

Prevalence of Multidrug Resistant *Mycobacterium tuberculosis* among Tuberculosis Patients Admitted to Adama Hospital Medical College, Adama, Ethiopia: A Retrospective Study

Bayissa Chala*, Ahmedin Usmael

Department of Applied Biology, School of Applied Natural Science, Adama Science and Technology University, Adama, Ethiopia
Email: baychal07@gmail.com, *bayissa.chala@astu.edu.et

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Abstract

Multidrug resistant tuberculosis (MDR-TB) is an emerging challenge for TB control programs globally. Ethiopia ranks 7th among the world's 22 high TB burden countries. According to report of WHO (2017), TB is one of the leading infectious causes of death in Ethiopia claiming the life of more than 30 thousand people annually. The surge of MDR-TB has been compounding the problem further. Facility-based MDR-TB researches have not been generated in equal pace with community-based ones. The aim of this study was to assess the prevalence of MDR-TB using clinical records of MDR-TB patients in Adama Hospital Medical College (AHMC) from 2014 to 2018. All clinical data of MDR-TB from 2014-2018 was collected from AHMC TB department. Socio-demographic and risk factor data were collected from patients using semi-structured questionnaire. Data were analyzed using Microsoft excel and SPSS version 20. Out of a total 2332 TB suspected cases admitted to AHMC from 2014 to 2018, 175 (7.5%) were confirmed MDR-TB cases or confirmed Rifampicin resistant cases. In particular, 97 (4.2%) presented presumptive MDR-TB alone and 78 (3.3%) showed confirmed Rifampicin resistance alone. Comparison among age groups showed the highest prevalence for 24 - 44 years with 1.8% and 1.5% confirmed MDR-TB and Rifampicin resistance. The overall prevalence of MDR-TB was moderate indicating for possible rise of the problem due to course of time. Further study combining both community and health facility based is recommended to highlight the need to make useful strategies for testing, surveillance and effective clinical management of MDR-TB cases.

Keywords

Multidrug Resistance, *Mycobacterium*, Prevalence, Rifampicin Resistance, Tuberculosis

1. Introduction

Tuberculosis (TB) is one of the world's deadliest communicable diseases with most cases in Asia and Africa, including Ethiopia [1] [2]. The emergence of multi drug resistant TB (MDR-TB) is a challenge for the global control and prevention of the disease [3]. Multi drug resistant tuberculosis is a type of TB that is resistant to at least the two main first-line anti-TB drugs, namely, Rifampicin and Isoniazid. People become infected with MDR-TB either when they are exposed to a resistant strain or when improper treatment leads to selection of a resistant strain [4]. Annually, about 3.3% of new TB patients and approximately 20% of previously treated patients become infected with MDR-TB, leading to the deaths of 190,000 individuals [5].

The MDR-TB has become a major public health problem and presents new barriers to the control of TB [5]. Drug-resistant TB is a man-made problem, largely being the consequence of human error as a result of poor supply management and quality of anti-TB drugs and inadequate or improper treatment, which is further exacerbated by human immunodeficiency virus (HIV) [6].

Globally, from 1994 to 2010 multidrug resistance was observed in 3.4% and 19.8% of all new TB cases and previously treated TB cases, respectively. Based on the prevalence rate from the survey and TB case notification in 2000/8 the magnitude of MDR-TB in Ethiopia was estimated to be 997 cases, which includes 651 and 346 MDR-TB cases among newly diagnosis and retreatment cases, respectively [7].

According to FMOH [8], the national TB prevalence report of Ethiopia was 240/100,000. Ethiopia is among the 30 high tuberculosis, human immunodeficiency virus and multidrug resistance tuberculosis burden countries that accounted for 87% of all estimated TB cases worldwide with annual estimated TB incidence of 164/100,000 population and death rate of 28/100,000 population for 2017 [9]. Likewise, Ethiopia is one of the countries with the highest MDR-TB burdens, with 2.3% of newly confirmed TB patients affected and 17.8% of previously treated TB patients affected [5]. According to the recent global report, 2900 (1800 - 4000) MDR-TB cases were estimated among notified pulmonary TB in Ethiopia [10]. Studies reported multidrug-resistant tuberculosis in Addis Ababa, capital city of Ethiopia [11]. In Oromia region treatment centre-based management of MDR-TB has been implemented at different hospitals, including Adama Hospital Medical College and Bishoftu Hospital, both being located at eastern of the capital Addis Ababa.

Several factors have been associated with the development of MDR-TB [6].

Studies reported that previous exposure of patients to anti-tuberculosis treatment, treatment failure and alcohol use were among the commonly identified risk factors of MDR-TB in Ethiopia [12] [13]. Addressing the underlying risk factors is one of the five principal pathways for preventing drug-resistant TB [2]. At the same time, determining the proportion of drug resistance among new cases is vital in the assessment of the effectiveness of national TB control programme [14].

In Ethiopia, the incidence of MDR-TB appears to be a continuing challenge to the national TB control program. It is important to note that facility-based MDR-TB epidemiological information is crucial to complement community-based studies so as to understand the whole picture of the episode in the country and take appropriate clinical interventions. Therefore, the present study was designed to assess the prevalence and magnitude of MDR-TB among tuberculosis patients attended Adama Hospital Medical College from 2014 to 2018.

2. Materials and Methods

2.1. Description of Study Area

The study was conducted in Adama Hospital Medical College (AHMC) which located in East Showa Zone, Oromia Regional State, Adama city. The City located on 99 km south east of Addis Ababa, the capital city of Ethiopia. The hospital lies at 8°54'N latitude and 39°27'E longitude. The town is found in area of average altitude about 1712 m above sea level and has annual rain fall of 7600 mm and mean annual monthly temperature of 21°C. The climate of an area is hot or arid.

2.2. Study Design

Descriptive cross-sectional study design was used to assess the magnitude of MDR-TB patients among tuberculosis patients. Socio-demographic and clinical data was retrieved from medical records, bacteriological laboratory reports, expert consultation reports. The risk factor information including HIV status of the patients, the previous treatments for tuberculosis, MDR-TB contacts history were also collected.

2.3. Data Collection

All clinical data of MDR-TB patients recorded in AHMC for treatment of tuberculosis and related medical purpose from 2014 to 2018 were included. Data were extracted using designed forms including socio-demographic and background information.

Additionally, questionnaires were prepared and administered to 100 randomly selected TB and MDR-TB patients following treatment during the end of December 2018. The English language questionnaire was translated into the regional language of Afan Oromo, and then translated back to English to maintain the consistency of the questionnaires.

2.4. Data Analysis

Before analysis, the data were coded, organized, and cleaned, followed by statistical analysis using MS-excel and SPSS software version 20. The extracted data from medical records, and bacteriological laboratory reports were separately organized and analyzed. Descriptive statistics such as proportion, mean, and standard deviation were calculated. Results were presented in text, tables, and figures.

2.5. Ethical Consideration

The study was carried out after obtaining ethical clearance from Adama Hospital Medical College ethical review committee. After the review, the committee wrote approval letter to concerned AHMC officials for smooth running of data collection. The information gathered from records was treated confidentially and norm of the hospital was followed in the process of data collection.

2.6. Operational Definition

- Bacteriologically confirmed TB case: a biological specimen is positive by smear microscopy or culture.
- Clinically diagnosed TB case: not bacteriologically confirmed but diagnosed with active TB by a clinician.
- Extrapulmonary tuberculosis (EPTB): any TB case with involvement of organs other than the lungs such as pleura, lymph nodes, abdomen etc.
- Monoresistance: resistance to one first-line anti-TB drug only.
- Multidrug resistance: resistance to at least both isoniazid and rifampicin.
- Polydrug resistance: resistance to more than one first-line anti-TB drug (other than both isoniazid and rifampicin).
- Presumptive TB: a patient who presents with symptoms or signs suggestive of TB.
- Pulmonary tuberculosis (PTB): any TB case with involvement of the lung parenchyma or the tracheobronchial tree.
- Rifampicin resistance (RR): resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs.
- Treatment failure: previously treated for TB and whose treatment failed at the end of their most recent course of treatment.

3. Results

3.1. Clinical Features of Multidrug-Resistant/Rifampicin-Resistant-Tuberculosis Cases

Out of 2332 TB suspected cases admitted to AHMC from 2014 to 2018, 175 (7.5%) were confirmed MDR-TB cases or confirmed Rifampicin resistant cases. In particular, 97 (4.2%) presented presumptive MDR-TB alone and 78 (3.3%)

showed confirmed Rifampicin resistance alone. Comparison among age groups showed the highest prevalence for 24 - 44 years with 1.9% and 1.5% confirmed MDR-TB and Rifampicin resistance. Detail data is shown for age category (<15, 15 - 24, 25 - 44 and >45) of 2014-2018 years (**Table 1**). Comparatively, higher proportion of MDR-TB or Rifampicin resistance of 3.4% and 2.9% were registered in 2014 and 2015, respectively while a sharp decline was observed from 2015 to 2018.

The admission of MDR-TB patients was compared for the past five years. The proportion of MDR-TB among new cases was 41 (1.8%) while among previously admitted cases were 159 (6.8%). The highest and lowest admission for previous MDR-TB cases was registered in 2018 and 2017, respectively. Similarly, relatively higher and lower new MDR cases were recorded in 2014 and 2017, respectively (**Figure 1**). Relative proportion of HIV/AIDS positive MDR-TB cases was higher for 2018 whereas least cases were detected in 2017 (**Figure 2**).

3.2. Demographic Features of Multidrug-Resistant/Rifampicin-Resistant Tuberculosis Cases

In the present study, analysis of respondents of 100 TB outpatients was included with the response rate of 99.5%. Of the total respondents, 62% and 38% of them were males and females, respectively. The age of the cases ranged from 1 to 75 years with median age of 29 years. Relatively, larger proportions of respondents (45%) were in age group 25 - 44 years (**Table 2**).

Table 1. Age and gender distribution of the MDR-TB suspects with drug susceptibility test (DST) in Adama hospital medical college from 2014-2018.

Year	Sex	Confirmed MDR-TB Cases				Confirmed Rifampicin Resistant cases				Total
		Age category (year)				Age category (year)				
		<15	15 - 24	25 - 44	>45	<15	15 - 24	25 - 44	>45	
2014	M	1	6	11	8	1	9	6	3	45
	F	1	3	12	2	1	4	7	3	33
2015	M	0	4	10	9	1	5	9	1	39
	F	1	3	7	5	1	1	7	4	29
2016	M	1	1	2	0	0	0	0	0	4
	F	0	6	3	1	0	0	0	0	10
2017	M	0	0	0	0	0	1	3	1	5
	F	0	0	0	0	0	1	1	1	3
2018	M	0	0	0	0	0	1	2	1	4
	F	0	0	0	0	0	1	1	1	3
Total		4	23	45	25	4	23	36	15	175

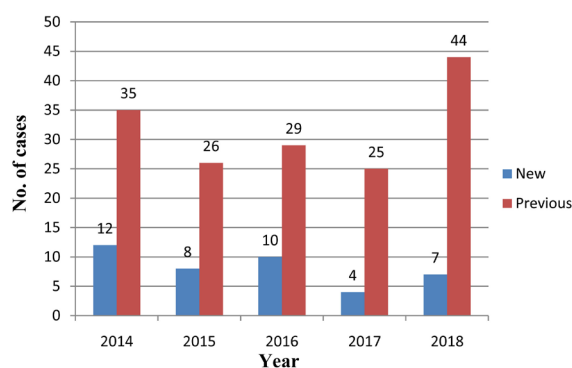


Figure 1. Comparison between new and previous MDR-TB enrolled patients admitted for second line treatment in AHMC from 2014-2018.

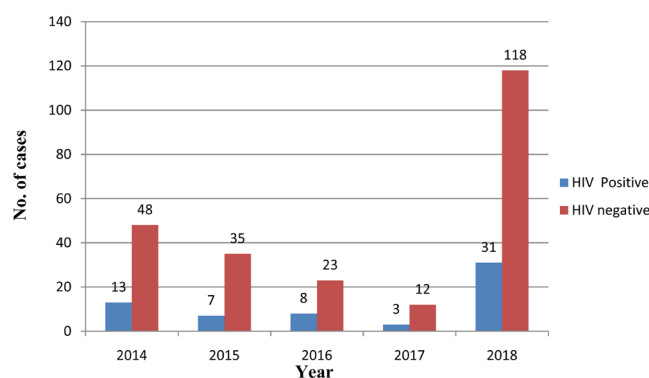


Figure 2. HIV/AIDS Screened MDR-TB patients admitted for second line treatment in AHMC from 2014-2018.

Table 2. Sex-stratified demographic and clinical characteristics of multidrug-resistant/Rifampicin-resistant tuberculosis cases, Adama Hospital College, 2014-2018.

Characteristics	Male Frequency (n)	Female Frequency (n)	Total (%)	p-value
Age (years)				
<15	3	2	5	0.01
15 - 24	19	13	32	
25 - 44	29	16	45	
≥45	11	7	18	
Residence region				
Adama town	11	8	19	0.23
Outside Adama town	45	36	81	
Treatment history with anti-TB				
Previously treated	45	34	79	0.02
Newly admitted	14	7	21	
Microscopic sputum test				
Positive	38	43	81	0.001
Negative	11	8	19	
HIV status				
Positive	18	10	28	0.41
Negative	39	33	72	

4. Discussion

In the present study, the average prevalence of both confirmed MDR-TB cases and confirmed Rifampicin resistant cases admitted to AHMC during 2014 to 2018 years was 175 (7.5%). According to the national population based TB prevalence survey conducted in 2010-2011 the prevalence of smear-positive TB among adults and all age group was 108 and 63 per 100,000 head of population, respectively [15]. Studies reported that TB is one of the leading infectious causes of death in Ethiopia [16] killing more than 30 thousand people annually [17]. Our finding reported a higher resistance rate than 5.8%, 5.7%, and 4.5% studies in Central African Republic [18], Somalia [19] and Zambia [20], respectively.

The proportion of MDR among new cases of the present study was 41 (1.8%) while among previously admitted cases were 159 (6.8%). Similar studies elsewhere in Ethiopia revealed that the proportion of MDR-TB was 4.3% in new patients and 6.7% in previously treated patients [21], 2.18% in newly diagnosed and 21.07% and previously treated patients [22], 2% of new cases and 17% among previously treated patients [23], 2.3% among new cases and 13.9 % among previously treated cases [24] and 2.3% among new and 17.8% among previously treated patients [25]. It is to be noted that 20 years ago, reports showed that the prevalence of MDR-TB was almost nil or 1% in different parts of Ethiopia [26]. It has been suggested that determining the proportion of drug resistance among new cases is vital in the assessment of the effectiveness of national TB control programme [14]. From the previous study reports it is evident that the burden of MDR-TB among newly admitted TB patients shows an increasing trend.

The admission of MDR-TB patients in AHMC was compared for the past five years. The peak admission of MDR-TB among retreated patients was registered in 2018, implying that MDR-TB appears to be on increasing trend from past to two years in Ethiopia (Figure 2). On the contrary, relatively significant decline in MDR-TB was reported in Ethiopia from 2010 onwards [27] [28] [29] [30].

The variations in overall prevalence of drug resistance among the different study settings including the present study area could be due to difference in sample size, irregular supply of anti tuberculosis drugs, and poor TB case management. In the present study, 97 (4.2%) presented presumptive MDR-TB alone and 78 (3.3%) showed confirmed Rifampicin resistance alone. Previous studies in Ethiopia reported that the proportion of resistance to Rifampicin was within a range of 1.9% - 21.4% [31]. More recent studies reported 15% resistance to any of the first-line anti-TB drugs including Rifampicin among new TB cases [29].

From socio-demographic and associated risk factors, close to two-third of respondents were males. Treatment history with anti-TB of respondents showed that previously treated patients accounted for 79% and newly admitted patients were 21% with strong statistical significance ($p < 0.02$). Microscopic sputum test positivity showed 81% with $p < 0.001$. From the questionnaires response slightly larger proportions (45%) of MDR victim respondents were in age group 25 - 44 years.

Relative proportion of HIV/AIDS positive MDR-TB cases was higher for 2018 whereas least cases were detected in 2017. Studies reported statistical significant association between HIV infection and any drug resistance [28]. Although factors linked with MDR-TB vary from study time to study time and from study place to study place risk factor that was commonly identified as a predictor of MDR-TB was HIV/AIDS [32].

It is obvious to imagine that the proportion observed in the present study might actually not reflect the true burden of the disease in the study area. The other point is that secondary data obtained from a single health facility may have its own limitation in showing the magnitude of disease impact in the area. Other shortcoming associated with recording and handling of data might have their own effect on the reliability of the outcome.

5. Conclusions and Recommendations

In the present study, the average prevalence of both confirmed MDR-TB cases and confirmed Rifampicin resistant cases admitted to Adama Hospital Medical College from 2014 to 2018 years was 175 (7.5%), which is moderate. The proportion of presumptive MDR-TB and confirmed Rifampicin resistance was 97 (4.2%) and 78 (3.3%), respectively. History of previous anti TB treatment and microscopic sputum test positivity showed a correlation as risk factor for MDR-TB with statistical significance, $p < 0.02$ and $p < 0.001$, respectively. The moderate proportion of MDR-TB in this study may indicate for possible rise of the problem due to course of time.

Consistent surveillance of emerging and increasing trend of MDR-TB is vital to optimize patient management. For early case detection and treatment, expanding diagnostic capacity of the disease is a vital step to limit further spread of drug resistant TB strains. Further study combining both community and health facility based will be recommended to highlight the need to make useful strategies for testing, surveillance and effective clinical management of MDR-TB cases.

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Conflicts of Interest

The authors declared that they have no competing interests.

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