

# Determinants of Drug Resistant Tuberculosis Among Tuberculosis Patients on Treatment in Gedeo Zone Public Healthcare Facilities, Southern Ethiopia, 2025. Unmatched Case–Control Study

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## Abstract

**Introduction:** Drug-resistant tuberculosis (DR-TB) is a form of tuberculosis caused by *Mycobacterium tuberculosis* strains that do not respond to standard anti-TB drugs. Ethiopia ranked among the top 30 countries burdened by DR-TB in the world. Although drug-resistant tuberculosis is a growing public health concern in the Gedeo Zone, determinants of DR-TB are still inadequately explored, as few studies have been undertaken in this area. Therefore, this study aimed to assess the determinants of drug-resistant tuberculosis among TB patients receiving treatment.

**Objectives:** To assess the determinants of drug-resistant tuberculosis among TB patients receiving treatment in Gedeo Zone public healthcare facilities, southern Ethiopia, 2025

**Methods:** An institution-based unmatched case–control study was conducted from July 21--August 19, 2025, with a total of 177 participants (59 cases and 118 controls) who attended public healthcare facilities in the Gedeo zone. A simple random sampling technique was used to select a study participant. The data were collected with the Kobo Toolbox and then exported to SPSS version 27 for analysis. Associations between dependent and independent variables were assessed via binary logistic regression. At the 95% CI, in bivariable analysis, a *p* value of <0.25 was used to select candidate variables for multivariable analysis. In the multivariable analysis, a *p* value of less than 0.05 was considered statistically significant.

**Result:** In this study, 177 participants (59 cases and 118 controls) were enrolled, resulting in a 100% response rate. This study revealed that five factors were significantly associated with DR-TB in this study area: lack of formal education (AOR = 3.37, 95% CI: 1.09–10.42), urban residence (AOR = 2.54, 95% CI: 1.07–6.03), previous TB treatment history (AOR = 3.34, 95% CI: 1.57–7.09), counselling on DR-TB (AOR = 0.28, 95% CI: 0.10–0.78), and social stigma (AOR = 3.27, 95% CI: 1.56–6.84).

**Conclusion:** Lack of formal education, urban residence, previous TB treatment history, counselling and social stigma was found to be determinants of DR-TB. Effective DR-TB control interventions focused on the above determinants need to be implemented.

**Keywords:** Drug Resistance, Tuberculosis, Healthcare Facility, Gedeo Zone

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## Abbreviations

AOR	Adjusted Odds Ratio
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
COR	Crude Odds Ratio
DM	Diabetes Mellitus
DR-TB	Drug Resistant Tuberculosis
DURH	Dilla University Referral Hospital
ETB	Ethiopian Birr
HF	Heart Failure
HIV	Human Immunodeficiency Virus
HR-TB	Isoniazid Resistant TB
HTN	Hypertension
MDR-TB	Multidrug Resistant Tuberculosis
RR	Relative Risk
RR-TB	Rifampicin resistant tuberculosis
TIC	Treatment Initiation Center
WHO	World Health Organization
XR-TB	Extensive Drug Resistant Tuberculosis

## 1. Introduction

According to the World Health Organization, tuberculosis (TB) is a communicable infectious disease caused by the bacterium *Mycobacterium tuberculosis* that primarily affects the lungs but can, in some cases, extend its impact to other organs throughout the body [1]. Drug-resistant tuberculosis (DR-TB) is a severe bacterial infectious disease caused by strains of *Mycobacterium tuberculosis* that are nonresponsive to one or more antimicrobial medications intended to treat tuberculosis [1]. Drug-resistant tuberculosis encompasses several forms, including multidrug-resistant tuberculosis (MDR-TB), which is characterized by resistance to at least two of the most potent first-line antitubercular drugs, isoniazid (INH) and rifampicin (RIF), and rifampicin-resistant tuberculosis (RR-TB), which is characterized by resistance to rifampicin (RIF), which may or may not present with resistance to other antitubercular drugs, and extensively drug-resistant tuberculosis (XDR-TB), representing a more severe form of drug resistance characterized by resistance to isoniazid (INH) and rifampicin (RIF) and at least one fluoroquinolone, such as moxifloxacin or levofloxacin, and at least one second-line injectable antitubercular drug, such as amikacin, kanamycin, or capreomycin [2].

The development of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) strains of the disease, which are highly resistant to first- and second-line antitubercular drugs, has made the global TB crisis even more critical, as standard treatment protocols are no longer effective and the challenge of managing and controlling this deadly infectious disease becomes even more difficult [3,4]. Tuberculosis, particularly drug-resistant tuberculosis, disproportionately burdens already fragile health systems in Africa, widens health inequalities, and erodes public health gains, most severely in southern Africa, due to high HIV prevalence, limited health care resources, and widespread socioeconomic challenges [5]. Southern Ethiopia, like other regions of the country, experiences a significant burden of TB

and, as such, a high DR-TB prevalence. The rates in this particular region, which are likely higher than the national average, place an extra burden on the already fragile health infrastructure [6]. The WHO has set a target to reduce tuberculosis (TB) by 50 percent by the end of 2025, but thus far, only a small 8–3 percent reduction has been achieved, and the deadline is approaching [7]. This lack of progress is largely due to the growing prevalence of drug-resistant tuberculosis (DR-TB), which makes effective treatment and control strategies very challenging [2]. Although DR-TB prevention and treatment programs are in place according to national guidelines and recommendations of previous studies, the number of new cases continues to increase, which indicates that currently available evidence is insufficient to control the disease and that context-specific research is urgently needed [8]. In this study area, therefore, locally relevant, evidence-based information is critical to guide effective interventions and reduce the burden of DR-TB in this area.

Although drug-resistant tuberculosis is an increasing public health problem in the Gedeo Zone, determinants of DR-TB remain inadequately explored, as only a few studies have been conducted in this area thus far [5]. Those previous studies identified several determinants of DR-TB, such as social stigma, living in a household with one or two rooms, having a previous history of TB treatment, having a baseline body mass index (BMI) less than 18.5 kg/m<sup>2</sup>, and having pulmonary TB or DM [8]. However, the continuing increase in DR-TB cases suggests that additional social, environmental, and clinical factors may also play a role. Additionally, important regional perspectives are provided by a prior study that included the Dilla University Referral Hospitals (DURH) TIC center as one of four study areas in southern Ethiopia; however, further context-specific investigations focused on the Gedeo Zone are warranted for a deeper understanding of the local determinants of drug-resistant tuberculosis [6]. The existing evidence gap emphasizes how urgently more research in this area is needed to fully comprehend the complex and context-specific factors that lead to drug-resistant tuberculosis. The current lack of deep understanding makes designing an effective control strategy difficult. Generating up-to-date and locally relevant evidence is therefore essential to identify more determinants of DR-TB, guide focused interventions and strengthen ongoing efforts to reduce the burden of DR-TB in this area. Therefore, this study was aimed to assess the determinants of drug-resistant tuberculosis among TB patients receiving treatment in Gedeo Zone public healthcare facilities, southern Ethiopia.

## 2. Methods and Materials

### 2.1. Study Area and Period

This study was conducted in healthcare facilities in the Gedeo Zone, which is located in southern Ethiopia and is approximately 360 km south of Addis Ababa. The zone has 45 public health facilities distributed across 13 districts and serves a population of 1,330,796 people, according to the woreda-based plan of the 2017 Ethiopian fiscal year (EFY). Drug-resistant tuberculosis (DR-TB) is diagnosed at Dilla University Referral Hospital (DURH), which functions as a treatment initiation center (TIC). Treatment is started

at DURH, and once a patient's sputum test becomes negative, they are linked to their local health center for close follow-up. According to the Gedeo Zone Health Department's report, 3,380 drug-susceptible TB patients and 65 drug-resistant TB (DR-TB) patients currently receive treatment across various health facilities in the Gedeo Zone [9]. The study was conducted from July 21–August 19, 2025.

## 2.2. Study Design

An institution-based unmatched case–control study was employed.

## 2.3. Source and Study Population

The source population of the study included all new and previously treated TB patients registered for treatment in Gedeo Zone healthcare facilities with documented drug susceptibility testing (DST). With respect to the study population, all randomly selected DR-TB patients currently receiving treatment at Gedeo Zone healthcare facilities were cases, whereas all randomly selected drug-susceptible TB patients receiving treatment at Gedeo Zone health facilities were controls.

## 2.4. Eligibility Criteria

For cases, all confirmed DR-TB patients currently receiving treatment were included, and for controls, all confirmed drug-susceptible TB patients after 2 months of treatment were included in the study. For cases, patients with previous treatment for DR-TB were excluded, and for controls, patients in the intensive phase of treatment for drug-susceptible TB and patients with previous treatment for DR-TB were excluded from the study.

## 2.5. Sampling Size Determination

To determine the proportion among cases and controls, the sample size was computed via the double population proportion formula by considering a ratio of cases to controls of 1:2, a power of 80, a 95% confidence interval, and an adjusted odds ratio of 0.26, with a proportion among cases of 0.743 and among controls of 0.429 from a study of drug-resistant tuberculosis patients in southern Ethiopia [7]. For determinants of drug-resistant tuberculosis among tuberculosis patients receiving treatment, the sample size was computed via Epi Info version 7.2.5.0 software by considering a ratio of case to control of 1:2, a power of 80, a 95% confidence interval, and an odds ratio varying according to the variable. The sample size formula for the method described in Fleiss w/CC was used. When the adequacy of the sample size is considered, the largest sample size is 161. By adding a 10% nonresponse rate, the total sample size for this study was 177. Therefore, the total sample sizes for this study were 59 cases and 118 controls.

## 2.6. Sampling Procedure

First, the list of all DR-TB patients diagnosed over 24 months as well as health care facilities where DR-TB patients were linked after being declared sputum negative was taken from the DURH TIC center. The sample was then proportionally allocated to all healthcare facilities on the basis of the number of DR-TB cases linked to them. One-third of the proportionally allocated sample was the number of cases needed from that facility, while 2/3rd

of that was the control needed from the same facility. Finally, a simple random sampling technique was employed to select study participants on the basis of their serial number in the TB registration book until an allocated sample was obtained for each healthcare facility. When the allocated sample was equal to the number of cases on follow-up at that facility, all of it was included in the study.

## 3. Variable of the Study

### 3.1. Dependent Variable

- Drug resistant Tuberculosis

### 3.2. Independent Variable

- **Sociodemographic and Economic Factors** (i.e., age, sex, residence area, educational status, occupational status, monthly income).
- **Behavioral Factors** (i.e., smoking, chat chewing, alcohol consumption, treatment interruption, social stigma, information about DR-TB, counselling on DR-TB, delay in seeking care).
- **Environmental and Household Factors** (i.e., number of rooms, crowding, contact with DR-TB patients, opening window habits, and distance of healthcare facilities from living areas).
- **Clinical and Comorbid Factors** (i.e., HIV status, nutritional status, hospitalization, previous treatment for TB, treatment failure, relapse).

### 3.3. Operational Definition:

- **MDR-TB:** Resistant to at least both isoniazid and rifampin on the basis of drug susceptibility testing [1].
- **XDR-TB:** DR-TB that fulfils the definition of MDR and is also resistant to any fluoroquinolone and at least one additional injectable anti-TB agent on the basis of drug susceptibility testing [1].
- **HR:** Resistant to isoniazid only
- **RR:** Resistant to rifampicin only
- **DR-TB:** Any one of the four categories of DR-TBs listed above.
- **Patient:** A patient with a confirmed diagnosis of MDR-TB or XDR-TB.
- **Control:** Drug-susceptible TB patients or TB patients declared to be drug susceptible by laboratory confirmation after 2 months of initial treatment.
- **New Patients:** Patients who have never been treated for TB or have taken anti-TB drugs for less than one month [1].
- **History of Contact with DR-TB Patients:** Sharing living, learning or working space with smear-positive pulmonary DR-TB patients for 1 or more nights or extended during the 3 months prior to the current diagnosis [6].
- **History of Drug Interruption:** History of missing even a single dose of anti-TB therapy [10].
- **Comorbid Illness:** Concurrently diagnosed conditions in TB patients, including under nutrition, HIV, diabetes mellitus and lung diseases (COPD, asthma) [6].
- **Alcohol Consumption:** Currently, alcohol consumption is

defined as drinking alcohol at least once a month [11].

- **Smokers:** Smokers who currently smoke or have smoked one or more cigarettes per day within the 12 months of TB diagnosis [11].
- **Stigma:** This is considered present if the patient reports experiencing isolation, discrimination, or reduced social support due to a current or past TB infection [6].
- **Undernutrition:** Age-specific WHO anthropometric tools were used to classify the nutritional status of patients as normal, mild, moderate or severe undernutrition, overweight or obese [12].
- **Hospitalization:** Documented or reported admission to the hospital for at least 2 days in the last 3 months before TB diagnosis [13].
- **Distance from the Nearest Treatment Center:** classified as 'near' if the one-way walking time is less than 1 hour and 'far' if it takes 1 hour or more [14].
- **The Monthly Income:** low (<1500 ETB), moderate (1500-3000) or high (>3000) [15].

#### 4. Data Collection Tool and Procedures

A structured interview questionnaire was developed {Look at supplementary file} from the literature to gather data on sociodemographic and economic factors, environmental and household factors, behavioral factors, and clinical and comorbid factors was used to collect data. Using checklists, clinically and comorbidity-related data were collected from the client's chart. At each healthcare facility, data were collected by two nurse professionals via the Kobo toolbox in two isolated chronic Tb clinic units.

#### 5. Data Quality Management

Before data collection, the structured questionnaire prepared for data collection was pretested in 5% of the study sample at Yirgalem Hospital, which is found in Sidama Regional State, Ethiopia. After the pre-test, the data collection questionnaire was carefully designed, translated and retranslated. The questionnaires were developed in English, translated to Amharic, and then returned to English to maintain consistency by a well-trained language expert. Two training sessions concerning the objective of the study, the study instruments, the consent form, how to interview, and the data collection procedure were given to the recruited data collectors. The data collection procedure was supervised closely. Supervision

was made on a daily basis to check completeness and consistency. Prompt clarifications were given whenever ambiguity occurred during data collection. The collected data were rechecked for completeness by the principal investigator.

#### 6. Data Processing and Analysis

After the data were collected via the Kobo toolbox, they were exported into SPSS software version 27 for analysis. Frequency distribution tables were used to describe some variables. A Hosmer–Lemeshow goodness-of-fit test was used to assess multicollinearity, and it was found that the variance inflation factor (VIF) was 2, which suggested that the model's predictions were well calibrated and that the model fit the data well. Bivariable and multivariable logistic regression were employed to test the associations between the dependent and independent variables. In the bivariable analysis, a P value of <0.25 was used to select candidate variables for multivariable analysis. In multivariable analysis, a P value of less than 0.05 was used to determine the statistical significance of the association, and an adjusted odds ratio (AOR) with a 95% confidence interval was used to determine the presence, strength, and direction of association between covariates and the outcome variable.

#### 7. Results

##### 7.1. Sociodemographic Characteristics of the Respondents

This study included a total of 177 participants, which included 59 drug-resistant TB patients (cases) and 118 drug-susceptible TB patients (controls), making a response rate of 100%. The majority of participants in both groups were 25 years of age or older, with male accounting for 40 (67.8%) of case, and 65 (55.1%) of the control group. The study participants ranged in age from 10-49 years, with a median age of 30 years (IQR ± 19.5). The most common occupation was farming overall, and there was a clear disparity in educational attainment, with 13 (22.8%) of the cases and 44 (77.2%) of the controls lacking any formal education. There was also variation in place of residence, with 63 (53%) of the controls living in rural areas and 37 (62%) of the cases living in rural areas. Similarly, the majority 34 (57.6%) of participants from cases and 73 (61.9%) from controls were married. Finally, over half of the cases 33 (55.9%) and more than one-third of the controls 43 (36.4%) reported earning less than 1500 ETB, indicating economic disparity (**Table 1**).

Variable	Category	Case (%)	Control (%)
Sex	Female	19 (32.2)	53 (44.9)
	Male	40 (67.8)	65 (55.1)
Age	Below 15 years	7 (53.8)	6 (46.2)
	15–24 years	21 (40.4)	31 (59.6)
	25 and older	31 (27.7)	81 (72.3)
Occupation	Farmer	15 (25.4)	29 (24.6)
	Housewife	11 (18.6)	27 (22.9)
	Merchant	9 (15.3)	34 (28.8)

	Other	24 (40.7)	28 (28.7)
Educational status	No formal education	13 (22.8)	44 (77.2)
	Primary	28 (37.8)	46 (62.2)
	Secondary and above	18 (39.1)	28 (60.9)
Marital status	Single	22 (37.3)	28 (23.7)
	Married	34 (57.6)	73 (61.9)
	Divorced	3 (5.1)	13 (11.0)
	Widowed	0 (0.0)	4 (3.4)
Religion	Protestant	47 (79.7%)	75 (63.6%)
	Orthodox	11 (18.6%)	30 (25.4%)
	Muslim	1 (1.7%)	11 (9.3%)
	Catholic	0 (0.0%)	2 (1.7%)
Residence	Rural	37 (62.7)	63 (53.4)
	Urban	22 (37.3)	55 (46.6)
Monthly income in ETB	Below 1500	33 (55.9)	43 (36.4)
	1500–3000	12 (20.3)	19 (16.1)
	Above 3000	14 (23.7)	56 (47.5)
ETB: Ethiopian Birr			

**Table 1: Sociodemographic Characteristics of TB Patients Receiving Treatment During the study of Determinants of Drug-Resistant Tuberculosis, Gedeo Zone Healthcare Facilities, 2025 (n=177)**

## 7.2. Behavioural and Social Characteristics of the Study Participants

In this study, the majority of 54 (91.5%) of the case, and 106 (89.8%) of the control did not have a history of smoking, while alcohol consumption varied, with controls using alcohol more frequently 37 (31.4%) than did cases 12 (20.3%). Similarly, only 21 (17.8%) of the controls and 4 (6.8%) of the cases reported having a

history of chat chewing. With respect to awareness, more than half 33 (55.9%) of the cases and 64 (54.2%) of the controls) of both groups did not hear about DR-TB. However, the majority of the respondents 53 (89.8%) of the cases and 85 (72.6%) of the controls did not receive counselling about DR-TB. Regarding social factors, 20 (33.9%) of the cases and 74 (62.7%) of the controls reported experiencing social stigma (**Table 2**).

Variable	Category	Case (%)	Control (%)
History of smoking	No	54 (91.5)	106 (89.8)
	Yes	5 (8.5)	12 (10.2)
History of alcohol drinking.	No	47 (79.7)	81 (68.6)
	Yes	12 (20.3)	37 (31.4)
History of chewing chat	No	55 (93.2)	97 (82.2)
	Yes	4 (6.8)	21 (17.8)
Ever heard about DR-TB	No	33 (55.9)	64 (54.2)
	Yes	26 (44.1)	54 (45.8)
Ever got counselling about DR-TB	No	53 (89.8)	85 (72.6)
	Yes	6 (10.2)	32 (27.4)
Social stigma	No	39 (66.1)	44 (37.3)
	Yes	20 (33.9)	74 (62.7)
History of drug interruptions	No	43 (72.9)	95 (80.5)
	Yes	16 (27.1)	23 (19.5)
Reason for drug interruption	Forget to take	3 (18.8)	12 (52.2)
	Side effect	1 (6.3)	2 (8.7)

	Symptoms resolved	12 (75.0)	9 (39.1)
DR-TB: Drug-Resistant Tuberculosis			

**Table 2: Behavioral and Social Characteristics Of the Study Participants During the Study of Determinants of Drug-Resistant Tuberculosis, Gedeo Zone Healthcare Facilities, 2025 (n=177)**

### 7.3. Environmental Characteristics of the Study Participants

Regarding family size, over half of the cases 29 (50.9%) had only one to two family members, whereas 29 (26.6%) of the controls did. The majority of the controls 81 (71.7%) resided in homes with two or more rooms, whereas 33 (55.9%) of the cases did. Almost all cases 55 (93.2%) and controls 97 (84.3%) had in a house which has windows. 49 (83.1%) of the cases and 36 (30.5%) of the

controls did not have a history of contact with DR-TB patients, and 34 (28.8%) of the controls were not sure of their contact status. Finally, the case group was relatively closer to healthcare facilities, with 50 (84.7%) of the cases were living within one hour of a healthcare facility, compared with 75 (63.6%) of the controls (**Table 3**).

	Category	Case (%)	Control (%)
Number of family members	1–2 people	29 (50.9)	29 (26.6)
	3–4 people	16 (28.1)	46 (42.2)
	5–6 people	11 (19.3)	28 (25.7)
	7 and more	1 (1.8)	6 (5.5)
Number of room in living home	Only one	26 (44.1)	32 (28.3)
	Two or more	33 (55.9)	81 (71.7)
Presence of windows in rooms	No	4 (6.8)	18 (15.7)
	Yes	55 (93.2)	97 (84.3)
Habit of opening windows	No	20 (36.4)	34 (35.1)
	Yes	35 (63.6)	63 (64.9)
History of contact with DR-TB patient	I don't know	1 (1.7)	34 (28.8)
	No	49 (83.1)	36 (30.5)
	Yes	9 (15.3)	48 (40.7)
Distance of healthcare facility from living area	Less than 1 hour	50 (84.7)	75 (63.6)
	More than 1 hour	9 (15.3)	43 (36.4)
DR-TB: Drug-resistant tuberculosis			

**Table 3: Environmental Characteristics of the Study Participants During the Study of Determinants of Drug-Resistant Tuberculosis, Gedeo Zone healthcare facilities, 2025 (n=177)**

### 7.4. Clinical Characteristics and Comorbidities of the Study Participants

Among the cases, rifampicin-resistant TB (RR-TB) was the most prevalent form of drug-resistant TB, accounting for 42 (71.2%) of the cases. A considerable proportion 18 (30.5%) of the cases and 66 (55.9%) of the controls had a history of previous TB treatment. Relapsed cases accounted for 18 (30.5%) of the cases and 13 (11.0%) of the controls. The majority 51 (86.4%) of cases

and 96 (81.4%) of the controls had negative HIV serostatus, and in both groups, the majority of participants did not report having diabetes mellitus, cardiovascular disease, or chronic lung disease concurrently. There was a noticeable difference in nutritional status between the cases and the controls. 94 (79.6%) of the controls maintained a normal nutritional status, whereas only 28 (47.5%) of the patients were found to have a normal nutritional status (Table 4).

Variable	Category	Case (%)	Control (%)
Types of Drug-Resistant TB cases	HR-TB	4 (6.8)	0 (0.0)
	MDR-TB	13 (22.0)	0 (0.0)
	RR-TB	42 (71.2)	0 (0.0)
History of previous TB treatment	No	41 (69.5)	52 (44.1)

	Yes	18 (30.5)	66 (55.9)
History of hospitalization	No	45 (76.3)	87 (73.7)
	Yes	14 (23.7)	31 (26.3)
Category of the patient	New	33 (55.9)	91 (77.1)
	Relapse	18 (30.5)	13 (11.0)
	Return after default	8 (13.6)	14 (11.9)
HIV sero-status of the patient	Negative	51 (86.4)	96 (81.4)
	Positive	8 (13.6)	13 (11.0)
	Unknown	0 (0.0)	9 (7.6)
Have concomitant DM	No	56 (94.9)	107 (91.5)
	Yes	3 (5.1)	10 (8.5)
Cardiovascular diseases (HTN, HF, Stroke)	No	56 (94.9)	107 (91.5)
	Yes	3 (5.1)	10 (8.5)
Concomitant lung diseases (Asthma, COPD, other)	No	58 (98.3)	114 (96.6)
	Yes	1 (1.7)	4 (3.4)
Nutritional status (Based on age appropriate anthropometry)	Normal	28 (47.5)	94 (79.6)
	Mild undernutrition	15 (25.4)	16 (13.6)
	Moderate undernutrition	11 (18.6)	5 (4.2)
	Severe undernutrition	5 (8.5)	3 (2.5)

**Table 4. Clinical Characteristics and Comorbidity Condition of the Study Participants During the Study of Determinants of Drug-Resistant Tuberculosis, Gedeo Zone Healthcare Facilities, 2025 (N=177).COPD: Chronic Obstructive Pulmonary Disease; DM: Diabetes Mellitus; Dr-Tb: Drug-Resistant Tuberculosis; Hf: Heart Failure; Hiv: Human Immunodeficiency Virus; Htn: Hypertension**

### 7.5. Determinants of Drug-Resistant Tuberculosis

The associations of each independent variable with the outcome variable were assessed separately via binary logistic regression, and variables with  $p < 0.25$ , such as age, educational status, area of residence, history of alcohol consumption, previous TB treatment, history of anti-TB drug interruption, DR-TB counselling, and social stigma, were considered candidates for the final model. After all the assumptions of logistic regression were confirmed to be fulfilled, all the variables with  $p < 0.25$  in the bivariate analysis were tested in the final model. Then, variables with a significance level of  $p < 0.05$  were considered significant determinants of DR-TB. After adjusting for other covariates, five variables, educational status, area of residence, previous TB treatment, DR-TB counselling, and social stigma, were found to be significantly associated with DR-

TB in this study area. Accordingly, the odds of developing DR-TB were 3.37 times greater for participants without formal education than for those with secondary education or higher (AOR = 3.370; 95% CI: 1.09, 10.416). Similarly, living in an urban area was also linked to higher odds; the odds of DR-TB were 2.54 times higher for urban dwellers than for rural dwellers (AOR = 2.535; 95% CI: 1.067, 6.025). One important protective factor was receiving counselling regarding DR-TB; those who received counselling had a 72% lower chance of contracting DR-TB than those who did not (AOR = 0.281; 95% CI: 0.102, 0.777). Moreover, those who had previously received TB treatment had 3.34 times greater odds of developing DR-TB (AOR = 3.340; 95% CI: 1.574, 7.087). Finally, the likelihood of developing DR-TB was considerably increased by social stigma (AOR = 3.268; 95% CI: 1.562, 6.835) (Table 5).

Variable	Case (%)	Control (%)	COR (95% CI)	AOR (95% CI)
<b>Age in year</b>				
Below 15 years	7 (53.8)	6 (46.2)	1	1
15–24 years	21 (40.4)	31 (59.6)	1.77 (0.886, 3.534)	1.483 (0.605, 0.632)
25 and above	31 (27.7)	81 (72.3)	0.58(0.171, 1.973)	0.432 (0.093, 2.003)
<b>Educational status</b>				
Secondary and above	18 (39.1)	28 (60.9)	1	1
Primary	28 (37.8)	46 (62.2)	1.056 (0.496, 2.249)	1.973 (0.747, 5.210)
No formal education	13 (22.8)	44 (77.2)	2.176 (0.924, 5.123)	3.370 (1.09, 10.416)*

<b>Residence area</b>				
Rural	37 (62.7)	63 (53.4)	1	1
Urban	22 (37.3)	55 (46.6)	1.468 (0.774 – 2.784)	<b>2.535 (1.067, 6.025)*</b>
<b>History of drinking alcohol</b>				
No	47 (79.7)	81 (68.6)	1	1
Yes	12 (20.3)	37 (31.4)	1.789 (0.850 – 3.764)	1.634 (0.610, 4.375)
<b>Ever got counselling about DR-TB</b>				
No	53 (89.8)	85 (72.6)	1	1
Yes	6 (10.2)	32 (27.4)	0.301 (0.118 – 0.767)	<b>0.281 (0.102, 0.777)*</b>
<b>History of previous TB treatment</b>				
No	41 (69.5)	52 (44.1)	1	1
Yes	18 (30.5)	66 (55.9)	2.891 (1.490 – 5.609)	<b>3.340(1.574, 7.087)*</b>
<b>History of drug interruptions</b>				
No	43 (72.9)	95 (80.5)	1	1
Yes	16 (27.1)	23 (19.5)	0.651 (0.313 – 1.354)	<b>0.556 (0.235, 1.315)</b>
<b>Social stigma</b>				
No	39 (66.1)	44 (37.3)	1	1
Yes	20 (33.9)	74 (62.7)	0.305 (0.158 – 0.587)	<b>3.268 (1.562, 6.835)*</b>
AOR: Adjusted Odds Ratio; COR: Crude Odds Ratio; DR-TB: Drug-Resistant Tuberculosis; TB: Tuberculosis*; a Significant Variable with a p value < 0.05				

**Table 5. Bivariate and Multivariate Analyses Were Performed During the Study of Determinants of Drug-Resistant Tuberculosis in Gedeo Zone Healthcare Facilities, 2025 (n=177).**

## 8. Discussion

This study assessed determinants of drug-resistant tuberculosis among patients receiving treatment in Gedeo Zone health facilities in southern Ethiopia. Five factors, namely, educational status, urban residency, counselling on DR-TB, previous TB treatment, and social stigma, were found to be statistically significant determinants of DR-TB. These results demonstrate that the occurrence of DR-TB is multifactorial and influenced by a combination of behavioral, environmental, sociodemographic, and clinical factors rather than being attributed to a single cause.

This study revealed that educational status is a significant determinant of drug-resistant tuberculosis (DR-TB). Individuals with no formal education had 3.37 times greater odds of developing DR-TB than those with at least a secondary education. This finding is consistent with a number of prior studies that reported that a lack of formal education was a significant risk factor for DR-TB [7-16]. According to those studies, the risk of developing DR-TB was 2.2–4.4 times higher for those without formal education than for their counterparts. The consistency of findings across studies may be accounted for by the role of education in health literacy, awareness, and treatment adherence. The importance of early health-seeking behaviour, appropriate medication use, and ongoing adherence to long-term TB treatment regimens are more likely to be understood by those with higher levels of education, whereas those with lower levels of education may struggle to understand health information, which could result in delayed diagnosis, inappropriate medication use, and a greater risk of drug resistance.

Furthermore, socioeconomic position and education are strongly correlated. People with higher levels of education typically have better employment, incomes, and living conditions, which makes it easier for them to obtain high-quality healthcare. Each of these factors can lower the chance of contracting tuberculosis and the development of drug-resistant strains.

Urban residents were 2.54 times more likely to have DR-TB than rural residents were in this study area. This finding contrasts with several studies that reported that rural residents are 2.54–3 times more likely to develop DR-TB than urban residents are [17-19]. This discrepancy is likely due to differences in healthcare access, environmental conditions, and demographic characteristics. As illustrated by several studies and reports, the Gedeo Zone has a high population density, and the urban area of the zone has an even higher population density, which could account for this discrepancy [20-21]. Higher population densities can facilitate the transmission of DR-TB due to the crowded living conditions and frequent social interactions that are characteristic of urban settings. Despite the fact that people residing in rural areas have less access to healthcare, rural areas may have lower transmission rates because of their less crowded populations and less social interaction. The diagnostic and reporting rates of medical conditions are also better in urban areas, which could explain the greater number of DR-TB patients in urban regions than in rural regions. In this study, counselling about DR-TB was identified as a strong protective factor, with a 72% lower odd of DR-TB in participants who received counselling from healthcare providers than in those who did not. This finding

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is consistent with the finding that patients who did not receive counselling had a fivefold greater risk of developing DR-TB [22,23]. This consistency of findings may reflect the fact that counselling educates patients on the need for adherence to their drug regimen and treatment interruption, which reduces the risk of resistance, while building patient-provider trust and psychological support, which also play important roles in effective treatment. In general, the consistency of findings reinforces the necessity for appropriate counselling as part of tuberculosis control.

This study also revealed that previous TB treatment was a significant risk factor for DR-TB, which was 3.34 times greater than the risk for people who did not have a history of previous TB treatment. Previous TB treatment has been identified as one of the best predictors of DR-TB in several other studies, and in some studies, the risk is even greater (up to 11.8 times greater) [24-26]. It is scientifically plausible that lung cavities and fibrotic tissue, which are commonly found in patients after TB episodes, serve as reservoirs of Mycobacterium, as anti-TB drugs poorly penetrate these areas, allowing bacilli to survive and evolve, encouraging the development of mutations that are resistant to these drugs. Strengthening the follow-up of previously treated patients is essential to prevent both the emergence of new resistant strains and the spread of existing strains.

This study also demonstrated that social stigma was a significant predictor of drug-resistant tuberculosis (DR-TB). The participants who experienced stigma had 3.27 times higher odds of developing DR-TB than did those who did not. This finding is in line with other studies in other settings that identified stigma as one of the most significant predictors of DR-TB, with adjusted odds ratios ranging from 5.1-8.9 [11-27]. These similarities among studies demonstrate that stigma is a critical component of the epidemiology of DR-TB because it often leads to nonadherence to treatment, hiding of illness, and delays in seeking care, all of which contribute to the emergence and transmission of resistant forms of the disease. Social stigma can lead patients to delay or avoid seeking care, stop their drugs, or hide their illness, all of which facilitate the emergence and spread of resistant forms of the disease. Thus, control of TB and DR-TB will require more than just improvements in diagnostic and treatment regimens; efforts must include community education, patient empowerment, and a reduction in discrimination to increase adherence to treatment and reduce the burden of drug resistance.

### 9. Limitations of the Study

One of the study's weaknesses could be attributed to its limited sample size. This limitation may be reflected in the large confidence intervals for factors that showed relationships and those that did not. A large sample size, which requires more resources, might be necessary for an exact assessment. Furthermore, because the data were collected at a health facility, participants may have given information in support of hospital staff out of frustration, which could have resulted in social desirability bias.

### 10. Conclusion

This study identified multiple significant factors contributing to the development of drug-resistant tuberculosis (DR-TB), including social stigma, previous TB treatment, lack of formal education, urban residence, and insufficient counselling, emphasizing the necessity of integrated multidimensional interventions that combine counselling, psychosocial support, and community engagement, which are essential for enhancing treatment adherence and reducing stigma. Furthermore, close monitoring of patients with a history of TB treatment and targeted interventions in urban settings are critical to effectively address drug-resistant tuberculosis (DR-TB).

Addressing these challenges requires multifaceted interventions. Efforts should focus on launching sustained, multiplatform public health campaigns (using local radio, community meetings, and religious institutions) that emphasize that TB is a curable disease and not a moral failure or a curse. Testimonials from successfully treated patients can be used to humanize the condition. Moreover, engaging respected community and religious leaders as "TB champions" to speak openly about TB, counter misinformation, and encourage community support for affected individuals and families is essential to create awareness in the community to prevent disease transmission from individuals to individuals. The implementation of enhanced adherence support for all first-time TB patients through directly observed therapy (DOT) short course, ideally by a trained family member or community health worker, will help patients who are not susceptible to MDR-TB. The goal is to ensure a 100% cure rate for new cases to prevent the emergence of resistance. Finally, implementing a standardized, simple counselling checklist for all patients and their treatment supporters is an essential asset in preventing the disease. Key messages should be repeated, and understanding should be verified through "teach-back" methods (where the patient explains the information in their own words) to enhance their knowledge about the nature of the disease.

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### Author Contributions

Mebrat Mengesha, Alemselem Zebdewos, Taye Gari and Alemayehu Tadesse all contributed significantly and equally to the work reported, whether in the study design, execution, acquisition of data, analysis, and interpretation, or in all of these areas; they also participated in the article's drafting, revision, and critical review; endorsed the final version for publication; and decided which journal to submit it to.

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## Declarations

### Ethical Approval and Consent to Participate

All procedures used in this study adhered to the ethical principles of the Declaration of Helsinki for medical research with human beings. The ethical review committee of Hawassa University's College of Medicine and Health Science provided approval for this study. An official letter was given to the MDR-TB Diagnostic Centre at Dilla University College of Medicine and Health Science. Written informed consent was obtained from all the participants and from the legal guardians of the participants who were illiterate and minors. The information collected from the respondents had never been used for purposes other than this study. The confidentiality and privacy of the information were ensured.

### Clinical Trial Number

Not applicable.

### Consent for Publication

Not applicable.

### Competing Interests

The authors declare that they have no competing interests.

### Conflict of Interest

The authors declare that there are no conflicts of interest among the authors or between the authors and institutions.

### Data Availability

The datasets generated and/or analysed during the current study are not publicly available [as it is the word of the participants, it may contain the privacy of an individual or maintain the privacy and confidentiality of the participants but are available from the corresponding author upon reasonable request.

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