BMJ Open Respiratory Research

Determinants of multidrug-resistant tuberculosis among adults undergoing treatment for tuberculosis in Tigray Region, Ethiopia: a case–control study

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To cite: Zereabruk K, Kahsay T, Teklemichael H, *et al*. Determinants of multidrug-resistant tuberculosis among adults undergoing treatment for tuberculosis in Tigray Region, Ethiopia: a case–control study. *BMJ Open Respir Res* 2024;**11**:e001999. doi:10.1136/bmjresp-2023-001999

Received 15 August 2023
Accepted 19 April 2024

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ABSTRACT

Background Multidrug-resistant tuberculosis is a type of tuberculosis that is resistant to at least the first-line antituberculosis drugs namely, rifampicin and isoniazid. However, most of these studies were limited only to a single hospital. Therefore, this study aimed to identify the determinants of multidrug-resistant tuberculosis among adults undergoing treatment for tuberculosis in the Tigray region of Ethiopia.

Methods Hospital-based unmatched case–control study was conducted from 1 April 2019 to 30 June 2019. A simple random sampling method was used to select the required sample size. Variables at a p value less than 0.25 in bivariate analysis were entered into a multivariable analysis to identify the determinant factors of multidrug-resistant tuberculosis. Finally, the level of significance was declared at p<0.05.

Results Rural residence (adjusted OR (AOR) 2.54; 95% CI 1.34 to 4.83), HIV (AOR 4.5; 95% CI 1.4 to 14.2), relapse (AOR 3.86; 95% CI 1.98 to 7.5), return after lost follow-up (AOR 6.29; 95% CI 1.64 to 24.2), treatment failure (AOR 5.87; 95% CI 1.39 to 24.8) were among the determinants of multidrug-resistant tuberculosis.

Conclusion Rural residence, HIV, relapses, return after lost follow-up and treatment failure were the identified determinant factors of multidrug-resistance tuberculosis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Tuberculosis (TB) is one of the leading causes of morbidity, the fourth cause of hospital admission and the second cause of hospital death in Ethiopia and the prevalence of multidrug-resistant TB (MDR-TB) was found to be 18.5% in the Tigray region.

WHAT THIS STUDY ADDS

⇒ The previous studies were limited only to a single hospital but our study was conducted in the whole of Tigray region and we have used Gene-Xpert to select cases and controls, unlike other studies.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings would be used as input for policymakers to improve MDR-TB treatment and prevention in Ethiopia.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* (MTB). It usually affects the lungs but can also affect other organs.[1] Multidrug-resistant TB (MDR-TB) is a form of TB that can resist at least two of the most effective anti-TB drugs, namely rifampicin and isoniazid, making it much harder to treat.[2] When an individual who has no history of first-line TB treatment develops MDR-TB, it is termed primary. When insufficient treatment leads to the selection of spontaneously resistant strains (ie, drug resistance is acquired), the disease is termed secondary MDR-TB.[3] Unless the individuals infected with resistant strains of MTB are treated appropriately, resistant strains will continue to spread in the community, accelerating the epidemic.[4] Both primary and retreatment or secondary cases of MDR-TB have already been reported in Ethiopia.[5]

MDR-TB has continued to be a challenge for TB control globally.[6 7] According to 2016 WHO report, 600 000 people were newly eligible for MDR-TB treatment.[8] Although MDR-TB is a growing concern in Africa where limited resource exists, it is largely under-reported.[9 10] According to a 2010 WHO report, the number of MDR-TB cases was rising in Africa.[2] The prevalence varies among countries and regions while high prevalence has been observed in developing countries.[6] Sub-Saharan Africa represents 14% of the global burden of new MDR-TB cases.[9] Seven countries including Ethiopia in Africa (new/retreatment% accordingly) Angola (2.6/18%), DR Congo (2.2/17%), Kenya (1.3/9.4%), Nigeria (4.3/25%), Somalia (8.7/47%) and Zimbabwe (4.6/14%) are

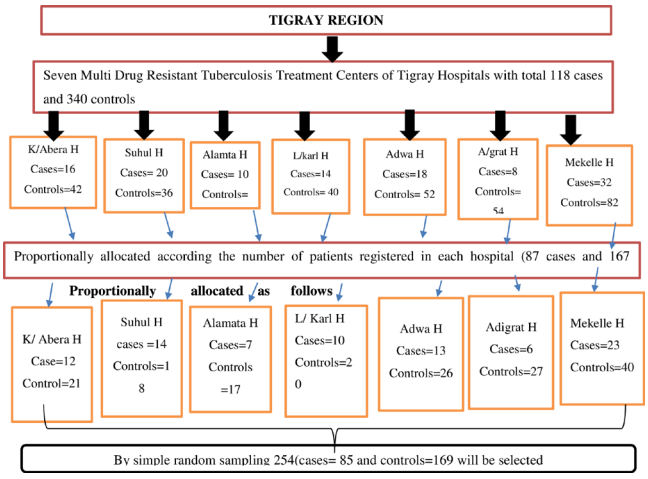

Figure 1 Sampling procedure for MDR-TB among adults undergoing treatments for TB in Tigray Region, Ethiopia, 2019. MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

also listed among the 30 high MDR-TB burden countries in the world.[11] WHO in 2016 listed Ethiopia as 8th out of 30 high MDR-TB burden countries in the world with a prevalence of 2.7% (1.5%–4.0%) in newly and 14.0% (3.6%–25.0%) in previously treated patients.[12]

MDR-TB is a cause of death for more than 240 000 deaths annually.[8] Patients infected with MDR strains are less likely to become cured.[13] The cure rate for MDR-TB is poor ranging from 6% to 59%.[14] According to the Ministry of Health statistics, TB is one of the leading causes of morbidity, the fourth cause of hospital admission and the second cause of hospital death in Ethiopia.[15]

The treatment of MDR-TB with second-line drugs is long which is more than 2 years, complex process and has a considerable rate of adverse effects and making MDR-TB more costly and more difficult to manage than drug-susceptible TB.[2 16] The cost of drugs alone for treating the average MDR-TB patient is 50–200 times higher than for treating a drug-susceptible TB patient.[17] The cost per patient treated is usually in the range of US$100–US$1000 for drug-susceptible TB and US$2000–US$20 000 for MDR-TB.[8]

MDR-TB mostly affects the poor, illiterate, productive age group and immune compromised individuals.[7] Inadequate treatment (due to shortage of the drug, the increasing cost of drug and physician errors), inadequate adherence (such as poor compliance, alcoholism, drug addiction, length of treatment and adverse drug reactions) and poor infection control have been also identified contributing factors for the occurrence of MDR-TB.[18–20] In Ethiopia, the low socioeconomic status of the people, high prevalence of infectious diseases and limited access to well-equipped healthcare facilities worsen the effect of MDR-TB.[2]

Globally, the prevention of new infections of *MTB* and their progression to TB disease is critical to reduce the burden of disease and death caused by TB and to achieve the end TB Strategy targets set for 2030 and 2035. Health interventions have been tried for latent TB infection, prevention of transmission of *MTB* through infection prevention and control, and vaccination of children with the bacilli Calmette-Guérin vaccine.[21] Ethiopia has also designed a strategy to provide culture and drug susceptibility testing services at least to all MDR-TB suspected cases and apply directed observed therapy (DOT) for first-line anti-TB medications. However, MDR-TB is becoming a major challenge of the TB control programme in Ethiopia and is continuing a public burden in our country.[22–24]

There are limited numbers of MDR-TB studies in different regions of Ethiopia.[25–27] However, most of these studies are restricted only to a single hospital, have inconsistent results and there is no published information regarding MDR-TB in the Tigray region. Thus, this study will be used as baseline data or input on determinants of MDR-TB among adult patients undergoing first-line drug treatment in MDR-TB treatment centres of Tigray Hospitals. The findings would be used as input for policymakers to improve MDR-TB treatment in Ethiopia.

Identifying determinant factors in a given region has a substantial role in the reduction of mortality and morbidity by collaboratively preventing the infection. Therefore, for regional health bureau, this research will be used as source of information to identify the determinant factors of MDR-TB and to develop a strategy for the factors and to tackle MDR. Therefore, the main aim of this study was to identify the determinants of MDR among adults undergoing treatment for TB in Tigray region, Ethiopia.

METHODS AND MATERIALS

Study area and period

The study was conducted in Tigray regional state public hospitals. Tigray is found in the northern part of Ethiopia. Tigray's surface Area is 53 638 km² and according to the 2007 population and housing census projection, Tigray population size is 6.8 million.[28] Tigray Regional State has two comprehensive specialised hospitals, 15 general hospitals, 22 primary hospitals and 223 health centres. From the 15 general hospitals, 7 hospitals namely Kahsay Abera, Suhul, Adwa, Adigrat, Mekelle, Lemlem Karl and Alamata are giving MDR-TB treatment services. There were 118 registered MDR-TB patients in the Tigray region. Cases were all registered MDR-TB patients who were confirmed by gene xert and attending the MDR-TB treatment centre hospitals of Tigray. In this study, controls were all confirmed non-MDR-TB patients by gene xpert who are registered and taking first-line anti-TB medications. Critically ill (unconscious) patients who could not respond were excluded from the study. The study was conducted from 1 April 2019 to 30 June 2019 in MDR-TB treatment centre hospitals of Tigray.

Table 1 Sociodemographic characteristics of MDR-TB in Tigray Region, Ethiopia, 2019 (n=254)

	Cases (n=85		Controls (n=169)	
Variables	Number	Percentage	Number	Percentage
Age				
18–25	23	27.1	37	21.9
26–45	44	51.8	93	55
>45	18	21.2	39	23.1
Sex				
Male	55	64.7	99	58.6
Female	30	35.3	70	41.4
Religion				
Orthodox Christian	76	89.4	157	92.9
Muslim	9	10.6	12	7.1
Occupation				
Farmer	26	30.6	49	29
Merchant	10	11.8	32	18.9
Government employer	7	8.2	14	8.3
Unemployed	29	34.1	40	23.7
Others*	13	15.3	34	20.1
Family size				
1–3	26	30.6	57	33.7
4–6	49	57.6	91	53.8
7–11	10	11.8	21	12.4
Marital status				
Single	32	37.6	52	30.8
Married	37	43.5	78	46.2
Divorced/widowed	16	18.8	39	23.1
monthly income				
Up to 500	10	11.8	14	8.3
501–1500	48	56.5	94	55.6
1501–2000	13	15.3	18	10.7
>2001	14	16.5	43	25.4
Number of rooms				
1	32	37.6	70	41.4
2–3	40	47.1	83	49.1
≥4	13	15.3	16	9.5
Presence of widows				
No	20	23.5	40	23.7
Yes	65	76.5	129	76.3
number of windows (n=65)				
1	30	46.2	46	35.7
2–3	29	44.6	67	51.9
≥4	6	9.2	16	12.4
Open window				
No	9	13.8	19	14.7
Yes	56	86.2	110	85.3

*Others in occupation include private employees, students, daily worker and pensioned.
MDR-TB, multidrug-resistant tuberculosis.

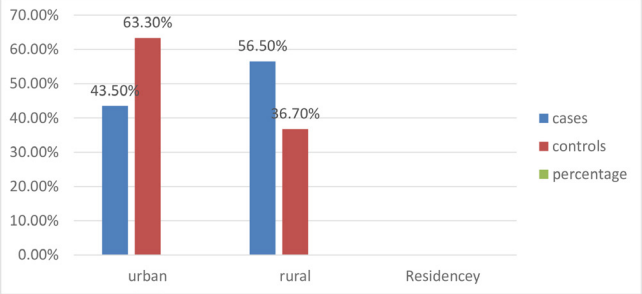

Figure 2 Residence of MDR-TB among adults undergoing treatment for tuberculosis In Tigray, Ethiopia, 2019. MDR-TB, multidrug-resistant tuberculosis.

Patient and public involvement

We did not involve patients or the public in the design, conduct, reporting or dissemination plans of our research.

Study design

A hospital-based unmatched case–control study was conducted.

Study population

The study populations for cases were all MDR-TB patients undergoing treatment in the selected hospitals during the data collection period. The study population for controls was all TB patients (not MDR-TB) undergoing treatment for TB in the selected hospitals during the data collection period.

Sample size determination and sampling technique

Sample size determination

The required sample size was determined by using the Epi-Info V.7.2.2.12 from the previous study conducted in Ethiopia. The estimated sample size was determined based on the following assumptions: a CI of 95% at the power of 80%, with a ratio of 1:2 (case to control). Finally, by comparing the three results, the first variable (no job)[29] that brings the largest sample size was selected with a total sample size of 242 by adding a 5% non-response rate the total sample size was 254 (85 and 169 controls) (figure 1).

Sampling techniques and procedures

First, the sample size was allocated proportionally to the seven MDR-TB treatment centres of Tigray according to the number of patients registered to take the treatment. Then a frame of MDR-TB patients enrolled in second-line drug treatment at MDR treatment centres of Tigray was created using the medical registration number. Finally, a simple random sampling technique was used to select the MDR-TB cases. MDR-TB patients enrolled in the second line drug at MDR treatment centre hospitals of Tigray were taken as cases and a simple random sampling technique was used to include 85 study participants from the list of MDR-TB patients' registration book. 169 Controls were also selected by a simple random sampling technique from the TB registration book in similar hospitals.

Data collection tools and procedures

Primary data were collected by face-to-face interview using pretested structured questionnaires, whereas secondary data were collected by reviewing patient medical charts/registration logs using checklists for the corresponding study participants. Seven trained BSc nurses were employed to conduct interviews with the participants and review the corresponding records. Three senior BSc nurse supervisors were assigned to supervise the whole data collection process during the data collection period. The questionnaire contained sociodemographic-related factors, behavioural-related factors and clinical-related factors. The data collection period was from 1 April 2019 to 30 June 2019. The dependent variable is divided into two, MDR-TB and non-MDR-TB. The independent variables included the sociodemographic variables (age, sex, religion, socioeconomic status/income, education, occupation, marital status, living residence, family size, the number of rooms in the patient's household and the number of windows), clinically related variables (HIV status, history of contact with known TB patient, history of contact of with known TB patient, another underlying/chronic disease, number of TB episodes TB, outcome, history of interruption the first-line anti-TB, DOT, encountered side effects, category of TB, and duration of first-line treatment) and behavioural-related variables (prison status, alcohol consumption and cigarette smoking). Data on sociodemographic characteristics, behavioural characteristics and some clinical characteristics were collected through face-to-face interviews. The remained clinical characteristics were collected through the review of the patient records and registration books.

Data quality assurance

Data quality was ensured by giving 2 days of training for data collectors and supervisors and by providing supervision during the data collection period. First, the questionnaire was adapted from a published paper in English form,[29] then translated into Tigrigna (local language) and back-translated into English to ensure its consistency. Each questionnaire was checked for completeness, and missed values were then manually cleaned up on such indications before leaving the study area. The questionnaire was pretested on 5% of other patients who did not participate in the study for completeness and appropriateness to the local context. Based on the findings, necessary amendments have been made. Every questionnaire was checked by the principal investigator on the spot.

Data processing and analysis

The data were coded and entered into Epi data manager V.4.4.3.1 and then exported to SPSS V.20 for further statistical analysis. Descriptive statistics such as frequencies, percentages, median and IQR were computed. Finally,

Table 2 Behavioural factors of MDR-TB among adults undergoing treatment for TB in Tigray, Ethiopia, 2019 (N=254)

Variables	Cases (n=85)		Controls (n=169)	
	Number	Percentage	Number	Percentage
Drinking alcohol				
No	67	78.8	127	75.1
Yes	18	21.2	42	21.2
Cigarette smoking				
No	78	91.8	152	89.9
Yes	7	8.2	17	10.1
Lived with cigarette smoker				
No	79	92.9	149	88.2
Yes	6	7.1	20	11.8
Imprison status				
No	72	84.7	148	87.6
Yes	13	15.3	21	12.4

MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

the report was summarised and presented using, texts, tables and figures. A binary logistic regression model was used to test the association between independent and dependent variables. All variables at p<0.25 in bivariate logistic regression were entered into a multivariable logistic regression to determine the association between a set of independent variables and the dependent variable. The OR was estimated at 95% CI to show the strength of an association and a p<0.05 was used to declare statistical significance. Model fitness was checked using Hosmer-Lemeshow goodness-of-fit which was fitted (0.436). The variance inflation factor was used to assess multicollinearity between the independent variables.

RESULTS

Sociodemographic characteristics

A total of 254 participants with 85 cases and 169 controls were included in this study with a 100% response rate.

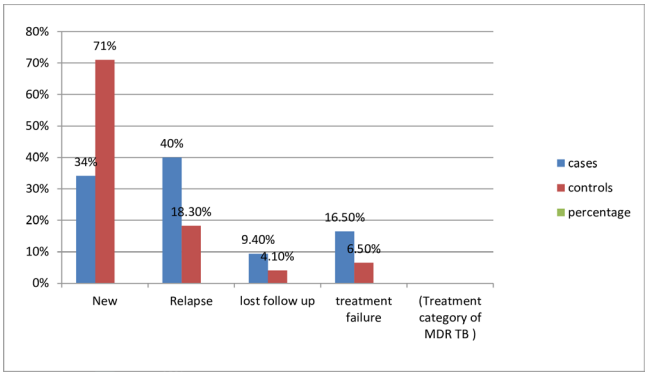

Figure 3 Treatment category of MDR-TB tuberculosis among adults undergoing treatment for TB in Tigray, Ethiopia, 2019. MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

Of the participants, 55 (64.7%) were males among cases and 99 (58.3%) were females among controls (table 1). Regarding educational status, around 34 (40%) participants among the cases and 60 (35.5%) participants among controls had no formal education, 26 (30.6%) participants among cases and 55 (32.5%) participants among controls had finished their primary school, 14 (16.5%) participants among cases and 34 (20.1%) participants among controls were secondary school, 11 (12.9%) participants among cases and 20 (11.8%) participants among controls were college and above.

Of the respondents, 62 (36.7 %) among the controls and 48 (56.5%) among the cases were living in rural residence (figure 2).

Behavioural-related factors

More than three-fourths, 67 (78.8%) cases and 127 (75.1%) controls did not drink any alcohol. Of the cases, 7 (8.2%) and 17 (10.1%) from controls were cigarette smokers (table 2).

Clinical-related factors

Of the respondents, 29 (34.1%) of cases (MDR-TB patients) and 120 (71%) of controls (TB patients) were new patients. Eight (9.4%) and 14 (16.5%) cases were returned after lost follow-up and treatment failure, respectively. Of the participants, 34 (40%) among cases and 31 (18.3%) among controls were relapse patients (figure 3).

Of the cases, 56 (65.9%) faced two or more episodes of tuberculosis and 120 (71%) among controls faced only one episode. 70 (82.4%) and 163 (96.4%) were non-reactive among cases and controls, respectively. From the participants, 15 (17.6%) among cases and 6 (3.6%) among controls were HIV reactive patients (table 3).

Table 3 Clinical-related factors of MDR-TB among adults undergoing treatment for TB in Tigray, Ethiopia, 2019 (N=254)

	Cases (n=85)		Controls (n=169)	
Variables	Number	Percentage	Number	Percentage
Number of TB episodes				
Once	29	34.1	120	71
≥2	56	65.9	49	29
Interruption first-line anti-TB treatment				
No	44	78.6	40	81.6
Yes	12	21.4	9	18.4
Reason of interruption				
Side effects	5	41.7	8	88.9
Forgetting	1	8.3	0	0
Feeling better	6	50	1	11.1
DOT				
No	6	10.7	5	10.1
Yes	50	89.3	44	89.9
Place of treatment				
Health centre	34	60.7	21	42.9
Hospital	22	39.3	28	57.1
Contact with known TB				
No	22	25.9	62	36.7
Yes	23	27.1	43	25.4
I don't remember	40	47.0	64	37.9
Contact with known MDR-TB				
No	27	31.8	97	57.4
Yes	15	17.6	4	2.4
I don't remember	43	50.6	68	40.2
Outcome of first-line TB Rx				
Cured	15	26.8	15	30.6
Completed	21	37.5	25	51.1
Lost follow-up	10	17.9	8	16.3
Failure	10	17.9	1	2
Chronic disease status				
No	78	91.8	149	88.2
Yes	7	8.2	20	11.8

DOT, directed observed therapy; MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

Determinants of MDR-TB

The bivariate logistic regression analysis showed that rural residence, TB episodes greater than or equal to two, treatment category (treatment after lost follow-up, relapse and treatment failure), HIV and history of close contact with known TB were statistically associated with development of MDR-TB. However, after multivariable logistic regression analysis rural residence, HIV, relapse, lost follow-up and treatment failure were significantly associated with MDR-TB at a p<0.05.

The odds of MDR-TB among residents were 2.6 times as compared with urban residents (adjusted OR (AOR) 2.58; 95% CI 1.4 to 4.6). The odds of being MDR-TB among HIV-reactive participants were 4.4 times as compared with HIV non-reactive participants (AOR 4.4;95% CI 1.5 to 12.6). Treatment after lost follow-up participants had a 5.4 times higher risk for MDR-TB as compared with the newly diagnosed patients (AOR 5.4;95% CI 1.69 to 17). Relapse patients had a 3.9 times higher risk for the development of MDR-TB as compared with new patients (AOR 3.86; 95% CI 1.98 to 7.5). Participants with first-line treatment failure patients were found five times more likely to develop MDR-TB as compared with new patients (AOR 5.1; 95% CI 2 to 13) (table 4).

Table 4 Determinant factors of MDR-TB among adults undergoing treatment for TB in Tigray Region, Ethiopia, 2019

Variables	Controls n (%)	Cases n (%)	COR (95% CI)	AOR (95% CI)	P value
Residence					
Urban	107 (63.3)	37 (43.5)	1	1	
Rural	62 (36.7)	48 (56.5)	2.24 (1.3 to 3.8)	**2.58 (1.4 to 4.6)***	**0.002**
Patient category					
New	120 (71)	29 (34.1)	1	1	
Relapse	31 (18.3)	34 (40)	4.5 (2.4 to 8.5)	**3.86 (1.98 to 7.5)***	**0.001**
Return after lost follow-up	7 (4.1)	8 (9.4)	4.7 (1.5 to 14.1)	**5.4 (1.69 to 17)***	**0.004**
Treatment failure	11 (6.5)	14 (16.5)	5.3 (2.1 to 12.8)	**5.2 (2 to 13)***	**0.01**
History of close contact with known TB					
No	62 (36.7)	22 (25.9)	1	1	
Yes	43 (25.4)	23 (27.1)	1.5 (0.75 to 3.0)	1.67 (0.76 to 3.6)	0.197
I don't remember	64 (37.9)	40 (47.1)	1.76 (0.94 to 3.3)	1.57 (0.78 to 3.2)	0.2
HIV status					
No	163 (96.3)	70 (82.4)	1	1	
Yes	6 (3.6)	15 (17.6)	5.8 (2.2 to 15.6)	**4.4 (1.5 to 12.6)***	**0.006**

The bold values are the determinant factors siginificantly associated with the MDR-TB.
*P<0.05 shows independent variables associated with the outcome variable and '1' indicates reference.
AOR, adjusted OR; COR, crude OR; MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

DISCUSSION

As per our knowledge, this is the first study to identify the determinants of MDR-TB among adults undergoing treatment for TB in the Tigray region of Ethiopia. There are limited numbers of MDR-TB studies in different regions of Ethiopia. However, most of these studies are restricted only to a single hospital, have inconsistent results and there is no published information regarding MDR-TB in the Tigray region. Living in a rural setting, return after lost follow-up, relapse, treatment failure and HIV were found to be significantly associated with the occurrence of MDR-TB. MDR-TB was significantly associated with residence areas; living in a rural area increased the occurrence of MDR-TB compared with living in an urban area. This is similar to the studies conducted in East Shoa, Oromia region and Amhara regional state, Ethiopia.[29–31] This might be due to the large proportion of people living in rural settings, differences in access to TB services, socioeconomy and the level of awareness about adherence to first-line TB treatment, as rural communities have poor adherence to treatment that likely leads to MDR-TB.[29] In contrast, a study conducted in southwestern Ethiopia showed that rural residents were not associated with the development of MDR-TB.[25] This might be due to the sample size difference and sociodemographic difference.

In this study, HIV was significantly associated with the occurrence of MDR-TB. This is supported by a study conducted in Oromia which found that HIV is a risk factor for the development of MDR-TB.[30] This could be due to drug malabsorption in HIV-infected patients since the patient is taking both ART and anti-TB medications, especially rifampicin and ethambutol, which can lead to drug resistance and has been shown to lead to treatment failure.[32] In contrast, HIV was not associated with the development of MDR-TB in a study conducted in southwestern and, east Shoa, Ethiopia.[25 29] This discrepancy might be due to sample size difference and the highest prevalence of HIV in Tigray region.

In this study, MDR-TB was significantly associated with return after lost follow-up (defaulting). This finding is similar to the study conducted in Brazil, Thailand and Addis Ababa, Ethiopia.[33–35] This can be explained by the increased exposure to anti-TB drugs. A study conducted in 11 countries has shown that the longer the time of exposure to anti-TB drugs, the greater the chance of occurrence of resistance.[36] This might be due to poor management of the patient, unsatisfactory patient or clinician compliance, lack of supervision of treatment and the absence of infection control measures in hospitals.[37 38] This study found that relapse was significantly associated with the occurrence of MDR-TB. This study found that relapse was significantly associated with the occurrence of MDR-TB. This finding is supported by a study conducted in Brazil.[35] In contrast, relapse was not associated with the occurrence of multidrug resistance TB in a study conducted in the Amhara regional state.[31] This difference might be due to the different selection of study participants and a relatively small proportion of relapse patients in a study conducted in the Amhara regional state.

It has been found that there is a significant association between treatment failure and the development

of MDR-TB. This finding is in line with a study that was conducted in Jimma southwest Ethiopia, Addis Ababa, Amhara regional state, Ethiopia.[31 33 39] The possible reasons behind this association could be unsatisfactory compliance by patients or clinicians, lack of supervision during the treatment, usage of improper drug regimens and inadequate or irregular drug supply that may potentiate drug resistance(.[26 40] As a strength, this study was conducted in the seven MDR-TB treatment centres and used gene-Xpert to select cases and controls which helped control selection bias compared with other studies. This study had a weakness in its recall bias since some of the information such as interruption of anti-TB, and contact history with known TB and MDR-TB patients was based on the recall of the study participants. For clinicians, enhancing health education for patients to adhere to first-line anti-TB medications since relapse, lost follow-up and treatment failure were determinant factors for the occurrence of MDR-TB, and they should invest time to explain clearly to patients what medication should be taken, how much, how often and when. The findings would be used as input for policy-makers to improve MDR-TB treatment and prevention in Tigray, Ethiopia. Future researchers better study prospective cohorts on determinants of MDR-TB and it is better to conduct community-based case–control since patients reporting to a clinic/hospital are likely to differ from people seeking alternative treatments in their homes.

CONCLUSIONS

This study identified rural residence, HIV, relapse, return after lost follow-up and treatment failure as determinant factors for the occurrence of MDR-TB.

Acknowledgements Authors thank to Mekelle University, advisors, supervisors, data collectors and study subjects.

Contributors KZ made substantial contributions to the conception, design of the work, methodology, analysis, data interpretation and wrote the final manuscript. TK and HT had equally contributed to the analysis and interpretation of the data. WA, AH, GB and GM have made substantial contribution in reviewing overall the study in analysis, interpretation of data, have drafted the manuscript and substantively revised the work. KZ takes full responsibility for the work, conduct of the study, had access to the data, and controlled the decision to publish. All authors read and approved the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval Ethical clearance was obtained from the Mekelle University College of Health Science institutional review board (IRB) (ERC 1283/2019). Official supportive letters were obtained from Tigray Regional Health Bureau and respective hospitals. Moreover, before conducting the study, the purpose and objective of the study were described to the study participants and informed consent was obtained. Respondents were allowed to refuse or discontinue participation at any time they wanted. Confidentiality was assured and maintained throughout the study period.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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