

Characteristics of Multidrug Resistance Tuberculosis Cases in Baghdad

Arwa Tahrir Ramadhan*, Layth Salihi **, Mohammad Yahya
Abdulrazaq***, Hayder H. Ali Al-Sikafi ****

ABSTRACT:

BACKGROUND:

Multidrug-resistant tuberculosis (MDR-TB) is caused by strains of *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, the two most effective bactericidal agents currently available for TB treatment. It has emerged as a global public health emergency. It requires treatment with combination therapy consisting of four to six medications for up to 2 years. Additionally, the treatment is generally more toxic and far more expensive than the standardized treatment regimen used to treat drug-susceptible TB. The latest estimates of the World Health Organization (WHO) arrive at 650 000 prevalent MDR-TB cases among the 12 million tuberculosis cases worldwide.

OBJECTIVE:

To identify the Characteristics of multidrug resistance tuberculosis cases attending the specialized center for chest and respiratory disease in Baghdad during the period 9th of September 2012 – 9th of December 2012.

METHODS :

A cross sectional study was done in the specialized center for chest and respiratory disease in Baghdad during the period 9th of September 2012 – 9th of December 2012. Any patient attending the specialized center for chest and respiratory disease in Baghdad during the study period diagnosed as a case of MDR TB was enrolled in this study.

RESULTS:

The sample is composed of 42 MDR-TB patients (29 male and 13 female), with age mean of 38.3 ± 12.8 year. Male sex significantly dominates and exceeds two thirds of the sample (69.0%) ($P < 0.05$). The study finds ages between 25-45 year contribute to about two thirds (62.0%) of patients, and ages between 55-65 years constitute about one fifth (19.0%) of the sample. ($P < 0.05$). Body habit significantly showed that half the sample (50.0%) were underweight and only 10% were overweight or obese ($P < 0.05$). Smoking is found in 21.4% of total sample.

The duration of taking first line antituberculosis drugs (FLD) before being labeled as MDR-TB varied from 14 to 72 months, with mean duration of 27.3 ± 15.2 months with no significant difference in mean duration between the two sexes ($P > 0.05$). Time required to diagnose these cases as MDR-TB varied from 0 to 24 months with mean time of 9.0 ± 6.5 months. There was no significant difference in mean diagnosis time between males and females ($P > 0.05$). This study found that around one fifth (19.0%) of the sample have a history of default from treatment with FLD. Only one female was significant to be a case of primary MDR-TB ($P > 0.05$). Two cases (both were males) significantly had history of reaction to FLD treatment ($P < 0.05$). None of the sample had positive HIV testing.

CONCLUSION:

Most MDR patients in this study were males aged between 25-45 years. Most cases had acquired MDR TB and primary MDR-TB was rare finding in this study. Around one fifth of the sample have a history of default from treatment with FLD.

KEY WORDS : tuberculosis, multidrug resistance.

*Bacteriologist, Ph.D, Al-Kindeg College of Medicine.

**Community Medicine Specialist, Specialized Center for Chest and Respiratory Disease.

***Pulmonologist, Internist, Specialized Center for Chest and Respiratory Disease.

****Pulmonologist, Specialized Center for Chest and Respiratory Disease.

INTRODUCTION:

The emergence of drug resistance in the course of treatment for tuberculosis (TB) is a phenomenon that was recognized shortly after the introduction of streptomycin in 1946–1947. Acquired drug resistance in TB patients is largely an iatrogenic

phenomenon, which results from the artificial selection of spontaneous drug resistance mutations in *Mycobacterium tuberculosis* during inadequate or incomplete therapy. These drug-resistant strains can subsequently be transmitted in the community, limiting the effectiveness of combination drug regimens used in treatment programs. ⁽¹⁾ The global epidemiology of drug resistance has worsened over the past 40 years, particularly with the emergence and increased recognition of multidrug-resistant (MDR)-TB and, more recently, extensively drug-resistant (XDR)-TB ⁽²⁾.

Multidrug-resistant tuberculosis (MDR-TB) caused by strains of *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, the two most effective bactericidal agents currently available for TB treatment, has emerged as a global public health emergency. It requires treatment with combination therapy consisting of four to six medications including a fluoroquinolone and an injectable anti-TB agent, as well as bacteriostatic agents administered for up to 2 years. Additionally, the treatment is generally more toxic and far more expensive than the standardized treatment regimen used to treat drug-susceptible TB ⁽³⁾. The latest estimates of the World Health Organization (WHO) arrive at 650 000 prevalent MDR-TB cases among the 12 million tuberculosis cases worldwide ⁽⁴⁾. The epidemic of highly drug-resistant TB threatens to undermine advances in TB control. The diagnosis, treatment and management of MDR-TB and XDR-TB cases require substantially greater financial and human resources, yet yield worse outcomes ⁽⁵⁾.

PATIENTS AND METHODS:

A cross sectional prospective study was done in the specialized center for chest and respiratory disease in Baghdad during the period 9th of September 2012 – 9th of December 2012. An official permission to undertake the study was granted by Public Health Office in the Ministry of Health and by the Ethical Committee of Al-kindey college of medicine. During the study period about 250 suspected patient referred to the MDR Tuberculosis Unit in the specialized center for chest and respiratory disease in Baghdad.

Forty two patients of them diagnosed as a case of MDR TB by culture and drug sensitivity test so included in this study (29 male, 13 female). A full medical history and physical examination was done for each patient. A pre-tested questionnaire was designed to obtain information by patients interview including age, gender, a detailed past TB history mainly the history of

first line antituberculosis drugs (from the patients themselves and the records) and focusing on drug defaulting history, drug interaction, smoking history and stigmatizing history due to TB.

Multidrug-resistant tuberculosis (MDR-TB) in this study is defined as strains of *Mycobacterium tuberculosis* that resistant to at least isoniazid and rifampicin. Primary MDR tuberculosis defined as those patients presented with MDR TB with no previous personal history of tuberculosis. Body Mass Index (BMI) calculated by weight (in Kilogram) divided by the square of height (in Meter), weight and height were measured using the same scale for all patients. According to the BMI, patients classified to under weight (BMI < 18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25-30 kg/m²) and obese (BMI > 30 kg/m²).

Statistical Package for Social Sciences-version 20 (SPSS v.20) used for data input and analysis. Continuous variables presented as mean ± standard deviation. t test for two independent variables used to test the significance on observed difference in means. Chi-square test of goodness of fit is used to verify the significance of observed proportions (observed distributions). All P values were asymptotic and two sided. Findings with P value < 0.05 considered significant.

RESULT:

The total number of patients included in this study was 42 MDR-TB patients. Their age varied from 17 to 61 year with mean of 38.3±12.8 year with no significant difference in mean age between males and females (P > 0.05, table 1). Age group (25-45) year contribute about two thirds (62.0%) of patients, and ages between 55-65 years constitute about one fifth (19.0%) of the sample. (P < 0.05, table 1). Male sex significantly dominates and exceeds two thirds of the sample (69.0%) (P < 0.05, table 1). Body Mass Index (BMI) of the sample varied from 12.9-35.3 kg/m², with mean of 21.0±5.9 kg/m² with no significant difference in mean BMI between males and females. (P > 0.05, table 1). The study showed that half the sample (50.0%) were underweight and only 10% were overweight or obese (P < 0.05, table 1). The study showed that 21.4% of patients were smokers, 27.6% of males and 7.7% (one woman), and these findings were significant (P < 0.05, table 1). One third of our patient said that tuberculosis was a social stigma, including 11 (37.9%) of males and three (23.1%) of females (P < 0.05, table 1). Only one female patient was

a case of primary MDR-TB ($P > 0.05$, table 2). The duration of taking FLD before being labeled as MDR-TB varied from 14 to 72 months, with mean duration of 27.3 ± 15.2 months, with no significant difference in mean duration between the two sexes ($P > 0.05$, table 2). Time required to diagnose these cases as MDR-TB varied from 0 to 24 months with mean time of 9.0 ± 6.5 months and 95%CI of 6.9-11.0 months. There was no significant difference in mean diagnosis time between males and females ($P > 0.05$, table 2).

This study found that around one fifth (19.0%) of the sample have a history of default from treatment with FLD. This finding was also found significant among males with a proportion of 17.2% ($P < 0.05$, table 2). Two cases (both were males) had history of reaction to FLD treatment. None of the sample had positive HIV testing. Regarding associated medical history; though the majority of patients (61.9%) had no associated medical illnesses; diabetes mellitus was affecting 35.7% of the MDR-TB patients ($P < 0.05$, table 2).

Table 1: Socio-demographic characteristics of study sample.

Characteristic	Description	ALL
Age (year)	Mean $\pm$ SD	38.3 $\pm$ 12.8
	95% CI	34.2-42.4
	Min - Max	17 - 61
Age Group (year) ; N (%)		
	• 15-24.9	5 (11.9)
	• 25-34.9	13 (31.0)
	• 35-44.9	13 (31.0)
	• 45-54.9	3 (7.1)
	• 55-64.9	8 (19.0)
		P = 0.042
Sex; N (%)	• Male	29 (69.0)
	• Female	13 (31.0)
		P = 0.014
BMI (Kg/m ²)	Mean $\pm$ SD	21.0 $\pm$ 5.9
	95%CI	19.1-22.8
	Min - Max	12.9-35.3
Body Habitus; N (%)	• Under Weight	21 (50.0)
	• Normal Weight	11 (26.2)
	• Overweight	5 (11.9)
	• Obese	5 (11.9)
		P = 0.002
Smoker; N (%)		9 (21.4)
		P < 0.001
TB is Stigmatizing (attitude) ; N (%)		14 (33.3)
		P = 0.031
N; number, %; percentage, SD; standard deviation, Min; minimum, Max; Maximum, P; P value.		

Table 2: Treatment characteristics and medical history of study sample.

Characteristic	ALL N = 42	Male N = 29	Female N = 13
Primary MDR-TB; N (%)	1 (2.4)	0 (0.0)	1 (7.7)
Duration (month) of taking FLD; Mean±SD	27.3±15.2	28.1±17.1	25.3±10.1
;95% CI	22.4-32.1	21.5-34.7	18.9-31.7
;Min - Max	14-72	14-72	14-48
		0.563	
Time of Diagnosis (month); Mean±SD	9.0±6.5	9.1±5.8	8.5±8.2
;95% CI	6.9-11.0	6.9-11.4	3.3-13.7
;Min - Max	0-24	0-24	0-24
		0.663	
Defaulted from FLD Treatment; N (%)	8 (19.0)	5 (17.2)	3 (23.1)
	P <0.001	P <0.001	P = 0.052
Reaction to FLD; N (%)	2 (4.8)	2 (6.9)	0 (0.0)
Close Contact to Regular TB Patient; N (%)	15 (35.7)	10 (34.5)	5 (38.5)
	P = 0.064	P = 0.095	P = 0.405
Close Contact to MDR-TB Patient; N (%)	2 (4.8)	2 (6.9)	0 (0.0)
	P <0.001	P <0.001	---
Associated Medical Illness; N (%)			
• Non	26 (61.9)	16 (55.2)	10 (76.9)
• Diabetes Mellitus	15 (35.7)	13 (44.8)	2 (15.4)
• Thyrotoxicosis	1 (2.4)	0 (0.0)	1 (7.7)
	P <0.001	---	P <0.001
N; number, %; percentage, MDR; multidrug resistant, TB; Tuberculosis, FLD; first line anti-TB drugs, Min; minimum, Max; Maximum, P; P value.			

DISCUSSION:

Recently MDR-TB has increased from an occasional infection to outbreak proportions ⁽⁶⁾. The pattern of drug resistance varies from place to place and at different periods of time. It is important to know the drug resistance pattern in that area to formulate an effective drug regime ⁽⁷⁾. The spread of MDR-TB can only be prevented by rapid identification of these cases and treatment with combination of effective drugs ⁽⁸⁾. In this study mean age was 38.3±12.8 yrs, representing the period of physical, mental and

occupational stress .The majority of MDR patients were males (69%).Similar finding was reported in Egyptian studies(9,10] and in Turkey ⁽¹¹⁾. Smoking is reported in 21.4% of total sample(27.6% of males and 7.7% of females)and these findings were significant (P < 0.05) .This is differ from what is reported in a study in Egypt where 35% of MDR patients were smokers. Acquired resistance predominates in the present study and only one patient found to be a case of primary MDR-TB (P > 0.05, table 2).This finding

is differ from that of Egyptian study where primary resistance was found in 30.6% of cases⁽⁹⁾. Also it is differ from findings in Indian studies (18.8%)⁽¹²⁾. However, it similar to findings in Turkish study⁽¹¹⁾. This is very important finding because secondary drug resistance is a measure of the quality of a TB control program and should be vigorously sought and reported. So in this study one fifth (19.0%) of the sample have a history of default from treatment with FLD. This finding was also found significant among males with a proportion of 17.2% ($P < 0.05$, table 2).

In the present study the duration of taking FLD before being labeled as MDR-TB varied from 14 to 72 months, with mean duration of 27.3 ± 15.2 months with no significant difference in mean duration between the two sexes ($P > 0.05$). Time required to diagnose these cases as MDR-TB varied from 0 to 24 months with mean time of 9.0 ± 6.5 months. There was no significant difference in mean diagnosis time between males and females ($P > 0.05$). (table 2).

None of the MDR patients in this study had positive HIV testing. This is similar to the findings of Egyptian study⁽⁹⁾. The most common co-morbid disease was diabetes mellitus, reported in 35.7% of MDR patients in this study ($P < 0.05$). Similar results were reported by others⁽⁹⁾.

CONCLUSION:

Most MDR patients in this study were males aged between 25-45 years. Most cases had acquired MDR TB and primary MDR-TB was rare finding in this study. Around one fifth of MDR patients had a history of default from treatment with FLD. TB as a stigmatizing disease found in one third of MDR patients

RECOMMENDATIONS:

It is important to manage patients with tuberculosis according to DOTS strategies in the national Iraqi TB program clinic to decrease the emergence of MDR cases. Also it is important to increase awareness of people about real story of tuberculosis to fight the attitude of stigmatizing to tuberculosis.

REFERENCES:

1. Giovanni B. Migliori¹, Giovanni S, Neel R. Gandhi. Drug resistance beyond extensively drug-resistant tuberculosis: individual patient data meta-analysis. *Eur Respir J* 2013; 42:169-79.
2. World Health Organization. Towards universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis by 2015. WHO progress report 2011. Geneva, World Health Organization, 2011.
3. Orenstein EW, Basu S, Shah NS, et al. Treatment outcomes among patients with multidrug-resistant tuberculosis: systematic review and meta-analysis. *Lancet Infect Dis* 2009; 9: 153-161.
4. World Health Organisation (2011) Global Tuberculosis Control. Report 2011: WHO/HTM/TB/2011.16.
5. Gandhi NR, Nunn P, Dheda K, et al.. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. *Lancet* 2010; 375:1830-43.
6. Bloom BR and Murray CJL Commentary on a reemergent killer. *Science* 1992; 257:1055-59.
7. Johnson R, Streicher EM, Louw GE, Warren RM, van Helden PD, Victor TC. Drug resistance in Mycobacterium tuberculosis. *Curr Issues Mol Biol* 2006; 8:97-111.
8. Johansen IS, Thomson V, Marjamaki M, et al. Rapid, automated, non-radiometric susceptibility testing of mycobacterium tuberculosis complex to four drugs used in standard short course line chemotherapy. *Diagn Microbiol Infect Dis*. 2004; 50:103-7.
9. Tarek M. Safwat, Ahmed A. Elmasry, Abdel-Kader M. Mohamed. PREVALENCE OF MULTI-DRUG RESISTANT TUBERCULOSIS IN ABBASSIA CHEST HOSPITAL FROM JULY 2006 TO DECEMBER 2009 ; 5:2011.
10. Nada M, Elnaggar T, Dewidar I. M.Sc. thesis submitted in Ain Shams University. Evaluation of outcome of multi-drug resistant anti-tuberculous treatment in Abbassia Chest Hospital between July 2006 and June 2008. 2009.
11. Levent Kart, Remzi Altın, Meltem Tor, et al. Antituberculosis drug resistance patterns in two regions of Turkey: a retrospective analysis. *Annals of Clinical Microbiology and Antimicrobials* 2002; 1:6.
12. Sarala Menon, Sujata Dharmshale, Chhaya Chande, et al. Drug resistance profiles of Mycobacterium tuberculosis isolates to first line anti-tuberculous drugs: A five years study. *Lung India*. 2012; 29:227-31.

