Bangladesh Med Res Counc Bull 2016; 42:67-71

Prevalence of Latent Tuberculosis Among Children Living in Households with Smear Positive Pulmonary Tuberculosis Patients

Islam S[1], Chowdhury SA[2], Karim MR[3], Samad R[4], Chowdhury Z[4], Barua PC[5]

[1]*Department of Paediatrics, Bangabandhu Memorial Hospital, USTC, Chittagong, Bangladesh*
[2]*Department of Haematology, Chittagong Medical College, Chittagong, Bangladesh*
[3]*Department of Pediatrics, Cox's Bazar Medical College, Cox's Bazar, Bangladesh*
[4]*Department of Pediatrics, Chittagong Medical College, Chittagong*
[5]*Office of the Vice Chancellor, USTC, Chittagong*

e-mail: sanjana36@gmail.com

Abstract:

This multicentre cross sectional analytical study was conducted in 2012 in Chittagong, Bangladesh, to evaluate the prevalence of latent tuberculosis infection (LTBI) among children living in households with smear positive pulmonary tuberculosis patient. Two groups of subjects were selected. Sixty five children of 3-12 years living with selected smear positive TB patient and children of same age living with healthy parents were included. For this purpose, sputum positive adult TB patients were selected. Mantoux test (TST) was done in 130 children. To exclude active TB disease in TST positive children, CXR P/A view was taken. Sociodemographic information were also included. The study found that the prevalence of LTBI among children who have household TB contacts was 41.5%, and Children who did not have household TB contact had the prevalence of LTBI of 9.2%. Parents' educational status showed that 74.1% of MT positive children had illiterate father and 63% children had illiterate mother. Ninety two percent of MT positive children were from lower and lower middle class family and only 7.2% were from upper class family. It was found that, mean family members were much higher (4.39±0.77) in MT positive cases comparing with MT negative cases (3.7±0.85). 88.9% of MT positive children were living in the same bed and 55.6% were living in different beds in the same house. The present study found that the prevalence of LTBI among children with household contacts of TB patient was higher than non-contact children. Parents' illiteracy, lower socio-economic status, large family, sharing of same indoor environment further increased the prevalence of LTBI among the contacts.

Keywords: LTBI, TB contact, Smear positive.

Introduction:

Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis* that spreads from person to person through the air. Persons with latent TB infection do not feel sick and do not have any symptoms. They are infected with *M. tuberculosis*, but do not have TB disease. Their sign of TB infection is only a positive reaction to the tuberculin skin test (TST).[1] Overall, without treatment, about 5-10% of infected persons will develop TB disease at some time in their lives. About half of those people who develop TB disease will do so within the first two years of infection.[1] *Styblo*has estimated that a single bacillary case would infect around 10 persons annually in a developed country. And, as per his estimation, in a developing country about 20 persons would get infected from a single case over an observed period of two years.[2]Another study showed that the overall prevalence of LTBI was 8.5% (152/1797)[3]. LTBI was diagnosed in 26.7% of the children with a known TB contact, as opposed to 6.4% of the children without such contact.[3] Nguyen et al found a prevalence of LTBI of 26–36% in children living with TB patients in remote settings of NorthernLaos.[4]

Another cross sectional study of children in contact with adults who had pulmonary TB in Abuja, Nigeria was conducted. TST readings were available for 193 (93%) children, and

positivity varied according to the number of AFB in sputum of the adults. Similar proportions of control children (6/48 [15%]) and children in contact with adults with smear-negative TB (13/80 [16%]) were TST positive. A larger proportion (38/78 [53%]) of children in contact with adults with smear-positive TB were TST positive (p <0.001).[5]

In TB endemic areas majority of the population develops primary mycobacterium tuberculosis infection during childhood. It is estimated that with accurate diagnosis and good reporting systems, children are likely to contribute 10-20% of the disease burden in areas where the TB is poorly controlled. With excellent TB control and active provision of preventive therapy to children with active TB contacts, the burden of childhood TB can be reduced to below 5%.[6] Detection of the latent TB infection among children with TB patients provides an accurate measure of ongoing transmission within communities, which is a key indicator of epidemic control. Childhood TB control programme is not yet well designed with underreported incidence and prevalence. LTBI among children is an unfocused area. Findings of this study may be a baseline for exact estimation of LTBI and for early identification, evaluation and treatment; which eventually improve the childhood TB control programme through determining the priority issues.

Materials and methods

In this study, the prevalence of LTBI among children with household contacts of TB patient was assessed using tuberculin skin tests (TST). This is a cross sectional analytical study done in Chittagong Medical College Hospital, Chittagong General Hospital and Chest Disease Clinic, Chittagong during July to December, 2012. Two groups of subjects were selected. Group A was test group and Group B was control group. Sample size was 65 from both groups. In Group A, children of 3-12 years living with selected smear positive TB patients and in Group B, children of same age living with healthy parents were enrolled. For this purpose, sputum positive adult TB patients were selected. After taking written informed consent from the parents, Mantoux test (TST) was done. If there is no induration, the result was recorded as "0 mm". Based on the size of the induration, there were cut-off points for defining a positive TST result: ≥5 and ≥10 of induration. For individuals who are at highest risk of developing TB disease if infected with *M. tuberculosis*, including malnourished child and child receiving immunosuppressive therapy or with immunosuppressive condition and recent contact of persons with active TB disease with ≥5 mm induration was considered positive. An induration of ≥10 mm should be considered positive for all other children.[6] In this study, induration ≥10 mm was defining a positive TST result. BCG vaccination may cause false-positive reactions, but these generally last only a few years after vaccination and were in the moderate range (5 to 10 mm).[7] So, age < 3 years as MT interpretation was doubtful due to BCG vaccination were excluded from the study. Chest X-Ray PA view was also done to exclude active TB disease for all study children. After detection of the positive cases, disposition was done to the proper authority for further management. Other socio-demographic information were also included. All the data were recorded and analysed by SPSS programme.

Persons infected with *M. tuberculosis* but do not feel sick or have any symptoms, have a normal chest x-ray and a negative sputum test, can not spread TB infection to others considered as LTBI. The only sign of TB infection is a positive reaction to the tuberculin skin test**.**

Results

Tuberculin test was positive in 27 (41.5%) of test group (Group A) subjects and 6(9.2%) of control group (Group B) subjects. Pearson's Chi-square test was done to find out the association between the MT results of both the study groups. Highly significant (p < 0.001) association was found in between these two groups (table I).

Table I: Distribution of Mantoux test results in study groups.

Mantoux Test	Study Groups				Total	
	GROUP A		GROUP B			
	N	%	N	%	N	%
Positive	27	41.5	6	9.2	33	25.4
Negative	38	58.5	59	90.8	97	74.6
Total	65	100.0	65	100.0	130	100.0

χ^2 value = 17.910; p = <0.001. Highly Significant.

In Group A 74.1% MT positive children had illiterate father and 63% children had illiterate mother. Persons at least with primary education

considered at literate. Statistically highly significant association to be was found with fathers' education ($p < 0.001$) and significant association was found with mothers' education ($p < 0.05$).

Table II: Relationship Between Parents' Educational Status And Mantoux Test Results Among Study Group A.

Parent's Educational Status		Mantoux Test: Positive N	%	Negative n	%	Total N	%	χ^2
Father's Education	Illiterate	20	74.1	11	28.9	31	47.7	$p = 0.000^{HS}$
	Literate	7	25.9	27	71.1	34	52.3	
Mother's Education	Illiterate	17	63.0	10	26.3	27	41.5	$p = 0.032^{S}$
	Literate	10	37.0	28	73.7	38	58.5	

HS = Highly Significant ($p < 0.001$); S = Significant ($p < 0.05$)

Table III: Relationship between parents' educational status and Mantoux test results among study group b.

Parent's Educational Status		Mantoux Test: Positive N	%	Negative N	%	Total N	%	χ^2
Father's Education	Illiterate	3	50.0	24	40.7	27	41.5	$p = 0.66^{NS}$
	Literate	3	50.0	35	59.3	38	58.5	
Mother's Education	Illiterate	5	83.3	13	22.0	18	27.7	$p = 0.00^{HS}$
	Literate	1	16.7	46	78.0	47	72.3	

NS = Not Significant ($p > 0.05$); HS = Highly Significant ($p < 0.01$)

In Group B, 50% MT positive children had illiterate father and 83.3% children had illiterate mother.The association between fathers education and MT results was not significant ($p > 0.05$); and that of mothers education was highly significant ($p < 0.01$).

Table IV: Distribution of socio-economic status according to the Mantoux test results among the study groups

Socio-Economic Status		Mantoux Test: Positive N	%	Negative n	%	Total n	%	χ^2 Test Significance
In Total	Lower & Lower Middle Class	31	93.9	73	75.3	104	80.0	$p = 0.020^{S}$
	Upper Middle Class	2	6.1	24	24.7	26	20.0	
In Group A	Lower & Lower Middle Class	25	92.6	24	63.2	49	75.4	$p = 0.007^{HS}$
	Upper Middle Class	2	7.4	14	36.8	16	24.6	
In Group B	Lower & Lower Middle Class	6	100.0	49	83.1	55	84.6	$p = 0.273^{NS}$
	Upper Middle Class	0	0.0	10	16.9	10	15.4	

S = Significant ($p < 0.05$)
Highly significant = ($p < 0.01$); NS = Not significant ($p > 0.05$)

About 92.2% MT positive children were coming from lower and lower middle class family and only 7.2% were from upper class family in group A. Here highly significant association was found with socio-economic status ($p < 0.001$). In Group B 100% MT positive children were coming from lower and lower middle class family and none were from upper class family shown in table IV. The t test was done to find out mean differences between MT results. It was found that mean family members were much higher (4.39±0.77) in MT positive cases comparing with MT negative cases (3.7±0.85) in Group A.

Table V: Relationship between family members and Mantoux test results (with independent samples t- test significance).

	Mantoux Test	N	Mean	± SD	Median	Range	Sign.
Family Members	**Positive**	33	4.64	0.77	4.00	3 – 5	**t** = 4.02
	Negative	97	3.82	1.52	4.00	3 – 11	
	Total	130	4.43	1.41	4.00	3 – 11	$p = 0.00^{*}$
Group A	**Positive**	27	4.39	0.77	4.00	3 – 5	**t** = 3.33
	Negative	38	3.70	0.85	4.00	3 – 6	
	Total	65	4.11	0.89	4.00	3 – 6	$p = 0.00^{*}$
Group B	**Positive**	6	4.80	0.52	4.00	4 – 5	**t** = 0.62
	Negative	59	4.33	1.82	5.00	3 – 11	
	Total	65	4.75	1.74	4.00	3 – 11	$p = 0.539$

* Highly significant

Table VI: Relationship between sharing of same indoor environment and Mantoux test results among study Group A

		Mantoux Test: Positive N	%	Negative N	%	Total N	%	χ^2
Living in Same Bed	**Yes**	24	88.9	21	55.3	45	69.2	$p (0.004^{HS})$
	No	3	11.1	17	44.7	20	30.8	
Living in Different Bed In Same Room	**Yes**	15	55.6	6	15.8	21	32.3	$p (0.001^{HS})$
	No	12	44.4	32	84.2	44	67.7	
Living in Different Room in Same House	**Yes**	0	0.0	11	28.9	11	16.9	$p (0.002^{HS})$
	No	27	100.0	27	71.1	54	83.1	

T-test was done to find mean differences between MT results. It was found that mean family members were much higher (4.39±0.77) in MT positive cases comparing with MT negative cases (3.7±0.85) in group A (table V).

About 88.9% MT positive children were living in same bed and 55.6% were living in different bed in same house. A highly significant association was to be found with same indoor environment ($p < 0.001$).

Discussion

Prevalence of LTBI among children after exposure to adults with smear-positive TB, as determined by TST, was 41.5% show in table I This corresponds nearly to the values of 30% to 50% in high-incidence countries[5] like India (41%)[4] and Nigeria (53%).[4]

Children not having household TB contacts had the prevalence of LTBI was 9.2% shown (table-I). This is consistent with the prevalence reported from other parts of the world like Laos, which was 5.8% with prevalence of 289/100,000 in 2007[4] and Greenland, which was 6.4% with incidence of 130/100,000 in 2010[3], of the children without such contact.

With this reference, it may be roughly estimated that the children of this study living in households with TB patients had a 4.5-times (41.5% versus 9.2%) greater risk of TB infection compared to those who do not have TB affected family member.

The households of persons with active TB serve as breeding places for TB due to lack of awareness about the tuberculosis transmission in the family. As because of a comparatively high proportion of new cases of pulmonary TB were sputum smear positive in Bangladesh (82%)[9], there was a high chance of development of LTBI among the contacts. Therefore, it seems to be that there is a large number of reservoirs of LTBI in the country, though there are no available information on the contact investigation using TST.

This study showed that the effects of several socio-demographic variables like parents' level of education, socio-economic status and number of family members can modify the prevalence of LTBI among the contacts.

Parents' educational status showed that 74.1% MT positive children had illiterate father and 63% children had illiterate mother (table II). Socio-economic condition also modifies the MT results. Ninety two percent of MT positive children were from lower and lower middle class family and only 7.2% were from upper class family. (table IV). It was also to be found that, mean number of family members was much higher (4.39±0.77) in MT positive cases comparing with MT negative cases (3.7±0.85), shown in table V. Study in Greenland revealed that different variables whose effect was significantly modified by the presence of a known TB contact were domestic crowding (increased risk: p= 0.009) and mother's education (decreased risk: p= 0.05).[3] This revealed domestic crowding and low parental educational level were significant risk factors for LTBI.

Among the children with a known TB contact, the increased risk of LTBI associated with living in crowded conditions may be the result of both easier transmission of *M. tuberculosis* because of closer contact between family members or because more family members are infected with *M. tuberculosis*. Similarly, low parental education, so far as it is linked to low socioeconomic status, may favour transmission of LTBI within the household because of suboptimal hygienic standards and care for TB patients. Other studies have also found low socioeconomic status to be associated with poorer general health, which may increase susceptibility to LTBI among children living in households with fewer resources.[3]

Sharing of the same indoor environment is another factor for high prevalence of LTBI found in this study. Some eighty nine percent MT positive children were living in same bed and 55.6% were living in different bed in same room in table VI. Similar results found in another study revealing sharing of the same indoor environment with a source patient for prolonged periods increases the probability of TB infection.[10] This in turn is also related to economic status.

Results of this study have shown a high risk of infection among children living in households with sputum positive TB patients. This risk has been further compounded by large family size, lower income group and low parental education. Furthermore, household contact investigation using TST is an efficient method for discovering LTBI which can progress to TB disease.

Conclusion

In TB endemic areas like Bangladesh majority of the population acquire Mycobacterium tuberculosis infection during childhood due to

active transmission from family. Children with LTBI are the future reservoir of TB cases. Early identification and detailed evaluation including TST should be a major component of Tuberculosis control efforts. Therefore, any possible intervention that minimises the risk of progression of LTBI to active TB is important. To prevent active TB cases, it needs to be find out latent cases of TB which have the potential to develop active TB disease in a favourable period.

Acknowledgements: Authors express their gratitude to all teachers and doctors of Department of Paediatrics, Chitttagong Medical College; Chittagong General Hospital and Consultant, Chest Disease Clinic, Chittagong.

Conflicts of interest: The authors declare that they have no competing interest.

References

1. "Fact Sheets: The Difference Between Latent TB Infection and TB Disease". Centers for Disease Control and prevention. Sep 1, 2012. www.cdc.gov/**tb**/publications/factsheets/general/ltbiandactivetb.htm
2. Murthy MSK, Channabasavaiah R, Nagaraj AV, Chandrasekhar P. Incidence of Tuberculosis Infection in a South Indian Village with Single Sputum Positive Case: An Epidemiological Case Study. Ind J Tub. 1991;38:123-30.
3. Søborg B, Andersen AB, Melbye M, et. Al. Risk factors for Mycobacterium tuberculosis infection among children in Greenland. Bull World Health Organ. 2011; 89:741-48.
4. Nguyen TH, Odermatt P, Slesak G, Barennes H. Risk of latent tuberculosis infection in children living in households with tuberculosis patients: a cross sectional survey in remote northern Lao People's Democratic Republic. BMC Infectious Diseases. 2009; 9:96.
5. Nakaoka H, Lawson L, Squire SB, Coulter B, Ravn P, Brock I et al. Risk for Tuberculosis among Children. CDC: Centers for Disease Control and Prevention. 2006; 12(9):1383.
6. Bangladesh. National Guidelines for the Management of Tuberculosis in Children. Dhaka: National Tuberculosis Control Programme, Director General of Health Services, Ministry of Health and Family welfare; 1st ed. 2012.
7. Suhail Ahmad. Pathogenesis, Immunology, and Diagnosis of Latent *Mycobacterium tuberculosis* Infection. Clin Dev Immunol. 2011; 2011: 814943.
8. Andrews RH, Devadatta S, Fox W. Prevalence of Tuberculosis among Close Family Contacts of Tuberculosis Patients in South India, and Influence of segregation of the Patient on the Early Attack Rate. Bull. World Health Org.1960; 23:463-510.
9. World Health Organization. Global Tuberculosis Report. Geneva: World Health Organization; 2012.
10. Wang PD and Lin RS. Tuberculosis Transmission in the Family. Journal of Infection. 2000; 41:249–05