Assessment of Treatment Outcomes of Multidrug-Resistant Tuberculosis in Bangladeshi Population: A Retrospective Cohort Study

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Abstract

Introduction: Every year millions of people fall sick with Tuberculosis (TB). Multidrug-resistant tuberculosis (MDR-TB) has a life threatening public health crisis globally.

Objective: To determine the successful treatment outcomes of MDR-TB in Bangladeshi population.

Methods: This retrospective cohort study was conducted at the National Institute of Diseases of the Chest and Hospital (NIDCH) Mohakhali, Dhaka, on 224 patients enrolled within July 2014 to June 2015. Data were collected by face-to-face interview and reviewing medical records.

Results: A total of 224 MDR-TB patients' histories were studied, among them male and female were 71% and 29% respectively. The average age was 37.6± 13.7 years. Of the total MDR-TB patients, 49(21.9%) were successfully treated, 124 (55.4%) had completed, 3(1.3%) had treatment failure, 5(2.2%) were lost to follow-up, 1(0.4%) was XDR-TB and 29 (12.9%) died. This study also found out that the patient with advanced age (≥55;p<0.001), living in rural areas (p<0.01), history of missing dose(p<0.001) and co-morbidity after treatment (p<0.05) were significantly associated with poor treatment outcomes of MDR-TB.

Conclusion: The study concluded that the successful treatment outcomes were 77.2% and the mortality rate was 12.9% of MDR-TB patients. Living in rural areas and missing dose were significantly associated with poor treatment outcomes. So, the study demonstrated that it is necessary to ensure the completion of whole treatment course to manage TB patients effectively in order to prevent MDR-TB.

Key-Words: Tuberculosis (TB), Multidrug resistant tuberculosis (MDR-TB), Extensive drug resistant tuberculosis (XDR-TB), Life threaten public health crisis, Successful treatment outcome.

Introduction

Every year millions of people continue to fall sick with TB. Globally 3.5% of new cases and 18% of previously treated cases had MDR/rifampicin resistant (RR) TB reported by WHO[1]. Management of MDR/RR TB is challenging because it involves the use of second-line drugs that cause a high frequency of adverse drug reactions and the treatment is lengthy. In Bangladesh MDR-TB prevalence is estimated at 1.6% among new cases and 29% among previously treated TB cases and overall 4% is reported by WHO[1]. Multi-Drug Resistance Tuberculosis (MDR-TB) is increasingly affecting the people and it is now a major concern for disease prevention. Despite research advances in the microbiological and clinical aspects of MDR-TB, research on the management of treatment outcome context of MDR-TB in Bangladesh is limited and less understood. Successful Treatment outcomes were defined as the cured and completed entire course and poor treatment outcomes defined by WHO guideline (relapse, treatment failure, lost to follow up, died). In this situation, we study the management issues which complicate the MDR-TB treatment and may result poor outcome have been addressed where scientific evidence is still lacking. Therefore, the present study was performed to determine the prevalence and management of treatment outcome of the MDR-TB patients in Bangladesh.

Materials and Methods

This was a retrospective cohort study and conducted at the National Institute of Diseases of the Chest and Hospital (NIDCH) Mohakhali, Dhaka on 224 patients enrolled within the period of July 2014 to June 2015. Data were collected though a pretested semi structured questionnaire by face-to-face interview, reviewing medical records and also MDR TB patients attending for review at NIDCH outdoor, various centers of BRAC in Dhaka city and some household basis. Data collection was started in July' 2016 and ended in June 2017 and patients were enrolled in the study if they were new MDR-TB patients, MDR-TB patients previously treated with only first-line drugs or MDR-TB patients previously treated with second-line drugs according to WHO guideline which is presented in Table-I.

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Table-I: Definition of TB types, resistance, and final treatment outcomes according to WHO

Category	Definition
Pulmonary TB	Lung parenchyma affected by Mycobacterium TB
Extra pulmonary TB	TB affects body organs other than lung
RR	Rifampicin resistance. It also includes other types of rifampicin resistance like MDR-TB and extensive drug resistance (XDR)
MDR-TB	Isolate of Mycobacterium exhibits resistance to at least rifampicin and isoniazid
New patients	Patient who has never exposed to TB drugs or administer TB medications for less than one month
Cure	Is when at least three consecutive sputum samples taken at least 30 days apart are negative during the continuation phase and without evidence of treatment failure
Treatment completed	Patients complete treatment without evidence of three consecutive sputum samples taken at least 30 days apart are negative during the continuation phase and without evidence of treatment failure
Relapse	TB patient remains sputum negative during treatment but becomes smear-positive at the end of the treatment period
Treatment defaulter	Interruption of treatment for at least 2 consecutive months
Treatment failure	Total change of treatment regimen or at least two drugs are terminated due to (a) sputum test remains positive by the end of intensive phase; (b) during continuation phase, reversion after conversion; (c) adverse drug effect; (d) evidence of resistance to fluoroquinolones or parenteral SLD
Lost to follow up	Treatment outcome is not assigned. It includes transferred out cases and those of unknown treatment outcome
Died	Recorded as died during treatment course irrespective of cause

Successful Treatment outcomes were defined as the cured and completed entire course and poor treatment outcomes defined by WHO guideline (relapse, treatment failure, lost to follow up, died).

Data included socio-demographic, disease and treatment related data. The socio-demographic variables were age, gender, residence, marital status, educational level and main occupation. Disease related variables included signs and symptoms, site of TB, contact history, status of conversion of sputum test, treatment related variables, regularity of treatment, development of co-morbidity after treatment and observation. Ethical approval was taken from ethical committee of National Institute of Preventive and Social Medicine. Data were analyzed by SPSS (Statistical Package for Social Sciences) version 20.0. Statistical test such as t-test, Chi-square and Fisher's exact test were used. Finally, the predictors were identified and a p value <0.05 was considered for statistical significance.

Results

This study was conducted in 224 patients and of them 71% were male and 29% were female. The average age was 37.6 ± 13.7 years. Among the total patients, 34.2% had no schooling, 35.7% patients completed their primary and secondary education, graduate and higher were only 19.6% and 10.6% respectively. Occupationally, 64.5% patients had done the sedentary work and 35.5% patients were involved in high labor intensive and 68.0% patients had come from urban resident. Most of the patients (75.0%) were married and majority (59%) were from nuclear family. Of the total patients, 101 (50.2%) were smoker and substance user were 23(11.5%). As per frequency distribution of clinical characteristics most of the cases (n=216, 96.4%) were smear positive pulmonary TB where as there were only 08 extra-pulmonary TB cases (3.6%). The number of new and old cases of TB were 32 (14.3%) and 192(85.7%) respectively. Among the total patients, 57 (25.8%) had history of having tuberculosis in their family members or sources of any contact and remaining 164 (74.2%) developed MDR-TB without any history of contact of TB persons. After MDR-TB treatment, most of the patients (94.6%) became negative with sputum smear test. The study also showed that about 1.9% patients had the history of reconversion of sputum test to positive. About 31.49% patients had faced social consequence and 22.8% patients had developed co-morbidity after treatment. The treatment outcomes were broken down into successful treatment (cure and treatment complete) and poor treatment outcomes (death, treatment failure and lost to follow-up) is shown in Table-II.

Table-II: Treatment outcome of MDR-TB patients in the study subjects.

Treatment Outcome		Frequency	%
Successful Treatment	Cured	49	21.9
	Completed	124	55.4
Poor Outcomes	Death	29	12.9
	Treatment Failed	3	1.3
	Lost to Follow-up	19	8.4
	Total	**224**	**100.0**

Of the 224 MDR-TB patients 49 (21.9%) were cured, 124 (55.4%) completed the treatment, 29 (12.9%) died, 19 (8.4%) were loss to follow-up and 3 (1.3%) were with treatment failure. The association between characteristics (socio-demography and clinical) and outcomes of treatment are shown in Table-III.

Table- III: Socio-demographics and clinical characteristics of MDR-TB patients grouped by treatment outcome.

Variables		Treatment outcome		p-value
		Poor Event (%)	Successful Censored (%)	
Gender:	Male	38(23.9%)	121(76.1%)	.528
	Female	13(20.0%)	52(80.0%)	
Age (years):	15-34	16(15.1%)	90(84.9%)	.000
	35-54	17(20.0%)	68(80%)	
	>=55	18(54.5%)	15(45.5%)	
Educational Status:	No Schooling	7(10.3%)	61(89.7%)	.404
	Primary	11(15.5%)	60(84.5%)	
	SSC and HSC	7(17.9%)	32(82.1%)	
	Graduate & Above	1(4.8%)	20(95.2%)	
Occupation:	Sedentary	22(17.1%)	107(82.9%)	.047
	High Labor Intensive	5(7.0%)	66(93.0%)	
Family Status:	Nuclear	13(11%)	105(89%)	.218
	Joint	14(17.1%)	68(82.9%)	
Residency:	Urban	25(16.6%)	126(83.4%)	.004
	Rural	24(33.8%)	47(66.2%)	
Smoking:	Smoker	18(17.6%)	84(82.4%)	.122
	Non-smoker	10(10.1%)	89(89.9%)	
Substance:	User	2(8.7%)	21(91.3%)	.746
	Non-user	25(14.1%)	152(85.9%)	
History of Family Contact:	Yes	7(12.3%)	50(87.7%)	.045
	No	41(25.0%)	123(75.0%)	
Increase Body Weight:	No Increase	6(60.0%)	4(40.0%)	.002
	Increase	28(14.4%)	166(85.6%)	
History of missing the dose:	Yes	15(62.5%)	9(37.5%)	.000
	No	14(8.0%)	161(92.0%)	
Development of Co-morbidity after treatment:	Yes	6(14.3%)	36(85.7%)	.02
	No	6(4.2%)	136(95.8%)	

NB: Event= death or treatment failure or lost to follow up; Censored= cured or completed or transferred out.

No significant difference was found in gender, marital status, education level, family status, smoking and substance user between successful and poor treatment outcomes of the study subjects. The study found that poor and successful treatment outcomes were significantly associated by their ages (p=0.000),

occupational categories (p=0.047) and places of residence (p=0.004). The study revealed that TB patients with older age (>55yrs), sedentary occupations like service holder, businessman, house wife and student and those who lived in rural areas were more likely to develop poor treatment outcomes of MDR-TB than their counterparts. In this study, regarding change of body weight had significantly increased (<0.01) in successful treatment outcomes of MDR-TB patients after treatment. The study also found that significantly more successful treatment outcomes in patients who were involved in history of family contact (<0.01) than compared with history of no family contact of MDR-TB subjects. The study also proved that the patients who did not miss the dose, had shown the significant association with successful treatment outcome (p<0.001). There were significant association between development of co-morbidity and treatment of MDR-TB of the study subjects. The study also revealed that some patients had significantly (p<0.05) developed co-morbidity such as deafness, diabetes, renal disease etc. after MDR-TB treatment.

Discussion

Accurate diagnosis and effective treatment of drug resistance tuberculosis (DR-TB) is essential not only to cure the affected population, but also to prevent further transmission of resistant strains. The study was designed to determine the prevalence of MDR-TB and to identify the critical predictors of poor treatment outcomes. A total of 224 patients were included in this study, among them 159 (71%) were male and 216 (96.4%) had pulmonary TB. Patients were followed for a mean of 19.5 month and the overall success rate was 77.3% and mortality rate was 12.9%. According to global Plan to End TB: 2018-2022, at least 90% success rates need to be the global target[2]. The treatment success rate of MDR-TB patients in our study was 77.3% which was comparably higher than other low-resource countries such as Pakistan (71.6%)[3] and Egypt (69.3%)[4], although lower than high-income countries such as the United States (78%)[5]. Several studies conducted in different time by Orenstein EW et al in 2009, Weiss P et al in 2014 and Eshetie S et al in 2017, it was found that the death rate was 11% ,13% and 12.7% respectively[6,7,8]. In this study the death rate was 12.9% of MDR-TB patients which was comparable to the previous studies. This study also found that older age (>55yrs and above) was a significant risk factors to develop MDR-TB than compared with younger age group. Among patients who were≥55 years old, 54.5% had poor treatment outcomes, may be due to co-morbidities in older age. So a better strategy to address co-morbidities will be important to reduce the poor treatment outcomes of MDR-TB patients in Bangladesh and this result also comparable to other studies[9,10]. Occupationally, sedentary worker groups were significantly more prone to develop poor treatment outcomes compared to high labor intensive of MDR-TB patients. May be immune system of high labor intensive was more potential than sedentary worker. In this study majority

of the respondents 151 (68.0%) were from urban area and 71 (32%) from rural area. The patients who lived in rural areas had poorer treatment outcomes than those who lived in urban area. A similar study in Bangladesh revealed that TB patients from rural areas were fourteen times more likely to develop MDR-TB than in urban area[10]. Possibly distance of the treatment center from rural areas and lack of awareness may be attributable. In this study 164(74.2%) patients were without any history of contact with TB patients in their families nad were found to have significant association with successful treatment outcomes (p < .05). In some other studies by Diande S et al[11] and Brewer TF et al[12] The same association of contact was found with MDR TB. This study also found that 175(87.9%) patients did not miss the treatment dose ever which had significant association with successful treatment outcome (p < .001). A study by Flora MS et al[13] also revealed that inappropriate treatment or patients missing doses or failing to complete their treatment were more likely to develop extensive drug resistance TB. This study also found that 42 (22.8%) patients had developed co-morbidities like renal disease, liver disease, diabetes etc. and it had significant (p < .05) association with MDR-TB subjects. Yu MC et al[9] also found that co-morbidities were significantly associated with tuberculosis. This experience supports a previous report that monetary incentives may help enhance adherence to treatment of MDR-TB[14].

Conclusion

This study concluded that the successful treatment outcomes of MDR-TB were 77.2%, which was comparable with other studies. Significantly poor treatment outcomes were observed in rural patients. The study also proved that missing dose was significantly associated with poor treatment outcomes. So, the study demonstrated that it is necessary to ensure the completion of whole course of treatment to obtain the better treatment outcome of MDR-TB.

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