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## RELATIONSHIP BETWEEN SUBSTANCE ABUSE AND MULTIDRUG-RESISTANT TUBERCULOSIS

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### Abstract

This case control study was conducted between January to June 2010 to determine the relationship between substance abuse and multidrug-resistant tuberculosis. A total of 73 cases were selected purposively, from culture-positive multidrug-resistant tuberculosis patients admitted in the National Institute of Diseases of the Chest and Hospital, Dhaka and compared with 81 un-matched controls, recruited from the cured patients of pulmonary tuberculosis who attended several DOTS centers of 'Nagar Shastho Kendra' under Urban Primary Health Care Project in Dhaka city. Data were collected by face to face interview and documents' review, using a pre-tested structured questionnaire and a checklist. Multidrug-resistance was found to be associated with smoking status ( $\chi^2 = 11.76$ ;  $p = 0.01$ ) and panmasala use ( $\chi^2 = 8.28$ ;  $p = 0.004$ ). The study also revealed that alcohol consumption and other substance abuse such as jarda, sadapata, gul, snuff, heroine, cannabis, injectable drugs was not associated with the development of multidrug-resistant tuberculosis. Relationship between substance abuse and multidrug-resistant tuberculosis are more or less similar in the developing countries. Bangladesh is not out of this trend. The present study revealed the same fact, which warrants actions targeting specific factors. Further study is recommended to assess the magnitude and these factors related to the development of multidrug-resistant tuberculosis in different settings in our country.

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**Key words:** Tuberculosis, Multidrug-resistant tuberculosis, Substance abuse.

### Introduction

Pulmonary tuberculosis remains a major public health problem and economic burden worldwide. Despite advances in chemotherapy policies, the prevalence of tuberculosis is still high.<sup>1</sup> Presently tuberculosis (TB) is the second greatest contributor among infectious diseases to adult mortality causing approximately 1.7 million deaths a year worldwide. World Health Organization (WHO) estimates that one-third of the world's population is infected with *Mycobacterium tuberculosis*.<sup>2</sup> Control of TB remains one of the most serious challenges to global health. In 2005 there were an estimated 8.8 million new cases and 1.6 million deaths. The continued rise of TB in this region may be largely attributed with weak healthcare delivery

systems.<sup>3</sup> TB has returned back in a deadly form called 'multidrug-resistant tuberculosis (MDR-TB)' which is a specific form of drug resistant TB due to a bacillus, resistant to at least isoniazid and rifampicin, two most powerful anti-tubercular drugs.<sup>2</sup>

Estimates suggest that daily about 880 new TB cases and 176 TB deaths occur in the country.<sup>4</sup> In Bangladesh the number of MDR-TB cases is increasing gradually despite the government's success in TB treatment by 92% and the detection rate of 72% in 2007. From July 2007 to Feb 2008, 165 cases of MDR-TB were detected in the National Institute of Diseases of Chest and Hospital (NIDCH).<sup>5</sup> According to the WHO report 2008, the MDR-TB rate in Bangladesh is estimated at

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3.6% and 19% among new and previously treated TB cases, respectively.<sup>4</sup> In such a situation, the emerging drug resistance in Bangladesh needs further exploration.<sup>6</sup>

A hospital based case- control study in 2008, identifies a few risk factors of MDR-TB including poor management of TB patients, non-DOTS regimen and non-observed therapy. TB patients having inadequacy in treatment regarding drug, dose and duration are more likely to develop MDR-TB.<sup>5</sup> Smoking and drug abuse are among the insignificant variables.<sup>7</sup> Although, worldwide many studies reveal significant relationship between smoking and multidrug-resistant tuberculosis.<sup>1,8-10</sup> In Samara region, Russia among the civilian and prison patients with tuberculosis shows that for isoniazid resistance smoking is a significant risk factor.<sup>8</sup> A study of MDR-TB among young Korean soldiers in a communal setting showed 65 (43.9%) patients are current smokers.<sup>1</sup> A retrospective cohort study done in Madrid, Spain shows the association of MDR-TB with alcohol abuse (OR: 0.12; 95% CI: 0.03 to 0.55;  $p=0.003$ ).<sup>11</sup> Alcohol use is significantly associated with default from MDR-TB ( $p \leq 0.05$ ).<sup>2,9,11,12</sup> In a Pakistani study, smoking cigarettes, birri, hukka, cigar or clay pipe, drug abuse such as cannabis, opiates or both as type of cannabis shows association.<sup>13</sup> Drug abuse is found to associate with MDR-TB in a few other studies.<sup>12,14</sup> In Georgia risk factors for MDR-TB includes injectable drug abuse (PR=1.59, 95% CI 1.21-2.09).<sup>12</sup>

Those factors are required to be assessed, evaluated and weighted in terms of their role in increasing the risk of MDR-TB in our perspective. In order to adopt and implement the strategies and changes that may be necessary at present or in future, to combat this deadly form of TB, accurate and comprehensive information regarding its development, is a prime requirement.

This study was an attempt to find out the relationship between substance abuse and the multidrug-resistant tuberculosis infection defining control in a more appropriate manner.

## Material and Methods

Seventy three cases were selected as defined by WHO<sup>2</sup>, diagnosed by the physician from National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka which is the only tertiary referral center for complicated TB patients in Bangladesh.

Eighty one un-matched controls were selected from the cured patients of TB (defined by NTP<sup>4</sup>), a smear-positive patient who completed the entire course of 6 and 8 months of treatment and sputum smears were negative on at least two occasions: the end or during the last month of treatment and on at least one previous occasion, at least one month apart treated at different DOTS centers in Nekibari, Kallyanpur, Agargaon, Hazaribagh and Pallabi 'Nagar Shastho Kendra' in Dhaka city. The sample size was calculated based on data from a small scale case- control study in Dhaka city.<sup>5</sup> At 95% confidence level and with 80% power of the test, and taking anticipated odds ratio 11.82 the estimated sample size was 86 for cases and 86 for controls. One control for each case was attempted. Available and consented 73 cases and 81 controls were recruited by purposive sampling. Data were collected ensuring the privacy and confidentiality by face to face interview and documents' review, using a pre-tested structured questionnaire in Bangla and a checklist. Data were collected on background characteristics of the samples, socio-economic status and substance abuse. Identity of the researcher and purpose of data collection was explained to the respondents and informed written consents were taken before data collection. Cases were interviewed in the NIDCH hospital and controls were invited in different DOTS centers of Dhaka city from where they had received their TB treatment. Statistical package for Social Science (SPSS) version 16.0 for Windows was used to analyze the data. Statistical comparisons between exposure and outcome variables were made using Chi-square tests. All the tests were 2 tailed and  $p < 0.05$  was considered to be statistically significant. The odds ratio (OR) with 95% confidence interval (CI) for risk factors was calculated.

## Results

### *Smoking status of the respondents*

The respondents were asked about their habits of smoking and other smokeless tobacco. Among the cases 24.7% were past smokers which was higher than the controls (19.8%;  $p = 0.01$ ). Cases and controls were further stratified by their gender to find the smoking data precisely. Among the male cases 54.8% were past smokers whereas it was 39% among the controls ( $p = 0.02$ ). There was no difference in number of cigarettes smoked per day or proportion of heavy/moderate smokers, even when it stratified by gender.

**Table-1: Smoking status of the cases and controls**

Smoking status of the respondents	Case (n=73)		Control (n=81)		$\chi^2$	p	OR
	Number	%	Number	%			
Never <sup>#</sup>	52	71.2	47	58.0	11.76	0.01	-
Current smoker	0	0.0	8	9.9			
Past smoker	18	24.7	16	19.8			
Occasional smoker	3	4.1	10	12.3			
<b>Number of cigarettes smoked/day</b>							
Light smoker	62	84.9	69	85.2	0.002	ns	
Moderate/ heavy smoker	11	15.1	12	14.8			
Mean $\pm$ SD	19.50 $\pm$ 13.798		13.17 $\pm$ 11.838		-0.04*	ns	

\*t- test; # = Reference group; OR: Odds ratio; CI: Confidence interval

Odds ratio showed that the past smokers were 1.02 times more likely to develop MDR- TB in reference to those who never smoked.

#### Smokeless tobacco use

The respondents were asked about their history of other smokeless tobacco use. Some of them answered 'no' and some of them answered either regular or occasional history of tobacco use. The regular/ occasional users were recorded as 'yes'.

Equal proportion of cases (23%) and controls (24%) used to take Jarda. Whereas sadapata use were seen in only two cases and gul use in two controls. No one was found to use Snuff. The higher proportion of cases (54.8%) had a history of panmasala use than the controls (22%). The  $\chi^2$  test showed that the difference was significant ( $\chi^2 = 8.28$ ;  $p = 0.004$ ).

**Table-2: Other substance abuse by the respondents**

Smokeless tobacco use	Case (n=73)		Control(n=81)		$\chi^2$	p
	Number	%	Number	%		
Jarda use	7	22.6	10	24.4	0.03	ns
Sadapata use	2	6.5	0	0.0	2.72	ns
Gul use	0	0.0	2	4.9	1.56	ns
Panmasala use	17	54.8	9	22.0	8.28	0.004
<b>History of Alcohol consumption</b>						
No	69	94.5	77	95.1	0.02	ns
Yes	4	5.5	4	4.9		
<b>History of cannabis abuse</b>						
No	78	93.2	79	97.5	1.70	ns
Yes	5	6.8	2	2.5		

#### Other substance abuse

The history of alcohol consumption was almost equal among the cases and controls (5.5% vs. 4.9%); Heroin abuse was also equal in cases (1.4%) and controls (1.2%). Cannabis abuse was more common in cases (6.8%) than in controls (2.5%) but not statistically significant. No respondents had a history of injectable drug abuse.

#### Discussion

This un-matched case control study was designed to determine the relationship between substance abuse and multidrug- resistant tuberculosis. A total of 73 culture- proved MDR- TB patients admitted in the National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka, and 81 control from the cured patients of pulmonary TB attending different DOTS centers in different 'Nagar Shastho Kendra' under Urban Primary Health Care Project (UPHCP) in Dhaka city were selected.

Statistically smoking status was found to be significant for the development of MDR- TB ( $p = 0.02$ ). A study in Russia reveals that for isoniazid and rifampicin resistance male sex, smoking is the significant risk factor.<sup>15</sup> In a Pakistani study smoking shows an association with MDR- TB.<sup>9</sup>

Past smokers were 1.02 times (OR = 1.02; 95% CI: 0.47-2.22) more likely to develop MDR- TB in reference to those who never smoked. Among the male respondents cases (54.8%) were more commonly past smokers than the controls (39%). According to a study

of tobacco prevalence among adult Bangladeshis if a person smokes > 20 sticks/ day he/ she is a heavy smoker followed by 10- 20 sticks/ day is moderate smoker and < 10 sticks/ day is the light smoker.<sup>16</sup> In this current study, only 15.1% of the cases was moderate/ heavy smokers which were higher than in the controls (14.8%).

Among the smokeless tobaccos only panmasala found to be statistically significant ( $p = 0.004$ ) in this study. Alcohol consumption was not associated with the development of MDR-TB although a number of studies showed association.<sup>9,17,18</sup> This study did not found any association of MDR-TB with drug abuse as heroine, cannabis. Overall substance abuse was less common in this study sample. A similar study in Iran showed no significant difference in case of MDR-TB groups in terms of drug abuse ( $p = 0.63$ ).<sup>11</sup>

Relationship between substance abuse and multidrug-resistant tuberculosis are more or less similar in the developing countries. Bangladesh is also with this trend. The present study supports the same fact.

### Conclusion

The study revealed that, smoking status and panmasala use of the TB patients were significantly associated with the development of multidrug- resistance. Alcoholism and other drug abuse had no association to develop MDR-TB. Relationship between substance abuse and multidrug- resistant tuberculosis are more or less similar in the developing countries. Bangladesh is not out of this trend. The present study supports the same fact, which warrants actions targeting specific factors.

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