Original Research Article

Pediatric tuberculosis in close contacts: prospective study

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Abstract

Introduction: Tuberculosis continues to be a major cause of morbidity and mortality among children in developing country like India. Early detection and treatment of infection can reduce morbidity and mortality. Screening of children in close contact with high risk groups is universally recommended but seldom practiced in resource limited settings. **Aims and objectives:** Primary objective to find prevalence of tubercular infection in children who are household contacts of PTB, and HIV-PTB coinfected adults. To identify subset of contacts who are at higher risk of contacting infection. **Settings and Design:** Prospective study conducted in tertiary care center. Children aged <10years in contact with adult PTB and PTB with HIV were enrolled and evaluated for tuberculosis infection by clinical, radiographic, and tuberculin testing. Transverse in duration of greater than 10 mm was defined as positive tuberculin test suggestive of tubercular infection. **Results:** About 33.6% of contacts exposed were found to be infected. Tuberculin test was found to be significantly positive in contacts exposed to PTB and HIV-PTB co-infected adults groups ($p > 0.0001$, with an odds ratio of 0.36 (1.10 - 1.74)), $P>0.0001$, 2.77 (1.33 - 5.79). Majority of children exposed to HIV negative PTB adults were infected compared to contacts exposed to HIV-PTB co-infected adults (35 vs 14) and the difference is statistically significant ($p>0.001$). Absence of scar is not associated with any significant risk. **Conclusions:** Prevalence of tuberculosis is high in contacts with high risk groups. HIV-PTB co-infected adults transmit infection less in comparison to HIV negative TB adults. Young children and those with severe malnutrition need to be targeted in contact screening.

Keywords: Contact tracing, Risk factors, Latent tuberculosis

Introduction

Pediatric tuberculosis infection and disease is widely prevalent in developing countries. It is estimated that around 10% of the 10.4 million global incident TB cases and 250,000 of the 1.7 million TB deaths in 2016 were amongst children (<15 years) [1]. In high TB burden settings, it is estimated that childhood TB contributes to 15–20% of all TB cases and is one of the leading causes of childhood mortality [2]. Most children usually acquire infection from household contact.

Among the household contacts, 10% of children less than 5 years and 8% older children will develop TB [3]. Children have a higher risk of progression to active tuberculosis than adults and there is increased risk of extra pulmonary complications [4]. Early detection is important to break the chain of transmission and reduce morbidity and mortality [5]. Hence importance and urgent need for contact tracing is recognized but rarely practiced in high burden countries. Contact screening and management of child contacts has great potential to reduce TB-related morbidity and mortality in children [6]. This study has been undertaken with the aim of studying the prevalence of tuberculosis infection among children in household contact with adults having HIV negative pulmonary tuberculosis and pulmonary tuberculosis with HIV and to identify possible risk factors. Identification of risk factors for disease among contacts may guide clinicians and public health practitioners on subsets of population that may benefit the most from contact tracing.

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Subjects and Methods:

Setting and design: This prospective study was conducted in tertiary care institution of Andhra Pradesh from October 2017 to September 2018. Adults cases of pulmonary TB and adults with HIV and pulmonary TB co-infection were identified from registers of RNTCP and NACO units respectively.

Sampling: Simple random sampling done and convenient sample technique adopted for the study. Total of 200 contacts were identified and called for screening. Total of 154 children came for screening and enrolled in study.

Approval of the institutional ethics committee and written informed consent of parents was obtained prior to enrolments of contacts.

Inclusion criteria: Children below 10 years living in same house as adult with tuberculosis

Exclusion criteria: Children who had been previously treated for tubercular infection, with comorbid conditions like HIV infection, hematological, or reticulo-endothelial system malignancies, diabetes and those who were previously or currently on immuno-suppressive drugs including corticosteroids were excluded.

Detailed history noted and clinical examination of children was performed by senior resident in pediatrics. History of BCG vaccination was especially enquired after, and scars examined. Height was measured using a stadiometer (erect position for children older than 2 years and supine position for younger children); weight was recorded using a single pre-calibrated beam balance. Malnutrition classified according to the Indian Academy of Pediatrics (IAP) classification [7]: Grade 1, weight 71-80% of expected; grade 2, weight 61-70% of expected; grade 3, weight 51-60% of expected; and grade 4, weight less than 50% of expected. Grades 1 and 2 were categorized as mild malnutrition and grades 3 and 4 as severe malnutrition.

Each of the children underwent tuberculin skin testing, performed by the intradermal injection of 1 Tuberculin Unit of Purified Protein Derivative PPD-RT23 with Tween 80 into the volar surface of the left forearm using a 26 gauge needle and disposable syringe.

This was read 72 hours later in good light with the forearm slightly flexed. Transverse in duration of greater than 10 mm was defined as a positive tuberculin test suggestive of tuberculosis infection.

A single technician trained in administration and interpretation of tuberculin test performed the procedure in all children.

All children underwent postero-anterior erect chest radiography which was reported by a single experienced radiologist (unaware of the results of tuberculin testing) and labelled as consistent or not consistent with tuberculosis.

Statistical analysis: Data analysis done by SPSS V22 software. Descriptive statistics calculated by frequency and percentage. Parameters between contacts of PTB and HIV PTB were done using Student's t test for continuous variables and the x2 test (with or without Yates's correction) for qualitative variables. $P<0.05$ will be considered as statically significant

Results

Total of 154 children in contact with 108 index cases enrolled as subjects of which 8 children lost to follow up. Total of 146 cases were included in final analysis. The number of females (54.1%) outnumbered the number of male subjects in the study. Majority of children were malnourished, out of which 42 (28.8%) contacts had mild malnutrition and 57(39%) had severe malnutrition. BCG scar was observed in 92 contacts (Table 1). In remaining contacts parents gave history of BCG vaccination but no documentation of same

Among the total subjects 81 children had exposure to adults with pulmonary tuberculosis and 65 (44.5%) were exposed to adults with HIV and pulmonary tuberculosis.

Among the symptomatic contact most common symptom observed was chronic cough (n=17) followed by documented weight loss (n=11). Table 2 Children exposed to PTB adults are more symptomatic than those exposed to adults with HIV and PTB. Chest radiograph was consistent with tuberculosis in nine children, seven of whom were contacts of PTB patients.

TST positive (>10mm) in 49 contacts of which 35 contact has exposure with adults with PTB, while 14 were exposed to HIV and PTB. The difference is found to be statically significant (p=0.001). The effect of contact with PTB and HIV and PTB patient on the occurrence of positive tuberculin test was analysed and found to be highly significant in both the group of contacts (p>0.0001) (Table 3). Tuberculin skin test was positive in 23.8%, 26.3%, and 29,8.% contacts with normal nutrition, mild malnutrition, and severe malnutrition respectively. The size of in duration of positive tuberculin skin test among contacts with increasing grades of malnutrition (Figure 1)

Table-1: Demographic characteristics of study subjects.

characteristic	Number
Male	67 (45.9%)
Female	79 (54.1%)
Contact with PTB	81 (55.5%)
Contact with HIV & PTB	65 (44.5%)
No malnutrition	42 (28.8%)
Mild malnutrition	57 (39%)
Severe malnutrition	47 (32.2%)
BCG scar	91 (62.3%)

Table-2: Clinical characteristics in children.

Clinical finding	Total	PTB contacts	HIV-PTB contacts
Cough > 4 weeks duration	17	12	5
Weight loss	11	7	4
Loss of appetite	6	1	4
Lymphadenitis	13	8	5
TST-positive	49	35	14

Table-3: Risk factors analysis in contacts

Variable	Infection positive	Infection negative	P-value	Odd's ratio (95% C I)
<5 years	29	32	0.002*	1.02 (1.21-2.34)
Severe malnutrition	24	28	0.05*	0.47 (0.21-1.06)
Absence of BCG	19	36	0.85	1.07 (0.53-2.18)
Contact with PTB	35	46	0.0001*	0.36 (1.10-1.74)
Contact with HIV PTB	14	51	0.0001*	2.77 (1.33-5.79)

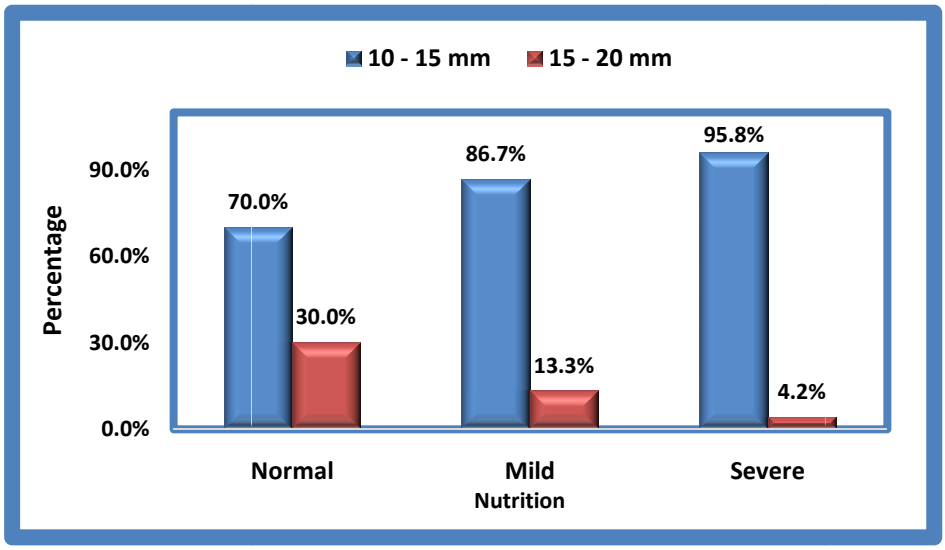

Fig 1: Nutrition

Discussion

Exact prevalence of tuberculosis in India is not known. It is estimated that childhood TB constitutes 10–20% of all TB in high-burden countries [2]. Prevalence of tuberculosis in high risk contacts observed in this study was high (33.6%). Similar observations made in other studies using TST cut off > 10mm stressing the need for contact tracing in high risk children [8,9]. A meta-analysis of contact investigation in low- and middle income countries by Morrison and colleagues revealed a prevalence of TB infection of 40% in children aged under 15 years [10]. Despite high prevalence of infection contact screening rarely implemented. A cross-sectional study in India reported that only 14% children younger than 14 years living in the same house as adults with pulmonary TB were screened for TB [11].

Early identification of tubercular infection in children relies heavily on tuberculin testing despite rapid advances in the diagnosis. Tuberculin test depends on administration of reagent and interpretation of test result. Multiple persons involved in the interpretation of test may lead to varied inference. In the present study the major limitation of tuberculin test is not a factor as the test is administered and interpreted by single person.

BCG vaccine known to protect from severe tubercular infection in children. BCG scar is observed in 62.3% of subjects. Kumar et al observed BCG scar in 81% of children [12]. BCG vaccination interferes with tuberculin reactivity but in duration of > 10mm in a BCG vaccinated child is more likely due to tubercular infection rather than vaccination [13, 14]. High prevalence of tubercular positivity in the present study population and majority of them having in duration > 10mm give indirect evidence of tubercular infection.

Malnutrition depress the hypersensitivity of Mantoux test and give false negative result [15]. Some studies reported significant difference in prevalence of Mantoux positivity among malnourished compared to normal children [16, 17]. Malnourished child can mount hypersensitivity reaction but size of in duration will be smaller. In the present study there was a significant difference in the prevalence of positive tuberculin test among malnourished compared to normally nourished children and mean duration of in duration in severely malnourished contacts was less. Young children aged ≤5 years were at significant risk of developing disease, probably because the pathogenesis of tubercular infection is different in younger than older children [17]. Older children who were at the risk of reactivation of latent infection, younger children are usually at risk of primary disease after infection from the index case [18]. HIV epidemic has significant influence on the epidemiology of tuberculosis. Adults with TB-HIV co-infection may be less likely to infect their close contacts than HIV-negative TB cases [19,20]. Factors like duration of cough and cavitory lesion on chest radiograph, associated with transmission of tuberculosis could differ significantly between HIV-seropositive and HIV-seronegative TB patients [21, 22]. In this study HIV-TB co infected adults transmitted infection to significant more number of contacts as compared to the transmission by HIV negative TB adults.

Limitations: Smaller sample size and lack of follow up of infected children is the major drawback. All the children who were TST positive were referred to RNTCP for further evaluation and treatment.

Conclusions

The findings from the present study suggest that there is a high prevalence of infection among children in household contact with adult cases of tuberculosis. The risk is higher for contacts of HIV negative PTB patient, severe malnutrition, younger age (>5 years) are significant risk factors for the transmission of infection First author was major contributor in the collection of data and compilation of data, while second author helped in planning of study and compilation of data

What this study adds to existing knowledge? Adults with co-infection (HIV-PTB) transmit infection significantly to close contacts. However, risk of transmission of infection is more in contacts of HIV negative PTB adults. Malnourished children under 5 years of age are at greater risk. Absence of BCG scar is not a risk factor.

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