awareness; particularly among individuals with low educational status; improved contact tracing, evaluation, and testing of all household contacts at healthcare facilities; implementation of community-wide awareness programs on alcohol and substance use through various media platforms; promotion of early contact screening and case identification by public health authorities; reinforcement of DOTS implementation, treatment adherence support, and laboratory capacity for drug susceptibility testing in line with national guidelines; and further research to explore additional determinants as well as the physical and physiological impacts of MDR-TB.

Authors' contributions

MJ was the principal investigator and conceived the study and was involved in the study design, supervised data collection, analyzed and interpreted the data, report writing. KZ wrote the manuscript. EA reviewed and edited the manuscript. NG reviewed and edited, interpretation of data and approved the final manuscript. All authors have made substantial contributions to this manuscript.

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Availability of data and materials

The datasets produced and/or analyzed throughout the current study are available from the authors upon reasonable request.

Ethics approval and consent to participate

Ethical approval to start the study was obtained from Institutional Research Ethics Review Committee (IRERC) office of Pharma College. In addition, permission letter was secured from Yirgalem General Hospital. Written informed consent was obtained from participants after a detailed explanation of the purpose and benefit of the study right before the individual data collection. The confidentiality issue was assured for study participant and their response were kept private. The participants were informed as having full right to stop or jump any question that is uncomfortable to them any time.

Consent for publication

Not applicable.

Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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