Scientific Research Publishing

Open Journal of Respiratory Diseases, 2019, 9, 1-17
http://www.scirp.org/journal/ojrd
ISSN Online: 2163-9418
ISSN Print: 2163-940X

Risk Factors for Multidrug-Resistant Tuberculosis and Characteristics of Cases: A Case-Control Study of Patients Attending ALERT General Hospital in Addis Ababa, Ethiopia

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How to cite this paper: Shimeles, E., Enquselassie, F., Tilahun, M., Mekonnen, A., Wondimagegn, G., Hailu, T. and Aseffa, A. (2019) Risk Factors for Multidrug-Resistant Tuberculosis and Characteristics of Cases: A Case-Control Study of Patients Attending ALERT General Hospital in Addis Ababa, Ethiopia. *Open Journal of Respiratory Diseases*, **9**, 1-17.
https://doi.org/10.4236/ojrd.2019.91001

Received: December 17, 2018
Accepted: January 15, 2019
Published: January 18, 2019

Abstract

Background: Tuberculosis remains a major public-health problem in the world, despite several efforts to improve case identification and treatment. Particularly multidrug-resistant tuberculosis is becoming a major threat to tuberculosis control programs in Ethiopia which seriously threatens the control and prevention efforts and is associated with both high death rates and treatment costs. **Methods:** A case-control study was conducted to assess risk factors and characteristics of MDR-TB cases at ALERT Hospital, Addis Ababa, Ethiopia, where cases were 167 MDR-TB patients, while controls were newly diagnosed and bacteriologically confirmed pulmonary TB cases of similar number, who were matched by sex and age of 5-years interval. **Results:** The socio-demographic characteristics of the participants indicated that majority (53.3%) were males and 46.7% females; a little over half of cases (55.1%) were in the age group 26 - 45 years, whereas 46.7% of controls were in this age group. According to the multivariable logistic regression analysis, previous history of hospital admission was the only factor that was identified as predictor which increased risk to develop MDR-TB by almost twenty times (AOR = 19.5; 95% CI: 9.17 - 41.62) and P-value of <0.05. All other studied factor such as being unemployed, family size, having member of household member with TB, and history of visiting hospital in past 12 months etc., didn't show any statistically significant association. **Conclusion:** The study identified previous history of hospital admission as independent predictors

for the occurrence of MDR-TB, while other studied variables didn't show any strong association. The findings added to the pool of knowledge emphasizing the need for instituting strong infection control practice at health care facilities to prevent nosocomial transmission of MDR-TB.

Keywords

Mycobacterium Tuberculosis, Multidrug-Resistant Tuberculosis, Risk Factors, Characteristics

1. Background

Tuberculosis (TB) remains a major public-health problem in the world, despite several efforts to improve case identification and treatment compliance. It is the single highest curable infectious killer in today's world. TB kills nearly two million people a year—5000 every day—mainly in the poorest communities in the developing world. TB takes its greatest toll on developing countries, which account for 98% of deaths from the disease [1]. In Africa, in contrast to many other parts of the world, the incidence rate is rising by approximately 6% per year [2]. High rates of human immunodeficiency virus (HIV) infection have been a key driving factor in this [3]; however, even in countries with relatively low HIV prevalence, the TB case notification has been rising [4].

Multidrug-resistant tuberculosis (MDR-TB) is a form of TB, caused by bacteria that are resistant to treatment with at least two of the most powerful first-line anti-TB medications, Isoniazid and Rifampin, and its resurgence has seriously threatens the control and prevention efforts and is associated with both high death rates and treatment costs [5] [6].

MDR-TB cases may arise by direct transmission of an MDR-TB strain from one individual to another, but also by inadequate treatment of an individual who was initially infected by a fully sensitive strain, or one with only single drug resistance. Either transmission of MDR-TB strains or selection of single drug resistant strains may have contributed to the increase in the prevalence of MDR-TB [7].

Resistance is caused by a genetic mutation that makes a drug ineffective against the mutant bacilli. Factors such as poor adherences to therapy, poor drugs quality or poor prescribing practice like insufficient dosage and inadequate duration of therapy have been reported to contribute to development of resistance to therapies [8].

Treatment of MDR-TB is more complex, involving use of expensive drugs and prolonged therapy period with more adverse events [9]. Poor adherence to treatment remains a major obstacle in the global fight against TB and the reasons for non-adherence are complex. Studies have reported low literacy levels, household members' fear of catching the disease, discriminatory behavior by health care providers, delays in care seeking behavior and self-denial due to

stigma experienced by TB patients as some of the challenges facing adherence to TB treatment [10].

Ethiopia is one of the 30 high TB, TB/HIV and MDR-TB burden countries in the world [11] and recent total estimated incidence of TB stands at 177 per 100,000 populations [12]. The prevalence of MDR-TB in the country has been rising with estimated annual incidence of 5800 MDR-TB cases, and estimated cases among notified pulmonary TB cases of 2900. In 2016, the country reported that 700 laboratory confirmed MDR-TB cases were tested for both Rifampicin and/or Isoniazid resistance and all of them were enrolled in treatment [13]. This is much higher than 2015 and 2014, which were reported to be 597 and 503 respectively [14] [15].

National TB program of Ethiopia has supported a sustained public education campaign through the media on the symptoms of TB, mode of transmission, the importance of seeking treatment, risk of MDR-TB and the fact that TB is curable. To further step up the fight, the government has also put a lot of effort in ensuring adequate availability of drugs and trained health workers. However, the question who gets ill with MDR-TB is not sufficiently answered.

Therefore, the study aimed at assessing the factors contributing to development of MDR-TB and the characteristics of MDR-TB patients enrolled for treatment at ALERT General Hospital, Addis Ababa, Ethiopia. The findings of the study will help for planning and policy improvement for successful tuberculosis control in Ethiopia.

2. Materials and Methods

2.1. Study Population

A case-control study was carried out to assess the risk factors and characteristics of MDR-TB. Cases were MDR-TB patients that were admitted and reported to outpatient unit for follow-up at ALERT Hospital, Addis Ababa, Ethiopia, in 2017. While controls were bacteriologically confirmed pulmonary TB cases, diagnosed by Xpert MTB/RIF as rifampicin sensitive, at 20 health centres in Addis Ababa. These are newly diagnosed cases who have never been treated for TB in the past. All were controls were matched with cases by sex within 5 year age bands.

National TB programme of Ethiopia notified 127,407 TB cases in 2016, of which 1571 were previously treated cases. Among them 68% were pulmonary, and of which 55% bacteriologically confirmed. About half (45%) of these cases were females. Treatment coverage rate was 69% and great majority (81%) knew their HIV status, of whom 8% were found to be positive. The number of laboratory confirmed MDR-TB cases was 700. Treatment success was 84% for new cases and 70% for MDR-TB cases [12].

2.2. Sample Size

The sample size for studying the contributing factors for MDR-TB was calculated by using double proportion formula, considering the assumptions that at

95% confidence level with 5% precision and z value of 1.96, and prevalence of MDR-TB among new cases of 1.6%. Thus, considering 10% nonresponse rate, the minimum sample size was found to be 167 cases. All consecutive MDR-TB patients who were put on second line anti-tubercular drugs for atleast one month, and attending ALERT hospital were selected for the study. Similarly 167 bacteriologically confirmed pulmonary TB patients were included as controls.

2.3. Sampling Procedure

All patients who are enrolled for treatment at ALERT hospital were informed of the study objectives and were recruited into the study upon leaving the consultation rooms during their treatment follow-up phase. The data collection continued by enrolling all patients consecutively till completion of the required sample size. Similarly the control bacteriologically confirmed TB patients were recruited consecutively into the study at time of diagnosis at the respective health centres.

The interviews educed information on the socio-demographic information of the participants including age, sex, marital status, education level and occupation, and other information like history of previous treatment, focusing on treatment adherence, reasons for non-adherence to treatment, and about current medical problem, duration between diagnosis and commencement of treatment, etc. The patients' medical files were also reviewed and appropriate data such as participants' case investigation and treatment related information was retrieved.

2.4. Data Analysis

The data captured in the questionnaires was grouped and examined for errors, then cleaned, and entered into RedCap version 8.03. Data was analysed using STATA version 11 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 likelihood of MDR-TB development. P-value of <0.05 was considered as statistical significance.

The potential associated factors that were analysed in the model include:

- Sociodemographic factors: focusing on marital status, education and occupation;
- Living conditions: this includes size of the family, average household monthly income, number of rooms, number of windows, having a members of household who had TB;
- Life style: this includes mainly about smoking and alcohol consumption;
- Medical history: this includes BCG vaccination, history of visiting hospital and history of hospital admission.

2.5. Ethical Considerations

The research proposal was subjected to screening for scientific and ethical integ-

rity by Ethical review committee at School of Public Health, and institutional review board of the College of Health Sciences, Addis Ababa University. Further screening was done by institutional review board of ALERT/AHRI and management of ALERT hospital, as well as Addis Ababa health bureau. A support obtained from these organizations gave a green light to carry out the study. The management of each of the selected health facilities were given orientation to ensure their support and facilitation of the data collection process.

Permission and consent to participate in the study was obtained from every individual respondent and patient's disease status were kept confidential. Every selected respondent had been briefed by the research team regarding the purpose of the study, any potential harms or benefits of the study, and were given full assurance that, under no circumstances findings of the interview and other information will be disclosed to any unauthorized persons or the authority other than the researcher. This was followed by seeking written agreement of the participant by the use of consent form. Those willing to participate signed an informed consent form and were then interviewed using a short pre-tested questionnaire.

2.6. Time Frame

The duration of the study was more than a year, commencing in July 2016. The data was collected in the period from 04 January to 30 December 2017.

3. Results

3.1. Socio-Demographic Characteristics of the Participants

The socio-demographic characteristics of the MDR-TB patient population that participated in the survey are presented in Table 1. More than half (53.3%) of the participants were males while 46.7% females for both cases and controls. A little over half of cases (55.1%) were in the age group 26 - 45 years, whereas 46.7% of controls were in this age group.

Close to half (47.9%) of the cases have never been married among and 52.1% were married, while among controls the married (48.5%) were less than those never married (51.5%).

About two third of the cases (60.2%) and controls (62.4%) had attained at least secondary level of education, and, only a third (31.7%) of cases and 43.7% of controls reported to have formal employment or merchants or daily wage.

3.2. Living Conditions, Life Style, Medical History

The median family size for cases was 4 with a range from 1 to 13, and it was 3 for controls with a range from 1 to 10. Many (41.3%) of the cases live in households with average monthly income of up to 1000 Birrs, while majority (51.1%) of controls live in households with more than 2000 birrs, as seen in Table 2. Less than a third (29.9%) of cases live in single room house, 34.7% live in a house with two rooms and 35.3% in a house of three or more rooms. The median was

Table 1. Socio-demographic characteristics of the study participants, at ALERT Hospital, and selected health centres, 2017 (n = 334).

Characteristics	Cases (n = 167)		Controls (n = 167)	
	Frequency	Percent	Frequency	Percent
Sex				
Male	89	53.3	89	53.3
Female	78	46.7	78	46.7
Age category (Years)				
≤25	61	36.5	71	42.5
26 - 45	92	55.1	78	46.7
>45	14	8.4	18	10.8
Marital status				
Never married	80	47.9	86	51.5
Married	87	52.1	81	48.5
Educational status				
Illiterate	5	3.0	13	7.8
Read and write	10	6.0	11	6.6
Up to elementary	51	30.5	37	22.2
Secondary school	59	35.3	61	36.5
College or more	42	25.2	45	26.9
Occupation				
Employed/merchants/wage	53	31.7	73	43.7
Unemployed	114	68.3	94	56.3

two rooms. Regarding the controls 37.7% live in single room house, 37.1% have two rooms and 25.1% in houses with more rooms. In terms of number of windows, just over half of cases (52.1%) and 59.9% of controls live in houses without any window or single window.

Almost fifth (18.0%) of the cases and 8.4% of controls had household members who had TB.

Some (9%) of the cases and 6.6% of controls smoke cigarettes, and just over a quarter (28.1%) of cases and 26.9% of controls reported alcohol consumption.

BCG vaccination was 46.7% for cases and 52.7% for controls as seen in Table 3. Majority (87.4%) of cases had history of visiting hospital during the 12 months before the diagnosis of current illness and 71.9% of controls had similar experience. More than half (55.7%) of cases reported history of hospital admission of different duration while only 7.2% of controls had history of admission.

3.3. Predictors of Developing MDR-TB

The bivariate analysis revealed that, being unemployed, household size of more than 4 people, history of visiting hospital in past 12 months and history of admission to health facility were found to have a crude association with developing

Table 2. Living conditions, life style and some medical history of the study participants, at ALERT Hospital, and selected health centres, 2017 (n = 334).

Characteristics	Cases (n = 167)		Controls (n = 167)	
	Frequency	Percent	Frequency	Percent
Size of the family*				
Up to 4	91	54.5	115	68.9
More than 4	76	45.5	52	31.1
Average household monthly income (ETB)				
Up to 1000 birrs	69	41.3	27	16.2
From 1001 to 2000 birrs	46	27.5	47	28.1
More than 2000 birrs	52	31.1	93	55.7
Number of rooms**				
One	50	29.9	63	37.7
Two	58	34.7	62	37.1
Three or more	59	35.3	42	25.1
Number of windows				
0 - 1	87	52.1	100	59.9
>1	80	47.9	67	40.1
Members of household who had TB				
Yes	30	18.0	14	8.4
No	137	82.0	153	91.6
Cigarette smoking				
Yes	15	9.0	11	6.6
No	152	91.0	156	93.4
Alcohol consumption				
Yes	47	28.1	45	26.9
No	120	71.7	122	73.1
BCG vaccination				
Yes	78	46.7	88	52.7
No	89	53.3	79	47.3
History of visiting hospital				
Yes	146	87.4	120	71.9
No	21	12.6	47	28.1
History of hospital admission				
Yes	93	55.7	12	7.2
No	74	44.3	155	92.8

*Size of family: Cases: Mean = 4.24, Median = 4, Range 1 - 13; Controls: Mean = 3.6, Median = 3, Range 1 - 10. **Number of rooms: Cases: Mean = 2.35, Median = 2; Controls; Mean = 2, Median = 2.

MDR-TB (Table 3).

The Overall Predictors of Developing MDR-TB

All variables which had shown statistically significant association during the

Table 3. Bivariate analysis of study participants with MDR-TB, at ALERT Hospital, and selected health centres, 2017: cases = 167, Controls = 167.

Characteristics	Cases (n = 167)		Controls (n = 167)		
	Frequency	%	Frequency	%	COR (95% CI)
Marital status					
Never married	80	47.9	86	51.5	1.15 (0.75, 1.77)
Married	87	52.1	81	48.5	1.00
Educational status					
Up to elementary	66	39.5	61	36.5	1.00
High school and above	101	60.5	106	63.5	1.14 (0.95, 3.85)
Occupation					
Unemployed	114	68.3	94	56.3	**1.67 (1.07, 2.88)***
Employed or merchants	53	31.7	73	43.7	1.00
Size of the family*					
Up to 4	91	54.5	115	68.9	1.00
More than 4	76	45.5	52	31.1	**1.84 (1.18, 2.30)**
Number of rooms					
One	50	29.9	63	37.7	1.00
Two	58	34.7	62	37.1	1.17 (0.7, 1.96)
Three or more	59	35.3	42	25.1	1.67 (0.97, 2.88)
Number of windows					
0 – 1	87	52.1	100	59.9	1.00
>1	80	47.9	67	40.1	1.37 (0.88, 2.11)
Members of household with TB					
Yes	30	18.0	14	8.4	**2.39 (1.21, 4.7)***
No	137	82.0	153	91.6	1.00
Smoking					
Yes	15	9.0	11	6.6	1.39 (0.62, 3.14)
No	152	91.0	156	93.4	1.00
Alcohol					
Yes	47	28.1	45	26.9	1.06 (0.65, 1.71)
No	120	71.9	122	73.1	1.00
History of chronic illness					
Yes	41	24.6	30	18	1.48 (0.87, 2.52)
No	126	75.4	137	82	1.00
BCG scar					
Yes	78	46.7	88	52.7	1.00
No	89	53.3	79	47.3	1.27 (0.82, 1.95)
History of visiting hospitals in the past 12 months					
Yes	146	87.4	120	71.9	**2.72 (1.54, 4.80)***
No	21	12.6	47	28.1	1.00
History of hospital admission					
Yes	92	55.1	12	7.2	**15.84 (8.17, 30.17)***
No	75	44.9	155	92.8	1.00

Notes: *Variables that showed significant association during bivariate analysis at $P < 0.05$, COR. Abbreviations: MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis; COR, crude odds ratio; CI, confidence interval.

bivariate analysis, such as being unemployed, family size, having member of household member with TB, history of visiting hospital in past 12 months and history of admission to health facility were collectively entered in the multivariable logistic regression analysis. Accordingly, previous history of hospital admission was the only variable identified as an independent predictor for the occurrence of MDR-TB, after controlling possible confounders. Previous history of hospital admission was found to increase likelihood to develop MDR-TB by almost 20 times (AOR = 19.5; 95% CI: 9.17 - 41.62) and P-value of 0.00 (Table 4).

3.4. Medical Condition of the MDR-TB Patients

Additional information was gathered from the MDR-TB patients about history of previous TB treatment and current medical condition, and the findings are seen in Table 5 and Table 6 respectively.

Almost two third (59.3%) reported history of TB treatment while 40.7% had never been treated. Among those treated, majority (80.8%) were treated three or more times, 15.2% twice and 4.0% only once. Regarding the history of treatment adherence during the first time they were treated for TB, majority (74.7%) of the

Table 4. Multivariate analysis for the risk factors of multidrug-resistant tuberculosis at ALERT Hospital, 2017: cases = 167, controls = 167.

Characteristics	Cases (n = 167)	Controls (n = 167)	COR (95% CI)	AOR (95% CI)	P-value
Occupation					
Employed/merchants	53	73	1.00		
Unemployed	114	94	**1.67 (1.07, 2.88)***	1.20 (0.69, 1.09)	0.511
Size of the family*					
≤4	91	115	1.00		
>4	76	52	1.84 (1.18, 2.30)	0.57 (0.32, 1.01)	0.057
Members of household with TB					
Yes	30	14	**2.39 (1.21, 4.7)***	2.12 (0.92, 4.88)	0.075
No	137	153	1.00		
History of visiting hospital in the past 12 months					
Yes	146	120	**2.72 (1.54, 4.80)***	1.91 (0.97, 3.78)	0.061
No	21	47	1.00		
History of hospital admission					
Yes	92	12	**15.84 (8.17, 30.17)***	**19.5 (9.17, 41.62)**	**<0.001**
No	75	155	1.00		

Notes: *Variables that showed significant association during bivariate analysis at P < 0.05, COR. Abbreviations: MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis; COR, crude odds ratio; AOR, adjusted odds ratio, CI, confidence interval.

Table 5. History of previous TB treatment among the MDR-TB study participants, at ALERT Hospital (n = 167).

Characteristics	Cases (n = 167)	
	Frequency	Percent
History of TB treatment		
Yes	99	59.3
No	68	40.7
Number of times treated		
1	4	4.0
2	15	15.2
3 or more	80	80.8
Regularity of treatment and adherence: First episode		
Took properly	74	74.7
Some times	23	23.2
Usually not taking	2	2.1
Type of health facility		
Government	90	90.9
Private	9	9.1
Major reasons for irregularly		
Developed drug side-effects	8	32.0
Improvement of symptoms	7	28.0
Treatment facility very far	4	16.0
Health workers not friendly	2	8.0
Other reasons	4	16.0

participants reported that they took their medication regularly without interruption, while 23.2% confessed had they sometimes had interrupted treatment and 2.1% didn't take the drugs most of the time. Majority (90.9%) of the patients had their previous treatment at government facilities and 9.1% in private health facilities. The most frequently perceived reasons for non-adherence according to the participants were developing drug side-effects (32%), improvement of symptoms and felt no need for completing treatment (28%), treatment facility was very far from residence (16%), health workers were not friendly (8%) and other reasons (16%).

Regarding current medical condition, Majority (56.3%) of the MDR-TB patients were smear positive TB cases, 43.1% smear negative and only one patient had extra-pulmonary TB. Majority (85.6%) knew their HIV status, of whom 23.8% were reactive. Cough was the major symptom and it lasted up to one month (48.3%), 2 - 3 months (25.5%) and for more than three months (25.8%). The mean duration between date of confirmation of diagnosis of MDR-TB and commencement of treatment was 61 days, with range from 16 to 251 days. After put on second line anti-TB treatment, 65.3% had developed adverse drug reaction, and great majority (82.6%) had it more than 3 times. In terms of severity,

Table 6. Current medical problem of the study Participants, at ALERT Hospital, 2017 (n = 167).

Characteristics	Number	%
Type of TB*		
Smear positive	94	56.3
Smear negative	72	43.1
EPTB	1	0.6
HIV test status		
Know	**143**	**85.6**
Not-reactive	109	76.2
Reactive	34	23.8
Do not known	**24**	**14.4**
Any adverse reaction		
Yes	109	65.3
No	58	34.7
Number of episodes of adverse drug reaction		
1	4	3.7
2	15	13.8
3 and above	90	82.6
Degree of adverse drug reaction		
Minor	35	32.1
Moderate	45	41.3
Severe	29	26.6
***Body mass index (in kg/m^2)**		
Underweight, less than 18.5	75	44.9
Normal, 18.5 to 24.9	86	51.5
Overweight, 25 to 29.9	4	2.2
Obese, 30 or more	2	1.5

NB. *Duration between date of confirmation of diagnosis and date of commencement of treatment: Mean = 61, range 16 - 251.

41.2% had moderate, 32.1% minor and 26.6% severe.

According to the body mass index, which was calculated based on the weight and height measured at the time of diagnosis, 51.45% of the participants were normal and 44.93% were underweight.

4. Discussion

There is a high burden of multidrug-resistant Tuberculosis in many countries which may be attributed to its demographic and socio-economic profile like poverty, lack of knowledge, attitude and practice, overcrowding, malnutrition, care during illness and lack of social security. Adequate information on risk factors for MDR-TB, such as epidemiological factors is essential in formulating a national policy and to redirect health resources in order to control the transmis-

sion of MDR-TB as well as ensure better patient management. As no single factor can be attributable for emergence of MDR-TB, and study regarding its risk factor is scarce, this study has tried to explore different socio-demographic, life style and medical related factors.

Ethiopia is among the 30 high burden countries for TB, TB/HIV as well as drug resistant TB that collectively contribute about 85% - 89% of the global burden (11). The socio-demographic characteristics of the study participants indicated that 55.1% were in the 26 - 45 years age bracket, which is the most agile and economically active age group. This is similar to another study among MDR-TB patient in North Ethiopia, Gondar and Borumeda, which showed (54.9%) of the cases were within the age ranges of 26 - 45 years [16]. Whereas other study at St Peter hospital, Addis Ababa, showed that 29.9% were in the age bracket 26 - 45 [17]. This finding is consistent with other studies, which reported a rapid rise in TB morbidity and mortality among this young adult population mostly between 15 - 44 years of age [18]. High risk of infection in this age group relates to having a higher number of social contacts in the community during young adulthood [19].

Majority (87.4%) of MDR-TB cases had history of visiting hospital during the 12 months before the diagnosis of current illness while 71.9% of controls had similar experience. Although the bivariate analysis demonstrated statistically significant association between history of visiting health facility in past 12 months and development of MDR-TB, this was not confirmed by multivariate analysis. However another study demonstrated a strong association where visiting hospital was identified as important predictor of MDR-TB (AOR = 3.34, P = 0.044) [20].

More than half (55.7%) of cases reported history of hospital admission of different duration while only 7.2% of controls had such history. The multivariable logistic regression analysis demonstrated that, respondents who had previous history of hospital admission were almost twenty times more likely to develop MDR-TB compared to those who had no previous history of hospital admission (AOR = 19.5; 95% CI: 9.17 - 41.62) and P-value of <<0.05. Similar finding was reported in other studies where hospital admission increased risk of MDR-TB by more than threefold (AOR = 3.49, P = 0.005) [20] and more than fourfold (AOR: 4.4 95% CI: 2.2 - 7.8) [21]. The findings were also in line with other studies in other countries (AOR: 3.8 and 2.08) [22] [23]. This has important implication that hospital-acquired infection of MDR-TB strains is common, and it requires concerted effort to cut the chain of transmission.

Almost two-third (59.3%) of MDR-TB patients had history of TB treatment, among them significant majority (96%) were treated twice or more times. Most (90.9%) of the treatment happened at government facilities. Other studies reported very high percentage of patients with previous history of TB treatment, 91.1% [19], 75.65% [16] and 100% [17]. In all of these cases, over three quarters of the patients were treated at least twice. A quarter (25%) of the MDR-TB pa-

tients had history of irregular treatment during the previous treatment. Similar history of treatment irregularity was also reported by other study 14.4% in rural setting [16], in urban area 16.7% [20], and in some studies even higher rate of 60.5% [17]. Case-control studies observed that respondents who had previous history of treatment for TB were 21 times more likely to develop MDR-TB compared to those who had no previous history of TB treatment (AOR = 21; 95% CI: 17.80% - 28.80%) [24], (AOR = 5.47; 95% CI 3.87% - 7.74%) [25]. TB therapy requires more than 90% adherence to facilitate cure [26], hence individuals who do not take anti-TB medication regularly have increased risk for MDR-TB created by inadequate or improper administration of drugs. Because of the length of treatment required for TB, as patients start to feel better, they stop taking their medication. The TB bacteria not fully eradicated from the body so the bacteria builds resistance to the first-line drugs that the patient has already taken. When the patients fall ill again, their TB strain will not respond to first line drugs.

Based on a meta-analysis of 16 studies in Ethiopia, the pooled prevalence of MDR-TB among newly diagnosed and previously treated TB cases was 2% (95% CI 1% - 2%) and 15% (95% CI 12% - 17%), respectively, with odds ratio of 8.1 (95% CI 7.5% - 8.7%) [27]. Similarly, according to a nationwide anti-TB drug resistance survey conducted in 2005, 1.6% of newly diagnosed TB cases had MDR-TB, while 11.8% previously treated TB cases had the MDR-TB [28].

Unlike many other studies, the current study showed that 40.7% of participants did not have any history of TB. This could be due to high prevalence of primary MDR-TB which results from transmission of resistant TB bacilli. It entails further big scale research to understand the dynamics of the MDR-TB transmission at population level.

The study has its own limitation and generalizability of the findings should be cognizant of this. Some of the data elements could have been better verified through observation in a house visits and with additional detail, such as practice of how often the windows are opening, the volume of house, frequency of visit to health facilities, duration of hospital admission, etc. The study team has tried its best to minimize recall bias by allowing respondents sufficient time to provide most reliable information. The study could have benefited by expanding the list of potential risk factors, including the type of TB of the household member they had contact with, information related to access barriers, however gathering such level of detail require big scale research with appropriate design and resource. The study was conducted in urban setting where hospital are overcrowded, poorly designed old buildings, limited space, poor ventilation etc., and this compromises generalizability of the findings to other settings.

5. Conclusions

The study assessed the risk factors and characteristics of MDR-TB patients at hospital level in Addis Ababa, where sociodemographic factors, life style, living condition, previous medical history and current medical problem were the vari-

ables of the study.

Many of the study participants had history of contact with a household member who suffered from TB, and hence transmission among close contacts concerns. This shows the importance of contact tracing for early detection of cases, and ensures timely treatment and containing transmission. According to the multivariable logistic regression analysis, previous history of hospital admission was found to be independent predictors for the occurrence of MDR-TB.

Therefore it is imperative that infection control in health care facilities is an important intervention to prevent transmission of MDR-TB in order to protect visitors, patients as well as health care providers. This needs to be implemented across the health system.

Acknowledgements

This research was conducted under school of public health, college of health sciences at Addis Ababa University and it was funded by Armauer Hanson research Institute in Addis Ababa, Ethiopia.

The authors wish to thank the research participants for their cooperation and willingness to participate in the study. We thank the research team members for their hard work and amazing support throughout the process. We appreciate staff and management of ALERT hospital, MDR-TB ward, the twenty study health centers and Armaer Hanson Research Institute for their support in data collection and data management. The valuable contributions of professors at school of public health and experts at AHRI in overall assistance and technical support are highly acknowledged. We thank Addis Ababa health bureau and regional laboratory and research unit for their cooperation.

Conflicts of Interest

The authors declare that they have no competing interests.

Ethics and Approval and Consent to Participate

The research proposal was subjected to screening for scientific and ethical integrity and approved by Ethical review committee at institutional review board of ALERT/AHRI with Project Reg. No. PO30/16.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding

The research was fully funded by Armauer Hanson's Research Institute, Addis

Ababa, Ethiopia.

Author's Contributions

ES conceived and designed the study, prepared protocol, coordinated data collection, conducted data analysis, and drafted manuscripts. FE, AA provided technical supported with the preparation of the proposal and the interpretation of data, advising on participated in data analysis, and critically reviewed the manuscript. MT, AM, GW supported preparation of protocol, coordinated field work, supported data analysis and interpretation. TH coordinated data entry and analysis.

All authors read and approved the final manuscript. All authors participated in critical appraisal and revision of the manuscript.

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List of Acronyms

AHRI	Armauer Hanson Research Institute
AOR	Adjusted odds ratio
CI	Confidence interval
COR	Crude odds ratio
DOT	Direct observation of treatment
EPTB	Extra-pulmonary tuberculosis
FDC	Fixed dose combinations
HIV	Human immunodeficiency virus
MDR-TB	Multi-drug-resistant tuberculosis
RR/MDR-TB	Rifampicin resistant or Multi-drug-resistant tuberculosis
TB	Tuberculosis
WHO	World Health Organization