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Epidemiology and factors of tuberculosis treatment outcome, Bangladesh, 2012-13

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ABSTRACT

Tuberculosis (TB) treatment outcome is an important indicator to improve TB control efforts. We assessed factors associated with unfavorable treatment outcomes among smear-positive pulmonary TB patients reported to the national TB program from January 2012 to December 2013 in Bangladesh. Favorable outcomes were cured and treatment completed with unfavorable outcomes as failed, defaulted, died and lost to follow-up. We retrieved 98,932 patients with outcome data; 65,458 (66%) were male and 7,956 (8%) had unfavorable outcomes (3,737 (47%) died, 1,641 (21%) defaulted, and 1,599 (20%) lost to follow-up). In multivariable analysis, male gender (adjusted odds ratio [aOR] 1.41; 95% confidence interval [CI] 1.34-1.49) and treatment at a chest disease hospital (CDH) (aOR 1.44; 95% CI 1.25-1.66) were risk factors. The association between male gender and unfavorable outcomes may result from the high smoking rates among males in Bangladesh. The association of treatment at a CDH with unfavorable outcomes may occur because complicated cases (e.g., TB with co-infections) are usually treated in a chest hospital in Bangladesh. A case-control study could further confirm and explain these findings.

Keywords: TB, Unfavorable outcome, Treatment outcome

INTRODUCTION

Tuberculosis (TB), is a re-emerging infectious disease and one fourth of the world's population is latently infected with TB and thus at risk to develop active TB disease anytime during their lifetime. Despite being a preventable and curable infection, the global TB report of 2018 highlighted TB as one of the top ten leading causes of death.² In 2017, approximately 10 million people in the world developed TB disease.² TB occurs in all countries and in all age groups but two thirds of all cases happens in eight countries; Bangladesh is one of them where three percent of global TB cases were reported in 2017.²

In Bangladesh, since 2012, the significant increase in TB case notifications is driven by increased numbers of extra-pulmonary and clinically diagnosed pulmonary

cases.3 Newly infected smear-positive pulmonary TB (NSP PTB) is the most infectious form that causes secondary infections.⁴ In 2012 to 2014, among the 22 high burden countries (HBCs), the percentage of newly registered pulmonary TB cases that are smear-positive was highest in Bangladesh (81%) and the democratic republic of the Congo (84%).5

The Bangladesh national tuberculosis control programme (NTP) has been conducting TB surveillance since 2007. Bangladesh was one of 11 HBCs that are not on track to reduce incidence, prevalence and mortality of TB in line with 2015 global millennium development goals targets.⁶ Since the surveillance system was implemented the data collected on epidemiological indicators of TB diseasesuch as factors affecting treatment outcome-have not been analyzed in detail. Understanding reasons

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poor treatment outcomes can help improve TB control efforts. Therefore, we analyzed the NTP surveillance data to evaluate the epidemiological indicators and assess factors associated with TB treatment outcomes among persons with NSP PTB in Bangladesh.

METHODS

We analyzed NSP PTB data reported to NTP from January 2012 to December 2013. These data are patients reported to NTP as having NSP PTB and TB treatment outcome data reported to NTP. Variables included were age group (e.g., 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64 and >65 years), gender, health-care facility and six TB treatment outcomes. Field level (sub-districts) surveillance staff report the data to NTP. Data were from all sub-districts in Bangladesh.

According to WHO, NSP PTB is based on the presence of at least one acid fast bacillus (AFB) in at least one sputum sample in countries where an external quality assurance system is functioning well. Case notification rate (CNR) is defined as number of cases registered and reported per one hundred thousand population per year.

NTP categorizes outcomes into six types: Cured (sputum smear test results negative for AFB after full treatment course), treatment completed (sputum smear test results for AFB not available after treatment completion), failed (sputum smear test results for AFB positive at the end of treatment), defaulted (treatment interrupted for ≥ 2 consecutive months) (Replaced by lost to follow up in the revised definition by WHO), died (death during TB treatment due to any cause) and lost to follow up (treatment outcome not known because of loss to follow up due to transfer or other).

We considered cured and treatment completed (I and II) to be favorable outcomes as favorable and all other outcomes (III-VI) to be unfavorable outcomes. Reporting sites were categorized as-sub-districts (primary, rural level), metropolitan health-care facility (secondary, urban level; MHF) and CHD (tertiary, urban level; CDH).

The chi-square test was used to compare treatment outcomes by health-care facility and gender of the patients. Descriptive characteristics are presented as percentages. We used logistic regression to assess association of demographic and treatment delivery factors with unfavorable outcomes. Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) and p values were calculated. We included factors with p \leq 0.10 into a multivariable logistic regression model and retained factors with p \leq 0.05 for the final model. All analyses were done using Stata 13 software.

As we used the program data and not personal identifiers, no ethical clearance was submitted and written approval was obtained from the national tuberculosis program, Bangladesh.

RESULTS

A total of 106,833 new patients were registered as having NSP PTB, of whom 66% were male. There were very few cases notified among <15 years age and >52% of patients were between 25-54 years age group. Case notification rate was about two times higher in 15-24 years and \geq 55 years age groups. A large increase from 0-14 years to greater than 15 years was observed (Table 1). The overall male-to-female ratio and male-to female ratios for all age groups except the 15–24-year-old group differed, male being significantly more (p<0.01); the male-to-female ratio was >1 for persons aged 0-4 years and \geq 35 years and was <1 for those aged 5-14 years and 25-34 years (Figure 1). There was a direct increase in male-to-female case ratios in each age group from 35-44 years to \geq 65 years.

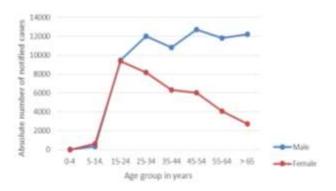
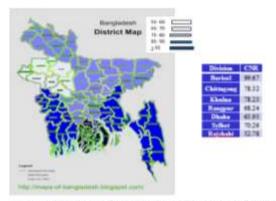


Figure 1: New smear positive pulmonary TB cases according to age and sex in Bangladesh, Bangladesh national tuberculosis control programme, 2012-13.

Analysis of case notification data by reporting sites indicates that the Southern costal parts of Bangladesh (i.e., Barisal division) had highest CNR at 99.67/100,000 population. The CNR in Chittagong, Khulna and Rangpur divisions were 78.32, 78.23 and 68.24 per 100,000 populations respectively. Rajshahi division had lowest CNR as 52.78/100,000 populations (Figure 2).



Overall case notification rate (CAR) new snear positive patronney TB in different dissions of Bengladesh in 2012, Highten notification noted in Berial division which is situated at the Sauthern part of the country, Also Chittagong and Khulna showed higher CHR than the other devisions of Bangladesh.

Figure 2: Case notification rate of NSP-PTB cases by divisions; Bangladesh national tuberculosis control programme, 2012-2013.

Table 1: New smear-positive pulmonary tuberculosis cases according to age distribution, Bangladesh national tuberculosis control programme, 2012-13.

Age group (years)	Male	Female	Total	Percentage (%)	Cumulative (%)	CNR/100,000 population
0-4	5	1	6	0.005		
5-14	311	649	960	0.9	0.9	2(0-14)
15-24	9479	9355	18834	17.6	18.5	220
25-34	12021	8175	20196	18.9	37.4	107
35-44	10837	6342	17179	16.1	53.5	105
45-54	12742	6044	18786	17.6	71.1	166
55-64	11843	4073	15916	14.9	86.0	229
≥65	12236	2720	14956	14.0	100	268

Table 3: New smear-positive pulmonary TB treatment outcomes stratified by health care facility, Bangladesh national tuberculosis control programme, 2012-2013.

Outcome	Sub-district facility (%)	CDH (%)	MHF (%)	Difference between sub- district and CDH	Difference between CDH and MHF	Difference between sub district and MHF
Favorable	81040 (89)	1535 (2)	8401 (9)	p<0.01	p<0.01	p<0.01
Unfavorable	6651 (84)	281 (3)	1024 (13)			

Treatment outcome data were available for a total of 98,932 patients. Among them, 65,458 (66%) were male. Unfavorable outcomes were seen in 7,956 (8%) of patients. Of these, 3,737 (47%) died, 1,641 (21%) defaulted, and 1,599 (20%) were lost to follow up. Favorable and unfavorable outcomes significantly between types of health-care facility where patients received TB treatment (Table 3). Among those with unfavorable outcomes, the proportion who died was highest in sub-district hospitals (53.3%), the proportion of those defaulting was highest at CDHs (44.4%), and the proportion who were lost to follow up was highest for MHFs (56.6%). On univariate analysis, factors associated with an unfavorable outcome were being male (p<0.001), treatment at a CDH (p<0.001), treatment at a MHF (p<0.001), and urban residence (p<0.001). On multivariable analysis, factors associated with an unfavorable outcome were gender (male) (adjusted odds ratio [aOR] 1.41, 95% confidence interval [CI] 1.34-1.49), treatment at a CDH (aOR 1.44; 95% CI 1.25-1.66) and treatment at an MHF (aOR 1.51; 95% CI 1.41-1.62).

DISCUSSION

In this analysis, we found that the age group with the highest percentage was 25-34 years, but the percentages were fairly comparable over a 40-year age range. Whereas Rao found large proportion of TB patients in the young and reproductive age group between 30 to 45 years.⁸ This might be because in this subcontinent, people at this age group (25-40 years) work outside and are commonly infected by others. Also, there might be a possible link with smoking.⁹ We also found the higher CNR in the ≥65 years age group. This might be because in Bangladesh, 62% of the older people (age>60 years) are at risk for malnutrition and malnutrition could lead to

secondary immunodeficiency which increases the host's susceptibility to infection. Also, there might be some biological changes with aging. Older persons being more susceptible to developing TB as body cellular immunity declines. Also, the chance of reactivation of primary infections increases with comorbidity (e.g., diabetes).

We found that men were more likely to have TB disease and to have unfavorable outcomes. Similar male to female ratio is noted in many studies.^{8,14} Possible explanations may be that women are less likely to seek health care or access care due to cultural and other barriers. 15,17 It is possible that the incidence of TB is higher in men. Men work outside the home leading to more frequent social contacts. Also, men in Bangladesh go overseas to work for periods of time and often live in crowded quarters which is a risk factor for developing smear positive TB disease.¹⁸ They also smoke more frequently which is considered risk factor.9 In addition, there are biological differences between men and women (e.g., hormonal differences, differences in the cellular immunity and antibody response, naturally lower level of CD4 T lymphocytes etc.) which might lead to a risk difference between men and women. 19 However, this relationship is not well established.

With regard to TB notification rate and treatment outcomes, we found that the Southern costal part of Bangladesh (i.e., Barisal division) had the highest CNR of NSP-PTB. This part of Bangladesh is divided by three big rivers and often the poor transportation and communication system making it difficult to travel to health-care facilities. According to 2006 CPD report, Barisal (52.0%), Rajshahi (51.2%) and Khulna (45.7%) have the highest incidence of poverty compared to the remaining divisions of Bangladesh. ²⁰ Factors associated

with low socio-economic status, include malnutrition with attendant decreased immunity, and these can predispose to communicable diseases like TB.²¹

We found treatment outcomes for urban and rural health care facilities differed significantly. Although only 2% NSP PTB cases were treated in CDHs, which are in urban settings, unfavorable outcomes were significantly higher in these facilities. Persons seeking medical care at MHFs were also found to be more likely to have unfavorable outcomes. One explanation for this is that in Bangladesh, persons with more complicated illness (e.g., TB associated with other diseases, multi-drug resistant TB, etc.) are often referred to and treated at CDHs and MHFs. CDHs and MHFs located in urban settings, which likely explains the univariate finding that unfavorable outcomes were associated with urban residence. Default rates were highest at CDHs and loss to follow up rates were highest at MHF. Usually there is rapid turnover of population in urban areas. Also, because of their urban location, the increased rate of unfavorable outcomes might lead to increased transmission.

Limitations

We only analyzed outcomes of NSP PTB cases. It would be important to analyze patients with other types of TB (e.g., those with new smear-negative PTB and extrapulmonary TB), to determine if factors associated with unfavorable outcomes for these persons are similar to those of persons with NSP PTB. Also, these data did not contain information about factors related to gender differences, other data that might have been available from medical records (e.g., smoking history, health-care seeking behaviors, specific comorbidities, etc.). Having medical record data would have provided additional important adjustment factors for the multivariable analysis.

CONCLUSIONS

Reinforcing adherence counselling and additional followup during treatment of patients being treated in CDHs and MHFs could increase favorable treatment outcomes. It would be important to institute rigorous tracing of patients who default or are lost to follow up. Further studies (e.g., a case-control study) would be warranted to confirm our findings and elucidate reasons for the association of males, treatment at particular facilities, and differences by regions with unfavorable outcomes.

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Institutional Ethics Committee

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