Risk factors of childhood tuberculosis: a case control study from rural Bangladesh

Mohamed R Karim¹, Mohamed A Rahman², Shaikh AA Mamun³, Mohamed A Alam⁴ & Shahnaz Akhter⁵

Background: Childhood tuberculosis (TB) is one of the major causes of childhood morbidity and mortality; however, it is relatively a neglected disease. Hence, we explored the risk factors for childhood TB.

Methods: Ninety-five cases and 94 controls were selected during January to May 2011 from DOTS centres located in four sub-districts of Bangladesh. The exposure status of recently diagnosed childhood TB patients (<18-year-olds), who were sputum-positive, were compared with children who were sent to the laboratory with suspected tuberculosis but were found to be sputum-negative. Data were collected by a structured questionnaire. Crude odds ratios (OR), adjusted odds ratio (AOR) and 95% confidence intervals (CI) were estimated. Stepwise logistic regression model was used to identify independent predictors.

Results: Children under 14 years of age (AOR: 0.25; 95% CI: 0.10-0.66), having completed primary education (AOR: 0.28; 95% CI: 0.10-0.74), whose fathers’ were in business or service (AOR: 0.24; 95% CI: 0.08-0.72), and who slept in a less crowded room (AOR: 0.32; 95% CI: 0.14-0.76), lived in a house with a separate kitchen (AOR: 0.39; 95% CI: 0.16-0.96) had less chance of having TB. Those who had contact with cases of TB among relatives or neighbours were less likely to have TB (AOR: 0.28; 95% CI: 0.16-0.70) compared to those who had contact with a TB case in the family.

Conclusion: Age, education, father’s occupation, crowding, kitchen location and intimate contact with a TB case were significantly associated with smear-positive childhood TB.

Key words: Tuberculosis, children, risk factors, prevention, Bangladesh.

Introduction

In today’s world, tuberculosis (TB) continues to contribute to an unacceptably high toll of disease and death among children. Of the 9.2 million new tuberculosis cases, about one million (11%) are children. Childhood tuberculosis carries much higher risk of severe disease and death among young children than adults.¹⁻³ It is now estimated that every year 300 000 people in Bangladesh develop active tuberculosis; children aged less than 14 years constitute only 3% of them. Childhood tuberculosis is under-reported in Bangladesh due to difficulties in confirming diagnosis, lack

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of guidelines for systematic screening and referral of suspected childhood TB cases. High prevalence of malnutrition renders the skin test for TB ineffective and lack of laboratory facilities is also an impediment for diagnosis of children with TB. Absence of awareness about TB in children also plays a role in the low detection rate of the disease.4-8

Risk of childhood tuberculosis depends on the probability, duration, and proximity of exposure to an infectious case, and also the infectiousness of the source cases (usually an adult with active pulmonary disease, although older children may also contribute to transmission). Studies have shown that younger children (<5 years) who were contacts of TB cases had significantly greater likelihood of being infected with increasing smear-positivity. The risk of positive Tuberculin Skin Test response in children increased with household TB infection proximity and with the degree of activities shared with the individual with tuberculosis.9,10

Malnutrition and tuberculosis are two problems which tend to interact with each other. Malnutrition increases the host’s susceptibility to infection especially in case of children. Both, protein-energy malnutrition and micronutrient deficiencies increase the risk of tuberculosis.11 Social factors, community TB prevalence and age determine where exposure is most likely to occur and may vary between communities. Children under 14 years of age have a lower risk of developing active TB compared to those above 14 years. A household TB case is most commonly implicated for infection among young children. Older children are increasingly likely to be infected from outside the household. Poverty, lack of education, poor housing, urban environments and overcrowding are all associated with increased transmission.12-15 Studies reported that use of biomass fuel for cooking substantially increases the risk of tuberculosis. Studies have also shown that this effect is reduced when availability of a separate kitchen, house type, indoor crowding, age, gender, urban or rural residence, etc. are statistically adjusted.16

In Bangladesh, childhood tuberculosis is a relatively neglected problem and factors responsible for its aggravation have not been studied adequately. This study was conducted to determine the risk factors that may be helpful in taking preventive measures against childhood tuberculosis to reduce morbidity and mortality related to this disease.

Methods
This case control study was carried out to identify risk factors for tuberculosis among children (<18-year-olds). The exposure status of recently-diagnosed childhood TB patients, who were sputum-positive at the peripheral laboratory were collected and compared with the exposure information of the children who were sent to the laboratory with suspected tuberculosis but were sputum-negative. Cases were diagnosed as TB patient at four sub-district DOTS service centres (Trishal, Bhaluka, Gofargaon, from Mymensingh, and Kapasia from Gazipur districts of Bangladesh) from January to May, 2011. Children who visited the DOTS laboratory but were sputum-negative during the same time period were taken as control. Addresses were taken from the sputum microscopy register with a view to trace study subjects at home for exploring exposure information.

Sample size was determined using EpiInfo software assuming anticipated probability of “exposure” given “no disease” 32%, anticipated odds ratio 2.44, 5% level of significance and 80% power. Estimated sample size was 91 cases and 91 controls. A total of 95 childhood tuberculosis patients (cases) and 94 controls were enrolled in the study. Each of the respondents was informed about
the objective of the study. They were assured about confidentiality prior to taking verbal consent. Data were collected by a researcher in face-to-face interviews using a structured questionnaire and by reviewing records. All the questionnaires were checked for consistency and completeness. A subset of questionnaires was also re-checked in the field.

**Operational definitions**

Literacy was determined by asking whether a respondent ever had education in any institution or not. The occupational status of the parents was collected in all possible categories and afterwards these were combined into two broad categories. Change in the composition of the family was determined by regular or irregular displacement of family members from their residence. Person per bedroom was calculated and then this variable was categorized taking two groups, i.e. <2 persons, and >2 persons per bedroom.

Household condition was assessed by the type of materials used for the floor, wall and roof of the house. It was first classified into very poor, poor, average, and good, which was further summarized as poor and good category. The location of the kitchen was taken as a proxy variable for “exposure to household smoke”. A kitchen attached to the house or indoor cooking arrangement was termed as “in-house kitchen”. Cooking outside, e.g. courtyard, shed etc. was termed as “outside kitchen”. A kitchen with windows and chimney (vent for expulsion of smoke), positioned separately in the house was stated as a “separate kitchen”. In rural Bangladesh, almost all the houses are constructed as mono-unitary spaces which are subsequently partitioned into several spaces based on utility and requirements (sleeping space, store place etc.). The number of windows per house was taken as a proxy for bedroom ventilation status.

The information on contact with a TB patient was collected as four different states; (i) Patients reported no contact; (ii) Patients who reported casual contact (e.g. sharing a transport route regularly or living in the same subdistrict); (iii) Patients who reported knowing each other by name, but had casual contact; and (iv) Patients who knew each other well and had prolonged or intimate contact (e.g. family members, friends). Based on the relationship and proximity of source cases, contact status was further subdivided into two categories, i.e. contact with family members, and contact with relatives/neighbours. Duration of contact with a tuberculosis patient was recorded in months. Those who could not understand this issue and who responded “do not know” were excluded while analyzing contact exposure data.

**Statistical analysis**

The data were entered, cleaned and edited using SPSS programme. Statistical tests ($\chi^2$) were performed to determine the association between exposure and outcome variables. The Yate’s corrected values were considered significant at a p value of <0.05. Crude odds ratios (OR) and 95% confidence intervals (CI) were estimated in the univariate analysis. Important predictors of univariate analysis were included in a stepwise logistic regression model to identify independent predictors. Adjusted odds ratios (AOR) and 95% CI were reported.

**Results**

Almost all the households of the respondents used tubewell water for drinking and cooking. Seventeen percent of the households (32/189) used kerosene lamp for lighting and the rest of the households had electricity. The mean age of the respondents was about 14 years (Figure 1), and 52% were females.
In univariate analysis, educational status of the children was found to be associated with TB (p 0.006) (Table 1). It is important to mention that seven of the study children were illiterate, and all of them had tuberculosis. Fathers’ educational status as well as occupational status did not have a significant association. However, association with maternal education was statistically significant (p 0.002). Almost all the respondents (96%) were permanent residents who lived in their own houses. Childhood tuberculosis was found to be related with regular or irregular displacement of the family members (changes in composition) (p 0.001). Bedroom occupancy (persons per bedroom) was statistically significantly associated with childhood tuberculosis (p <0.001) (Table 1).

Several household conditions showed association with childhood tuberculosis in univariate analysis (Table 2). Children living in families having only one bedroom had a greater chance of developing tuberculosis than those possessing two or more bedrooms (p <0.0001). The location of the kitchen was found to be significantly associated with childhood TB (p 0.001). Children living in houses with the kitchen inside the house were more likely to develop tuberculosis than those living in houses with a separate kitchen or when cooking was done outside the house. Children exposed to family members having TB were five times more likely to develop tuberculosis than those who came in contact with relatives or neighbours suffering from tuberculosis (p <0.0001). History of contact

Figure 1: Distribution of respondents by age
with a TB case for two years or more had three times more chance of having tuberculosis than those who had a shorter contact history (p<0.005).

In univariate analysis, several socio-demographic and household-related factors were found to be associated with childhood tuberculosis. Hence, a binary logistic regression model was constructed to find out the predictors of childhood tuberculosis adjusting for other factors (Table 3). The predictors in the model revealed that children less than 14 years of age...
### Table 2: Association of household characteristics and contact with TB case with childhood TB

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Controls N=95</th>
<th>Cases N=94</th>
<th>Crude odds ratio (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household condition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>†Poor</td>
<td>42(47)</td>
<td>48(53)</td>
<td>0.79(0.45-1.4)</td>
<td>0.5</td>
</tr>
<tr>
<td>Good</td>
<td>52(53)</td>
<td>47(47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedroom category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One bedroom</td>
<td>59(41)</td>
<td>86(59)</td>
<td>0.18(0.08-0.39)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Two or more bedrooms</td>
<td>35(79)</td>
<td>9(21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kitchen position</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>†In-house kitchen</td>
<td>21(30)</td>
<td>50(70)</td>
<td>0.29(0.11-0.78)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Outside kitchen</td>
<td>13(59)</td>
<td>9(41)</td>
<td>0.25(0.13-0.49)</td>
<td></td>
</tr>
<tr>
<td>Separate kitchen</td>
<td>60(63)</td>
<td>36(37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact with TB case</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>†In the family</td>
<td>18(26)</td>
<td>52(74)</td>
<td>0.20(0.10-0.38)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Relatives/neighbours</td>
<td>76(64)</td>
<td>43(36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of contact with TB case</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>†Less than two years</td>
<td>22(69)</td>
<td>10(31)</td>
<td>0.28(0.12-0.66)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Two years or more</td>
<td>33(38)</td>
<td>54(62)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† reference category, * statistically significant, CI = confidence interval

### Table 3: Predictors for smear-positive childhood tuberculosis: logistic regression

<table>
<thead>
<tr>
<th>Predictors*</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child less than 14 years of age</td>
<td>0.25</td>
<td>0.10-0.66</td>
<td>0.005</td>
</tr>
<tr>
<td>Respondents education - primary and above</td>
<td>0.28</td>
<td>0.10-0.74</td>
<td>0.01</td>
</tr>
<tr>
<td>Mother’s education - literate</td>
<td>1.35</td>
<td>1.06-1.73</td>
<td>0.01</td>
</tr>
<tr>
<td>Father’s occupation - service and business</td>
<td>0.24</td>
<td>0.08-0.72</td>
<td>0.01</td>
</tr>
<tr>
<td>Two or less persons per room</td>
<td>0.32</td>
<td>0.14-0.76</td>
<td>0.009</td>
</tr>
<tr>
<td>Outside kitchen</td>
<td>0.17</td>
<td>0.05-0.61</td>
<td>0.007</td>
</tr>
<tr>
<td>Separate kitchen</td>
<td>0.39</td>
<td>0.16-0.96</td>
<td>0.04</td>
</tr>
<tr>
<td>Contact with TB case - relatives/neighbors</td>
<td>0.28</td>
<td>0.16-0.70</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*Reference categories shown in table 1 and 2, CI = confidence interval, Logistic Regression: Cox & Snell $R^2 = 0.36$, Nagelkerke $R^2 = 0.49$, model $\chi^2_{(10)} = 76$, $p < 0.0001$
age had four times lower risk of developing TB compared to children 14 years or older. Those who had completed primary education had three times less chance to develop childhood TB than the illiterate children. Mothers’ education had a significant positive association with childhood TB (Adjusted OR: 1.35; 95% CI: 1.06-1.73). Fathers’ occupation as labourer had significant risk for childhood TB. Children sleeping in a less crowded environment (two or less persons per room) had three times less chance of having TB. Children residing in houses with an outside kitchen or a separate kitchen had five times and 2.5 times lower risk of developing childhood TB respectively compared to those having a kitchen inside the houses. Contact with a TB case in the family carried a higher risk than contact with a TB case among relatives or neighbours. There were nine children who had no BCG scar and eight of them had active tuberculosis.

Discussion

According to national statistics of Bangladesh, the male to female ratio is 2:1 among TB patients below 14 years of age. In this study, the frequency of male and female child TB cases was almost equal in the age category of 14 years or less but child TB cases were two times higher in girls than boys in the more than 14 years age category (Figure 2) which is consistent with other reports. It is important to note that, girls who develop tuberculosis at the start of their reproductive age are difficult to trace after marriage as their family may conceal the disease status for various social reasons (stigma). This situation increases the chance of spreading tuberculosis in a new setting (husband’s family) and also imposes long-term risk on her nutritional and reproductive status. In this study a higher proportion of cases were among older children (>14 years) which corresponds with a previous study.

Educational level of the children was low among cases than the controls. National data show that 51% children have completed the primary level of education. The study showed that children of literate mothers had a greater chance of developing tuberculosis which contradicts a previous study. Literate mothers are supposed to have better health seeking behaviour than their illiterate counterparts.

Children of daily labourers faced a higher risk of TB than those hailing from better occupational categories. Other studies have
also shown that childhood TB in different economic groups in the community tends to vary inversely with their economic levels.\textsuperscript{11,19} Increased size of the household was found to be important and overcrowding has been documented as a risk factor for TB in several studies in a variety of settings.\textsuperscript{10,19,20} Measurement of the bedroom area may not reflect the actual usable bedroom space because in a rural setting, it is always occupied by some furniture, utensils, stored crops, agricultural tools, bundles of firewood, jute-straw, and sometimes pet animals. The number of windows reflects a vague expression of ventilation status (there are many variables regarding window(s), such as: size of the window, position or placement, how often it is kept open, window material – glass, wood or metal, etc.). Children living in households with a separate kitchen were less likely to have active TB as was also found in India.\textsuperscript{16}

This study showed household contact as an important risk factor for tuberculosis which is consistent with the findings of some previous studies in West Africa and Lao People’s Democratic Republic where family history of TB was two to three times more frequent among childhood TB cases compared to the controls.\textsuperscript{12,19-21} Presence of BCG scar was higher among controls than among the cases. It was suggested that when given to children at an early age BCG provides about 75% protection for 15 years.\textsuperscript{22}

Childhood TB usually has nonspecific clinical signs, variable chest X-ray features; and infection is paucibacillary in nature with low bacteriological confirmation rates. Diagnosis of tuberculosis in children is relied mainly on clinical case-definition; tuberculin skin testing and chest radiography.\textsuperscript{23,24} In this study, cases and controls were selected on the basis of sputum microscopy, a highly specific test with low sensitivity, which might have resulted in increased volume of false negatives among controls. Children who had smear-negative pulmonary TB or were unable to produce adequate sputum samples (as expected in young children) and or children who had extra-pulmonary tuberculosis might have a chance to be misclassified as controls. So risk factors found to be associated with childhood TB in this study would be more valid for smear-positive tuberculosis cases.

As it was a case control study, there was a potential for recall bias. The controls were reluctant to provide information regarding frequency and duration of the exposure as well as contact history. As the controls were also taken from the DOTS microscopy center register, they were seemingly more health conscious or may have had easy access to the centre and thus might not be representative.

To conclude, improvement in the living standard of children (education and housing condition etc.) will help in reducing childhood TB in the community. The tuberculosis prevention programme in Bangladesh mostly focuses on detecting and treating index cases. Contact tracing and contact screening should also be incorporated as part of the National TB Control Programme for early diagnosis and treatment.

References


Responding to measles outbreak: closing the immunity gap in children of Timor-Leste

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**Background:** An outbreak of measles was reported in Timor-Leste during 2011. A concerted response at national level utilized this opportunity to improve measles immunization coverage rates.

**Methods:** Health Management Information System and Surveillance System data were utilized to describe the outbreak. Attack rates and case fatality rates (CFR) were calculated using standard methods. Evaluation surveys were used to access immunization coverage. Proceedings of weekly meetings of the National Committee for Control of Disease Outbreaks were reviewed.

**Results:** A total of 739 cases and 8 deaths were reported to the Surveillance Unit. Most (>82%) of the measles cases were reported from Dili and Ermera districts. The attack rate was 1.3 per 1000 population and CFR was 1.1%. The response was coordinated by the National Committee for Control of Disease Outbreaks, which included case management, active and passive surveillance, communication and measles immunization among six-month to 14-year old children. Immunization activity targeted 495 000 children, i.e. almost one-half of the Timor-Leste population and achieved high coverage (85%).

**Conclusions:** The outbreak highlighted gaps in the immunity against measles. The National Committee for Control of Disease Outbreaks ensured a coordinated response which led to prevention of deaths from measles due to early case management with vitamin A supplementation, and high measles immunization coverage.

**Key words:** Measles, outbreak, immunization, surveillance, Timor-Leste.

**Introduction**

In May 2010, the World Health Assembly endorsed a new measles mortality reduction goal.\(^1\) A South-East Asia Regional Consultation in 2009, agreed that measles elimination was technically, biologically and programmatically feasible. In 2010, the sixty-third session of the Regional Committee adopted the regional interim goals towards measles elimination as approved by the sixty-third World Health Assembly. The interim goals to

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