

# Risk factors for multidrug resistant tuberculosis patients in Amhara National Regional State.

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## Abstract

**Background:** Multidrug resistant tuberculosis (MDR-TB) is becoming a major threat to tuberculosis control programs in Ethiopia.

**Objectives:** To determine risk factors of MDR-TB patients in Amhara National Regional State, Ethiopia.

**Methods:** Case-control study was conducted from May 2013 to January 2014. Resistance to rifampicin and isoniazid were done molecularly using line probe assay. TB patients infected with MDR-*M.tuberculosis* and non MDR-*M.tuberculosis* strain were considered as cases and controls, respectively. Data was collected using structured questionnaire with face to face interview. Patients' clinical record review was also done. Multivariate analysis was computed to determine the risk factors of MDR-TB.

**Results:** A total of 153 MDR-TB and equal number of non MDR-TB patients' participated in the study. Patients who had TB treatment failure (AOR=13.5, CI=2.69-70), cavitations on chest x-ray (AOR=1.9, CI=1.1-3.38) and contact with MDR-TB patients (AOR=1.4, CI=0.19-0.39) were more likely to be MDR-TB patients. Low monthly income (AOR=1.1, CI=0.34-0.47), alcohol consumption (AOR=1.5, CI=0.2-0.98) and young age (AOR=2.9, CI=1.07-7.68) were the other risk factors of MDR-TB.

**Conclusions:** TB treatment failure, cavitation on chest X-ray, contact with MDR-TB patients and low socioeconomic status were important risk factors for development of MDR-TB. Therefore, strict adherence to directly observed therapy, appropriate management of TB patients and advice on the value of nutrients are helpful to control the spreading of MDR-TB.

**Key words:** Risk factors, MDR-TB, Ethiopia.

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## Introduction

Drug resistance is a major threat to tuberculosis (TB) control programs worldwide<sup>1</sup>. Multidrug resistant TB (MDR-TB) is defined as a simultaneous resistance to at least rifampicin (RMP) and isoniazid (INH)<sup>2</sup>. Patients infected with MDR strains are less likely to be cured from TB particularly if they are co-infected with HIV or suffer from other immuno suppressive diseases<sup>3</sup>.

MDR-TB is associated with a two to four fold period of treatment, psychological problems, economic wastage, poor treatment adherence and consequently treatment failure<sup>4,5,6</sup>. It is also associated with higher case fatality rates (50 - 80%) as a result of drug toxicity<sup>4,5</sup>.

Globally, 3.5% of new TB cases and 20.5% of previously treated cases are estimated to have MDR-TB<sup>7</sup>. In developing countries, due to poverty, migration and HIV infection, MDR-TB is associated with spread and persistence in high incidence<sup>4,5,6</sup>. Despite the lack of comprehensive surveillance data from Africa, MDR-TB has been recognized as an emerging public health concern. In South Africa, clusters of MDR-TB cases have been documented in institutional and community settings among HIV-infected patients<sup>8</sup>. Ethiopia is among the 27 countries with the highest TB burden in the world<sup>7</sup>. The annual TB incidence and prevalence of Ethiopia is estimated to be 247 and 470

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cases per 100,000 in 2013<sup>9</sup>. These days, drug resistant TB has become a common problem and challenge in Ethiopia<sup>7</sup>. Drug resistant TB is estimated as 1.6% and 12% among new and previously treated TB cases, respectively<sup>7</sup>.

Factors such as inadequate chemotherapy, poor drug quality, poor adherence to treatment, treatment failure, prior treatment, cavity pulmonary TB, HIV infection and diabetes accounted for the development of drug resistance in TB<sup>10,11</sup>. Of these, the most powerful predictor for the presence of MDR-TB is a previous history of treatment of TB<sup>10</sup>. Many new cases of MDR-TB develop due to error in TB management such as the use of a single drug to treat TB, the addition of a single drug to a failing regimen, the failure to identify pre-existing resistance, the initiation of an inadequate regimen using first line anti-TB drugs<sup>10,11</sup>. Variations in bioavailability of anti-TB drugs predispose the patient to the development of MDR-TB<sup>10,11</sup>.

Other major factors significantly contributing to the higher complexity of the treatment of MDR-TB is non-adherence to prescribed treatment<sup>12</sup>. Psychiatric illness, alcohol consumption, and travel to different places, symptom relief, adverse drug reactions, drug addiction, homelessness and inability to afford treatment do predict non-adherence to treatment. Poor compliance with treatment is also an important factor in the development of acquired drug resistance<sup>10,12,13</sup>.

Previous studies done in Ethiopia, reported that being male, prior exposure to anti-TB treatment, non-adherence for first line anti-TB treatment, drug side effects during first line treatment, treatment not directly observed with a health worker and interruption of treatment for at least a day were factors significantly associated with MDR-TB<sup>14,15</sup>.

It is known that epidemiologic information on risk factors of MDR-TB is important for prevention and control of the spread of the disease in countries where drug resistance is a major threat. However, there is scarcity of information in the study area and at large to our country. Thus, the aim of this study was to determine the potential risk factors for MDR-TB patients among presumptive MDR-TB patients in the Amhara National Regional State (ANRS), Ethiopia.

## Methods

### Study design, period and setting

Unmatched case - control study was conducted from May 2013 to January 2014 in ANRS. The State of Amhara is the second largest region of Ethiopia that has an area of 157347sq.km<sup>16</sup>. It is located in the north western and north central part of Ethiopia. According to the 2007 census, the region's population was 17,221,976<sup>16</sup>. The region is divided into 11 administrative zones with 151 Woredas. Out of these, 128 are rural and 23 are town administration. ANRS has over 500 governmental and private health institutions that provide TB microscopy and directly observed treatment for short course (DOTS) centers<sup>14,16</sup>. Currently, Gondar University specialized and Borumeda Hospital are the only MDR-TB treatment initiation centers in the region. Data on risk factors was collected from MDR and non MDR-TB patients who had follow up in the above MDR-TB treatment initiation centers of the region.

### Sample size determination and sampling

The sample size for cases and controls was calculated using Epi Info 6.04 soft-ware by taking a proportion of males among the controls of 50% and among the cases of 69.5%<sup>10</sup>, 5% significance level, power (% chance of detecting) of 80%, a case to control ratio of 1: 1 and a non response rate of 10%. A total of 358 sample size was calculated. However, only 306 (153 cases and 153 controls) TB patients volunteered and participated in the study. All confirmed MDR-TB patients and patients with TB but sensitive to both RMP and INH were enrolled conveniently.

### Study population and participants

Study population included all presumptive MDR -TB patients living in ANRS during the study period. Cases were presumptive MDR-TB patients who were infected with MDR *M. Tuberculosis* confirmed with molecular line probe assay (LiPA)

Controls were presumptive MDR-TB patients who were infected with *M. tuberculosis* sensitive to both RMP and INH as per the result of LiPA.

### Variables

MDR-TB was the dependent variable where as socio demographic factors, tuberculosis and its treatment related conditions were the independent variables.

### Data collection

Specimens were collected from presumptive MDR-TB patients for Ziehl Neelsen stain and culture in Lowenstein Jensen medium. From smear and culture positive samples, DNA was extracted and resistance to rifampicin (RMP) and isoniazid (INH) were done molecularly using line probe assay (LiPA). Using a structured questionnaire data was collected by both face to face patient interviews and patient's clinical record review. Health officers and nurses who were trained about MDR-TB and working at TB treatment initiation center collected the data. The main variables included in the study were age, sex, monthly income, HIV status, category of TB treatment, number of previous TB treatments, treatment history, alcohol consumption, smoking, history of irregular treatment during intensive and continuous phase, cavitations on chest x-ray, history of close contact with MDR-TB patients, housing condition and site of tuberculosis.

### Operational definitions of terms according to WHO

**New patients:** A case of TB that has never had anti-TB treatment

**Previously treated:** Patients that have received 1 month or more of anti-TB drugs in the past, may have positive or negative bacteriology and may have disease at any anatomical site.

**Relapse:** A patient declared cured or treatment completed of any form of TB in the past, but who reports back to the health service and is now found to be acid fast bacilli smear positive or culture positive.

**Treatment failure:** - A patient who is sputum smear or culture positive at 5 months or later during treatment.

**Defaulter:-** A patient whose treatment was interrupted for 2 consecutive months or more.

**Presumptive MDR-TB:** Those TB patients who had any TB treatment failure, symptomatic close contact of confirmed MDR-TB cases, return after relapse, return after default and previously treated cases that remain smear positive at the end of intensive phase.

### Data management and statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 20 statistical software. Descriptive statistics were computed to get summary values. Association between variables were determined using odds ratio and 95% CI. Multivariate analysis was run by selecting those variables that appeared to have a P-value of < 0.05 in the bivariate analysis to control the confounding effect of different variables while assessing the effect of each variable on the likely hood of MDR-TB development. P-value of < 0.05 was considered as statistical significance.

### Ethical considerations

Ethical clearance was obtained from the Research and Ethical Review Board of Bahir Dar University. Moreover, all patients gave written informed consent to participate in this study.

### Results

#### Characteristics of study participants

A total of 153 MDR-TB and equal number of TB patients infected with non MDR strains participated in the study. Of these, 88 (57.5%) and 90 (58.8%) were males in cases and controls, respectively. Eighty four (54.9%) of the cases and 81 (52.9%) of the controls were within the age ranges of 26 - 45 years. Detail characteristics of the study participants are presented in table 1.

**Table.1. Sociodemographic characteristics of MDR-TB cases (N=153) and controls (N=153), ANRS, 2014.**

Variables	Cases N (%)	Controls N (%)	COR (95% CI)
<b>Sex</b>			
Male	88 (57.5)	90 (58.8)	1.1 (0.67 - 1.66) *
Female	65 (42.5)	63 (41.2)	1
<b>Age category (Years)</b>			
≤ 25	56 (36.6)	43 (28.1)	0.8 (0.48 - 1.31) *
26-45	84 (54.9)	81 (52.9)	0.3 (0.16 - 0.74) **
> 45	13 (8.5)	29 (19)	1
<b>Residence</b>			
Urban	114 (74.5)	97 (63.4)	0.6 (0.36 - 0.97) **
Rural	39 (25.5)	56 (36.6)	1
<b>Marital status</b>			
Single	56 (37.2)	53 (34.6)	1
Married	61 (39.9)	83 (54.3)	0.4 (0.18 - 0.7) **
Divorced/Widowed	35 (22.9)	17 (11.1)	0.5 (0.26 - 1.02) *
<b>Educational status</b>			
Illiterate	53 (34.6)	55 (36)	1.6 (0.65 - 3.68) *
Up to elementary	52 (34)	61 (39.8)	0.8 (0.4 - 1.6) *
High school	26 (17)	16 (10.5)	0.9 (0.45 - 1.87) *
College & above	22 (14.4)	21 (13.7)	1
<b>Occupation</b>			
Farmer	39 (25.5)	44 (28.8)	1
Student	13 (8.5)	17 (11.1)	0.9 (0.38 - 2.07) *
Merchant	13 (8.5)	17 (11.1)	0.9 (0.38 - 2.07) *
House wife	37 (24.2)	29 (19)	1.5 (0.77 - 2.86) *
Employee	22 (14.4)	22 (14.4)	1.2 (0.56 - 2.43) *
Daily laborer	29 (19)	24 (15.7)	1.5 (0.75 - 2.9) **
<b>Monthly income (ETB)</b>			
Up to 500	54 (35.3)	47 (30.7)	0.2 (0.04 - 0.85)**
501-1500	79 (51.6)	80 (52.2)	0.4 (0.09 - 1.33)*
1501-2000	10 (6.5)	16 (10.5)	(0.29 - 1.12) *
> 2001	10 (6.5)	3 (2.0)	1

Key: ANRS (Amhara National Regional State), COR (Crude odds ratio), 1: Reference category, \*\* P-value < 0.05, \* P - value > 0.05

### Tuberculosis related conditions

The majority of participants had pulmonary TB in cases 141 (92.2%) and controls 137 (89.5%). Proportion of AIDS patients were more in cases 30 (19.6%) compared to controls 21 (13.7%). Homeless participants accounted for 12 (7.8%) in MDR-TB patients and 6 (3.9 %) in controls. Majority of cases (62.1%) and 54

(35.3%) of controls had cavitation on chest x-ray. Of the 153 MDR-TB cases, 44 (28.8%) had history of contact with MDR- TB patients. In the control group, only 22 (14.4%) had history of close contact with MDR-TB patients. Living in a house of mud floor was higher in the MDR-TB cases (83.7%) than in the control group (71.2%). The percentage of alcohol drinkers was higher among cases (29.6%) than controls (13.1%) (Table 2).

**Table 2 Tuberculosis disease related conditions in each category (case/control), ANRS, 2014.**

Characteristics	Cases (N = 153)		Control (N = 153)		COR (95% CI)
	Number	Percent	Number	Percent	
<b>History of alcohol consumption</b>					
Yes	33	21.6	20	13.1	0.6 (0.29- 0.94)***
No	120	78.4	133	86.9	<sup>1</sup>
<b>Living situation</b>					
Individually in a home	25	16.3	28	18.3	<sup>1</sup>
Within family	116	75.8	119	77.8	0.92 (0.5 -1.67)*
Homeless /prisoner	12	7.8	6	3.9	2.1 (0.75 - 5.65)**
<b>History of Contact with MDR- TB</b>					
Yes	44	28.8	22	14.4	0.4 (0.23 - 0.14) **
No	109	71.2	131	85.6	<sup>1</sup>
<b>Floor of the house</b>					
Mud	128	83.7	109	71.2	2.1 (1.19 - 3.60)**
Cement	25	16.3	44	28.8	<sup>1</sup>
<b>Have sewer in the home</b>					
Yes	30	19.6	69	45.1	<sup>1</sup>
No	123	80.4	84	54.9	0.3 (0.18 - 0.49)***
<b>Number of people in a house</b>					
Average (2)	32	20.9	32	20.9	<sup>1</sup>
Below average (<2)	31	20.3	31	20.3	1.0 (0.49 - 2.03)*
Above average (> 2)	90	58.8	90	58.8	1.0 (0.56 -1.78) *
<b>HIV status</b>					
HIV Negative	110	71.9	119	77.8	<sup>1</sup>
HIV Positive	13	8.5	13	8.5	1.1(0.48 - 2.44)*
AIDS	30	19.6	21	13.7	1.5 (0.84 -2.86)*
<b>Site of TB the patient has</b>					
Pulmonary	141	92.2	137	89.5	1.4 (0.63 - 3.01) *
Extra-pulmonary	12	7.8	16	10.6	<sup>1</sup>
<b>Had cavitations on chest X-ray</b>					
Yes	95	62.1	54	35.3	3.0 (1.89 - 4.83)***
No	58	37.9	99	64.7	<sup>1</sup>

Key: ANRS (Amhara national Regional State), COR (Crude odds ratio),\*\*\* P-value < 0.001, \*\* P - value < 0.05, \* P-value > 0.05

Of the 153 MDR-TB cases, 1(0.7%) was a defaulter, 135 (88.2%) were treatment failure, 14 (9.2%) were relapse and 3 (2%) were new cases. While in the controls, defaulters were 3 (2%), treatment failures were 66 (43.1%), relapses were 57 (37.3%) and new cases were 26 (17%). Previous treatment for > 2 times with anti TB drug were encountered in 121(79.1%) and 89 (58.2%)

of the cases and controls, respectively. Irregular treatment during intensive phase occurred in 22 (14.3%) of cases and 9 (5.9%) of controls. Moreover, irregular treatment during continuous phase occurred in 26 (17%) of the cases and 13 (7.9%) of the controls. One hundred twenty nine MDR-TB cases (86.6%) and 100 (67.1%) controls had history of treatment at a health facility (Table 3).

**Table 3 Tuberculosis treatment-related conditions in MDR-TB cases and controls ANRS, 2014.**

Variables	Cases	Percent	Controls	Percent	COR (95% CI)
<b>Treatment history</b>					
Previously untreated	6	3.9	22	14.4	<sup>1</sup>
Previously treated	147	96.1	131	85.6	0.2 (0.1- 0.62)***
<b>Category of TB-treatment</b>					
Defaulters	1	0.7	3	2	2.9 (0.22 -37.4) *
Treatment failure	135	88.2	66	43.1	17.7 (5.1- 60) ***
Relapse	14	9.2	57	37.3	2.1 (0.56 - 8.05) *
New case	3	2	26	17	<sup>1</sup>
<b>Number of previous treatment</b>					
0 -1	32	20.9	64	41.8	<sup>1</sup>
2 and above	121	79.1	89	58.2	2.6 (1.6 - 4.39)***
<b>Place of TB treatment</b>					
In home	20	13.4	49	32.9	0.3 (0.19-0.59)***
In health facility	129	86.6	100	67.1	<sup>1</sup>
<b>Private TB diagnostic &amp; treatment center</b>					
Yes	41	26.8	45	29.4	1.1 (0.7 - 1.9)*
No	112	73.2	108	70.6	<sup>1</sup>
<b>Irregular treatment during intensive phase</b>					
Yes	22	14.4	9	5.9	0.4 (0.17 - 0.84)**
No	131	85.6	143	94.1	<sup>1</sup>
<b>Irregular treatment during continuous phase</b>					
Yes	26	17	13	7.9	0.5 (0.23-0.93)**
No	127	83	139	92.1	<sup>1</sup>
<b>Previous treatment with insufficient duration</b>					
Yes	10	6.5	11	7.2	1.0 (0.42 - 2.38)*
No	143	93.5	142	92.8	<sup>1</sup>

key: ANRS: Amhara National Regional State, COR (Crude Odds ratio),<sup>1</sup>(Reference category)

\*\*\*P-value < 0.001, \*\* P-value < 0.05, \* P-value > 0.05

### Logistic regression analysis

After adjusting for possible confounding factors, MDR-TB was significantly associated with previous history of TB treatment failure (AOR=13.5, CI = 2.69 - 70), cavitation on chest x-ray (AOR= 1.9, CI = 1.1 – 3.38), young age (AOR = 2.9, 95% CI = 1.07 – 7.68), low monthly income (AOR = 1.1, CI 0.34 - 0.47), history of contact with MDR-TB patients (AOR = 1.4, CI = 0.19-0.39) and alcohol consumption (AOR = 1.5, CI = 0.2-0.98) (Table 4).

TB patients who had previous history of treatment failure were 13.5 times more likely to develop MDR-TB than those who completed the course of TB treatment. Moreover, those TB patients who had >2 times previous anti - TB treatment were 1.9 times more likely to develop MDR-TB compared to those who had not. TB patients who had cavitations on chest x -ray were 1.9 times more likely to have MDR-TB than those who had not. Patients whose ages were below 26 years old were 2.9 times more likely to have MDR-TB than those TB patients with age group of 26 years and above (Table 4).

Table 4. Multivariate analysis for the risk factors of multidrug-resistant tuberculosis ANRS, 2014.

Characteristics	Case	Control	COR	AOR	P-value
<b>Age of participants</b>					
≤ 25	56	43	0.8 (0.48 - 1.31)	2.9 (1.07 - 7.68)	0.036
26-45	84	81	0.3 (0.16 - 0.74)	2.2 (0.89 - 5.49)	0.09
≥46	13	29	1	1	
<b>Residence</b>					
Urban	114	97	0.6 (0.36-0.97)	0.5 (0.25 - 0.92)	0.03
Rural	39	56	1	1	
<b>Marital status</b>					
Single	56	53	1	1	
Married	61	83	1.9 (0.98 - 3.9)	1.16 (0.52 - 2.58)	0.04
Divorced/widowed	35	17	0.7 (0.42 - 1.15)	2.4 (0.89 - 6.57)	0.08
<b>Monthly income ( ETB)</b>					
≤ 500	54	47	0.2 (0.04 - 0.85)	0.1 (0.34 - 1.47)	0.003
501-1500	79	80	0.4(0.09 - 1.33)	0.2 (0.03 - 0.79)	0.24
1501-2000	10	16	(0.29 - 1.12)	0.2 (0.03 - 0.75)	0.02
> 2001	10	3	1	1	
<b>Alcohol consumption</b>					
Yes	33	20	0.6 (0.29 - 1.00)	0.5 (0.2 - 0.98)	0.04
No	120	133	1	1	
<b>Contact with MDR-TB patients</b>					
Yes	44	22	0.4 (0.24 - 0.74)	0.4 (0.19 - 0.39)	0.012
No	109	131	1	1	
<b>Floor of the living house</b>					
Mud	128	108	2.1 (1.19 - 3.6)	2.1 (0.93 - 4.4)	0.08
Cement/Other	25	44	1	1	
<b>Had cavitations on chest X-ray</b>					
Yes	95	53	0.3 (0.21 - 0.53)	1.9 (1.07 - 3.38)	0.03
No	58	98	1	1	
<b>Category of TB treatment</b>					
Defaulters	1	3	2.9 (0.22 - 37.3)	2.7 (0.49 - 14.9)	0.26
Treatment failure	135	66	17.7 (5.2 - 60.7)	13.5 (2.69 - 70)	0.002
Relapse	14	57	2.1(0.56-8.1)	5.2 (0.31 - 88)	0.25
New case	3	26	1	1	
<b>Number of previous treatment</b>					
0 -1	32	62	1	1	
2 and above	120	88	0.2 (0.12 - 0.48)	1.9 (0.95 - 3.61)	0.07
<b>Place of TB treatment</b>					
Home	21	49	1	1	
Health facility	129	100	0.3 (0.19-0.59)	1.8 (0.9 - 3.49)	0.09
<b>Irregular treatment during intensive phase</b>					
Yes	22	9	0.4 (0.17 - 0.84)	1.1 (0.25 - 4.24)	0.97
No	131	143	1	1	
<b>Irregular treatment during continuation phase</b>					
Yes	26	17	0.5 (0.23 - 0.93)	0.8 (0.35 - 2.23)	0.89
No	127	83	1	1	

Key: ANRS (Amhara National Regional State), COR (Crude odds ratio), AOR (Adjusted odds ratio)

## Discussion

This study was conducted for the first time in the region to determine the risk factors for MDR-TB infection among presumptive MDR-TB patients. History of TB

treatment failure was one of the strongest predictors for having MDR-TB. This conforms to other studies conducted in different parts of the world<sup>14, 17- 21</sup>. Similarly, a nationwide anti-TB drug resistance survey conducted

in Ethiopia stated that 11.8% of the MDR-TB cases had history of anti-TB therapy while 1.6% were newly diagnosed MDR-TB<sup>22</sup>. The association between TB treatment failure and MDR-TB might be related to unsatisfactory compliance by patients or clinicians, lack of supervision of treatment, improper drug regimens and inadequate or irregular drug supply that may potentiate drug resistance<sup>14,17-21</sup>. Furthermore, those TB patients who had history of > 2 times anti TB treatment were 1.9 times more likely to be at risk of developing MDR-TB. This is in accordance with study done in Ethiopia<sup>14</sup> and Pakistan<sup>2</sup>. The association between increased number of previous TB treatments and MDR-TB might be due to poor adherence of patients that may potentiate secondary drug resistance.

Data on the relationship between cavitations on chest x-ray finding and MDR-TB is insufficient in the literature. In the present study lung cavities are a risk factor for MDR-TB. This finding was in agreement with studies conducted in Brazil<sup>23,24</sup>. The association between lung cavities and MDR-TB was attributable to existence of a higher probability of first step resistant mutants. The selection of mutants is facilitated by the fast multiplication to up to 108 or 109 bacilli inside the cavities, due to the high level of oxygenation and to the protection granted to the bacilli by thick walls which keep drugs from reaching adequate inhibitory concentrations. Concomitantly with inadequate treatments, cavities are a favorable environment for the development of MDR-TB<sup>23,24</sup>.

An association between history of close contact with MDR-TB patients and subsequent MDR-TB cases in this study conforms to other studies<sup>18,19,25</sup>. The association between history of close contact with MDR-TB patients and MDR-TB strain would be attributable to acquiring of primary drug resistant bacteria from the patient.

Many studies reported that poor treatment adherence and irregular treatment were the strongest risk factors for development of MDR-TB<sup>14,23,26</sup>. This study also revealed that the rate of MDR-TB was higher among patients who did not adhere to the proper treatment during intensive and continuous phase. This might be associated with increased bacterial death and growth cycles, giving more opportunities for individual mutations of different independent genes to accumulate<sup>27</sup>.

In this study, young age presumptive MDR-TB patients were more prone to MDR-TB which calls for some concrete steps to be taken to combat this disease in order to save the economically productive population. This finding is in accordance with other reports in Ethiopia<sup>2,14</sup>. To the contrary, a study in other setting stated that MDR-TB was more prevalent among older age groups<sup>20</sup>. Moreover, regarding socio-economic factors, majority of MDR-TB patients were from low socioeconomic status<sup>2,28,29</sup>. This might be due to poor compliance with TB treatment often due to poor living and housing condition and limited access to medical treatment and health care services which might facilitate the spread of infectious bacilli. Hence, these lower socioeconomic groups should be the highest priority in MDR-TB prevention and control efforts.

In the present study, alcohol consumption was also one of the risk factor for the development of MDR-TB. It might be associated with its significant role for default and failure rate among new TB cases. Hence, it increases the rate of MDR-TB cases. In another studies also alcohol consumption was frequently reported as one of the risk factors for MDR TB<sup>23</sup> and was also a risk factor for default<sup>24</sup>.

Similar to previous studies, HIV status had no significant association with MDR-TB<sup>14,23,30</sup>. In addition, in France<sup>31</sup> and Ukraine<sup>32</sup> being HIV positive was associated with primary MDR-TB but it was not associated with secondary MDR-TB in France<sup>31</sup>. This is because HIV is one risk factor for drug susceptible TB, which is associated to immune system suppression. Moreover, a study in South Africa<sup>33</sup> showed that in retreated patients, HIV had no significant association with MDR-TB. Although, we did not differentiate being HIV positive or treatment for TB which came first, greater than 95% of the MDR-TB study participants in our study were patients who had a history of TB treatment and the result could have been different if all study participants were primary MDR-TB cases rather than secondary MDR-TB cases.

The major strength of this survey was inclusion of presumptive MDR-TB patients living in all parts of the Amhara Region and selecting the cases and controls based on the result of molecular technique, line probe assay. However, this study could not differentiate whether MDR-TB cases were primarily MDR-TB or secondary MDR-TB.

## Conclusion and recommendations

This study revealed important information on risk factors for MDR-TB patients that would provide base line information for high TB burden countries like Ethiopia. In this survey, previous TB treatment failure, having cavitations on chest x-ray, contact with MDR-TB patients and low socioeconomic status were the major predictors for having MDR-TB. Therefore, strict adherence to DOTS, basic TB infection control practices, appropriate management of TB patients and advice on the value of nutrients are imperative to control the spreading of MDR-TB.

## Competing interests

The authors declare that they have no competing interests.

## Author's contribution

MW conceived and designed the study, collected and analyzed data and wrote the manuscript, MD designed the study, was involved in data collection, revised the questionnaire and the manuscript. YM revised the questionnaires and manuscript and AA revised the manuscript, AB designed the study, reviewed the questionnaire and critically revised the manuscript. All authors read and approved the manuscript.

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