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Prevalence of Rifampicin Resistance and Associated Risk Factors among Suspected Multidrug Resistant Tuberculosis Cases in TB Centers Mogadishu-Somalia: Descriptive Study

Ahmed Y. Guled[1,2,3], Ayub Hassan Elmi[2], Bashir Mohamud Abdi[2], Abdihamid Mohamed Ali Rage[1,2*], Fartun Mohamed Ali[2], Abdullahi Hassan Abdinur[2], Abdullahi Abdulle Ali[2], Anab Adam Ahmed[2], Khadra Abdullahi Ibrahim[2], Salah Osman Mohamed[2], Fos Ali Mire[2], Omar Abdi Adem[2], Ali Dirie Osman[2]

[1]Guuleed Hospital, Mogadishu, Somalia
[2]Faculty of Medicine, Benadir University, Mogadishu, Somalia
[3]Department of Internal Medicine, Benadir University, Mogadishu, Somalia
Email: *abdihamidmohamed10@gmail.com

Abstract

Introduction and Background: Multidrug-resistant tuberculosis (MDR-TB) has emerged as a significant global health concern. Patients who had failed previous TB treatment, relapsed after treatment, contacted known MDRTB patients or defaulted during previous treatment, and HIV patients are considered to be suspected and at high risk for developing drug resistant TB specially MDR-TB. However, there is little data available on the prevalence and trends of MDR tuberculosis in national level but luck of it in Mogadishu is our main concern. Methodology: This was a cross-sectional, descriptive study involving all suspected MDR TB patients attended at the Mogadishu three Tb centers. Results: A total of 138 cases of suspected MDRTB patients were included in the study. Of these, 70 patients (51%) had rifampicin resistant-TB. Of the 138 study participants, 94 (68.62%) were between 21 - 40 years old that indicates the dominance of productive age group (21 - 40 years). Previous Tuberculosis treatment has been noted to be a major risk factor for development of multidrug resistance tuberculosis. MDR-TB prevalence is significantly higher in male than female patients. Conclusion and Interpretation: The prevalence of Rifampicin resistance among these high risk groups was significant. The high association of previous TB treatment to

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*Corresponding author.

MDR-TB might be explained due to inappropriate anti-tubercular regimens, sub-optimal drugs, inadequate or irregular drug supply, unsatisfactory patient or clinician compliance, lack of super-vision of treatment and absence of infection control measures in healthcare facilities. As the pre-valence of MDRTB is high and yet the cases remain un-isolated in the community we recommend the MOH/NTP and funding agencies to facilitate establishment of MDRTB management centers earlier in Mogadishu in order to treat the MDRTB case otherwise it might Amplify of the incidence of this Emerging Disease.

Keywords

Prevalence, Risk Factors, Tuberculosis, Mogadishu

1. Introduction

Tuberculosis (TB) remains a major global health problem, responsible for ill health among millions of people each year. TB ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV) [1]. TB is the first infectious disease declared by the World Health Organization (WHO) as a global health emergency [1].

It's among the leading causes of death and disability among the economic active segment of the world's pop-ulation. Someone becomes newly infected with TB every second; and it is the leading cause of death among HIV-positive individuals. TB accounts for more than 1/4 of all preventable adult deaths in the developing world. There are an estimated half million (480,000) new cases of multi drug resistance tuberculosis around the world every year. TB creates more orphans than any other infectious disease [2].

TB has high morbidity and mortality rates despite its status as a treatable disease. Tuberculosis is almost al-ways curable if patients are given sufficient uninterrupted therapy. Despite the treatability of this infection, tu-berculosis has proven to be impossible to eliminate, and the number of drug-resistant cases has increased.

Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs. Multidrug-resistant tu-berculosis (MDR-TB) is an increasing global problem, with most cases arising from a mixture of physician error and patient non-compliance during treatment of susceptible TB. The extent and burden of MDR-TB varies sig-nificantly from country to country and region to region.

Drug-resistant TB (DR-TB) poses a major threat to control of TB worldwide. Patients infected with mul-tiple-drug resistant strains are less likely to become cured, particularly if they are infected by HIV or suffer from another immune disease. The treatment is much more toxic and much more expensive about 700 times than the one of patients with sensitive organisms [3].

The new and potentially devastating threat is the most feared diseases in the planet which is XDR tuberculosis. It's virtually untreatable. Extensively drug resistant-tuberculosis (XDR-TB) has been reported in all regions of the world [4].

After more than 2 decades of civil war, Somalia is one of the poorest, least developed, and most violent coun-tries in the world [5]. The conflict and violence, particularly in the south-central region, have caused massive population movements, exacerbated recently by severe drought, floods, and famine [5].

Since the collapse, National and regional hospitals specialized for TB control were closed, further more large number of populations are migrated to and from the neighboring countries which have high rank in TB prevalence.

The levels of MDR-TB in Somalia are among the highest in the Eastern Mediterranean and African region [6]. Drug resistance arises due to improper use of anti-TB medicines, including, administration of improper treat-ment regimens and failure to ensure that patients complete the whole course of treatment [7]. This study has done at Mogadishu TB centers; especially only those have the ability to perform GeneXpert assay tests namely: finsom TB center, buulo-hubey TB center and manhal TB center. The study was designed to assess the preva-lence and associated risk factors of MDR TB, which poses huge challenge against struggling with TB in Moga-dishu and Somalia.

We carried out this study to determine the prevalence of Rifampicin resistance and associated risk factors among suspected MDR TB patients.

2. Methodology

2.1. Ethical Consideration

Research Ethics Committee of Benadir University approved the study and the permission to conduct this research at the study site was obtained from the managers of the NTP/MOH. Interviewees were received full explanation about the study including the purpose, process and benefits of the study. Also informed consent by the interviewees considering: Willingness to participation, Freedom of withdrawal, Confidentiality and Assurance to data not to use for other purpose.

2.2. Research Design

Observational study Design in cross-sectional form: Prevalence of Rifampicin-Resistance among MDR suspected Patients attended TB Centers in Mogadishu 1st February 2015 to 31th July 2015.

2.3. Study Area

This study was done at TB centers in Mogadishu; the largest and capital city of Somalia. Located in the coastal Banaadir Region on the Indian Ocean, the city has served as an important port for centuries. As of 2015, it has a population of 1,280,000 residents [8]. More than 20 years of civil war has left Mogadishu virtually destroyed, but now things are starting to change.

We selected all Mogadishu TB centers those can perform GeneXpert test (a rapid diagnosis of TB disease and drug resistance, the test simultaneously detects Mycobacterium tuberculosis complex (MTBC) and resistance to Rifampin (RIF)); actually three, namely: Finsoma TB center (Yaqshiid District), Muslim AidTB center (wada-jir District) and Manhal TB center (waberi District).

2.4. Inclusion Criteria

All patients suspected to have multidrug resistance attended at Mogadishu TB centers during the data collection. Extra Pulmonary Tuberculosis was excluded from the study.

2.5. Sampling Population

All patients with pulmonary Tuberculosis enrolled in the all three TB centers and those were suspected to have MDR TB and investigated by Gene X pert machine during the study period 1st February to 31th July 2015.

2.6. Research Tool and Method of Data Collection

All the patients were subjected to Gene Expert test. Data was collected from February to July 2015, using semi-structured questionnaire and was precoded and analyzed by SPSS and STATA respectively. Data was collected from the above mentioned TB centers. The research tool used was semi structured questionnaire.

The questionnaire is written in English language and translated verbally to the Somali language. To test the reliability of the questionnaire and validity of the results, pre-testing of the questionnaire was conducted with 20 TB patients in Mogadishu TB centers. Generally the questionnaire consisted of 23 closed ended questions, arranged in three categories. We regarded demographic information, Basic knowledge & Awareness of TB as the main categories of the questionnaire.

2.7. Data Analysis and Management

Questionnaire was pre-coded for entry into the software **Epi Data** (version 3.0) and data analyzed using statistical software package **STATA** (Version 12). Continuous variables were categorized, rearranged and recoded, in order to get adequate number of observation for analysis. Where the strength of association was evaluated using odds ratio (OR), with the corresponding 95% confidence interval (CI) as parameter estimate, and P value of less than 0.05 as measurement of the significant of the statistics.

The collected data were organized and analyzed using quantitative method. Generally, the data obtained were presented using frequency tables, charts and percentages. One hundred and thirty eight of MDR suspected patients were selected for this study.

2.8. Operational Definitions

Relapse: are previously treated for TB, were declared cured or treatment completed at the end of their most recent treatment episode and are now diagnosed with a recurrent episode of TB.

Failure: are previously treated for TB and whose treatment failed at the end of their most recent treatment episode.

Contact: are defined as people from the same household sharing common habitation rooms.

Defaulter: DR-TB patient whose treatment was interrupted for two or more consecutive months for any non-medically approved reason.

MDRTB: a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs.

XDR-TB: MDR-TB plus resistant to fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycin, and/or capreomycin

Primary drug resistance: Drug-resistant TB in a person with no history of TB treatment, implying they were infected with a resistant TB. This reflects person-to-person transmission of drug-resistant TB bacilli.

Acquired drug resistance: Drug-resistant TB in a person with a history of TB treatment. This reflects drug resistance acquired during TB treatment but may also reflect infection or re-infection with resistant TB bacilli.

Suspected MDRTB: Patients, who had failed previous TB treatment, relapsed after treatment, contacted known MDRTB patients or defaulted during previous treatment, and HIV patients are considered to suspect MDRTB.

Rifampicin monoresistant TB: TB caused by strains of M. tuberculosis that are resistant to only Rifampicin. Rifampicin resistance is a predictor of MDR TB because resistance to RIF, in most instances, co-exists with resistance to isoniazid.

3. Results and Analysis

3.1. Socio-Demographic Characteristics

Of the 138 study participants were conducted to the study, of which 96 (69.6%) and 42 (30.4%) were male and females respectively. 94 (68.62%) were between 21 - 40 years old. age distribution of the study population indicates the dominance of productive age group (21 - 40 years).

According marital status of study participants more than half (52%) were married, (41%) were single and less number of participants (4.35%) and (2.17) were divorced and window respectively. Majority (89.1) of participants were lived in Mogadishu, only (10.9%) were come from outside of Mogadishu. One of third (34.1%) of study subjects were living in Internal Displaced Camps while (65.9%) were living outside IDP camps. the household numbers of the families that belong to the research subjects 18% of them were between 1 - 3 persons, 34.5% were 4 - 7 person, 26.6% were 8 - 12 members and 20.86% were more than 12 members. Nearly one third (32.6%) of participants were illiterate while (67.39%) were literate (**Table 1**).

3.2. Prevalence of Rifampicin Resistance Tuberculosis

In this study, the prevalence of Rifampicin resistance Tuberculosis was nearly half 71 (51.5%) of the patients Suspected with MDRTB as illustrated in **Figure 1**.
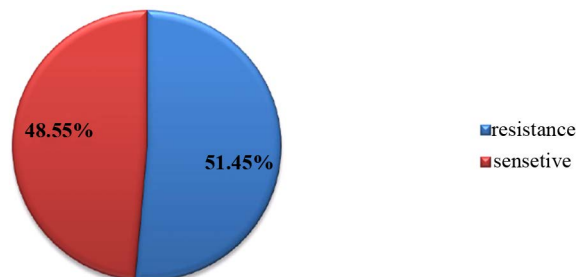
Figure 1. Prevalence of Rifampicin resistance among suspected MDRTB cases in Mogadishu TB centers from 1st February to 31th July 2015.

Table 1. Socio-demographic characteristics of study participants, Mogadishu, Somalia, 2015.

Variables	Frequency	Percentage
Age		
0 - 10	2	1.46
11 - 20	14	10.22
21 - 30	47	34.31
31 - 40	47	34.31
41 - 50	24	17.52
>50	3	2.19
Gender		
Male	96	69.57
Female	42	30.43
Marital status		
Married	73	52.89
Single	57	41.3
Divorce	5	3.62
Windowed	3	2.17
Residence		
Mogadishu	123	89.13
Outside Mogadishu	15	10.87
Living status		
IDP camp	47	34.06
Non-IDP camp	91	65.94
Household number		
0 - 3	49	35.51
4 - 7	59	42.75
8 - 12	22	15.94
>12	8	5.8
Level of literacy		
Literate	93	67.39
Illiterate	45	32.61
Employment status		
Employed	60	43.48
Unemployed	78	56.52
Total	**138**	**100**

3.3. Risk Factors Associated with Multidrug Resistance Tuberculosis

In this study, 93 (67.4%) of the study participants had a habit of smoking, chewing chat or both. Although convergence of the MDR-TB and HIV infection epidemics revealed in various studies only 1 (0.72%) of study participants were having HIV infection. On the other hand, 7 (5.07%) and 12 (8.7%) of the study participants were having Diabetes Mellitus and Asthma respectively.

Around one third 47 (34.31%) of study of patients suspected with MDRTB took their previous TB treatment outside of TB center. In spite of this, 58 (42.03%) of the study participants were believed that trauma and poverty are causative factor of Tuberculosis. according patient categories nearly half 80 (57.97%) were failure and relapsed cases (**Table 2**).

Multivariate Analysis of Factors Associated with Multidrug Resistance Tuberculosis

In the bivariate analysis, the Participants less than 30 yrs of age were more likely to have MDRTB compared to their counterpart of greater than 30yrs of age and this was statistically significant (p = 0.000). Females were not more likely to have MDRTB compared to the males, the association between gender and MDRTB was not statistically significant. (p = 0.21). There was no statistically significant association which was found among marital

Table 2. Frequency of risk factors associated with Multidrug resistance tuberculosis Suspected Patients, Mogadishu, Somalia, 2015.

Variables	Frequency	Percentage
Social habits		
Smoking	56	40.58%
Chewing chat	31	22.46%
Both	6	4.35%
Non	45	32.6%
Co infection with HIV/AIDs		
HIV/AIDs positive	1	0.72%
HIV/AIDs negative	137	99.28%
Diabetes		
Diabetes positive	7	5.07%
Diabetes negative	131	94.93%
Asthma		
Having asthma	12	8.7%
Not having asthma	126	91.3%
Opinion of patients on the cause of TB		
Germ	61	44.2%
Trauma	51	36.96%
Poverty	7	5.07%
All	19	13.77%
Location the patience took TB treatment		
TB centers	91	65.69%
Non-TB centers	47	34.31%
Categories of patients MDRTB		
Defaulter	12	8.7%
Failure	45	32.61%
Relapse	35	25.36%
HIV	1	0.72%
Contact	28	20.29%
Others	17	12.32%
Total	**138**	**100%**

and residency to MDRTB. Significant association was found the household numbers more than seven members and Multidrug resistance TB. It was also found that there was statistically significant association between treatment failure and MDRTB (p = 0.0160).

4. Discussion

The prevalence of Rifampicin resistance was found to be more than half, 51.4% of the patients Suspected MDRTB. This high level of prevalence in Mogadishu maybe reasonable, where the security situation is most volatile and disruption of care more frequent, [9] and has the most internally displaced people [10], factors that are expected to exacerbate disease progression and transmission of *M. tuberculosis*.

This high number of prevalence of MDRTB was found by many other studies; In a previous survey in Somalia 2011, multidrug-resistant tuberculosis (MDR TB) was found in 5.2% and 40.8% of patients with new and previously treated TB, respectively [11]. In *Georgia* the prevalence of MDR-TB was high: 6.8% in newly diagnosed cases, 27.4% in re-treatment cases and 14.8% of all cases [10].

Also studies conducted in South Africa [12], in Burkinafaso [13] and Ethiopia (12%) [9].

But relatively, a lower frequency of MDR-TB has been reported in Bangladesh (0.23% for new cases and 5.56% for previously treated patients) [14].

Based on of the 138 study participants, 94 (68.62%) were between 21 - 40 years old, as shown in **Table 3**. Age distribution of the study population indicates the dominance of productive age group (21 - 40 years) was found in our studies, this finding similar to other studies that shows More than 60% proportion of both MDR and non-MDR TB patients were among young adults aged 15 - 34 years old [15].

The association between age and the risk of MDR-TB is not well established in the literatures as different studies use different cut-off points for age groups.

In gender most reports, Men have been noted to be at increased risk for having susceptibility TB then females, but for MDR-TB females seem to be at higher risk [16].

Notably, our study noted that MDR-TB prevalence is significantly higher in male than female patients that are consistent to studies done in Ethiopia pointing out being male is a risk factor for MDR-TB [17]. This may be explained by the fact that women are more compliant with treatment and therefore less likely to receive inadequate treatment than men.

Furthermore, men are almost always outdoors and therefore more susceptible to community-acquired resistant strains.

Almost all (99.28%) of study participants were not having HIV/AIDs. Only 1 (0.72%) participants had HIV/AIDs, this may be attributed by the low level of HIV infection rates in Somalia, comparing to the other countries in the continent.

However, a positive association between HIV and MDRTB has not been reported from study results in east Africa [18]-[22].

Previous Tuberculosis treatment has been noted to be a major risk factor for development of multidrug resistance tuberculosis. Moreover, studies done in Ethiopia [23] and Nigeria [24], showed that there is significant association b/w MDRTB and previous TB treatment.

This finding is congruent to our study result illustrating that there is statistically significance association among previous treated patients and Multidrug resistance tuberculosis (p = 0.0160).

The extensive use of drugs of suboptimal quality, the widespread practice of using wrong medical prescriptions, and incomplete adherence of patients to treatment are the most likely reasons for this finding.

Surprisingly, positive history of close contact with an identified TB patient did not reveal significant difference between MDR-TB and non-MDR-TB cases. This similar finding was found in study carried out in Brazil [25].

In a study done by Bashar *et al*. on the increased incidence of multi-drug resistant tuberculosis among diabetic patients it was revealed that the proportion of MDR-TB cases was higher among those with diabetes resulting in a significant association between the two variables. [26], our study, however, showed no statistically significant association between diabetes and MDR TB.

5. Conclusion

Multidrug Resistance tuberculosis is major challenges to tuberculosis control, with a high rate of rifampicin resis-

Table 3. Multivariate analysis of variables associated with frequency of Multidrug resistance among study participants, Mogadishu, Somalia, 2015.

Variables	Frequency of multidrug resistance tuberculosis			Odd radio (95% CI)	P value
	Sub-total N (%)	Positive N (%)	Negative N (%)		
Age					
<30 yrs	63	18	45	1	……...
>30 yrs	75	49	26	4.7 [2.1, 10.2]	0.0000
Gender					
Male	96 (69.57%)	46 (47%)	50 (53%)	1	………….
Female	42 (30.43%)	25 (60%)	17 (40%)	0.7 [0.4, 1.3]	0.2110
Marital status					
Married	73	39	34	1	..
Single	57	27	33	1.4 [0.7, 2.8]	0.2468
Divorce	5	5	0	0.0 [….]	0.1690
Windowed	3	2	1	0.59 [0.05, 6.9]	0.6721
Residence					
Mogadishu	123	65	58	1.0	…..
Outside Mogadishu	15	6	9	1.7 [0.6, 5]	0.3491
Household number					
0 - 3	49	7	42	1.0	0.0000
4 - 7	59	35	24	0.11 [0.04, 0.34]	0.1948
8 - 12	23	21	1	0.01 [0.00, 0.24]	**0.0446**
>12	8	8	0	0.00	**0.0150**
Employment status					
Employed	71	18	53	1.0	….
Unemployed	67	42	25	0.2 [0.1 - 04]	0.0000
Asthma					
Having asthma	12	6	6	1.0	…
Not known Hx asthma	126	65	61	0.94 (0.3, 3.0)	0.9166
Diabetes Mellitus					
Having diabetes	7	1	6	1	…
Not known with diabetes	131	70	61	0.14 (0.01, 1.29)	0.0442
Categories of MDRTB					
Defaulter	12	5	7	1	….
Failure	45	35	10	2 [0.1, 0.9]	**0.0160**
Relapse	35	16	19	0.8 [0.2, 3.2]	0.8097
HIV+	1	1	0	……	0.4292
Contact case	28	13	15	0.8 [0.2, 3.3]	0.7841
Others	17	2	15	0.4 [0.7, 40.6]	0.0686
Total	138	71	67		

tance was observed on suspected multidrug resistance TB patients in Mogadishu, nearly half of the suspected patients confirmed to have Rifampicin resistance. Unless prompt interventions in management of MDR tuberculosis in Mogadishu put in place, the possibility remains that MDR strains could spread quickly to become the dominant form of tuberculosis. Previous exposure to anti-TB drugs were an important determinant of development of drug resistance.

The high association of previous TB treatment to MDR-TB might be explained due to inappropriate anti-tubercular regimens, inadequate or irregular drug supply, unsatisfactory patient or clinician compliance, lack of supervision of treatment and absence of infection control measures in healthcare facilities.

Patient's adherence to anti-TB drugs (especially re-treated cases) and scaling up of gene X pert service at district hospital level will help to reduce the development of drug resistance in the study area.

We recommend:

1) Proper diagnosis along with a full course of directly supervised treatment is the key to saving lives threatened by TB and to halt the spread of the dangerous Drug-resistant strains of TB, to achieve this goal we recommend stakeholders including local authorities, MOH/NTP, and funding agencies to consolidate, strength and decentralize DOTs strategy, since some of the respondents claimed that distance of TB centers were the cause of their defaulter.

2) Some of the respondents has still misconception about MDRTB, therefore It is suggested to the health care workers, media, and local NGOs; that TB related knowledge and facts should be disseminated to cover all of the community particularly IDP living people.

3) As the prevalence of MDRTB is high and yet the cases remain un-isolated in the community we recommend the MOH/NTP and other concerning agencies to facilitate establishment of effective MDRTB management and isolation centers earlier in Mogadishu.

4) We recommend researchers, funding agencies and health institutions including universities, to stress, surveillance of drug resistance trends, and health seeking behavior related studies, in order to be used by health policy makers.

5) Since privately imported suboptimal anti-tubercular drugs are widespread available in Mogadishu which is an important contributing factor for developing multi drug resistance, We recommend to the local authority MOH to create quality control programs of anti-tubercular treatment entering the country other than global drug facilities.

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Competing Interests

No competing interest of this paper.

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