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Prevalence and associated factors of multi drug resistance tuberculosis among presumptive tuberculosis patients at public health facilities in Dire Dawa City, Eastern Ethiopia

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Abstract

Background: Tuberculosis is one of the top 10 causes of death worldwide. The emergence of multi-drug resistant tuberculosis threatens global tuberculosis care and prevention and continues to be a public health threat in many countries. Ethiopia is among 30th high multi drug resistance tuberculosis burden countries, but evidence regarding on prevalence and associated factors among presumptive tuberculosis patients in Ethiopia was scarce, especially in Dire Dawa. Therefore, this study aimed to assess the prevalence and associated factors of multi-drug resistant tuberculosis among presumptive tuberculosis patients in public health facilities in the area.

Methods: Institutional based cross-sectional study was conducted in seven health centers and one hospital in Dire Dawa from August 2020 to July 2021. Data were collected by face-to-face interview from patients and data extraction sheet from Gene Xpert registration books. The data was entered and cleaned using Epi- Data version 3.1 and analysis was done using SPSS version 20. Bivariate and multivariate logistic regressions were used and variables which had a significant association were identified on the basis of 95% CI and $P< 0.05$.

Results: The estimated prevalence of mycobacterium tuberculosis in presumptive tuberculosis patients was 487/3638 (13.4%) and multi-drug resistance tuberculosis was 25 (5.1 %). The prevalence of multi-drug resistant tuberculosis among new and previously treated presumptive TB patients was 10 (0.3%) and 15 (8.3%), respectively. Educational status (AOR= 0.042, 95% CI 0.003-0.534, P = 0.015, history of previous tuberculosis treatment (AOR= 27.6, 95% CI 11.78- 64.85, P< 0.001) and HIV sero status (AOR= 5.8, 95% CI 2.438- 13.95, P< 0.001) were found to be statistically significant and independent predictors of multi-drug resistance tuberculosis.

Conclusion: The prevalence of multi-drug resistance tuberculosis in this study was lower than national estimates. Educational status, history of previous tuberculosis treatment and HIV serostatus were factors associated with multi-drug resistance tuberculosis in this study.

Keywords: Mycobacterium Tuberculosis, Multi-drug Resistance Tuberculosis, Rifampicin Resistance Tuberculosis, Prevalence, Associated Factors, Dire Dawa

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1. Introduction

Tuberculosis (TB) is an infectious disease caused by bacilli from mycobacterium tuberculosis complex and one of the top 10 causes of death worldwide [1]. The emergence of multi-drug resistance tuberculosis (MDR-TB) is a critical treat to tuberculosis control and a major public health concern in several countries. Multi-drug resistance tuberculosis is defined as resistance to at least two first line anti-TB drug (rifampicin and isoniazid) [1]. MDR-TB patient present with persistent and progressive cough, fever, night sweats, loss of appetite and weight loss and definitive diagnosis is reached on laboratory-based confirmation of bacilli. Globally, the incidence of multi-drug resistance tuberculosis estimated as 3.5% and 18% among new tuberculosis cases and previously treated cases respectively [2] and in Africa the prevalence of multi-drug resistance tuberculosis was 2.5% from new and 12% previously treated tuberculosis cases. It also emerges as a major clinical and public health challenge in sub-Saharan Africa [3]. Few studies in sub-Saharan Africa indicated that the prevalence of multi-drug resistance tuberculosis ranges from 2.1- 54 % [3-5]. Ethiopia is among 30th high tuberculosis, TB/HIV and multi drug resistance tuberculosis burden countries. Even if Ethiopia working towards preventing occurrence and spread of multi-drug resistance tuberculosis, it remains high [6]. Nationally, the prevalence of multi-drug resistance tuberculosis varies from 10.3% to 18.5% [7-9]. According to WHO 2018 tuberculosis report, 2.7% of new tuberculosis cases and 14% of previously treated tuberculosis cases are estimated to have multi-drug resistant tuberculosis [2]. Of annually notified MDR-TB cases, 70% are between 15-54 years of age, while around 12% are children younger than 15 years, 56% were males and, 7% had TB/HIV co-infection [2].

Early detection and high quality treatment of drug-susceptible TB, health system strengthening and regulation, integration of services, strengthen of lab capacity, strengthen of TB infection control and drug regulation, addressing underlying risk factors and social determinants, ensuring patient adherence, supervision of therapy and patient support are preventing the development of multi-drug resistance TB [10].

Drug resistant tuberculosis has been an increase in recent years in many countries, due to continued expansion in the use of rapid molecular tests. In spite of increased testing, a number of drug resistant tuberculosis cases detected show a slight increase. Globally, 160, 684 cases of MDR/RR-TB were detected in 2017 and 186, 772 in 2018, but coverage of testing was still 46% for new and 83% for previously treated tuberculosis patients [1, 2, 6].

In addition to high prevalence, multi-drug resistance tuberculosis incurs a high indirect cost catastrophe as a facility based survey done in 14 countries shown, cost catastrophe ranges from 67% to 100% [3]. Other study also shown 63% direct cost catastrophe, 37% and 10% productivity and income reduction respectively [11]. Similar study in Ethiopia indicated that 76% of MDR patients have no income after diagnosis and a 50% dropped monthly household income [12].

According to the End TB Strategy, the targeted cumulative reductions in cases and deaths by 2020 was 20 and 35%, respectively; however, only a 6.3% and 11% reduction in cases and deaths, respectively was possible by the end of 2018 [2]. In countries with high burden of tuberculosis, rapid detection, continuous surveillance and regular monitoring of multi-drug resistance tuberculosis are essential for disease management and earlier treatment initiation [3].

Ethiopia is one of high burden country; still, sputum smear microscopy is the commonly used laboratory diagnostic technique for TB. In line with the WHO's recommendations of implementing Gene Xpert MTB/RIF assay in all health facilities, a number of service points across the country has reached 314 from 28 when it was rolled out in 2014. There was also an improvement in the utilization rate from 28% in 2018 to 78% [13]. However, still, different factors have different impacts on the occurrence and diagnosis of multi-drug resistance tuberculosis. In addition to limited continuous surveillance, behavioral and occupational factors like contact history, poor drug adherence, previous treatment failure, and alcohol consumption were a major contributing factors for the development of multi drug resistance-tuberculosis in Ethiopia [14]. Therefore, the aim of this study was to determine the prevalence and associated factors of multi-drug resistant tuberculosis among presumptive tuberculosis patients at public health facilities in Dire Dawa City, Eastern Ethiopia.

2. Methods and Materials

An institution based cross-sectional study was conducted from August 2020 to July 2021.There are two public and four private hospitals, 15 health centers, and 52 private clinics in Dire Dawa City. All public and 19 private health facilities have provided Directly Observed Treatment (DOT) for tuberculosis patients. However, only one drug resistance treatment initiation center and four Gene Xpert diagnostic sites are available [15]. The study was conducted among 310 primary data and 3,328 secondary data. The presumptive cases were randomly selected from the Gene Xpert MTB/RIF assay registration logs at public health facilities in Dire Dawa City. The study excluded patients with incomplete records. The dependent variable of the study was diagnosis of tuberculosis. The independent variables included socio-demographic, behavioral, and clinical characteristics of patients. A pre-tested, structured questionnaire was used to gather socio-demographic and behavior information from patients. Clinical profiles of patients were gathered by medical record review using a data extraction checklist. Three trained diploma nurses on the study's objectives and tools collected the data.

A single sputum sample per patient for age greater than 5 years and gastric aspirate for age less than 5 years were used for the diagnosis of MDR-TB using Gene Xpert MTB/RIF assay. After the sputum sample was collected, it was mixed in the supplied cartridge with sample reagent. Then samples were diluted and decontaminated, and Gene Xpert MTB/RIF assay was performed according to the manufacturer's manual and the results were collected from the Gene Xpert computer after 2 hours [16].

The collected data was entered, coded, and cleaned using Epi- Data version 3.1. Statistical analysis was conducted using SPSS version 20. Descriptive statics such as frequency, percentage, and cross tabulation as well as bivariate and multivariate logistic regression were used to present the finding. Variables which had a p-value <0.25 in the bivariate analysis were carried into multivariate model. Finally, significant level identified based on odds ratio, with 95% CI and P-value < 0.05.

3. Results

3.1 Socio demographic and clinical characteristics of study participants

This study was conducted on 3638 presumptive TB cases. Of those, 310 were primary and 3328 were secondary data. The mean age of the study participants was 36 (36±18 SD) years. Majority of the participants were found with in age group of 16-30 years, which account 1375 (37.8%). Among total study participants, 1872 (51.5%) were males and 1766 (48.5%) were

females. About 209 (67.4%) of the study participants were from urban. Of 3638 presumptive TB patients, 3400 (93.5%) were HIV serostatus negative and 180 (4.9%) had previous TB treatment history.

Table 1. Socio demographic and clinical characteristics of presumptive TB patients in public health facilities of Dire Dawa, Eastern Ethiopia (n=3638), 2021

Variables		**Frequency**	**Percentage (%)**
Age	<15	351	9.6
	16-30	1375	37.8
	31-45	916	25.2
	>46	996	27.4
Sex	Male	1872	51.5
	Female	1766	48.5
Residence	Urban	209	67.4
	Rural	101	32.6
History of prior TB treatment	New	3458	95.1
	Relapse	75	2.1
	Lost to follow up	45	1.2
	Failure	20	0.5
	Defaulter	40	1.1
HIV status	Positive	238	6.5
	Negative	3400	93.5

Abbreviations: HIV: Human Immunodeficiency Virus, TB: Tuberculosis

3.2. **Prevalence of MTB and multi-drug resistance tuberculosis**

Among 3638 presumptive TB cases, the overall prevalence of MTB detected by using Gene Xpert MTB/RIF assay was 487 (13.4%). Of MTB, 282 (15.1%) were among males, 249 (18.1%) were observed in the age group 16–30 years, 64 (26.95) were among HIV positive and 56 (31.1%) had a history of TB treatment. Among 487 MTB, 25 (5.1 %) had MDR-TB. Of multi-drug resistance tuberculosis 9 (1%) were in age group of 31-45 years and 14 (0.8 %) were females, 10 (4.2%) HIV co-infection and 15 (18.3%) had TB treatment history.

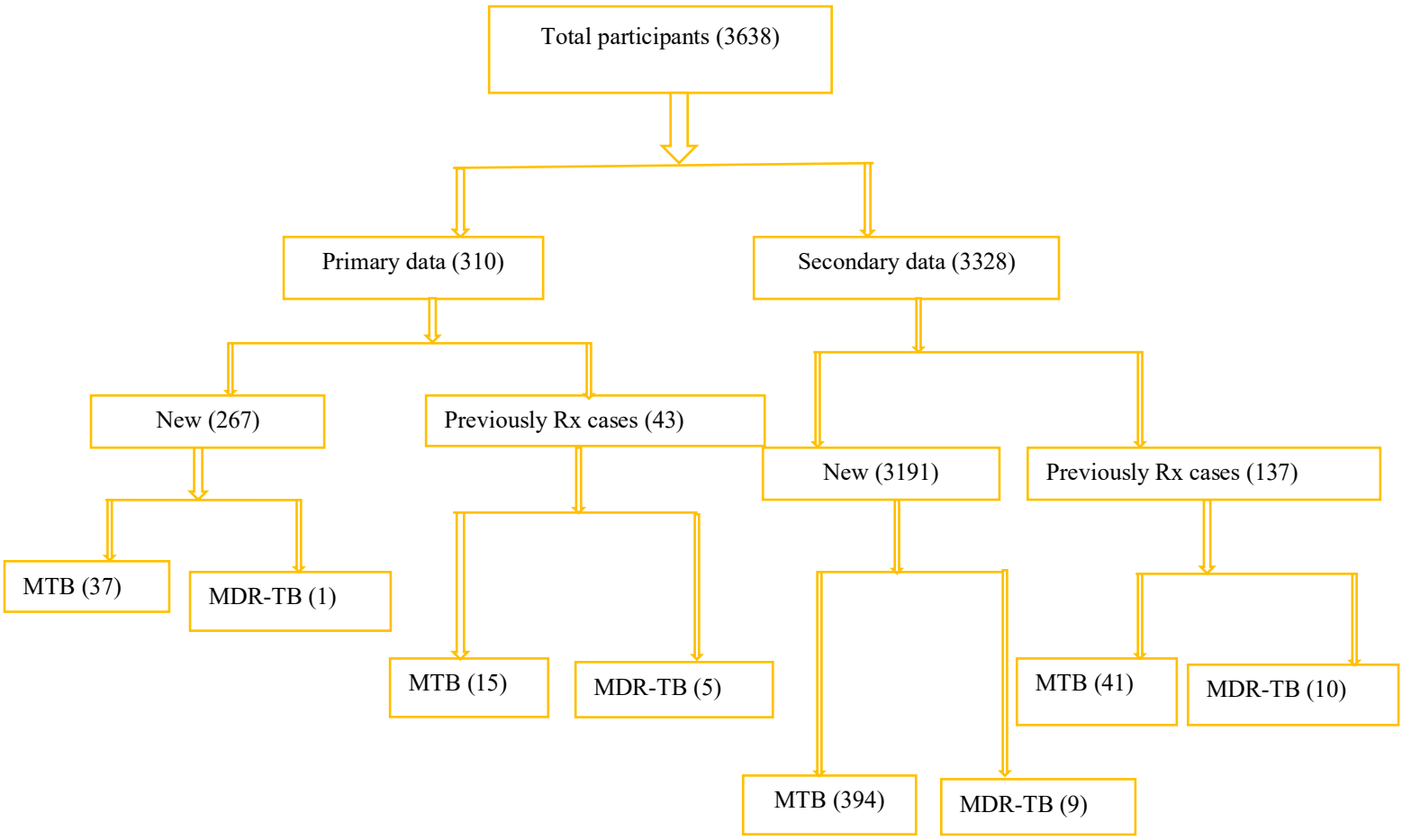

Figure 3. Prevalence of multi-drug resistance tuberculosis among primary and secondary data of presumptive tuberculosis patients in public health facilities of Dire Dawa, Eastern Ethiopia, 2021

3.3. Factors associated with MTB and MDR-TB diagnosis

As displayed in Table 2 below, from MTB cases, the highest positive finding, 249 (48.6 %) were observed in the age group 16-30 years, followed by 31-45 years 104 (20.3%). It showed a statistically significant difference over the different age groups. Being positive MTB was 1.4 times greater in male than female. The odds of being male among MTB cases was significantly higher (OR=1.38, 95% CI: 1.14-1.69, P=0.001). Similarly, the odds of MTB was 3.28 times greater in previously treated TB patients than new cases (P< 0.001) and showed a statistically significant difference with treatment history of patients.

Table 2: Association of clinical and socio demographic factors with M. Tuberculosis and bivariate and multivariate analysis among presumptive TB patients in public health facilities of Dire Dawa, Eastern Ethiopia (n=3638), 2021.

Variable		MTB status with frequency and percentage		COR (95%CI)	AOR (95%CI)	P-value
	Category	Positive	Negative			
Age	<15	46 (13.1)	305 (86.9)	1		
	16-30	249 (18.1)	1126 (81.9)	0.682 (0.486-0.957)	0.666 (0.472 - 0.940)	0.021*
	31-45	104 (11.4)	812 (88.6)	1.178 (0.812- 1.707)	1.286 (0.880 - 1.881)	0.194
	>46	88 (8.8)	908 (91.2)	1.556 (1.065-2.274)	1.696 (1.152 - 2.496)	0.007*
Gender	Male	282 (15.1)	1590 (84.9)	1		
	Female	205 (11.6)	1561 (88.4)	1.351 (1.114-1.638)	1.384 (1.136 - 1.686)	0.001*
Residence	Urban	36 (17.2)	173 (82.8)	1		
	Rural	16 (15.8)	85 (84.2)	1.11 (0.581- 2.104)	0.53 (0.210-1.314)	0.169
HIV status	Positive	64 (26.9)	174 (73.1)	1		
	Negative	423 (12.4)	2977 (87.6)	2.589 (1.910-3.509)	2.629 (1.911 - 3.617)	<0.001*
Previous TB treatment	Yes	56 (31.1)	124 (68.9)	1		
	No	431 (12.5)	3027 (87.5)	3.172 (2.277-4.418)	3.287 (2.326 - 4.644)	<0.001*

Note * means that there is a significant association

On bivariate analysis of the dependent and independent variables, previous history of TB treatment and patients' HIV serostatus showed significant association with MTB. When these variables were adjusted on multivariate analysis, previous history of TB treatment (AOR=3.28, 95% CI: 3.33–4.64; P<0.001) were found to be independent predictors of multidrug resistance tuberculosis among patients of presumptive tuberculosis in the study area (Table 3).

Table 3. Association of clinical and socio-demographic Factors with RR Tuberculosis bivariate and multivariate analysis among presumptive TB patients in public health facilities of Dire Dawa, Eastern Ethiopia (n=3638), 2021.

Variable		MDR-TB status with frequency and percentage		COR (95%,CI)	AOR (95% CI)	P-value
	Category	Positive	Negative			
Age	<15	2 (0.6)	349 (99.4)	0.880 (0.170- 4.559)	0.687(0.123- 3.839)	0.669
	16-30	9 (0.7)	1366 (99.3)	0.766 (0.256- 2.292)	0.450 (0.141- 1.433)	0.177
	31-45	9 (1.0)	907 (99)	0.508 (0.170- 1.523)	0.437(0.138 - 1.388)	0.160
	>46	5 (0.5)	991 (99.5)	1	1	
Gender	Male	11 (0.6)	1861 (99.4)	1.352 (0.612- 2.986)	1.396 (0.606 - 3.214)	0.433
	Female	14 (0.8)	1752 (99.2)	1	1	
Residence	Urban	5 (2.4)	204 (97.6)	1	1	
	Rural	1 (1.0)	100 (99.0)	2.45 (0.283- 21.260)	0.195 (0.003-13.788)	0.452
HIV status	Positive	10 (4.2)	228 (95.8)	1	1	
	Negative	15 (0.4)	3385 (99.6)	9.898 (4.397- 22.28)	5.83 (2.438- 13.95)	<0.001*
Previous TB treatment history	Yes	15 (8.3)	165 (91.7)	1	1	
	No	10 (0.3)	3448 (99.7)	31.35(13.87 - 70.83)	27.64(11.78- 64.85)	<0.001*

Note * means that there is a significant association

Patients with previously TB treated were 27.6 times more likely to be MDR- TB than patients who were untreated (AOR= 27.6, 95% CI 11.78- 64.85, $P< 0.001$). In this study multi-drug resistance tuberculosis showed a statistical significant association in tuberculosis treatment history ($P < 0.05$), but no association observed in age category, sex, residence.

4. Discussion

This is one of few studies from the eastern region of Ethiopia to measure the burden and risk factors of multi-drug resistance tuberculosis among presumptive cases. In the present study, the prevalence of M. tuberculosis was found to be 13.4 %. This prevalence is comparable with the study conducted in Nepal 13.8% [17], in eastern Amhara 11% [18] and in Addis Ababa, Ethiopia 13.5% [19]. However, it was lower than a study conducted in Nigeria 37.7% [20], northwest Ethiopia 24.6% [21] and in East Gojjam 20.2% [22]. The difference might be due to the heterogeneity nature of study participants, geographical variation and different criteria used for diagnosis of tuberculosis.

According to our study, MTB slightly predominated among males: 57.9%. This is higher than a study conducted in Nepal 14.08%, northwest Ethiopia 25.3% and Addis Ababa Ethiopia 15.1% [17, 19,21], but this finding was comparable with a study conducted in Nigeria 55%[20] .The difference of prevalence by sex might be due to health-seeking behavior, environmental factors, and the higher exposure of males to different factors that pose a risk of acquiring the TB bacilli.

In this study, the prevalence of MDR/RR TB among presumptive tuberculosis patients was 0.7% and 5.1% among tuberculosis detected. Furthermore, previous history of TB treatment, and HIV positive patients were found to be independent predictors of multidrug resistance tuberculosis among patients of presumptive tuberculosis in the study area. This finding was comparable with a study conducted in Botswana 5.4% [23] , in Afar 4.3% [24], in Metema 5.6% [14], but lower than a study conducted in Nigeria 23.4% [20], in Saudi Arabia 17.1% [25], in northwest Ethiopia 15.8% [21], in Amhara 15.3% [7], in Tigray 18.5% [9], in Nepal 10.2% [17], in Debre Markos 10.3% [8], in Addis Ababa 9.8% [19] and higher than study conducted in Nigeria 2.7% [26], in Ethiopia 1.8 % [27], in eastern Ethiopia 1.1% [28] and 1.4% systematic review in Ethiopia [29]. A probable reason for this variation might have been that we included presumptive cases to identify RR TB, while other studies included identified cases of TB by GeneXpert in study population. The method of diagnosis and study setting may account for the variation in prevalence across studies.

In the present study, the proportion of MDR-TB in previously treated cases was 8.3 %. The finding of this study was comparable with a study conducted in Botswana 7.7% (23) and lower than study conducted in Nepal 13.8% [17], Northwest Ethiopia 16.5% [21] , Debre Markos 17.5% [8], Metema 13.9% [14] , Easter Gojjam 16.7% [22], Afar 11.1% [24] and Global 2020 TB report 12% [30], but higher than a study conducted in Nigeria 4.4% [26]. This indicates might be a gap in continuous implementation of the DOTS, which is vital for effective adherence of patients to treatment, health service delivery, awareness of the public about the disease. Also, could be indicating the existence of ongoing transmission of drug resistant strains and weakness of TB prevention and control measures.

In the present study, the proportion of MDR-TB among HIV positive was 4.2%. This finding was lower than a study conducted in Afar 16.6% [24], northwest Ethiopia 18.7% [21], Addis Ababa 12.5% [31]. This might be due to HIV infection, which may lead to mal-absorption of anti-TB drugs, especially rifampicin, with adverse effects leading patients to non-adherence

and subsequent drug resistance. In the present study, findings indicate that sex and age of the patient are not the contributing factors for the occurrence of MTB and RR-TB. However, further supporting studies in this study area is needed to draw the conclusion.

This study has several limitations. First, a lower rate of MDR-TB in this study might has affected the results of logistic regression analysis for significance of association. Second, due to the cross-sectional natures of the study design, the temporal sequence of events cannot be determined, which limits the inference of a cause-effect relationship. Third, recent unprecedented COVID-19 crisis may have an impact on TB presumptive screening, prevention and control systems in different aspects however, the study finding will contribute for the literature as different sources of data were used.

5. Conclusion and recommendation

The prevalence of MDR/RR- TB in this study is lower than the national estimates. However, still, there is a need to reduce this burden through strengthening early detection and treatment and TB control programs to prevent further emergence of a public health threat of MDR TB. History of previous TB treatment and HIV sero-status were factors associated with MDR TB in this study. This calls health care providers and program managers to focus on counseling and supporting TB patients for compliance with the regimen to complete treatment without interruption. Health care workers should make early screening of patients who are at risk of tuberculosis, there by strengthening and providing early diagnosis and treatment. Asking symptoms of mycobacterium tuberculosis, HIV risk factories and history of previous treatment should be considered while screening and counseling patients in the study area. Since the prevalence of multi-drug resistance tuberculosis was high in HIV positive and patients previously treated for the TB.

Ethical approval and consent to participate

Ethical clearance was obtained from ethics review committee of Dire Dawa University and official letter was submitted to all selected health facilities and permission was obtained.

Consent for publication

Not applicable

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interests

The authors declare that they have no competing interests.

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Authors' Contribution

BZ- developed the project and took part in data collection, data analysis and developing the initial drafts of the manuscript and revising subsequent drafts. HM- involved from conception through end of manuscript. Finally, all authors agreed at the end for the publication of the manuscript on the Journal.

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