



Determinants of multi-drug resistant tuberculosis patients for treatment adherence: a cross sectional study in Bangladesh

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ABSTRACT

The aim of this study is to assess the determinants of multi-drug resistant tuberculosis patients (MDR TB) for treatment adherence. A cross sectional study was carried out for one year in National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka. One hundred and twenty MDR TB patients were selected for this study. Data were collected by treatment record review and face to face interview by using pre-tested semi-structured questionnaire and analyzed by SPSS version 20. Data revealed that the disease was most prevalent (42.5%) among age group from 21 - 30 years (mean age 30.61 years). Among enrolled patients 90.8% had medication adherence according to treatment regimen. Only 9.2% respondents had interruption of their medication due to side effect of the drugs and delivery disruption. 81.7% had received regular follow up visit. Among patients 87.5% had regular follow up sputum test done according to guideline. Most of the respondents were informed about MDR TB from doctors. It was observed that mass media had no active role in MDR TB. However, the treatment adherence rate of the MDR TB patients was moderately satisfactory. Treatment supporters, oral medication use, previous pulmonary TB disease were identified as determinants of MDR TB treatment adherence. To improve MDR TB treatment adherence, a patient -centered approach should be considered at the programmatic level.

INTRODUCTION

Multi-drug Resistant tuberculosis (MDR-TB) has become a significant public health problem globally and an obstacles to effective global TB control. Globally in 2016, an estimated 4.1% (95% confidence interval [CI]: 2.8–5.3%) of new cases and 19% (95% CI: 9.8–27%) of previously treated cases had MDR/RR-TB (Eshetie et al. 2018). Ten countries accounted for around 75% of the gap between enrolments in MDR-TB treatment in 2016 and the estimated number of incident MDR/RR-TB cases in 2016; China and India accounted for 39% of the total gap. In many countries, one of the barriers to adequate access to treatment of drug-resistant TB is that the network for the programmatic management of drug-resistant TB (PMDT) is too centralized and reliant

on hospital-based models of care. Greater decentralization and more use of outpatient models of care are needed. The 2035 targets are a 95% reduction in TB deaths and a 90% reduction in the TB incidence rate, compared with levels in 2015. The most immediate milestones, set for 2020, are a 35% reduction in TB deaths and a 20% reduction in the TB incidence rate, compared with levels in 2015 (WHO, 2017).

As of 31 December 2015, in Bangladesh a total of 4579 MD-R TB patients were enrolled for treatment including 880 in 2015. Among the 880 patients in 2015, 680 are under 24-month regimen and rest 200 under 9 month regimen (WHO, 2016). In Bangladesh 2014, noted that 769 TB patients tested for HIV. Among them 45 patients had TB with HIV positive (NTP, 2016).

The development of drug resistance is a highly man made problem resulting from inadequate treatment due to suboptimal adherence. Failure to the course of treatment or incomplete TB treatment (non-adherence) is a known cause of poor treatment outcomes, increased morbidity, depilation economy and mortality, relapse, development of drug resistance, and increased disease transmission. There are complex interactions of individual, interpersonal, socio-cultural, and health system factors that influence adherence. Treatment supporters, difficulties in taking drugs regularly due to complications, lack of mass media role were identified as affecting adherence to MDR TB treatment in this study. The current study, therefore, was aimed at determining factors of treatment adherence MDR TB patients.

METHODS AND MATERIALS

The descriptive type of cross sectional study of MDR TB patients was conducted from 1st January, 2017 to 31st December, 2017. All diagnosed Multi –drug Resistant Tuberculosis (MDRTB) patients who attending in MDR control room for follow up visit in National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali.

The inclusion criteria: 1) Patients who started their treatment from January 2016 including pulmonary and extra pulmonary Multi –drug Resistant Tuberculosis (MDRTB) patients at least four month. 2) Patients who had received long treatment regimen (20 months) & short treatment regimen (9 months) of Multi –drug Resistant Tuberculosis (MDRTB). 3) MDR TB patients who are under supervision of National Tuberculosis Control Programme (NTP) in BD. 4) Patients who had voluntarily given consent. Total study populations were 150 & Sample size was 120. Data were collected by face to face interview and treatment record review. The collected data were checked and verified. Statistical analysis was performed using SPSS (statistical package for social science) version 20 statistics.

RESULTS

A total of 120 registered MDR TB patients under NTP were participated in this study. Their age ranged from 21 to 30 years with mean age 30.61

years. Among the respondents 62.5% (n=75) were male and 37.5% (n=45) respondents were female. Majority of the respondents 85.8% were Muslim. Majority of the respondents 47.5% were primary passed. Most common occupation was service 39.2% and home maker 20.8%. Majority of the respondents 55.8% were married. Most of the respondents 73.3% family members were 2-5 members. Majority respondent's monthly family income from 5000-10000 Taka with average family income of 13762.5 Tk. (SD \pm 8637.6). Majority 74.2 % of the respondents were belong in nuclear family and most of them 69.2% had residence made of Tin (Table 1).

Table 1: Socio-demographic characteristics of the respondents

characteristics	Frequency	%	Mean \pm SD
Age group (years)	11- 20 years	27	22.5
	21-30 years	51	42.5
	31-40 years	15	12.5
	41-50 years	15	12.5
	>50 years	12	10.0
Gender	Male	75	62.5
	Female	45	37.5
Religion	Islam	103	85.8
	Hindu & Christian	17	14.2
	Illiterate	24	20.0
Level of education	Primary	57	47.5
	Passed		
	S.S.C Passed	13	10.8
	H.S.C Passed	15	12.5
	Graduation	11	9.2
Occupation	Service	47	39.2
	Home maker	25	20.8
	Students	18	15.0
	Others	30	25.0
Marital status	Married	67	55.8
	Single	42	35.0
	Others (Divorced, Separation)	11	9.2
Monthly income (in taka)	5000-10000	61	50.8
	11000-15000	28	23.3
	16000-20000	19	15.8
	>20000	12	10.0
Family members	2-5 members	88	73.3
	6-9 members	29	24.2
	>9 members	3	2.5
Family Types	Nuclear	89	74.2
	Joint	31	25.8
Residence	Tin shed	83	69.2
	Semi pacca	16	13.3
	Pacca	15	12.5
	others	6	5.0

Adherence to medication is a crucial part of patient care and indispensable for reaching clinical goals. Majority of the respondents 92.5 % (n= 111) had retreated. Only 7.5% were new MDR TB cases in this study. Most of the respondents had started their MDR treatment immediately after diagnosis. 30.0% (n=36) respondents had received 11-15months MDR TB treatment. 28.3% (n= 34) respondents had received 16- 20 months. 25.8% (n= 31) respondents had received 5-10 months. Rest of them 15.8% (n=19) respondents had received <5 months MDR TB treatment. Most of the respondents 84.0% (n=101) had received 20 months treatment regimen according PMDT guideline). Most of the respondents 72.5 % (n= 87) having no family members affected previously by MDRTB. Among them 53.3% (n=64) respondents had collected their MDR TB drugs from non- governmental organization (N.G.O). Rest of them 46.7% (n=56) respondents had collected their MDR TB drugs from government. Majority of the respondents 90.8% (n=109) had intake their MDR TB drugs daily at right time. 9.2% (n=11) respondents did not take their MDR TB drugs daily at right time. Among them 37.5% (n= 45) respondents had remind their spouse to intake of MDR TB drugs daily. 28.3% (n=34) respondents had remind their parents. 8.3% (n=10) respondents had remind their children. 25.8% (n= 31) respondents to intake of MDR TB drugs daily by themselves (Table 2).

Table 2: Adherence to MDRTB medication

Characteristics		Frequency	Percent
Previous history of TB	No	9	7.5
	Yes	111	92.5
Family history of MDRTB	No	87	72.5
	Yes	33	27.5
Started treatment after diagnosis	Within two weeks	118	98.3
	>Two weeks	2	1.7
MDRTB treatment regimen	9 month regimen	19	16.0
	20 month regimen	101	84.0
Duration of MDRTB treatment	<5 month	19	15.8
	5-10 month	31	25.8
	11-15 month	36	30.0
	16-20 month	34	28.3
Collection	Government	56	46.7

center of MDRTB drugs	N.G.O	64	53.3
Daily intake of MDRTB at right time	No	11	9.2
	Yes	109	90.8
Remind to daily intake of medicine	Spouse	45	37.5
	Parents	34	28.3
	Children	10	8.3
	No body	31	25.8

Loss of follow-up visit and sputum test is also interruption of treatment. Most of the respondents 81.7% (n=98) had receive regular follow up visit according to treatment regimen and they were adhere for MDR TB treatment.87.5% (n=105) had regular follow up sputum test done according to guideline. Rest of them 12.5% (n= 15) had no regular follow up visit sputum test done. In this study majority of the respondents received financial support from government to take nutritious diet & received support from hospital during critical situation (Table 3).

Table 3: Adherence of MDRTB follows up check-up

Characteristics		Frequency	Percent
Follow up visit according to treatment regimen	Regular follow up visit	98	81.7
	Irregular follow up visit	22	18.3
Follow up sputum test according to guideline	Regular follow up sputum test	105	87.5
	Irregular follow up sputum test	15	12.5
Carried transport cost during follow up visit	Government	37	30.8
	N.G.O	19	15.8
	By self	64	53.3
Financial support from govt. to take nutritious diet	No	11	9.2
	Yes	109	90.8
Hospital support during critical situation	No	10	8.3
	Yes	110	91.7

In this study 78.3% patients were informed about MDR TB by doctors. Mass media had no role in this study to informed patients. Majority 86.7%

(n=104) of the respondents know the availability of free treatment center of MDR TB. Presence of co-morbidity influence MDR TB patient's treatment. 77.5 % (n=93) of the respondents had no co-morbidity. 22.5% (n =27) of the respondents had presence co-morbidity. There is no HIV with TB positive patients in this study. Patients should be monitored closely for signs of both treatment and adverse drug reaction (ADR) of the medications. 58.3% (n=70) of the respondents had adverse drug effect. 41.7% (n =50) of the respondents had no adverse drug effect. Majority of them had hearing disturbances. In this study depression and suicidal tendency was not found as adverse drug reaction (ADR) of the medications.

According to the patients history it is noted that when disease is severe and symptoms are strong they took drug daily and regularly. Gradually when symptoms are disappearing and the patients feel better they do not complete the courses of medicine as per prescription. Majority 90.8% (n=109) of the respondents had medication adhere. 9.2% (n=11) respondents had interrupted their treatment due to side effect of drugs & unavailability of certain drugs (delivery disruptions). Maximum missing dose of the respondents were more than one days. In current study majority of the respondents had received helped from DOT (Directly Observed Therapy) provider (Table 4).

Table 4: Interruption of MDRTB treatment

Characteristics		Frequency	Percent
Knowledge regarding sources of MDR TB information	Doctors	94	78.3
	Health workers	18	15.0
	Family members	8	6.7
	Mass media	0	0.0
Knowledge regarding availability of free of treatment for MDRTB	Know	104	86.7
	Don't know	16	13.3
Presence of co-morbidity	No	93	77.5
	Yes	27	22.5
Presence of adverse drug effect	No	50	41.7
	Yes	70	58.3
Adverse drug effect	Hearing disturbances	38	39.2

	Nausea and vomiting	15	15.5
	Weakness	10	10.3
	Arthralgia	9	9.3
	Dizziness	12	12.4
	Headache	7	7.2
	Visual Disturbances	6	6.2
Missing dose of the medication	No	109	90.8
	Yes	11	9.2
Causes to take irregular drugs	Side effect of the drugs	8	72.7
	Delivery disruptions	3	27.3
Received help from DOT provider	No	6	5.0
	Yes	102	85.0
	Occasional	12	10.0

DISCUSSION

The objective of this study was to assess the determinants of MDR TB patients for treatment adherence. The socio-demographic variables including age, sex, religion, level of educational, occupation, marital status and marital relation with spouse during taking MDR TB drugs, monthly family income, family members, type of family and residence type of the respondents. It was found that among 120 respondents. In this study the most prevailing age group from 21 – 30 years. The mean age of the respondent was 30.61 years. The respondents 62.5% (n=75) were male and 37.5% (n=45) respondents were female. Majority of the respondents 85.8% were Muslim. Majority of the respondents 47.5% were primary passed. Most common occupation was service 39.2% home maker 20.8%. Majority of the respondents 55.8% were married. Most of the respondents 73.3% family members were 2-5 members. Majority respondent's monthly family income from 5000-10000 Taka with average family income of 13762.5 Tk. (SD ± 8637.6). Majority 74.2 % of the respondents were belonging in nuclear family and most of them 69.2% had residence made of Tin. A similar study was done in China, male: female ratio of MDR-TB patients was 69.81% & 30.19%. The age groups of 40–59 years and 20–39 years accounted for 43.87% and 31.13% respectively, consisting of more than three-fourths of all the participants. The' education level was relatively low with 164 (77.36%) patients who had only attended middle school or

primary school or had received no education at all. Farmer 25.47% and worker 22.64% groups were the two most common occupations of the participants. Married patients accounted for 70% of the total, and about half of the participants' families had two to three family members. Approximately 52% of the participants' annual family income was between 10,001 and 50,000 Yuan (1,640–8,197 dollars), which was the middle level of all the participants of MDR TB patients (Chen et al., 2016).

Adherence to TB treatment is crucial for effective tuberculosis control that involves complex issues improving the quality of care of patients with TB. The development of drug resistance is a highly man made problem resulting from inadequate treatment due to suboptimal adherence. This study revealed that majority of the respondents 92.5% (n= 111) had previous history TB. Only 7.5% had no previous history of TB .They were new MDR TB cases in this study. Most of the respondents 98.3% (n=118) had started their MDR treatment immediately after diagnosis. 30% (n= 36) respondents had received 11-15 months MDR TB treatment. 28.3% (n= 34) respondents had received 16- 20 months. 25.8 % (n= 31) respondents had received 5- 10 months. Rest of them 15.8 % (n=19) respondents had received <5 months MDRTB treatment. Most of the respondents 84% (n=101) had received long treatment regimen (20 months) according PMDT guideline. Most of the respondents 72.5 % (n= 87) having no family members affected previously by MDRTB. Among them 53.3% (n=64) respondents had collected their MDRTB drugs from non-governmental organization (N.G.O). Rest of them 46.7% (n=56) respondents had collected their MDR TB drugs from government. Previously a case control study in Bangladesh shows that History of tuberculosis in the past was more common in cases (22.1%) and 83.9% (n=115) cases started their treatment immediately within 2weeks. 62.5% (n=95) cases receive treatment from government of Bangladesh (GOB), and 34.2%(n=52) cases from non-governmental organization (N.G.O) out of 136 cases (Flora et al., 2013).

Prudent use of drugs (5 right including patients, drugs, dose, time and route) is very important for MDR TB treatment. Majority of the respondents

90.8% (n=109) had intake their MDR TB drugs daily at right time. 9.2% (n=11) respondents did not take their MDR TB drugs daily at right time. Among them 37.5% (n= 45) respondents had remind their spouse to intake of MDR TB drugs daily. 28.3% (n=34) respondents had remind their parents. 8.3% (n=10) respondents had remind their children. 25.8% (n= 31) respondents to intake of MDR TB drugs daily by themselves.

Loss of follow-up visit and follow up sputum test is also interruption of treatment. This study showed that most of the respondents 81.7 % (n=98) had receive regular follow up visit according to treatment regimen and they were adhere for MDR TB treatment. Rest of them 18.3% (n= 22) had no received regular follow up visit. 87.5% (n=105) had regular follow up sputum test done according to guideline. Rest of them 12.5% (n= 15) had no regular follow up visit sputum test done. 53.3% (n=64) respondents had carried their transport cost by self during follow-up visit. A case-control study of in Philippines, Among 91 case-patients those lost to follow-up and 182 control-patients those who adhered to treatment, independent factors associated with loss to follow-up included patients' higher self-rating of the severity of vomiting as an adverse drug reaction and alcohol abuse out of 477 respondents (COMDIS-HSD, 2016).

The current study showed that most of the respondents had informed about MDR TB by doctors. Mass media has no role in this study to informed knowledge about it. MDR TB drugs are taken through orally and by injection. Medication should be administered by a trained DOT provider. Majority of the respondents had medication adhere of MDRTB and minority respondents had interruption their treatment due to side effect of drugs and unavailability of certain drugs (delivery disruptions). In a study by Caminero (2013) it is noted that although the drugs were given free of charge, many patients were unable to adhere to their treatment because of one oral combination of the following factors; lack of adequate food, poor communication between health care providers and patients, beliefs in traditional healing system, unavailability of the service in nearby health facilities, side-effect and pill burden of the drugs, stigma and discrimination study (Caminero, 2013).

Missing dose is the most common cause of drug resistant against TB. Our study revealed that 36.4% (n=4) of the respondents missed dose for 2-4 days of medication. 27.3 % (n=3) of the respondents missed dose for one day. 18.2% (n=2) of the respondents missed dose for two weeks. 9.1% (n=1) of the respondents missed dose for one month. 9.1% (n=1) of the respondents missed dose for more than one month. A cross sectional survey in china shows that treatment interruption was defined as missing a dose for at least 1 day for less than 8 consecutive weeks. Severe interruption was defined as missing doses for 2–8 consecutive weeks. Of 110 patients, 75 (68%) interrupted treatment. 19(17%) patients reported severe interruption, with a median duration of 30 days (Xu et al., 2009).

In current study 85.0% (n=102) of the respondents had received helped from DOT. Majority 90.8% of the respondents had received financial support from government to take nutritious diet. Majority 91.7 % of the respondents had received support from hospital during critical situation. A similar study was reported in China by Chen et al. (2016).

Multi-drug resistant against TB (MDR-TB) and its long and arduous treatment can lead to major disruptions in physical and mental health in patients and depression. Family is a reliable shelter for the MDR-TB patients, upon which they can depend during treatment (Chen et al., 2016). In a study in Nepal it is noted that wives and mothers give crucial family support to their husbands and children with MDR-TB, but are sometimes denied even basic support from husbands/wives and family when they are the patient (COMDIS-HSD, 2016).

CONCLUSION

Globally Multi-drug resistant tuberculosis (MDTB) remains a major health problem including high burden country in Bangladesh. In BD the drugs and diagnosis are given free of charge, many patients were unable to adhere to their treatment. In conclusion, we found that incomplete treatment which includes treatment discontinuation due to treatment failure, adverse reactions to MDR TB medicine, and hospitalization for TB complications during

previous TB treatment is the main factors leading up to MDR-TB. We also found less time required to visit the treatment centre and the designated DOTS centre, it does not necessarily mean that supervised treatment, accessibility or being treated in a designated DOTS centre contributes to MDR-TB. These finding are based on the most recent episode of previous treatment of patients with MDR-TB, as most patients have more than one episode of previous TB treatment. In addition, the health system may be better prepared for the retreatment of patients. Therefore, basic DOTS services should be strengthened for new patients to prevent development of drug resistance. Patients who are hospitalized for TB-related causes could be tested for MDR-TB. Patient education could be strengthened for all patients with TB regarding adverse effect and compliance-related issues. Public awareness through social media or mass media is also very important.

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