DOI Number: 10.37506/v20/i1/2020/mlu/194656

Characteristics of Multidrug Resistant Tuberculosis in Minia, Egypt

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Background

Tuberculosis (TB) is a disease of great antiquity and has almost certainly caused more suffering and death than any other infection. A total of 40 patients were registered with a diagnosis of MDR-TB during 2010–2018 in Minia. The majority of patients were from rural areas (27; 67.5%) and male (27; 67.5%). Emergence of MDR-TB has the potential to be a serious public health problem in that necessitates strengthened TB control and improved continuous monitoring of therapy.

Keywords: *TB; MDR-TB; Therapy*

Introduction

TB is a major public health problem owing to its high risk of person-to-person transmission, morbidity, and mortality. TB still remains one of the major health miseries facing humans, particularly in developing countries (1).

Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. World Health Organization estimates that there have been 558 000 new cases with resistance to rifampicin – the foremost effective first-line drug, of that – 82% had MDR-TB.

According to the latest WHO estimation the incidence of tuberculosis (per 100,000 people) in Egypt was reported at 13 in 2017 (2). Screening, diagnosis, notification, and registration of TB cases were implemented all over Egypt according to the National TB Strategy of the National Tuberculosis Control Program (NTP). One of the registration sites is Minia Chest Hospital, Minia, Egypt where the current study was conducted.

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Method

This was a hospital-based retrospective study conducted to detect the pattern of prevalence, risk factors and treatment outcomes among patients with multidrug-resistant tuberculosis (MDR-TB) in Minia, Egypt and involving a record review of patients with TB notified and registered in Minia Chest Hospital. Data of 40 MDR-TB cases reported from January 1, 2010 to December 31, 2018 were analyzed. The diagnosis of MDR-TB in Minia Chest Hospital is made in line with the National Egyptian TB Control Program Guidelines of the Ministry of Health (NTP). Sociodemographic characteristics, associated co-morbidities, fate of outcome and regimens of previous antituberculous treatments received either category I (CAT1) (Isoniazid "H", rifampicin "R", pyrazinamide "Z", ethambutol "E" with or without streptomycin "S" for 2 months followed by isoniazid and rifampicin for 4 months {2HRZE(S)/4HR}), category II (CAT2) (2HRZES/1HRZE/5HRE) were collected. Cured patient was defined as a patient who is smear-negative in the last month of treatment and on at least one previous occasion. Treatment completed was defined as a patient who has completed treatment but who does not meet the criteria to be classified as a cure or a failure. Death was defined as a patient who dies for any reason during the course of treatment. Treatment default was defined as a patient whose treatment was interrupted for two months

or more. Treatment failure was defined as a patient who remained or became again smear-positive at five months or later during treatment or defined as a patient who was initially smear-negative before starting treatment and become smear-positive after completing the initial phase of treatment. Trend curve of prevalence rate of MDR-TB cases in Minia, Egypt from 2003 to 2018 was performed.

Limitation of the study

By using retrospective data there were unavailability of clinical data, radiologic and other laboratory investigations.

Statistical Analysis

Data analysis was performed using SPSS version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. US). Crude and adjusted odds ratios (ORs) and their 95% confidence intervals (CI95) were calculated. A binary logistic multivariate model was applied to determine the independent predictors of the treatment outcome out of those factors that demonstrated significant association by bivariate analysis at a level of significance of $p \leq 0.05$.

Results

A total of 40 patients were registered with a diagnosis of MDR-TB during 2010–2018 in Minia. The majority of patients were from rural areas (27; 67.5%) and male (27; 67.5%). The mean age of the patients was 38 years (SD ±14.3 years). Smokers represented 55% of patients. Married patients were 60% of patients (Table1).

Majority of patients received CAT1 treatment at home and about half of them were regular in treatment. The commonest side effects of drugs used in treatment of MDR-TB patients were GIT symptoms and peripheral neuritis as shown in (Table 1).

The adjusted odds ratios (OR) and 95% confidence intervals (CI) for the association between the combined effect of independent variables and the outcome variable (MDR-TB). These estimates were obtained by logistic regression analysis. Marital status, place of previous treatment, compliance and associated comorbidities were statistically associated with. Compliance to treatment was found to be the most important determinant (Table 2).

Regarding the associated co-morbidities, 2.5% of the included patients were positive for HIV,17.5% of them had cardiac diseases, 25% were diabetics, 10% had HCV and 10% had chronic chest diseases (Fig. 1).

Patients completed treatment performed 37.5% and cases with favorable outcome were 22.5% while failure of treatment were only 5% (Fig.2).

The trend curves of MDR-TB and TB cases in Minia were decreasing in the years 2004, 2010, 2012 and 2018. The trend curves were increasing in the years 2005and 2011 (Fig 3).

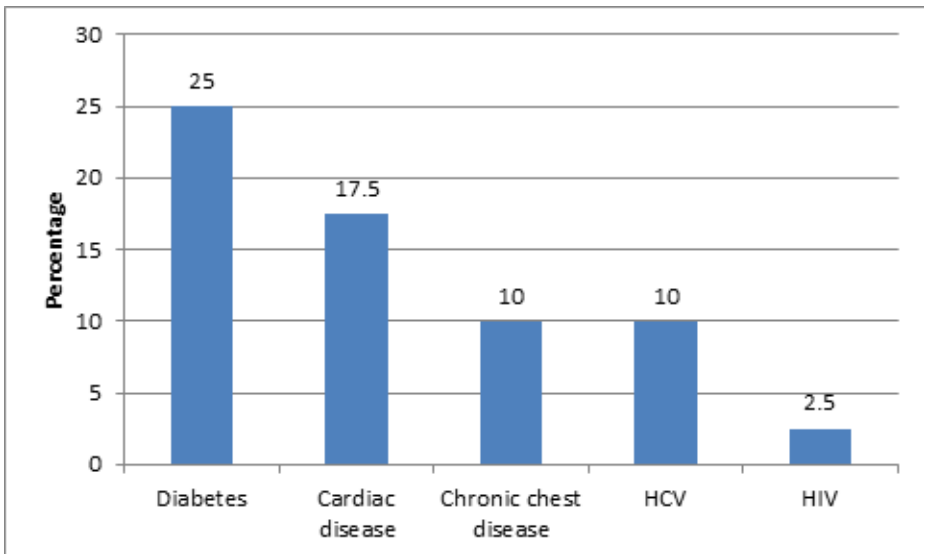

Fig (1) Associated co morbidities among the studied cases

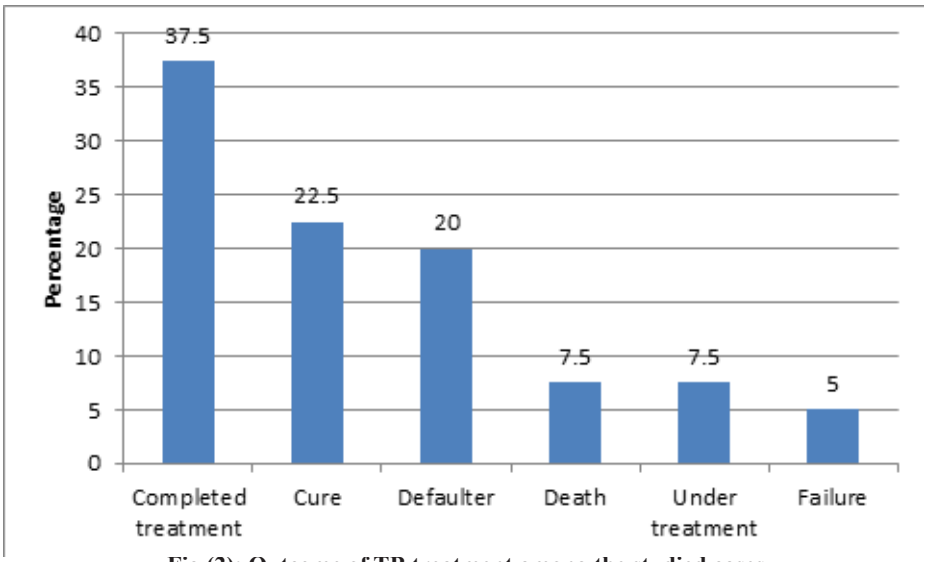

Fig (2): Outcome of TB treatment among the studied cases

Fig (3): Trend in prevalence of MDR- TB among TB patients in the period from 2003 to 2018

Table (1): Characteristics of MDR-TB cases in the period 2010-2018, Minia, Egypt

Age (years)	**Mean ± SD**	**38.6±14.3**	
		No.	%
Sex	Male	27	67.5
	Female	13	32.5
Smoking status	Smoker	22	55
	Non smoker	18	45
Residence	Rural	27	67.5
	Urban	13	32.5
Occupation	Non-worker	13	32.5
	Manual	6	15
	Farmer	13	32.5
	Housewife	8	20
Marital status	Single	5	12.5
	Married	24	60
	Widow	7	17.5
	Divorced	4	10
Place of treatment	Home	36	90
	Hospital	4	10
Regimen of treatment	CAT1	37	92.5
	CAT2	3	7.5

Cont... **Table (1): Characteristics of MDR-TB cases in the period 2010-2018, Minia, Egypt**

Compliance	Regular	21	52.5
	Irregular	7	17.5
	Uncertain	12	30
Side effects	Nothing	16	40
	GIT symptoms	18	45
	Peripheral neuritis	2	5
	Arthritis	4	10
Total		40	100

Table (2): Logistic regression analysis of factors affecting MDR-TB among the studied cases, Minia, Egypt

Variables	**OR**	**CI**	**P-value**
Age	0.95	0.86-1.04	0.26
Sex	1.1	0.075-16.5	0.9
Occupation	1.9	0.7-5.04	0.18
Residence	2.006	0.28-14.6	0.5
Marital status	5.6	1.1-28.7	0.03*
Smoking	4.5	0.4-51.5	0.2
Place of previous treatment	4.6	3.08-26.2	0.04*
Regimen of previous treatment	3.02	0.006-1509.8	0.7
Compliance to treatment	2.03	1.3-3.9	0.02*
Side effects of drugs	1.3	0.65-2.5	0.84
Associated comorbidities	1.95	1.57-2.6	0.04*

Discussion

Multi Drug Resistance Tuberculosis MDR-TB is a rapidly increasing public health problem with major socio-economic and individual consequences. The spread of MDR-TB can only be prevented by rapid identification of these cases and treatment with a combination of effective drugs [(5)].

In the present study, males constituted 67.5% while females represented 32.5%. This coincides with the epidemiological picture of tuberculosis where males spend more number of hours outdoor exposure and more challenging and hazardous working environments. Also this came in accordance with [(6)] who reported that the percentage of MDR-TB among males was 75.9% and that of females was 24.1% in three different governorates in Egypt.

In this study, we found that 55% of MDR-TB patients were smokers and this coincided with that of [(7)] in El-Abbasia Chest Hospital who revealed that in MDR TB, smokers were 61.53% and non-smokers were 38.47% among MDR-TB cases.

In many countries, differences in MDR-TB prevalence rates between urban and rural areas have been described. In the current study, 62.5% of patients were from rural areas and 32.5% were from urban areas. A study by [(8)]has reported similar findings that 90% were

from rural areas and only 10% were from urban area in the Dakahlia governorate from 2006 to 2011. Increased MDR-TB cases in rural areas could be explained by poverty, bad social conditions, milk sanitation, and occupational exposure to infected animals.

In this study, the most common co-morbidity associated with MDR TB was diabetes. This result agreed with those of [9] who reported that the highest co-morbidity among MDR-TB patients was DM 29.9%. Also, it was matched with those of [10], who reported that the highest co-morbidity among MDR-TB patients was DM (18.3%) of the patients.

In the present study, cured patients were (22.5%), dead patients were (7.5%) and defaulters were (20%). This result was matched with those of [11], who reported that (19.4%) were successfully treated, (20.9%) died, defaulted (13.4%). On the other hand, the result didn't agree with[12], who studied the outcome of treatment of MDR TB patients in Russia that 76.0% was cured. Again, the result didn't match with those of [13] who reported that 70.6% were cured in United Kingdom from 2004-2007. This difference might be due to patient compliance with treatment and regular drug in developed countries.

In the present study, 45% of patients suffered from gastrointestinal disorders. This result coincided with those of (14), who stated that the most frequent side effect of Anti TB drugs was gastrointestinal manifestations (64%). Also, this result agreed with those of (10), who reported that dominant adverse effect was gastrointestinal disorders (55%). Oppositely, the result did not coincide with those of (15) who reported that the highest adverse effects were ototoxicity 41.8%, psychological 21.3% and gastrointestinal 14%. This difference might be due to the fact that Törün study included 263 MDR TB patients who received individualized treatment for MDR-TB between April 1992 and June 2004 at Istanbul, Turkey and also the author said that the frequent and early occurrence of ototoxicity may be due to the extended exposure to amino glycosides and Capreomycin during or prior to MDR-TB treatment.

In the current study, the studied cases were resistant to CAT1 (rifampicin, isoniazid, ethambutol and streptomycin) represented 92.5%. This result agreed with the findings reported by (16) that 65% of patients were resistant to CAT1. Contrary to our results (17) in Bulgaria founded that only 52% of cases were resistant to CAT1 this high percent of acquired resistance may be due to alcoholism, number of previous treatments and irregular treatments. A study by (18) reported that only 42.8% of patients in a tertiary hospital in India were resistant to CAT1.Such variation may be due to varied geographical distribution, circulating strain patterns, demographic, ethnic, and epidemiological differences.

In this study comorbidities increased risk of MDR-TB ($p=0.04$) and this was observed by (19) in South Korea who found that relapse with resistant strains and poor treatment outcome of MDR-TB was documented among comorbid patients. Active screening for diabetes and HIV among TB patients is suggested as a cost-effective measure to be incorporated within the TB control program.

Our study revealed that MDR-TB infection had a statistically significant association with patients place of previous treatment ($p=0.04$) and this is in agreement with study done in Addis Ababa, Ethiopia by (20) on patients who visited health facilities ($p<0.005$). Compliance to treatment appeared to be a predictor for MDR-TB ($p=0.02$) and this finding was in agreement with a study by (21) in China ($p<0.005$), which requires strong commitment and collaboration among health organizations and greater compliance with TB treatment guidelines by service providers and patients.

In the present study, the trend curve of MDR-TB cases in Minia was decreasing in the years 2004, 2010, 2012 and this may be due to that the program of MDR-TB was approved and implemented in Egypt in the year 2003, by the Green Light Committee (GLC) (22). The trend curve was increasing in the years 2005 and 2011with more detection rate of drug resistant TB cases with drug susceptibility tests and increasing slum areas, low socioeconomic status and poor nutrition and political disturbance and 25th January revolution.

Conclusion

Emergence of MDR-TB has the potential to be a serious public health problem in that necessitates strengthened TB control and improved continuous monitoring of therapy. Emphasis on the need to complete medical records of patients in hospitals.

Declarations:

- There is no conflicts of interest and/or funding

- The paper has been read and approved by all authors.

- Ethical considerations: The study was approved by the ethical committee of the Faculty of Medicine, Minia University. Prior to data collection, official permissions were obtained from the authorities of Minia University Hospital. Following the ethical guidelines of epidemiological research, a written informed consent was taken from each participant.

- Data is available on request.

Ethical approval: Ethics approval to use, report, and publish the collected data was obtained from the administrator of Minia Chest Hospital. Patient information was anonymized and deidentified prior to the analysis. Research Ethics Committe at the Faculty of Medicine, Minia University, approved this study protocol.

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