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Risk factors, clinico-epidemiological profile of tuberculosis among children attending a tertiary care hospital: a two year study

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ABSTRACT

Background: TB remains as the one among the top 10 causes of death worldwide. In 2016, 10.4 million people fell ill with TB, and 1.7 million died from the disease with 0.4 million with HIV. At least 1 million children become ill with TB each year. Children represent about 10-11% of all TB cases. Having knowledge of the risk factors for tuberculosis infection in children is important to evaluate the level of ongoing transmission of infection and to help adapt activities within national TB control programs. The main objective is to study the risk factors and their association and variable clinical features in cases of pulmonary and extra pulmonary tuberculosis.

Methods: The main objective is to study the risk factors and their association and variable clinical features in cases of pulmonary and extra pulmonary tuberculosis.

Results: 98 cases of TB were confirmed out of total 628 with a prevalence of 17.07% in the study with 78 PTB cases and 20 EPTB. Females were more with male to female ratio of 0.7:1.5-9 years was the most common age group in the study. Statistically significant association was found between old history of ATT, HIV positivity, contact with an open case of TB and malnutrition (p value<0.05). TB meningitis was the most common EPTB (10/20 cases) followed by tuberculous lymphadenitis (5/20). 69.39% (68/98 cases) were smear positive, radiologically 59.18% of cases were positive and Tuberculin skin test was positive in 46.94%.

Conclusions: Childhood tuberculosis is a neglected entity in developing countries due to underreporting and difficulties in diagnosis due to variable clinical picture in children. Hence epidemiological surveillance studies in children are required to determine the actual prevalence of pulmonary and extra pulmonary cases of tuberculosis. Increased efforts are required to isolate TB bacilli from body fluids to identify early the childhood cases and manage them to prevent disease burden in the community.

Keywords: Extra pulmonary tuberculosis, HIV, Pulmonary tuberculosis, Tuberculous meningitis, Tuberculin skin test

INTRODUCTION

Tuberculosis an air borne infectious disease caused by Mycobacterium tuberculosis is still an alarming threat mainly in developing countries despite advances in diagnosis and management. TB remains as the one among the top 10 causes of death worldwide. In 2016, 10.4 million people fell ill with TB, and 1.7 million died

from the disease with 0.4 million with HIV.¹ Seven countries account for 64% of the total, with India leading the count. The problem of tuberculosis in children cannot be underestimated as the scope is not yet fully known. TB infection and disease among children are much more prevalent in developing countries, where resources for TB control are scarce. At least 1 million children become ill with TB each year. Children represent about 10-11%

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of all TB cases.² Researchers estimate that 67 million children are infected with TB (latent TB) and are therefore at risk of developing disease in the future. India is one of the countries with highest childhood cases of tuberculosis in all clinical types. Regional data from WHO indicate that the smear positive TB in children accounts for 0.6-3.6% of all cases reported.3 However, the data represents only a tip of the iceberg where most are unnoticed and unreported. Information on prevalence of tuberculosis infection among children is important to evaluate tuberculosis transmission in communities. Having knowledge of the risk factors for tuberculosis infection in children is important to evaluate the level of ongoing transmission of infection and to help adapt activities within national TB control programs.4 Development of drug resistance is an additional threat with an alarming rise of HIV-TB co infected cases. Most of the drug resistant cases are reported from India due to lack of appropriate awareness and failure in administration of health programmes in treatment. Monitoring of TB management in children is an essential part in national programmes to determine the success or failure of the programme.⁵ Most of the studies have reported the socio demographic profile of childhood tuberculosis. Hence there is an urgent need for further research into the epidemiology, diagnosis management of childhood tuberculosis.

This study focuses on the risk factors and their association, socio demographic characters and clinical profile of cases of tuberculosis in children. The main objective is to study the risk factors and their association and variable clinical features in cases of pulmonary and extra pulmonary tuberculosis.

METHODS

A prospective observational study was conducted by department of pediatrics in association with department of Microbiology at Narayana Medical College and hospital, a tertiary care hospital for a period of two years from January 2014 to December 2015 after obtaining ethical clearance from the institutional ethical committee. The study was conducted as per the guidelines and protocol of the committee. Written and informed consent was obtained from the parents of the enrolled cases included in the study and complete socio demographic particulars regarding age, sex, duration of the symptoms, family history of TB or HIV status of parents, old history of Anti tuberculosis treatment etc were obtained and noted in a separate predesigned questionnaire sheet.

A detailed clinical history and physical examination were done in all the suspected cases of the study. Suspected tuberculosis was defined as per the guidelines of revised National tuberculosis control programme [RNTCP] History of BCG vaccination, (Observation of BCG scar-4mm in size), history of contact with TB (Defined as person taking ATT or taken ATT in the past two years) was elicited from all the cases.⁶ All the cases suspected to

have tuberculosis were diagnosed as per the WHO guidelines.⁷ In cases of pulmonary tuberculosis cases sputum examination or gastric lavage was collected and performed Acid fast staining procedure for Acid fast bacilli. Regular sputum concentration technique using Nacetyl Cysteine as digestant was followed in specimens which were negative by regular method. In cases which were negative by smear microscopy, chest radiographs were done and observed for lesions suggestive of pulmonary TB. A standard tuberculin skin test [TST] was done as per the standard guidelines and cases with induration ≥10mm were considered positive. Malnutrition was assessed and if weight or height was elicited and less than the 5th percentile for age as per Agarwal's charts.⁸

Extra pulmonary cases of tuberculosis were suspected based on clinical signs and symptoms and diagnosed. Ultrasound abdomen in cases of Abdominal tuberculosis, histopathological examination in cases of TB lymphadenitis and CSF examination collected by lumbar puncture and CT brain was done as per the requirement in cases of TB meningitis. HIV testing was done for all the confirmed cases by Standard NACO guidelines and confirmed the HIV status in TB positive cases.

Statistical analysis

All the collected data was entered in Microsoft excel spread sheet by a technical person and corrected for any mistakes. Corrected data was entered in SPSS version 13 for windows 8. Data was presented as rates and proportions. Statistical significance of difference in proportions was tested using chi-square test and a p-value of <0.005 was considered significant.

RESULTS

In the present study conducted for a period of two years, 628 children with suspected tuberculosis (Pulmonary and extra pulmonary) were enrolled.54 were excluded from the study as 23 not consented for the study, 12 were lost on follow up, 8 cases refused for collection of gastric aspirate and 9 cases were transferred to other hospital due to personal reasons.

574 of the remaining were examined clinically and screened for TB following the standard TB diagnostic criteria as per RNTCP.⁹ 98 of the 574 cases were confirmed as tuberculosis with an overall prevalence of 17.07% in the study. 78 of 98 cases were identified as pulmonary tuberculosis (79.6%) and 20 cases as extra pulmonary (20.4%). Out of the 98 new cases of TB registered in our study, 58 (59.18%) were females and 40 were males (40.82%). Male to female ratio in the study was 0.7:1. The mean age of the children was 10.6±2.1 years with range of (1 year-12 years). The most common age group in the study was 5-9 years with 48.98%, followed by 10-14 years (32.65%) and 1-4 years (18.37%). Demographic details of the TB cases in the study are summarized in Table 1.

Table 1: Socio demographic profile of TB cases in study.

Demographic profile	No	%
Sex		
Male	40	40.82
Female	58	59.18
Age (Years)		
1-4 years (Pre school)	18	18.37
5-9 years (Primary School)	48	48.98
10-14 years (Adolescent age)	32	32.65
Residence		
Rural	64	65.31
Urban	34	34.69
Educational status of head of family		
Illiterate	54	55.10
Primary School	17	17.35
Secondary	13	13.27
Graduate	14	14.29
Type of family		
Nuclear	59	60.2
Joint	39	39.8
Family history of TB		
Present	28	28.57
Absent	70	71.43
Socio economic status		
Low	56	57.14
Middle	24	24.49
High	19	19.39
BCG vaccination status		
Yes	76	77.55
No	22	22.45

Majority of the cases were from rural areas (65.31%), where the head of the family was illiterate (55.10%). 60.2% of cases were from nuclear family and 28.57% of cases had a family history of TB. 57.14% of cases were identified from low socioeconomic status as per Prasad's socio economic status classification.¹⁰

Risk factors

Immunization history with evidence of BCG scar was present in 76 cases (77.55%) and absent in 22 cases (22.45%). Regarding the nutritional status of the cases in the study 44 cases were identified with PEM (44.9%) and 54 were moderately built (55.1%).

HIV spot test was done in all the confirmed cases and 8 cases were found reactive (8.2%). Regarding contact with an open case of TB 34 cases (34.7%) had a positive history of contact and 12 cases (12.2%) had an old history of administration of anti tuberculous treatment.

Statistically significant association was found between old history of ATT, HIV positivity, contact with an open case of TB and malnutrition (p value<0.05). History of BCG vaccination and TB was not found statistically significant in the present study (Table 2).

Table 2: Risk factor distribution of confirmed cases in the study.

Risk factor	Number	%
BCG Vaccination		
Yes	76	77.55
No	22	22.45
Malnutrition		
Yes	44	44.9
No	54	55.1
H/O of contact with Open case		
Yes	34	34.7
No	64	65.3
OLD H/o ATT		
Yes	12	12.2
No	86	87.8
HIV status		
Positive	8	8.2
Negative	90	91.8

Clinical profile

Clinical profile of the cases in the study is summarized in Table 3.

Table 3: Clinical signs and symptoms in TB cases of the study.

Signs and symptoms	Number	%
Fever	94	95.92
Cough	82	83.67
Loss of appetite and weight	69	70.41
Headache	41	41.84
Convulsions	10	10.20
Lymphadenopathy	19	19.39
Pain abdomen	12	12.24
Pallor	42	42.86
Altered sensorium	8	8.16
Hepatomegaly	4	4.08
Ascites	4	4.08
Spleenomegaly	4	4.08

Extra pulmonary tuberculosis was found in 20 cases (20.4%) and pulmonary in 78 cases (79.6%). Both pulmonary and extra pulmonary cases were more in age group of 5-9 years with pulmonary 46.2% and EPTB 60%.

Fever was the most common presenting symptom (95.92%) followed by cough (83.67%), loss of appetite and weight (70.41%). TB meningitis was the most common EPTB (10/20 cases) followed by tuberculous lymphadenitis (5/20) and pericarditis (1/20), abdominal tuberculosis (1/20) and osteo-articular tuberculosis (1/20) in one case each.

Disseminated tuberculosis was observed in two cases in the study (Figure 1).

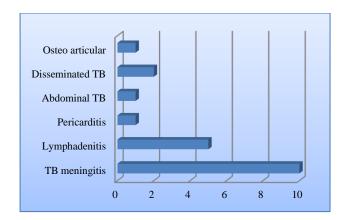


Figure 1: Distribution of cases of extrapulmonary tuberculosis in the study.

Diagnostic tests

Smear microscopy was performed on sputum, gastric aspirate and CSF specimens by Acid fast staining technique as per RNTCP guidelines by a trained technician and reported. 69.39% (68/98 cases) were smear positive and 30.61% (30/98 cases) were negative. All the cases were examined radiologically by chest X-ray and 59.18% of cases were observed with findings suggestive of tuberculosis and 40.82% of cases had no evidence of tuberculosis.

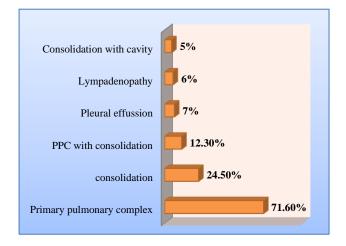


Figure 2: Radiological findings of chest X-ray positive cases in the study.

The most common X-ray chest findings in order of frequency are primary pulmonary complex (71.6%), consolidation (24.5%), primary complex with consolidation (12.3%), pleural effusion (7%), lymphadenopathy (hilar and paratracheal) (6%) and consolidation with cavity (5%) (Figure 2).

Tuberculin skin test was positive in 46.94% (46/98) cases. Mantoux positivity was more in cases of extra pulmonary tuberculosis than pulmonary tuberculosis and was statistically significant (p value <0.05) (Table 4).

Table 4: Diagnostic test distribution in cases of the study.

Diagnostic criteria	Number	%
Smear positive for AFB		
Yes	68	69.39
No	30	30.61
Radiologically positive		
Yes	58	59.18
No	40	40.82
Tuberculin skin test positive		
Yes	46	46.94
No	52	53.06

DISCUSSION

Tuberculosis is still an important communicable disease despite increased awareness and diagnostic methods with good sensitivity and specificity. Childhood cases of tuberculosis both pulmonary and extra pulmonary are often being underreported because of variable clinical manifestations. Present study mainly focused on the risk factors and variable clinical manifestations observed in cases of childhood tuberculosis.

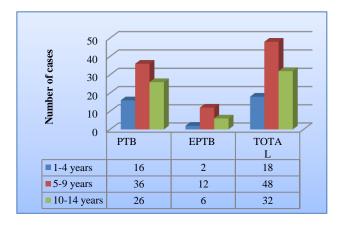


Figure 3: Age wise distribution of PTB and EPTB cases in the study.

In present study, most common age group of the children affected in both pulmonary and extra pulmonary tuberculosis was 5-9 years which is consistent with observations in many other studies also. In contrast a study conducted by Marais BJ et al reported 1-5 years as the most common group in his study and male children were more commonly affected than females with a ratio of 1.7:1 which is different from the findings in present study. In present study females outnumbered the male children with a ratio of 0.7:1. This can be due to high care taken in Indian scenario with regard to male children than female due to traditional beliefs.¹¹

Higher number of cases in this age group may be because children of less age may be missed or misdiagnosed. In a study conducted by Kabra SK et al, sex distribution was equal and more of males than females in their study.¹² In

present study, majority of the cases were residing in rural areas and belonging to low socio economic status. Findings in the various studies have already established that the prevalence of tuberculosis is higher in poor people residing in rural areas because of improper hygiene, lack of awareness and poor methods in controlling the air borne transfer of the pathogen. Illiteracy is also associated as one of the major factor in childhood tuberculosis and in present study, 55.10% cases had no knowledge about the disease which is observed in many studies.¹³

In present study, 77.55% of the cases were vaccinated with BCG and scaring was observed which reflects the immunization coverage of the children under national programme. This raises the efficacy of BCG vaccination as means of protection against tuberculosis. Various studies have reported that BCG protects for a period of 10 years and few studies from abroad has raised the status of protection with BCG as doubtful. But most studies from India have reported that BCG protects against tuberculosis which is a contrast finding in Present study.¹⁴ In present study significant association was found between extra pulmonary cases of tuberculosis and cases without BCG vaccination. This was a unique observation in Present study which was also reported by Baghaie N et al, a study from Iran.¹⁵ In the present study significant association was found with HIV status, old history of tuberculosis, malnutrition and contact with open case of tuberculosis with both PTB and EPTB. These findings are on par with findings of Sreeramareddy et al who also reported same risk factors association in his study. 16

Fever was the most common presenting complaint in both PTB and EPTB in Present study followed by cough, loss of appetite and weight which is also reported in many studies globally. However, few studies reported cough, loss of appetite and weight as most common features in pulmonary tuberculosis. ¹⁷ Clinical profile is variable from place to place and region to region depending upon multiple factors like HIV status, nutritional level of the children and type of tuberculosis. In a study from Africa, Schaaf H et al reported lymphadenitis and fever as the most common presenting signs and symptom in his study. ¹⁸

In present study, tuberculous meningitis was the most common form of EPTB followed by lymphadenitis. In Present study, tuberculous meningitis was associated with HIV cases in present study. Findings of present study were on par with findings of Gosai DK et al who also reported TB meningitis as the most common form of EPTB followed by abdominal tuberculosis in his study whereas TB lymphadenitis was next in present study. ¹⁹ Disseminated tuberculosis was seen in two cases in Present study and abdominal tuberculosis in one case of Present study. In a study conducted by Sheth Vet al TBM was the most common and disseminated was the next followed by osteo articular tuberculosis. ²⁰

Smear positive cases in present study was 69.39% with both pulmonary tuberculosis and in cases of TB lymphadenitis histopathological specimen was positive for Zn staining. In developing countries like India microscopy still remains as a gold standard in diagnosis of pulmonary tuberculosis. This is similar to findings in the study of Graham et al who also reported similar smear microscopy positivity in his study.²¹ 59.18% of childhood cases on chest X- ray showed evidence of radiological findings strongly suggestive of pulmonary tuberculosis which was similar to the reports of De villers RV et al in his study.²²

Primary pulmonary complex was the common radiological finding in the study followed by consolidation, which are on par with the findings of Nantongo et al in their study.²³ Mantoux test positivity was seen in 46.94% of cases in Present study in both pulmonary and extra pulmonary cases of TB. However, Mantoux positivity and size of induration was more in cases of EPTN than PTB in Present study. Vijayasekaran D et al have found in their study that Mantoux positivity in childhood TB varies from 21.2% to 53%. In cases of pulmonary tuberculosis overall positivity was 34.12% and more in TB lymphadenitis than TB meningitis cases, similar observations were found in study of Kiwanuka JP. 24,25

CONCLUSION

To conclude, Childhood tuberculosis is a neglected entity in developing countries due to underreporting and difficulties in diagnosis due to variable clinical picture in children. Hence epidemiological surveillance studies in children are required to determine the actual prevalence of pulmonary and extra pulmonary cases of tuberculosis. Increased efforts are required to isolate TB bacilli from body fluids to identify early the childhood cases and manage them to prevent disease burden in the community. A prospective research should be directed for better understanding the predictors of pulmonary and extra pulmonary TB in childhood. Health programmes should be directed to improve the socioeconomic conditions of the adult cases who act as source of transmission to children. Hence results of the research should be used cumulatively to modify strategies for better control of this devastating disease.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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