FACTORS ASSOCIATED WITH MULTIDRUG-RESISTANT TUBERCULOSIS

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Abstract

This case control study was conducted in selected centers of Dhaka City from March to July 2008 to determine the association of multidrug-resistant tuberculosis with the attributes related to treatment and socio-economic condition of tuberculosis patients. Sixty seven culture-proven multidrug-resistant tuberculosis cases and similar number of age and sex matched controls were selected purposively. 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 occupation (p=0.001) and residential status (p=0.001) of the tuberculosis patients. Tuberculosis patients who did not remain under directly observed treatment were 3 times more likely to develop multidrug-resistant tuberculosis (OR 3.21, 95%CI=1.59-6.52). Multidrug-resistance was associated with inadequacy of treatment (OR 2.56, 95%CI=2.03-3.23). Failure of sputum conversion at the end of 2 months of treatment was detected to be the best predictor of multidrug-resistant tuberculosis (OR 11.82, 95% CI=4.61-30.33), followed by treatment with non Directly Observed Treatment Short course regimen and high labor intensive occupations like agriculture, production and transport. The risk factors of multidrug-resistant tuberculosis warrant much improvement in the effective implementation of control programs.

Ibrahim Med. Coll. J. 2009; 3(1): 29-33

Key wards: Tuberculosis, MDR TB.

Introduction

Despite the availability of effective chemotherapy tuberculosis (TB) still remains a major health problem in most of the countries of the world.[1] Tuberculosis was on the verge of extinction from the western world due to effective introduction of chemotherapeutics.[2] Average number of cases declined in the 70's leading to a sense of relief. But, in the last two decades, the world has witnessed an alarming rise of tuberculosis.[3] Bangladesh ranks fifth among 22 high TB Burden countries in the world.[4] Unfortunately, TB has not only struck back, it has returned with vengeance in a deadly form called 'multi drug-resistant tuberculosis'. MDR TB is a specific form of drug resistant TB due to a bacillus, resistant to at least isoniazid and rifampicin, the two most powerful anti-tubercular drugs.[5]

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).[6] WHO estimated 14% MDR-TB rate among previously treated cases and 1.8% among new cases.[7]

In such a situation, the emerging drug resistance in Bangladesh needs further exploration.[8] In order to adopt and implement the strategies and changes that may be necessary at present or in future and to combat this deadly form of TB, accurate and comprehensive information regarding its development, is a prime

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requirement. This study is designed to identify the factors related to the development of MDR TB in a setting common in Bangladesh.

Materials and Methods

Sixty seven cases were selected, as defined by WHO[5] 'resistant to the two main first line drugs, Isoniazid and Rifampicin', from culture-proved MDR-TB patients admitted in National Institute of Disease of Chest and Hospital (NIDCH). Equal number of age and sex matched controls, the cured patients of TB, as defined by NTP,[9] who had been smear-positive initially but became smear negative in the last month of treatment and on at least one previous occasion, were selected from NIDCH and other DOTS centers in Mohakhali, North Badda, Adorsha Nagar and Rampura in Dhaka City. The sample size of 134 was estimated following WHO guideline.[10] Data were collected by face to face interview and documents' review, using a pre tested structured questionnaire and a checklist on background characteristics of the samples, socio-economic data and data related to anti tuberculosis treatment. Ethical clearance was obtained from the Ethical Committee of NIPSOM before data collection. Data were processed and analyzed by SPSS version 12.0.

Results

Socio-demographic characteristics of cases and controls

Cases and controls were matched for age and sex. No significant difference was observed in marital status,

Table-1: *Distribution of the respondents by socio-demographic characteristics*

Variables	Case n=67		Control n=67		χ^2	p	OR	95% CI
	No.	%	No.	%				
Religion								
Muslim	63	94.0	65	97.0	0.69	ns	–	–
Hindu	4	6.0	2	3.0				
Marital status								
Unmarried	24	35.8	23	34.3	0.03	ns	–	–
Ever married	43	64.2	44	65.7				
Education in years								
Illiterate	22	32.8	13	19.8	9.44	ns*	–	–
1 – 5 years	23	34.3	15	22.4				
6–10 years	18	26.9	28	41.8				
≥11 years	4	6.0	11	16.4				
Occupation								
Sedentary	10	14.9	27	40.3	13.66	0.001	5.03	2.06-12.71
Labor intensive	41	61.2	22	32.8			2.10	0.89-4.90
Non paid	16	23.9	18	26.9				
Place of residence								
Urban slum	2	3.0	18	26.9	16.85	0.001	14.73	3.11-69.68
Rural	36	53.7	22	32.8			1.27	0.53-3.06
Peri-urban	18	26.9	14	20.9			1.93	0.74-5.06
Urban	11	16.4	13	19.4				
Type of house								
Pucca	9	13.4	14	20.9	7.66	ns	–	–
Semi-pucca	18	26.9	29	43.3				
Kucha	40	59.7	24	35.8				
Income class by the severe poverty line								
Below	63	94.0	60	89.6	0.89	ns	–	–
Above	4	6.0	7	10.4				

ns = not significant, * Bonferroni correction

religion, house-type and income level between cases and controls (Table–1). Although initially showed, after Bonferroni correction no significant difference was observed in educational status between cases and controls. Cases and controls significantly differed by their places of residence (p=0.001) and occupational categories (p=0.001). TB patients with high labor intensive occupations like agriculture, production and transport were five times more likely and those who lived in rural areas were fourteen times more likely to develop MDR TB than their counterparts.

MDR-TB was associated with observation (p=0.001), adequacy (p<0.001), regularity (p<0.01), and completion of first course (p<0.001) of TB treatment and smear conversion after 2 months of initial treatment (p<0.001, Table-2). Drugs were available for most of the TB patients, only 6 MDR TB cases reported about non-availability. TB patients who were not under directly observed treatment, were 3.21 times more likely to develop MDR TB than those who did (OR=3.214, 95% CI=1.585 - 6.516). TB patients having inadequacy regarding dose and duration in treatment were 2.5 times more likely to develop MDR TB (OR=2.56, 95% CI=2.026-3.230), having irregular treatment were 2.98 (OR=2.98, 95%CI=1.37-6.48) times and having non compliance regarding completion of treatment were 2.34 (OR=2.34, 95% CI=1.9-2.9) times more likely to develop MDR TB. Twenty eight (52.8%) out of 53 cases remained smear positive at the end of 2 months of the intensive phase, whereas only 13.4% of controls remained as such. TB patients who remained smear positive at the end of 2 months of the intensive phase, were 11.82 times more likely to develop MDR TB than those converting to smear negative (OR=11.82, 95%CI=4.60–30.33).

Entering all independent variables together, a logistic regression model was constructed with overall 84% correct prediction. Failure of sputum conversion at the end of 2 months of treatment was detected as the best predictor of MDR TB, followed by treatment

Table-2: *Management of tuberculosis and MDR TB*

Variables	Case n=67		Control n=67		χ^2	p	OR	95% CI
	No.	%	No.	%				
Treatment regimen								
DOTs	43	64.2	65	97.0	23.09	<0.001	18.14	4.08-80.73
Non-DOTs	24	35.8	2	3.0				
Observation of Treatment								
Not observed	42	62.7	23	34.3	10.79	0.001	3.21	1.585-6.516
Observed	25	37.3	44	65.7				
Adequacy of treatment								
Inadequate	22	33.8	0	0.0	27.21	<0.001	2.56	2.026-3.230
Adequate	43	66.2	67	100				
Completion of 1st course								
Not completed	17	25.4	0	0.0	19.47	<0.001	2.34	1.9 - 2.9
Completed	50	74.6	67	100				
Irregularity in the course of treatment								
No	39	58.2	54	80.6	7.90	<0.01	2.98	1.37-6.48
Yes	28	41.8	13	19.4				
Availability of anti TB drugs								
No	6	9.0	0	0.0	6.28	ns*	–	–
Yes	61	91.0	67	100				
Smear conversion at 2nd month of treatment								
No	28	65.1	9	13.6	30.77	<0.001	11.82	4.60-30.33
Yes	15	34.9	57	86.4				

ns = not significant, * Bonferroni correction

Table-3: *Factors of MDR TB after adjusting for other variables*

Variables	χ^2	p	OR	95% CI of OR
Smear conversion at 2nd month of treatment				
Conversion*				
No conversion	26.41	0.000	11.82	4.61-30.33
Regimen of treatment				
DOTS*				
Non-DOTS	7.23	0.007	20.12	2.26-179.24
Occupation				
High labor intensive occupations*				
Sedentary occupations	6.99	0.008	0.127	0.028-0.587
Observation of treatment				
Not observed*				
Observed	5.46	0.020	0.501	0.28-0.895

*Reference group

with non-DOTS regimen, high labor intensive occupations and lastly non-observation of treatment (Table-3).

Discussion

This study was designed to determine the association of multidrug- resistant tuberculosis with the socio-economic and treatment related factors of TB-patients.

Among the socio-economic factors, occupation and residential status were found to be associated with the development of MDR TB. Several studies in India identified illiteracy and low socio-economic status of the patients, among the factors associated with the emergence of drug resistance.[11]

In the present study, highest proportion of the MDR TB cases (61.2%) were found to be involved in occupations like agriculture, production and transport. Occupation might have an association with MDR TB ($p < 0.01$). This might be because, these are the occupations where maintenance of a strict, meticulous and long course like TB-treatment seems to be difficult without special motivation.

The study revealed that, poor management of illness of TB patients might give rise to MDR TB. Non DOTS source and regimen of treatment and non observed therapy were associated with the development of multidrug-resistance. TB patients having inadequacy in treatment regarding drug, dose and duration were more likely to develop MDR TB. A Chinese study in northern Jiangsu province in 2002 concluded that, residing in an area without DOTS program was an independent predictor of MDR TB.[12] Statistically, association of MDR TB was observed with irregularity of treatment in this study. In a case control study in India researchers identified poor past compliance to treatment (OR 6.6) as an independent predictor of MDR TB.[13] Another study in Sao Paulo city, Brazil found the most frequent condition associated with MDR TB cases, was abandonment of therapy (45%).[14] Few other studies around the world in recent years concluded a similar outcome.[15,16]

The study revealed that, failure of sputum conversion at the end of 2 months of treatment was the best predictor of MDR TB. In a study in India in 2000, researchers found that more than half of the patients receiving category II treatment who remained sputum positive after 3 or 4 months of treatment, had MDR TB.[17]

Risk factors for multidrug-resistant tuberculosis are more or less similar in the developing countries. Bangladesh is also not out of this trend. These factors need to be taken into account while framing programs to ensure the complete and reliable cure of TB patients in order to prevent this deadly form of TB as well.

Acknowledgement

This study was supported by a grant from Bangladesh Medical Research Council (BMRC).

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