Smoking behaviour among Tuberculosis relapse cases attended at tertiary level hospitals in Dhaka city of Bangladesh

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ABSTRACT— Bangladesh is a high Tuberculosis (TB) burden country particularly due to the burden of drug resistant TB. Smoking increases the risk of relapses of TB, which remains to be explored in the context of Bangladesh. This case-control study was conducted in two tertiary level hospitals in Dhaka City to determine the association between smoking habit and relapse tuberculosis (TB). The study population was the registered adult TB patients who got complete treatment within 2-5 years. Relapse and non-relapse TB cases are listed serially in the hospital record books. The relapse cases were selected randomly as case group and age-matched (±2 years) with the respondent of the case group, cured patients were included as control groups. A total of 170 respondents in each case and control groups were selected with 80% power and assuming 14% differences between cases and controls. The selected respondents who visited the respective hospitals on the scheduled day were interviewed face to face for data collection. The mean age of the participants was 39.7±11.56 years. Significantly ($\chi2=20.767$; p=0.000) a higher proportion of the relapse cases were found among the respondents who got complete TB treatment 3 years before in comparison to that of the control group. Family size more than five, education of secondary level, two earning members in the family, past smoker, smoked more than 10 cigarettes per day and exposure to second-hand smoking were found to be significantly associated with a higher proportion of relapse cases. Regression analysis revealed that exposure to second-hand smoking and past smokers was 2.4 and 2.0 times respectively more likely to develop relapse TB. Thus, this study concluded that past smoking habit and exposure to second-hand smoking had the strongest likelihood of developing more TB relapse cases.

KEYWORDS: TB, Relapse TB, MDR-TB, Smoking, Second-hand smoker, NTP, Bangladesh.

1. INTRODUCTION

Tuberculosis (TB) is a major public health problem in the world. In 2014, among 100,000 people, 133 were estimated to be contracted TB [1]. Bangladesh ranks sixth among the high TB burden countries [2- 4]. The annual incidence and prevalence of TB for all cases in Bangladesh was 225 and 411 per 100,000 populations respectively [5]. WHO categorized smoking as a high burden for tuberculosis and reported that the burden of smoking among patients with tuberculosis was poorly defined [1]. Study findings revealed that people who smoked had approximately twice the risk of both Mycobacterium tuberculosis infection and active tuberculosis [6]. A recent systematic review and meta-analysis of 24 published studies showed that individuals who smoked had a 73% increased risk of becoming infected with tuberculosis and were more than twice as likely to develop active tuberculosis than those who did not smoke. This review further

revealed that smokers were 40 to 60 per cent more likely than non-smokers to develop tuberculosis after being infected with TB bacteria. Smoking could decrease immune response or damage the function of cilia in the airways and increase the risk for TB [7]. Smoking also increases the risk of relapses even after successful treatment of tuberculosis [8]. The National Tuberculosis Control Program (NTC) of the Government of Bangladesh has prioritized to eliminate Tuberculosis [9]. Smoking is a modifiable exposure, therefore, highlighting smoking as a risk factor for TB may have greater resonance in Bangladesh, very few published studies could address about how smoking behavior or smoking cessation influenced the outcome of tuberculosis [10]. This study aimed to examine the extent of the risk of smoking behavior among TB cases in selected tertiary level hospitals of Dhaka City.

2. Materials and methods

This was a case-control study conducted among the TB-relapse and non-relapse (cured) cases who got complete TB treatment from the National Institute of Diseases of the Chest and Hospital (NIDCH) and TB Hospital in Dhaka, Bangladesh. These two hospitals have specialized facilities. A major proportion of TB patients in the country are handled by them. These hospitals maintain patient's registration books and keep records of the relapse and cured TB cases serially. The study population was the registered adults (>18 years) TB patients who got complete treatment within 2 to 5 years from the respective hospitals. The registered relapse case was selected as the participants of the case group and who were registered as cured (non-relapse) were selected as the participants of the control group. The study sample size was calculated using the formula: $n=z^2_{1-\infty/2}(P1(1-P1)+P2(1-P2))/d^2$ where z=1.96 at 5% level of significance and 80% power of the test; d=acceptable level of error=10; P1 and P2 =anticipated prevalence of smoking with no recurrence or recurrence of relapse 24% and 38% respectively.[11] Thus, the Epi sample size calculator determined a sample of 340 (170 cases and 170 controls) as the calculated sample size.

A total of 2664 TB patients (>18 years) were recorded in the registration books of both the hospitals within 2 to 5 years, of them 205 were relapse cases and others were non-relapse cases. From the list, 170 relapse cases were selected randomly as the respondents of the case group while age-matched (± 2years) participants with the respondent of the case group from the nearest serial were included in the control group. The selected participants who could not attend or did not give consent to participate in the study were replaced with the individual from the nearest serial of the registration books. Ultimately 340 respondents (170 case and 170 control) who visited the respective hospitals on the scheduled day were interviewed face to face for collection of data. Ethical issues of the study were reviewed and approved by the Research Ethics Committee of Daffodil International University, Bangladesh.

3. Results

The mean age of the respondents was 39.8 (±11.44) years and 47.1% of them belonged to 26-40 years age group. The difference of age between case and control groups was not significant. About 86% of the respondents were married. A higher proportion of them was from the case group (88.8%). Among the respondents, 57.1% completed the secondary level of education and one-fourths (25.3%) of them completed graduation. However, significantly ($\chi2=7.705$; p=0.021) a higher proportion (31.8%) of the respondents of the control group had graduation. Occupation of the majority (43.8%) respondents of both the groups was service followed by business (38.2%) and a few (8.5%) were unemployed (Table-1).

Table 1: Socio-demographic characteristics of respondents

Characteristics	Case n (%)	Control n (%)	Total n (%)	Test of Significance

Age group (years)				
≤ 25	16 (9.4)	19 (11.2)	35 (10.7)	
26 to 40	79 (46.5)	81 (47.6)	160 (47.1)	χ^2=0.591; p=0.899
41 to 55	57 (33.5)	55 (32.4)	111 (32.6)	
55+	18 (10.6)	15 (8.8)	33 (9.7)	
Mean ±SD	40.58±11.47	38.97±11.37	39.78±11.44	t=-1.347; p=0.179
Marital status				
Ever Married	151 (88.8)	144 (84.7)	295 (86.8)	χ^2=1.255; p=0.263
Never married	19 (11.2)	26 (15.3)	45 (13.2)	
Education				
Primary	34 (20.0)	26 (15.3)	60 (17.62)	χ^2=7.705; p=0.021
Secondary	104 (61.2)	90 (52.9)	194 (57.1)	
Graduate &above	32 (18.8)	54 (31.8)	86 (25.3)	
Occupation				
Service	68 (40.0)	81 (47.6)	149 (43.8)	χ^2=7.129; p=0.068
Business	75 (44.1)	55 (32.4)	130 (38,2)	
Worker	15 (8.8)	17 (10.0)	32 (9.3)	
Unemployed	19 (11.2)	10 (5.9)	29 (8.5)	

Most of the respondents (68.5%) had family members up to 5 (Table-2). Significantly (χ^2=4.923; p=0.026) a higher proportion (37.1% Vs. 25.9%) of relapse cases were found among the families with more than 5 members. More than half (53.5 %) of the respondents had one earning member in their family. However, a higher proportion of the case group respondents had two or more than two earning members and the difference was statistically significant (χ^2=3.831; p=0.050). Majority (52.6%) of the respondents had monthly family income up to Taka 25000 and there was no significant difference in the monthly family income between the respondents of case and control groups. Fifty five percent of the respondents were found to live in a house having up to two living rooms, while significantly (χ^2=34.610; p=0.000) a higher proportion (61.8% Vs. 28.2%) of the respondents of case group respondents lived in the house more than two living rooms.

Table 2: Family characteristics of respondents

Family Characteristics	Case n (%)	Control n (%)	Total n (%)	Test of Significance
Family size				
≤ 5	107 (62.9)	126 (74.1)	233 (68.5)	χ^2=4.923; p=**0.026**
>5	63 (37.1)	44 (25.9)	107 (31.5)	
Earning members				
One	82 (48.2)	100 (58.8)	182 (53.5)	χ^2=3.831; p=**0.050**
Two or more	88 (51.8)	70 (41.2)	158 (46.5)	
Monthly Family Income (BDT)				
≤ 25000	87 (51.2)	92 (54.1)	179 (52.6)	χ^2=1.783; p=0.410
25001 to 50000	69 (40.6)	70 (41.2)	139 (40.9)	
> 50000	14 (8.2)	8 (4.7)	22 (6.5)	

Mean ± SD	29264±14095	28247±13084	28755±13588	
Living Room				
Up to 2	65 (38.2)	122 (71.8)	187 (55.0)	χ2=38.610; p=0.000
> 2	105 (61.8)	48 (28.2)	153 (45.0)	

Almost two-thirds (65.3%) of the total respondents completed TB treatment 3 years before. Among them significantly (χ2=53.979; p=0.000) a higher proportion of the respondents were from the case group (46.5%) in comparison to that of the control group (22.9%). A few (3.5%) respondents reported that their household members had been suffering from tuberculosis and of them significantly (χ2=5.529; p=0.019) a higher proportion (5.9% Vs. 1.2%) was the household members of case group (Table -3).

Table 3: Distribution of respondents by Tuberculosis

TB characteristics	Case n (%)	Control n (%)	Total n (%)	Test of Significance
Years of complete treatment				
3 years	91 (53.5)	131 (77.1)	222 (65.3)	χ2=20.767; p=**0.000**
>3 years	79 (46.5)	39 (22.9)	118 (34.7)	
TB of Household				
No	160 (94.1)	168 (98.8)	328 (96.5)	χ2=5.529; p=**0.019**
Yes	10 (5.9)	02 (1.2)	12 (3.5)	

Table 4: Distribution of respondents according to smoking habit

TB characteristics	Case n (%)	Control n (%)	Total n (%)	Significance test
Past Smoker				
No	20 (11.8)	43 (25.3)	63 (18.5)	χ2=10.307; p=0.001
Yes	150 (88.2)	127 (74.7)	277 (81.5)	
Post Treatment				
Non-Smoker	151 (88.8)	158 (92.9)	309 (90.9)	χ2=1.739; p=0.187
Smoker	19 (11.2)	12 (7.1)	31 (9.1)	
Smoking per day				
10 sticks	60 (40.0)	72 (56.7)	132 (47.7)	χ2=7.682; p=0.006
> 10 sticks	90 (60.0)	55 (43.3)	145 (52.3)	
Total	150 (54.7)	127 (45.2)	277 (100.0)	
Smoking duration				
10 years	83 (55.3)	80 (63.0)	163 (58.8)	χ2=1.666; p=0.197
>10 years	67 (44.7)	47 (37.0)	114 (41.2)	
Total	150 (100.0)	127 (100.0)	277(100.0)	
2nd hand Smoking				
No	91 (53.5)	111 (65.3)	202 (59.4)	χ2=4.879; p=0.027
Yes	79 (46.5)	59 (34.7)	138 (40.6)	

Before the diagnosis of TB, 81.5% of the respondents had the habit of smoking (Past smoker) and

significantly ($\chi2=10.307$; p=0.001) a higher proportion of them were found in the case group (88.2% Vs. 74.7%). A majority (52.3%) of the respondents smoked more than ten cigarettes per day. This was significantly ($\chi2=7.683$; p=0.006) higher among the case groups (60.0%). The proportion of smoking for more than ten years was also found higher (44.7%) among the case group. Overall 9.1% of the respondents had the habit of smoking after treatment. Of the total respondents, 40.6% had a history of exposure to second-hand smoking in their home and the exposure was significantly higher (46.5%) ($\chi2=4.879$; p=0.027) among the case group (Table-4).

Logistic regression analysis was carried out to see the impact of educational status, family size, earning member, living room, past smoker, exposure to second-hand smoking and years after complete TB treatment on the likelihood of developing relapse tuberculosis (table-5). The combined effects of all these predictors could significantly ($\chi2=80.411$; p=0.000) explain the occurrence of relapse tuberculosis of the participants. The participants who had exposure to second-hand smoking significantly (p=0.003) 2.3 times more likely to develop relapse tuberculosis than those who had no history of exposure. Similarly, the participant who was a past smoker significantly (p=0.035) 2.0 times more likely to develop relapse tuberculosis than who was not a past smoker. On the other hand, a participant who had more than 2 living rooms significantly (p=0.000) 0.27 times less likely to develop relapse tuberculosis. The participants who got complete tuberculosis treatment more than 3 years before, significantly (p=0.000) 0.25 times less likely to have relapse tuberculosis, inversely, a participant who got complete TB treatment within the last 3 years, 4.0 times more likely to have relapse tuberculosis.

Table-5: Logistic regression predicting likelihood of occurrence of Relapse Tuberculosis

Dependent Variables	Relapse Tuberculosis			95% Confidence Interval			
Independent Variables	B	S.E.	Wald	Sig	Exp (B)	Lower	Upper
Constant	.630	.514	1.504	.220	1.878		
Primary			8.036	**.018**			
Secondary	.219	.346	.402	.526	1.245	.632	2.453
Graduate and Above	-.625	.388	2.605	.107	.535	.250	1.143
Family Size (≥5)	.217	.319	.462	.497	1.242	.665	2.320
Earning member (≥2)	.115	.292	.155	.694	1.122	.633	1.988
Living room (>2)	-1.380	.278	24.574	**.000**	.252	.146	.434
Second hand Smoking	.835	.277	9.086	**.003**	2.305	1.339	3.968
Past Smoker	.711	.339	4.403	**.036**	2.035	1.048	3.953
TB Diagnosis (>3 Yrs)	-1.450	.293	24.447	**.000**	.235	.132	.417

$\chi2=80.411$; p=0.000

To predict the occurrence of relapse tuberculosis and the number of sticks smoking daily, a second logistic regression (table-6) was performed among the past smoker participants, using the same predictors. The combined effect of the predictors was found to explain significantly ($\chi2=52.284$; p=0.000) the status of occurrence of relapse tuberculosis of the participants. This analysis also revealed that participants having a history of exposure to second-hand smoking 2.4 times more likely to develop relapse tuberculosis than those who had no history of exposure to second-hand smoking. The participant of past smokers who had more than two living rooms and got complete tuberculosis treatment more than three years before, significantly (p=0.001 and p=0.000 respectively) less likely to have relapse tuberculosis. However, no significant ability to predict the likelihood of developing relapse cases was revealed with the increased number of sticks (>10) smoking per day.

Table-6: Logistic regression predicting likelihood of occurrence of Relapse Tuberculosis among the smoker participants

Dependent Variables	Relapse Tuberculosis			95% Confidence Interval			
Independent Variables	B	S.E.	Wald	P	Exp (B)	Lower	Upper
Constant	1.199	.403	8.874	.003	3.317		
Primary			8.665	.013			
Secondary	.262	.364	.519	.471	1.300	.637	2.650
Graduate and Above	-.704	.407	2.989	.084	.495	.223	1.099
Earning member (≥2)	-.042	.323	.017	.896	.959	.509	1.805
Living room (>2)	-1.054	.303	12.102	.001	.348	.192	.631
Family Size (>4)	.300	.342	.771	.380	1.350	.691	2.641
Second hand Smoking	.886	.308	8.276	.004	2.426	1.326	4.436
Sticks per day (>10)	-.368	.288	1.635	.201	.692	.394	1.216
TB Diagnosis (>3 Yrs)	-1.217	.306	15.814	.000	.296	.163	.539

$\chi^2=52.284$; p=0.000

4. Discussion

A recent WHO report revealed the definitive evidence of increased risk of occurrence of TB, recurrent TB and negative response to the treatment of TB by smoking [12]. Studies carried out elsewhere further revealed the increased risk of contracting TB by second-hand smoking, particularly among the children. Recurrent TB becoming an important public health challenge because of its increased MDR and high death rates. [12-15] Bangladesh government has made good progress in reducing the occurrence of TB during the last few decades. Yet TB is a major public health problem in the country. In 2016, about 223,921 cases of TB were reported. Of which 4.1% (9086) was reported to be the relapse cases. The overall TB case notification was 138/100,000 population and the TB mortality rate was 40/100,000 population. The incidence of MDR-TB was 5.3/100,000 population [16]. A study conducted in a tertiary level hospital in Bangladesh revealed that 56% of the MDR- TB cases were relapsed cases [15]. The current study was conducted among the TB relapse cases and non- relapse cases to assess the risk of smoking in developing relapse cases. Majority of the respondents of the current study were ex-smokers and significantly ($\chi^2=10.307$; p=0.001) a higher proportion of them belonged to the case group. Though not significant a higher proportion (11.2%) of the relapse cases continued smoking after the completion of their previous TB treatment. However, studies revealed the association of cigarette smoking with TB infection [17- 19]. Further, studies revealed the association of smoking with increased mortality from TB [19- 21] A study on hazard ratio analysis reported that the smoking relapse case compared with that of higher education and previously treated patients were 3.48 time higher for less educated and 4.30 time higher for newly treated patients [22]. However, another study reported differently that the hazard ratio of occurrence of relapse TB was higher among the current smokers compared to the ex-smokers and never smokers [23]. In this study above 11% of the relapse cases were found to be a current smoker but not significantly different from control group participants. The current study further revealed that those who smoked more than 10 cigarettes per day significantly suffered more from relapse TB, while the duration of the habit of smoking did not show any significant relationship with the relapse TB. Moreover, this study revealed a significant ($\chi^2=4.897$; p=0.027) association between exposure to second-hand smoking and increased occurrence of relapse TB. Similar to the current study; studies from elsewhere reported that both passive and active exposure to smoking had a significant association with tuberculosis infection. [23], [24].

Regarding the socioeconomic conditions of the respondents, it was revealed that majority of the respondents were middle-aged and comparatively the average age of the respondents of the case group was higher. The study identified a significant (p<0.05) inverse relationship between relapse cases and the higher educational level. It was also revealed that significantly ($\chi^2=4.923$; p=0.026) a higher proportion of the relapse cases lived in a bigger family (>5), had significantly more earning members (≥ 2) in the family and had more than 2 living rooms than that of the control group. A study carried out elsewhere reported the association

between the lower level of education, unemployment, low household income with the occurrence of TB [25]. This study revealed that the TB patients within 3 years of complete TB treatment and family members reported to be suffered from TB, significantly ($\chi2$=20.767; p=0.000 and $\chi2$=5.529; p=0.019 respectively) a higher proportion of them suffered from relapse TB. Similarly, in a study, it was reported that most of the TB recurrences occurred within the first three years and patients at higher risk of recurrence who were living in neighbourhoods with high TB incidence or with a history of TB treatment [18].

The logistic regression analysis revealed that the participants who had two living rooms and TB treatment completed over 3 years independently had less (0.27 and 0.25 times) ability to predict the likelihood developing of TB relapse cases. On the other hand, past smokers and exposure to second-hand smoking independently had the ability to predict the likelihood of developing more relapse cases. Among these predictors, the strongest predictor was second-hand smoking followed by past smokers, significantly (p=.003) 2.3 times and (p=.035) 2.0 times respectively more likely to develop relapse tuberculosis. It was reported in the studies that cigarette smoke increases the concentration of iron inside lung epithelial cells [26], has a harmful effect on lung function [27] and has a significant association with TB infection [23], [24]. However, the second logistic regression revealed that the number of sticks smoking per day had no significant ability to predict the likelihood of developing relapse cases. But the exposure to second-hand smoking remained the same strongest (2.4 times) ability as found among the total participants to predict the likelihood of developing relapse tuberculosis. Another study reported that the number of TB relapse cases decreased with the increase of the time interval from the first diagnosis of TB and the relapse rate decreased yearly as well [28]. Most episodes of recurrence TB occurred in the first three years of the previous diagnosis [18]. However, the current study revealed that after removing the effect of possible confounders, the past smoker and second-hand smoking both had the strongest ability to develop relapse tuberculosis. After adjustment of the confounders, the predictors having two living rooms and completed TB treatment over three years, independently 0.34 and 0.29 times respectively less likely to develop relapse tuberculosis among the smokers.

5. Conclusion
Tuberculosis relapse case was more likely to develop within three years of the complete TB treatment. Past smoking habits and exposure to second-hand smoking independently had the strongest likelihood of developing more TB relapse cases.

6. Funding

7. Declaration
The author(s) declare that they have no competing interest.

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