

## Original Research Article

# A study on screening of high risk children for tuberculosis infection

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### ABSTRACT

**Background:** Tuberculosis (TB) continues to be one of the most devastating and widespread infections in the world. Of the 9 million annual tuberculosis cases, about 1 million (11%) occur in children (under 15 years of age). Childhood tuberculosis is a neglected aspect of the tuberculosis epidemic. The objective of the study was to screen the children who are household contacts of TB, HIV and TB -HIV patients and identify the children with the type of tuberculosis (Latent and symptomatic) and treat accordingly there by reducing the transmission of disease, as these children may become open cases in the future.

**Methods:** All the registered cases of active TB, TB-HIV and HIV were traced out from district unit of RNTCP, PHC, CHC in and around Nellimarla town (10 kms radius). These patients were interviewed for medical history, treatment history, duration of treatment and degree and duration of house hold contacts (primarily children between 1 to 14 years).

**Results:** Out of 160 registered patients 91 patients were diagnosed as having symptomatic TB infection and 69 were diagnosed having latent TB infection, with most of the affected children being in the age group of 1 to 5 years). Majority of the symptomatic patients (46.15%) were household contacts of TB- HIV patients and majority of children (40.57%) with latent TB Infection are direct household contacts of open cases of TB alone. Of the symptomatic TB infection 74.72% had pulmonary TB and 25.28% had extra pulmonary TB.

**Conclusions:** Tubercular lymphadenopathy is the most common manifestation of extra pulmonary TB followed by tubercular meningitis and among the tubercular lymphadenopathy the cervical lymphnodes are most commonly involved.

**Keywords:** HIV, Pulmonary tuberculosis, Tuberculosis lymphadenopathy

### INTRODUCTION

Tuberculosis (TB) continues to be one of the most devastating and widespread infections in the world. Of the 9 million annual tuberculosis cases, about 1 million (11%) occur in children (under 15 years of age). In countries worldwide, the reported percentage of all tuberculosis cases occurring in children varies from 3% to more than 25%. Childhood tuberculosis is a neglected aspect of the tuberculosis epidemic. This “orphan disease

“exists in the shadow of adult TB and is a significant child health problem but is neglected because it is usually smear-negative and is thus considered to make a relatively minor contribution to the spread of TB.<sup>1</sup>

#### *Childhood TB prevalence indicates*

- Community prevalence of sputum smear-positive pulmonary tuberculosis.
- Age-related prevalence of sputum smear-positive pulmonary tuberculosis.

- Prevalence of childhood risk factors for disease

### **Stage of epidemic**

Many western nations have been experiencing a resurgence of TB with most of the new cases imported from countries with high rates of the disease. Young children carry the greatest burden of disease. They are the most likely to develop disease after infection and are significantly more likely to develop extra pulmonary and severe disseminated disease than adults. Infected children represent the pool from which a large proportion of future cases of adult TB will arise.<sup>2</sup> In addition, childhood TB is a sentinel event, indicating on going transmission of TB within communities.<sup>3</sup> Though an estimated 1 million new cases of tuberculosis (TB) occur in children worldwide each year, pediatric TB has not been given the same priority as its adult counterpart.<sup>4</sup> Childhood TB is a neglected aspect of the TB epidemic. This "orphan disease" exists in the shadow of adult TB and is a significant child health problem but is neglected.<sup>5</sup> Does this justify ignoring childhood tuberculosis? Proper identification and treatment of infectious cases will prevent childhood TB. However often Childhood TB is accorded low priority by National TB Control programme.

### **Probable reasons include**

- Diagnostic difficulties
- Rarely infectious
- Limited resources
- Misplaced faith in BCG
- Lack of data on treatment.

Interest in tuberculosis has been rekindled. But the interest in childhood tuberculosis continues to be lukewarm. Since the declaration by the WHO of a, global TB emergency" in 1993, a wealth of publications has addressed important aspects of the burden, management and control of tuberculosis (TB). In general, however, the emphasis has been on adult disease. By contrast, paediatric TB has been relatively neglected. As a result, both research and surveillance data in the field of childhood TB have been greatly limited. However, children are particularly vulnerable to severe disease and death following infection, and those with latent infection become the reservoir for future transmission following disease reactivation in adulthood, fuelling future epidemics. Further research into the epidemiology, immune mechanisms, diagnosis, treatment, and prevention of childhood tuberculosis is urgently needed. Advances in our understanding of tuberculosis in children would provide insights and opportunities to enhance efforts to control this disease.<sup>3</sup> Studies of pediatric TB are scantily available both in global and national contexts. Reliable data on the burden of all forms of TB amongst children who are in contact with adult open cases in India are not available. Hence, a study of pediatric TB cases was carried out to determine the prevalence of TB in high

risk groups, type of TB and treatment outcomes in the Tuberculosis units of Vijayanagaram District. knowing the prevalence and history of contact with open cases can help in understanding the groups that are vulnerable to the disease and treatment outcomes in the various groups can indicate as to the type of population that have favourable and non- favourable outcomes. This can help in focusing on those specific groups when diagnosing and treating childhood TB.

### **Objectives**

- To know the incidence of Tuberculosis infection in paediatric patients who belong to high risk group like contact with open cases of TB, HIV, TB and HIV of pediatric tuberculosis patients.
- To know the type of tuberculosis (latent or symptomatic) and risk factors involved in transmission of disease

### **METHODS**

This prospective study was conducted from October 2010 to September 2012, with an aim to study the incidence of tuberculosis infection (latent and symptomatic) in high risk group of children i.e. children who are household contacts with adult TB, TB-HIV, HIV cases in and around Nellimarla Town (10 km radius).

The Ethical committee of our college and hospital approved this study. All the children between 1-14 years who are household contacts were applied for Mantoux test and results were interpreted along with supportive evidence with chest-x-ray, complete blood picture, CSF-analysis, Ultrasound abdomen, detailed clinical examination, history of symptoms and signs. Before data entry, the investigator and statistician reviewed the forms of consent, accuracy and completeness.

### **Study population/sample size**

From October 2010 to September 2012, 389 children between 1-14 years who are household contacts of 200 patients (suffering with TB, TB-HIV, HIV) in and around 10km radius of Nellimarla town are enrolled. This number was chosen due to feasibility reasons and the available time frame.

### **Household contact**

Defined as any child who lives in a household with an index case taking anti- tubercular treatment or has taken ATT therapy in the past 2 years.

### **Index case**

Defined as a case of active pulmonary tuberculosis with sputum positive for AFB Smear and culture, who are either HIV seropositive or seronegative. It also included only HIV cases without active pulmonary tuberculosis.

### **Inclusion criteria**

- Children between 1-14 years (house hold contacts) exposed to
- Adult cases with tuberculosis (open cases).
- HIV-Cases.
- HIV-TB cases.

### **Exclusion criteria**

- Children who had been previously treated for tubercular infection
- Children with concurrent conditions identified as risk factors for tuberculosis. (HIV infection, haematological, or reticulo-endothelial system malignancies)
- Children who were previously or currently on immunosuppressive drugs. including corticosteroids.

All the registered cases of active TB, TB-HIV and HIV were traced out from district unit of RNTCP, PHC, CHC in and around Nellimarla town (10 kms radius). These patients were interviewed for medical history, treatment history, duration of treatment and degree and duration of house hold contacts (primarily children between 1 to 14 years). Knowledge of the transmission of disease and practices related to cough and spitting and also their socio-economic status was assessed.

All the index cases were explained about risk of exposure, burden and severity of the diseases and an informed consent was taken to test the children who are contacts

### **Data collection**

After obtaining informed consent of parent or guardian, children between 1 to 14 years who are house hold contacts and who are not previously diagnosed or on treatment with ATT are selected.

Detailed history and clinical examination of children between 1-14 years old who were in household contact with adult patients was performed. This included age, sex, religion, history of fever and/or cough of greater than two weeks duration, failure to gain weight, loss of appetite, decline in weight, and symptoms of extra-pulmonary tuberculosis such as lymphadenopathy, bone pains, neurological deficit (or any symptoms related to CNS involvement).

History of BCG vaccination was especially enquired after, and scars examined. A detailed history was also recorded regarding exposure to environmental tobacco smoke. Anthropometry (Height and weight) measurements were made, and malnutrition classified according to the Indian Academy of Pediatrics (IAP) classification: 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.<sup>4</sup> Grades 1 and 2 were categorized as mild malnutrition and grades 3 and 4 as severe malnutrition. 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 precalibrated beam balance.

### **Laboratory procedures**

#### *Tuberculin skin testing*

This is the standard method for identifying persons infected with *M. tuberculosis*. The Mantoux test (i.e., the intracutaneous administration of five units of purified protein derivative {PPD} tuberculin) best detects infection.

#### **Procedure**

The MANTOUX TUBERCULIN SKIN TEST is the intradermal injection of 0.1 mL containing 5 IU of purified protein derivative (PPD) stabilized with Tween 80, on volar surface arm using a 25-26 gauge needle.

#### ***Tuberculosis skin test (TST) recommendations for infants and children***

##### *Children for whom immediate TST is indicated*

- Contacts of people with confirmed or suspected contagious tuberculosis (contact investigation)
- Children with radiographic or clinical findings suggesting tuberculosis disease.
- Contacts of people with HIV
- Children who are infected with HIV.

##### *Children who have annual TST*

- Children infected with HIV

##### *Children at increased risk for progression of LTBI to tuberculosis disease*

Children with other medical conditions, including diabetes mellitus, chronic renal failure, malnutrition and congenital or acquired immunodeficiencies.

#### ***How the test is read?***

- Test is read by a trained health worker and authors, 48 - 72 hours after the tuberculin injection.
- Diameter of the indurated (swelling) area is measured across the forearm erythema (redness) is not measured.
- Test result is measured in millimeters (mm)

#### ***Definitions of positive tuberculin skin test (TST) results in infants and children***

*Induration >=10*

*Children at increased risk of disseminated tuberculosis disease*

- Children younger than 4 yrs age
- Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure or malnutrition.
- Children born in high -prevalence regions of the world
- Children frequently exposed to adults who are HIV infected, homeless. Users of illicit drugs, residents of nursing homes, incarcerated or institutionalised, or migrant farm workers.
- Children who travel to high prevalence regions of the world.

*Induration >= 15MM*

- Children 4 yrs of age or older without any risk factor
- Tuberculin skin-test results should be evaluated within the context of each patient's epidemiologic and environmental potential for infection.

**Chest X-ray**

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.

*Supportive diagnostic tests*

- Blood counts
- ESR (Erythrocyte sedimentation rate)
- CSF analysis
- Ultrasound abdomen
- FNAC of lymphnodes (on the basis of presentation of symptoms)
- CT-SCAN brain (for cases of neuro-TB)

**Definition**

*Latent TB*

Occurs after inhalation of infective droplet nuclei. A reactive tuberculin skin test and the absence of clinical and radiographic manifestations are the hallmark of this stage.

*Established TB*

It is a disease which occurs when signs and symptoms or radiographic changes become apparent. Untreated infants with latent TB have up to a 40% likelihood of developing TB. The greatest risk for progression occurs in the first 2 years after infection.

**RESULTS**

Out of 389 children, between 1-14 years who are Household contacts of 200 open cases of TB, TB-HIV, and HIV, 160 children had Significant positive Mantoux test, (reading of 10 mm or more is taken as significant)

Out of the 160 Mantoux positive children, 91 children were having symptomatic/established TB and 69 children were having latent TB.

**Table 1: Distribution according to age.**

Age	symptomatic /established	Latent	Total	Percentage
1-5	49	19	68	42.5%
6-10	26	19	45	28.1%
11-14	16	31	47	29.4%
Total	91	69	160	100%

Table 1 shows that maximum number of cases were in the age group of 1-5 years (42.5%) followed by age groups of 11-14. Similar findings were reported in a hospital based prevalence study done by Subrahmanyam S et al. In 1998 in Kottayam district of Kerala where they also observed that the maximum number of cases were in 1-5 years age group which was 49.5%.

The factors which led to high incidence of tuberculosis infection in children of this age group (1-5years) are:

- These children have some compromised immune status compared to children of other age group of same nutritional status.
- These children remain in close contact with adult cases.

**Table 2: Age/ sex distribution.**

Sex	1-5 yrs	6-10 yrs	11-14 yrs	Total	Percent
Male	32	17	18	67	41.9%
Female	36	28	29	93	58.1%
Total	68	45	47	160	100%

Table 2 shows that among all cases there were more female patients (58.1%) compared to males (41.9%) and this is correlating with Sharma S et al.<sup>6</sup> Observations which reported that the prevalence of TB is more in females (61.7%) than males in general.<sup>6</sup> This shows that the incidence is almost similar to prevalence both in high risk and in general population with regards to age/sex distribution.

Present study revealed a male to female ratio of 0.7:1, while a study done by Indumathi CK et al, for prevalence reported a male to female ratio of 0.8:13.

The high incidence of cases in females in my study could be explained by the fact that most of my study belonged to lower class (socioeconomic status) where the female child's nutrition and health may be neglected.

**Table 3: Distribution according to socioeconomic status (based on Kuppaswamy's classification).**

Status	Symptomatic	Latent	Total	Percent
Upper middle	11	07	18	11.25%
Lower middle	19	22	41	25.63%
Upper lower	49	34	83	51.87%
Lower	12	06	18	11.25%
Total	91	69	160	100%

This study showed that 88.75% of the cases belong to low socioeconomic status and 11.25% belonged to middle class. Thus, reem phasing that TB is associated with low socioeconomic status. This can be explained by the fact that usually people who belong to low socioeconomic status tend to live in small houses and these are usually overcrowded and this makes the spread easier. At the same time the children usually tend to be undernourished as they may not be supplied with good balanced diet due to financial aspects and undernourished children tend to be at more risk than general population of having TB when exposed to an open case (Table 3).

**Table 4: Distribution of patients according to religion.**

Religion	Symptomatic	Percent
Hindu	98	61.250%
Muslim	35	21.875%
Christian	27	16.875%

**Table 5: Distribution of patients according to educational status of parents.**

Education	Frequency	Percent
Illiterate	66	41.25%
Primary school certificate	43	26.87%
Middle school certificate	27	16.87%
High school certificate	17	10.62%
Intermediate or post high school certificate	07	4.40%
Total	160	100%

Table 4 shows that among all cases, the proportion of Hindus was 61.25%, which is more than the other 2 communities. It does not imply that cases were more in Hindus but because proportion of Hindus were more in the general population, more cases were reported among Hindus. While comparing between Muslims and

Christians, Muslims have higher percentage of frequency. This according to my observation basing on family history attributed to overcrowding in their houses which makes the spread easier.

This study showed that 68.12% of children were affected with TB, whose parents belong to low educational background and it was observed that paediatric TB cases progressively reduced with increasing educational status of parents (Table 5).

**Table 6: Distribution of patients according to presence of overcrowding.**

Overcrowding	Frequency	Percentage
Present	97	60.62%
Absent	63	39.38%
Total	160	100%

Table 6 shows that 60.62% of the patients lived in overcrowded households. Thus, authors can conclude that staying in overcrowded houses is associated with increased transmission of TB.

**Table 7: Distribution of patients according to BCG SCAR.**

BCG SCAR	Male	Female	Total (%)
Absent	16	27	43 (26.88%)
Present	51	66	117 (73.12%)
Total	67	93	160 (100%)

Table 7 shows that 73.12% of the patients have BCG Scar. Similar observations were made by Shivanandam S et al, in their study where 76% had received BCG Vaccination.<sup>7</sup> Study done by Gupta R et al, showed 77% cases were vaccinated with BCG.<sup>8</sup>

These two studies were done for prevalence in general population, but findings of my study also revealed the higher percentage of cases in the BCG Vaccinated children which is just correlating to the above study.

**Table 8: Distribution of patients according to nutritional status.**

PEM	Frequency	Percentage
Present	97	60.62%
Absent	63	39.38%
Total	160	100%

Table 8 shows that 60.62% of the patients were malnourished. This supports the fact that TB and malnutrition form a vicious cycle. Hence the incidence is more in malnourished children.

Table 9 shows that out of total 97 children with malnutrition 50.51% of children suffering with grade 1

malnutrition, 39.18% children grade 2, 7.22% belong to grade 3, and 3.09% belong to grade 4.

**Table 9: Distribution of patients according to grade of PEM (based on IAP classification).**

Grade of PEM	Frequency	Percentage
Grade 1	49	50.51%
Grade 2	38	39.18%
Grade 3	07	7.22%
Grade 4	03	3.09%
Total	97	100%

Previously there was a study for prevalence, according to PEM status by Sushmbhai et al, who observed that 42% has Protein Energy Malnutrition of which 37% has grade 1 or grade 2 PEM, 5% has grade 3 PEM with no children of grade 4. Since my study is based on Mantoux positive cases and there is likely chance of false negative Mantoux test in grade 3 and grade 4 PEM, there are less number of cases registered. But the fact is, contact children who are malnourished have higher risk of attaining TB infection than of normal nutritional status children and this is attributed to decreased immunity.<sup>9</sup>

**Table 10: Distribution according to type of contact.**

Type	TB (%)	TB-HIV (%)	HIV (%)	Total (%)
Symptomatic	36 (39.56%)	42 (46.15%)	13 (14.28%)	91 (56.87%)
Latent	28 (40.57%)	26 (37.68%)	15 (21.73%)	69 (43.12%)
Total	64 (40%)	68 (42.5%)	28 (17.5%)	160

Table 10 shows that 42.5% of children are suffering from TB (symptomatic and latent together) who are household contacts with TB-HIV, when compared to contacts with TB and HIV alone. This shows that children with household contacts with TB-HIV are at more risk of attaining infection compared to exposure to TB and HIV.

**Table 11: Distribution of patients according to types of symptomatic TB.**

Type	Pulmonary	Extra pulmonary
Symptomatic	68 (74.72%)	23 (25.28%)

Table 11 shows that there is a considerable higher proportion of pulmonary cases (74.72%) compared to extrapulmonary cases. The incidence of pulmonary cases is higher than extrapulmonary cases.

Table 12 showed that tubercular lymphadenopathy is the most common manifestation of extrapulmonary TB in our study population followed by TB-meningitis and cervical lymphnode is most commonly involved. Others include pleural effusion.

Arora VK et al, in their study reported that EPTB was seen in 47% of children with lymphadenopathy as 75%, pleural effusion in 9.6%, spinal and abdominal TB in 4.2% each and meningeal TB in 2.9% cases.<sup>10</sup>

**Table 12: Distribution of patients according to the type of extrapulmonary cases.**

EPTB	Frequency	Percentage
Neuro-TB	06	26.08%
Cervical lymphadenopathy	11	47.82%
Inguinal lymphadenopathy	01	4.34%
Abdominal TB	02	8.69%
Spinal TB	01	4.34%
Others	02	8.69%

## DISCUSSION

Most of the patients coming to the RNTCP centres belong to the under-privileged group. Out of 160 registered patients studied, 91 patients were diagnosed as having symptomatic tuberculosis infection and 69 were having latent tuberculosis infection. Most of the patients were in the age group of 1 to 5 years (which was around 42.5%) there were more females (58.1%) than males and male to female ratio was observed to be 0.8:1 which almost coincides with previous studies done for prevalence of Paediatric tuberculosis.

Majority of the patients were Hindus (61.25%) followed by Muslims (21.87%).

Majority of the study population (92%) belonged to low socioeconomic status as per Kuppusswamy classification, thus reemphasizing that TB is associated with low economic status.

Majority of the parents of paediatric patients were illiterates (41.25%) and it was observed that percentage of paediatric TB Cases progressively reduced with increase in education status of parents.

About (60.62%) study population gave a history of dwelling in overcrowded houses and nearly 80 to 90 % of them gave a history of being exposed to indoor Air pollution. More than half of the patients (97%) had wasting/under nutrition and of the total 160 children (50.9%) suffered grade-I under nutrition, 39.05% have grade-II under nutrition and 07.22% have grade-III under nutrition and 03.09 percent have grade-IV malnutrition.<sup>1</sup>

BCG Scar was present in 117 patients (73.12%) out of 160 patients.<sup>8</sup>

In this study 46.15% of children have symptomatic TB infection who are household contacts of TB HIV followed by those of household contacts of isolated TB (39.16%) and isolated HIV (14.28%). Out of 91

symptomatic children, 74.72% had pulmonary TB and 25.28% had extra pulmonary TB.<sup>6</sup>

This study also showed that 40.5% of children have latent infection who are in direct contact with adults having TB alone followed by those in contact with TB- HIV (37.68%) and HIV (21.73%). Usually the incidence of paediatric TB is 10% but above study is showing the incidence of TB in paediatric age group, especially who are household contacts of TB cases, as higher which explains the fact that there is still some lacking in the effective working of the RNTCP units. The deficiency may be due to inefficient supervision, deficiency in manpower, deficiency in reaching the adult cases and in counseling them. Hence early identification and screening of children who are household contacts of Adult TB, TB-HIV and HIV cases and treating them, accordingly, would help in decreasing the incidence of pediatric TB infection.<sup>11</sup>

The study showed that tubercular lymphadenopathy is the most common manifestation of extra pulmonary TB followed by tubercular meningitis and among the tubercular lymphadenopathy, the cervical lymph nodes were the most commonly involved. Pulmonary tuberculosis is more common across all age groups except in the group of 11-14 years where extra pulmonary tuberculosis is more common.

Paediatric tuberculosis still continues to be a major problem in children who are household contacts of TB, TB-HIV and HIV and especially, children of 1-5 years of age who are undernourished and belonging to low socioeconomic status are at increased risk of attaining infection. The high incidence of cases in females in our study may be due to the fact that most of present study population belonged to labor class where the female child's nutrition and health may be neglected. Poor housing conditions which continues to haunt our population is an important risk factor for TB transmission. Thus, prompt screening of all children who are household contacts, and to identify and treat the disease in them accordingly will lead to decreased morbidity and mortality. Steps to improve the socioeconomic conditions and the treatment of adult TB who are the source of infection to children will go a long way in preventing paediatric TB. Since a child with latent TB can become symptomatic within 1st year of infection, identifying the children and treating them at appropriate time can decrease the morbidity and mortality due to disease.<sup>4,12</sup>

## CONCLUSION

Diagnosis of paediatric tuberculosis still continues to be a challenge. The present definition of cure given by RNTCP is with reference to sputum positive cases only and cannot be applied to paediatric cases where most of the cases are sputum negative pulmonary cases and

extrapulmonary cases. Thus, the definition should be revised to include guidelines for cure in paediatric TB.

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