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Original Article

Prevalence and Risk Factors for Latent Tuberculosis Infection among Children in Contact with Smear-Positive Tuberculosis Cases in a Tertiary Care Center, South Tamil Nadu

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Abstract

Background: Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically active tuberculosis (TB). Knowledge of the prevalence of LTBI among children gives an understanding about the transmission of disease. Identification of risk factors associated with TB infection and treatment of the same among children reduce the chance of progression of tubercular infection to full blown disease.

Materials and Methods: This hospital-based cross-sectional study was done using a standard questionnaire and tuberculin skin test (TST) to evaluate the prevalence and risk factors for LTBI among children over 3 months of age and <72 months of age who were in contact with the smear-positive TB patient. Questionnaire used collected information on the socioeconomic status, household characteristics, index case characteristics, contacts anthropometric details, and proximity and activities of contact with the index case.

Results and Conclusions: Among the 104 children who were contacts of smear-positive index TB cases, 31 children (29.8%) had TB infection as assessed by TST. Relationship and proximity of the contact with the index case have a strong association for transmission of the TB infection. Bacterial load in the sputum of the index case and the number of lung zones involved in the chest X-ray of the index case are directly proportional to the risk of transmission of the infection.

Key words: Latent tuberculosis infection, Risk factors for tuberculosis, Smear-positive tuberculosis, Tuberculin skin test, Tuberculosis

INTRODUCTION

Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active tuberculosis (TB). As there is no "gold standard" test for LTBI, the global burden is not known with certainty; however, up to one-third of the world's population is estimated to be infected with *M. tuberculosis*.[1] In developing countries, the burden of TB infection and disease is much more compared to developed and Western nations. Despite modern treatment and health education to public, children are rarely investigated for TB. The proposed reason is difficulty in diagnosing in younger age group and children are mostly non-infectious. Additional reason is poor contact tracing in developing countries due to poor resources.

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Children mostly acquire infection from adults who are in their close proximity. TB infection among children has been considered as a marker of recent ongoing transmission in the communities.[2] Therefore, knowledge of the prevalence of TB infection among children gives an idea about the transmission of disease among the general population. Identification of risk factors for TB infection among

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children is very important in planning and reducing the burden of disease in the society.[3]

This study aims to find the prevalence and risk factors for TB infection among children who are in contact with adult smear-positive cases.

Aim of the Study

The aims of the study were as follows:

1. To study the prevalence of LTBI among household contacts aged 3 months and 72 months of smear-positive TB patients.
2. To identify the possible risk factors for transmission among household contacts and children.

MATERIALS AND METHODS

This is a hospital-based cross-sectional study which was done for a period of 12 months (July 2018–June 2019). The study population were household contacts of smear-positive TB patients being treated at district TB cell, Government Rajaji Hospital, Madurai, Tamil Nadu.

Any asymptomatic child over 3 months of age and ≤72 months of age in household contact with confirmed sputum-positive TB patients who are receiving treatment at district TB cell, Government Rajaji Hospital, Madurai, were included in the study. Household contacts who show symptoms or signs of TB were excluded from the study.

A standard questionnaire was generated and data were obtained from hospital records and interview with the index case. The questionnaire had details of the relationship with contact, duration of symptoms in the index case, their sputum load, and chest X-ray findings.

For children included in the study, information on age, sex, bacillus of Calmette and Guerin (BCG) status, nutritional status (by Indian Academy of Pediatrics [IAP] classification), activities spend by the contact with the index case, and proximity of the child with the index case were taken into account. The first-degree relation implies parents and siblings of the contact child who are sputum positive. The second-degree relation implies any other family member who is sputum positive.

Any symptoms suggestive of TB, namely, cough more than 2 weeks, evening rise of temperature, hemoptysis, loss of weight, and appetite were considered as significant symptoms in index case. Duration of symptoms was calculated from the onset of first symptom to the start of the antitubercular treatment. For the purpose of this study, the presence of these symptoms was categorized into ≤30 days and >30 days.

Sputum load in the household contact with confirmed sputum-positive TB is described as the amount of TB bacilli found in the oil immersion field when stained by Ziehl–Neelsen technique shown in below:

Smear grading	Number of bacilli in fields
+	1–99 bacilli/100 fields
++	1–9 bacilli/field
+++	10 or more bacilli/field

For the purpose of this study, radiologic findings of lung field in X-ray were divided into six zones, three in each lung (namely, upper, middle, and lower zones). The index cases were divided into two groups with Group 1 involving three or less zones and Group 2 involving more than 3 zones.

Family size or the household size is calculated by the no. of members in the family who live, eat, and sleep in the same house. It's divided into two groups with Group 1 comprising of a family with more than 4 members and Group 2 comprising of a family with four or less members.

The socioeconomic status of the family was calculated using the modified Kuppuswamy scale. For the convenience of this study, the socioeconomic class was divided into two groups, namely, Group 1 comprising Classes IV and V and Group 2 comprising Classes I, II, and III.

History of BCG administration to the contact was enquired. In addition, the child's left upper arm was examined for the presence of BCG scar. The contact children were classified into three groups, Group 1 – BCG administered with scar present, Group 2 – BCG administered but no scar, and Group 3 – BCG not administered.

The body weight of the child was measured using digital weighing machine, and nutritional status was calculated and classified based on IAP classification.

Activities of the contact with the index case were classified into three categories, namely, occasional, part of the day (<half a day in contact), or most part of the day (more than half a day).

Proximity of the contact child with the index case during sleep was categorized into three groups, namely, Group 1: Sleeps in the same house but not in same room, Group 2: Sleeps in the same room but not in same bed, and Group 3: Sleeps in the same bed.

An informed oral consent was obtained from the index case/guardian of the contact before the beginning of the interview, explaining the study and after completion of

the interview, the tuberculin skin test (TST) was done for the contact child.

TST

TST was given to the childhood contacts at the TB cell, Government Rajaji Hospital, Madurai, by a trained personal. The test was performed by giving intradermal injection of 0.1 ml of purified protein derivative (PPD) containing five tuberculin units PPD-RT 23 into the volar (ventral) surface of the forearm, in the long axis of the forearm using a short 26 gauge tuberculin syringe. A wheal of 6–10 mm in diameter was taken as successful administration. The test was read after 72 h both by palpation technique and ballpoint technique. An induration of size 10 mm or more at 72 h was taken as positive for TST.

OBSERVATIONS AND RESULTS

Out of 1239 cases diagnosed as smear-positive TB at TB cell, Government Rajaji Hospital, Madurai, 176 cases from the city limits were started treatment in TB cell. Out of these cases, 78 cases had contacts of children between 3 months and 72 months of age. Of them, 4 cases refused to join the study. One hundred and four contacts of the remaining 74 cases were brought to TB cell and after obtaining the informed consent from the contacts (parents), participated in our study.

We found that among our study population in the age of 3 months and 72 months, around 29.8% of household contacts of smear-positive index, TB cases had TB infection as assessed by TST. Among the 31 positive children, 19 were male and 12 were female. The mean age group among the contact children was 40 months [Tables 1 and 2].

The index case was a 1st-degree relation to 58.1% (18/31) infected contacts and 28.8% (21/73) of the non-infected contacts. Of the 104 contacts studied, 39 (37.5%) children had their first-degree relation as their index case of which 18 (46%) showed a positive TST test ($P < 0.04$) [Table 3].

Of the total 31 positive children, 80.6% (25/31) had contact with the index case whose symptoms were more than 30 days and 19.4% (6/31) had a contact with symptoms which were < 30 days. Among 73% of children whose contact had symptoms for more than a month, 33% showed a positive TST ($P = 0.25$) [Table 4].

Smear 3+ was present in 51.6% (16/31) of cases of infected contacts and 13.7% (10/73) of cases of non-infected contacts. Of the total contacts studied, 25% of children had contact with a smear 3+ positive patient and of them 61.5% had a positive TST ($P < 0.001$) [Table 5].

Table 1: Sex distribution of the contacts

Total contact cases	Mantoux positive	Mantoux negative
Male	19	40
Female	12	33
Total	31	73

Table 2: Age distribution of the contacts

Age group (in years)	Total	Mantoux positive	Mantoux negative
Between 3 months and 1 year	8	3	5
Between 1 and 2 years	9	4	5
Between 2 and 3 years	27	3	24
Between 3 and 4 years	16	7	9
Between 4 and 5 years	22	8	14
From 5 years up to 6 years	22	6	16
Total	104	31	73

Table 3: Correlation of Mantoux positivity to the relationship of the child to the index case

Relation of the children	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
1st degree	18 (58.1)	21 (28.8)	39 (37.5)
2nd degree	13 (41.9)	52 (71.2)	65 (62.5)
Total	31 (100)	73 (100)	104 (100)

($P<0.04$)

Table 4: Duration of symptoms in the index case and the influence on Mantoux test on the contacts

Duration of the symptoms	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
≤30 days	6 (19.4)	22 (30.1)	28 (26.9)
More than 30 days	25 (80.6)	51 (69.9)	76 (73.1)
Total	31	73	104

($P=0.25$)

Table 5: Correlation between sputum load in index case and Mantoux positivity in contacts

Sputum load	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
1+	2 (6.5)	31 (42.5)	33 (31.7)
2+	13 (41.9)	32 (43.8)	45 (43.3)
3+	16 (51.6)	10 (13.7)	26 (25)
Total	31	73	104

($P<0.001$)

Chest X-ray shadows involving three or more zones were present in 51.6% (16/31) of index cases of infected contacts and 9.6% (7/73) of non-infected contacts. Of the total 23 contacts, whose index cases had an X-ray shadow of three or more zones, 70% of them showed a positive Mantoux test ($P < 0.001$) [Table 6].

Among the infected contacts, 71% (22/31) belong to a family with more than 4 family members and among the non-infected contacts, 65.8% (48/73) come from a family with more than 4 family members ($P = 0.604$).

Of the 70 contacts, who belong to a family size of more than 4, 31% of them had a positive Mantoux test.

About 54.8% (17/31) of the infected contacts and 46.6% (34/73) of the non-infected contacts belong to a lower economic status of society (Classes IV and V according to modified Kuppuswamy's scale).

About 33% of the total 51 children who came from lower socioeconomic status tested positive for TB infection ($P = 0.4$).

BCG scar was absent in 38.7% (12/31) of the infected contacts and 9.6% (7/73) of the non-infected ones. It was seen in 61.3% (19/31) of the infected and 90.4% (66/73) of the non-infected children. Among children with a BCG scar, 22% showed a positive TST whereas in children without a scar, 63% showed a positive TST ($P < 0.001$) [Table 7].

Among the infected contacts, 58.1% (18/31) had Grade 1 malnutrition and 38.7% (12/31) and 3.2% (1/31) of them had Grades 2 and 3 malnutrition, respectively. Only 24% of the children with Grade 1 malnutrition showed positive test for TB infection whereas 45% of children with Grade 2 or 3 malnutrition turned out to be Mantoux positive ($P = 0.103$) [Table 8].

Nineteen out of 31 infected children gave a history of sleeping in the same bed with the sputum-positive index case whereas among the non-infected children, 28.8% (21/73) gave a similar history ($p < 0.004$). Among the 40 contacts who had slept in the same bed with the index case, 47% of children had a positive Mantoux test.

Around 35.5% (11/31) of the infected children gave a history of spending most of their day with the index case, whereas among the non-infected, 26% gave a similar history [Table 9]. Among the 30 contacts who had spent most of their day with the index case, 37% of children had a positive Mantoux test. In children who spent occasional activity or part of their day with the index case, 27% showed a positive test.

Table 6: Chest X-ray features of the patient and influence on the child Mantoux

Chest X-ray zones	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
±3 zones	15 (48.4)	66 (90.4)	81 (77.9)
>3 zones	16 (51.6)	7 (9.6)	23 (22.1)
Total	31	73	104

($P<0.001$)

Table 7: Association of BCG status and Mantoux result

BCG status	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
BCG administered and scar present	19 (61.3)	66 (90.4)	85 (81.7)
BCG administered but no scar	6 (19.4)	2 (2.7)	8 (7.7)
Not administered	6 (19.4)	5 (6.8)	11 (10.6)
Total	31	73	104

($P<0.001$). BCG: Bacillus of Calmette and Guerin

Table 8: Association of nutritional status and Mantoux result

Nutritional status	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
Grade 1	18 (58.1)	57 (78.1)	75 (72.1)
Grade 2	12 (38.7)	14 (19.2)	26 (25)
Grade 3	1 (3.2)	2 (2.7)	3 (2.9)
Total	31	73	104

($P=0.103$)

Table 9: Time shared by the contact with the index case

Time shared	Mantoux result		Total (%)
	Positive (%)	Negative (%)	
Occasional	2 (6.5)	8 (11)	10 (9.6)
Part of the day	18 (58.1)	46 (63)	64 (61.5)
Most of the day	11 (35.5)	19 (26)	30 (28.8)
Total	31	73	104

($P=0.543$)

DISCUSSION

Even in the era of modern medicine, TB is still a major health problem. It has been predicted that if at least 70% of new cases of smear-positive TB are diagnosed and treated and 85% of them are cured, TB transmission will decline by 7–11% per year.

Close contacts of smear-positive TB are at risk of being infected. Identification of risk factors for TB transmission as well the proportion of TB infection among the family contacts is important to evaluate ongoing TB transmission.

Our study demonstrated that among the study population in the age of 3 months and 72 months, around 29.8% of household contacts of smear-positive index TB cases were TB infected as assessed by TST. Among the 31 positive

children, 19 were male and 12 were female. The mean age group among the contact children was 40 months. The result is comparable with the various studies done in India.[4-7]

Our study shows that those children whose index cases are first-degree relatives are at a greater risk of developing the infection. Similar outcome has been shown in studies done by Tornee *et al*.,[8] Lienhardt *et al*.,[9] and Talay *et al*.[10] This can be explained by the fact that most children spend most of their time with parents.

In our study, it is found that the duration of symptoms of index case does not have a statistically significant association with the risk of infection in contacts. In our study, 21.4% of children who's index case showed symptoms ≤30 days showed positive Mantoux result when compared to 33% in children whose index cases had symptoms more than 30 days.

Bacterial load and the involvement of lung in the chest X-ray zones of the index cases showed a linear relationship with the risk of developing TB infection. Those children whose index cases had 3+ smear showed increased TST positivity (61.5%) when compared to children whose index case had smear of 2+ (28.8%) and 1+ (6.0%). About 69.5% of children whose index case had a chest X-ray with involvement of more than 3 lung zones had a positive tuberculin test when compared to 18.5% positivity in children whose index case X-rays had ≤3 lung zones involvement. It is comparable with the studies done by Tornee *et al*.,[8] Lienhardt *et al*.,[9] and Talay *et al*.[10]

The association between TB and socioeconomic factors has been reported in many studies. In our study, we did not find an association between risk of TB infection and socioeconomic status and household size.

However, many studies in the globe have shown association between socioeconomic status and the risk of TB infection [8,9,11] This difference in result may be attributed to smaller sample size and information bias by the index case.

Our study demonstrated a significant association between the presence of BCG scar and TB infection. In our study, 61.3% of contacts with BCG scar showed a positive result, whereas 38.7% of contacts without scar had a positive TST result. This result is similar to the study done in India by Miret *et al*.[12]

In our study, all the contact children belonged to the malnourished group according to IAP classification based on weight for age. As ours is a government run hospital, most of the patients attending this health-care facility belong to lower socioeconomic status. Of the 104 contacts, 24% with Grade 1 malnutrition showed positive tuberculin test, whereas 45% of children with Grade 2 or 3 malnutrition turned out to be tuberculin test positive. As all the contact children of the study were malnourished, we could not compare the risk of TB among normal child and malnourished child.

Proximity of the contact with the index case, especially during sleep at night, is directly proportional to the risk. Our study showed 35.5% of infected contacts gave a history of spending most of their day with the index case. This result was found to be statistically insignificant. In terms of proximity with the index case, 61.3% of the infected contact gave a history of sleeping in same bed with the sputum positive index case, whereas among the non-infected contact, 29% gave a similar history. These observations were similar to studies done by Lienhardt *et al*.[9] and Karima *et al*.[11]

Limitations of the Study

There were several limitations in this study, namely, study design, convenient sampling technique, and relatively small sample size.

Cross-sectional nature and convenience sampling technique based on hospital selection led to the limitation that the source cases are not fully representative of the TB population in the community.

This study lacked a true "gold standard" test for the diagnosis of TB infection and we are not able to make unequivocal assessments of the sensitivity and specificity of the tuberculin test.

We could not visit the subject's house to carry out observations on family details and socioeconomic status due to limited time and workforce. Moreover, questions on economic status could have been felt sensitive by some interviewees who may not have provided the right answers. The above-mentioned limitations may have led to information bias.

Recall bias occurred when interviewees who are the source cases, fear that they are the cause for disease transmission in the family. They might not give true answers about their contact with the children at home. Hence, the final conclusion based on their answers may have resulted in false-positive or false-negative results.

CONCLUSIONS

We found the prevalence of TB infection in children who are in household contact with smear-positive TB patients

at 29.8%. From the study, we could infer that active contact tracing and identifying the presence of TB infection among the contacts will play an important role in the control of TB. Making TST mandatory to all contacts of sputum smear-positive patients will enable to identify more LTBI of children and with ensuring treatment completion among them, the emergence of drug resistance TB and reservoir TB infection in the community could be prevented. Also ensuring that the diagnosed children complete their full course of treatment will prevent emergence of drug resistance TB and decrease the reservoir of TB infection in the community.

REFERENCES

1. World Health Organization. Latent Tuberculosis Infection: Updated and Consolidated Guidelines for Programmatic Management. Geneva: World Health Organization; 2018. p. 17.
2. World Health Organization. Global Tuberculosis Control: Surveillance, Planing, Financing. Geneva, Switzerland: World Health Organization; 2005.
3. Working Group on Tuberculosis, Indian Academy of Pediatrics (IAP). Consensual statement on childhood tuberculosis. Indian Pediatr 2010;47:41-55.
4. Andrews RH, Devadatta S, Fox W, Radhakrishna S, Ramakrishnan CV, Velu S. prevalence of tuberculosis among close family contacts of tuberculous patients in South India, and influence of segregation of the patient on early attack rate. Bull World Health Organ 1960;23:463-510.
5. Narain R, Nair SS, Rao GR, Chandrasekhar P. Distribution of tuberculous infection and disease among household in a rural community. Bull World Health Organ 1966;34:639-54.
6. Kumar R, Saran M, Verma BL, Srivastava RN. Pulmonary tuberculosis among contacts of patients with tuberculosis in an urban Indian population. J Epidemiol Commun Health 1984;38:253-8.
7. Rathi SK, Akhtar S, Rahbar MH, Azam SI. Prevalence and risk factors associated with tuberculin skin test positivity among household contacts of smear-positive pulmonary tuberculosis cases in Umerkot, Pakistan. Int J Tuberc Lung Dis 2002;6:851-7.
8. Tornee S, Kaewkungwal J, Fungladda W, Silachamroon U, Akaraswei P, Sunakorn P. Factors assoiciated with the household contact screening adherence of tuberculosis patients. Southeast Asian J Trop Med Public Health 2005;36:331-40.
9. Lienhardt C, Fielding K, Sillah J, Tunkara A, Donkor S. Risk factors for tuberculosis infection in Sub-Saharan Africa: A contact study in the Gambia. Am J Respir Crit Care Med 2003;168:448-55.
10. Talay F, Kumbetl S. risk factors affecting the development of tuberculosis infection and disease in household contacts of patients with pulmonary tuberculosis. Turk Respir J 2008;9:37-7.
11. Miret P, Pina JM, Juncosa S. Tiberculin reactivity in *Bacillus* Calmette-Guérin vaccinated subjects. Tuber Lung Dis 1996;77:52-8.
12. Karim MR, Rahman MA, Mamun SA, Alam MA, Akhter S. Risk factors of childhood tuberculosis: A case control study from rural Bangladesh. WHO Southeast Asia J Public Health 2012;1:76-84.

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