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Original Article

Clinical profile of children with pulmonary Tuberculosis

Anmol Goyal, Ira Shah*, Nikhil Patankar, Sujeet Chilkar

Pediatric TB Clinic, B.J. Wadia Hospital for Children, Mumbai, India

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ABSTRACT

Objective: To study the clinical profile of pulmonary TB in children at various ages.**Methods:** Forty-five children with pulmonary TB who were referred over a period of 12 months were included in the study. Clinical profile of various types of pulmonary TB and factors associated with them were compared.**Results:** Mean age of presentation was 5.4 ± 3.7 years. Male:female ratio was 32:13. Common clinical features were fever in 36 (80%), cough in 30 (66.7%), loss of appetite and malnutrition in 18 (40%) patients each. Raised ESR was seen in 28 out of 35 (80%) patients. Forty-two (93.3%) children had received BCG vaccination and 22 out of 37 (59.5%) were tuberculin skin test (TST) positive. Primary complex was seen in 22 (48.9%) patients, primary progressive TB in 17 (37.8%) and cavitary TB in 4 (8.9%) patients. Anemia ($p = 0.006$) and thrombocytosis ($p = 0.024$) was in patients with cavitary lesions. Children ≤ 5 years had primary complex followed by primary progressive and then by cavitary lesion (Odd's ratio: between primary complex vs primary progressive = 1.56; primary complex vs cavitary = 15.35; primary progressive vs cavitary = 10.06). In children > 5 years of age, it was found that cavitary lesions was more commonly seen followed by primary progressive and then by primary complex (Odd's ratio between cavitary and primary progressive = 10.06; cavitary vs primary complex = 15.35; primary progressive vs primary complex = 1.56).**Conclusion:** Primary complex is the commonest presentation of pulmonary TB. Primary complex is seen more commonly in children < 5 years of age while cavitary lesions are more commonly seen in children > 5 years of age.

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1. Introduction

Tuberculosis (TB) is a global health problem with India contributing more than 40% of the total infected population. The burden of childhood tuberculosis is unclear but 10% of the total tuberculosis load is found in children.¹ In children, due to difficulties in obtaining microbiological confirmation, timely

management of patients is affected, which leads to increased morbidity and mortality. An incidence rate of 2.85 cases per 100,000 children per year is reported in the United States while in India, an incidence rate of 100–299 per 100,000 person per year has been reported in different districts.² Pulmonary TB is more commonly seen in children less than 5 years of age.³ We thus undertook this study to determine the clinical profile of

* Corresponding author. 1/B Saguna, 271/B St Francis Road, Vile Parle (W), Mumbai 400056, India. Tel.: +91 22 32905610.

E-mail address: irashah@pediatriconcall.com (I. Shah).

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children with pulmonary tuberculosis and determine factors that can aid in diagnosis.

2. Methods and materials

This cross sectional observational study was done at our Pediatric TB clinic in a 200 bedded tertiary care children's hospital over a period of 1 year from October 2007 to October 2008 after approval from the institutional ethics committee and informed consent from the parents of the children. Patients with TB are followed up in the TB clinic and indoor admissions take place in the general pediatric wards. Children with open TB are admitted in the isolation wards. All children less than 15 years of age who were diagnosed to have Pulmonary TB were studied. Children were defined to have pulmonary tuberculosis if along with involvement of lung parenchyma, their culture from diseased site grew the tuberculous bacteria or histopathology was suggestive of caseous granulomas or they were in contact with an adult having tuberculosis or had positive tuberculin skin test (TST). Radiologically, patients with parenchymal opacities along with lymph node involvement were labeled as primary complex. Patients in which there was local progression of parenchymal disease with development of cavitation or atelectasis were labeled as primary progressive. Those with involvement of the tracheo-bronchial tree were labeled as Endobronchial TB. Patients with cavitary lesions were labeled as cavitary Pulmonary TB. Patients with innumerable, small, non-calcified nodules scattered throughout the lungs on radiological examination were labeled as Miliary TB.⁴ Patients with isolated pleural involvement without involvement of lung parenchyma or those with isolated mediastinal adenopathy and those with normal chest X-ray but positive tuberculin skin test (TST) were excluded from the study.

A detailed clinical history and physical examination was done in all patients. History of BCG vaccination, past TB or contact with TB was elicited and growth parameters such as height and weight were noted. Malnutrition was determined if weight or height was less than 5th centile for age as per Agarwal's charts.⁵ Investigations like hemogram, ESR, chest X-ray, TST by mantoux test (5 TU) were done at start of therapy. Specific investigations such as body fluid analysis, other imaging studies, biopsy and culture were done as and when required. All patients were receiving anti TB treatment (ATT) as per revised national tuberculosis control program (RNTCP) guidelines.⁶ Drug resistant (DR) TB was determined by drug sensitivity testing (DST) on positive TB culture tests.

Elevated ESR was defined when it was more than 20 mm at end of 1 h by Westergren method. Anemia was defined when hemoglobin was less than 10 g/dl, thrombocytosis was defined when platelet count was more than 4,50,000 cells/cumm, lymphocyte count more than 6500 cells/cumm was defined as lymphocytosis and less than 1500 cells/cumm was defined as lymphopenia.

Clinical and biochemical features associated with different types of TB were analyzed by SPSS software version 1. Statistical analysis was calculated by chi-square test or Fisher Exact test. Descriptive data was analyzed by percentage. $P < 0.05$ was considered significant.

3. Result

Total 45 (33.3%) children out of 135 were diagnosed as pulmonary TB in the study period. Mean age of presentation was 5.4 ± 3.7 years. Male:female ratio was 32:13. Common clinical features at presentation were fever in 36 (80%), cough in 30 (66.7%) and loss of appetite in 18 (40%). Among other clinical features, there was chest pain in 2 (4.4%), respiratory distress in 2 (4.4%), vomiting in 4 (8.9%) and abdominal pain in 3 (6.7%) patients.

On biochemical evaluation, 28 out of 35 (80%) records showed raised ESR levels. Anemia was recorded in 13 out of 40 (32.5%) patients, 9 out of 31 (29%) showed thrombocytosis and 15 out of 39 (38.5%) recorded lymphocytosis while none of them had lymphopenia. The mean duration of various symptoms and mean values of biochemical parameters are depicted in Table 1.

Forty-two (93.3%) children had received BCG vaccination and 22 out of 37 (59.5%) were found to be TST positive. Hepatomegaly was seen in 8 children (17.8%) while 4 (8.9%) had splenomegaly. Twenty-one children (46.7%) had cervical lymphadenopathy and 18 (40%) were malnourished. HRCT was done in 4 patients of whom 2 (50%) had mediastinal lymphadenopathy, 2 (50%) had consolidation and 2 (50%) had cavitary lesion.

Drug resistant (DR) TB was seen only in 2 (4.4%) children.

Primary complex was the most common of pulmonary TB seen in 22 patients (48.9%) followed by primary progressive in 17 (37.8%) and cavitary TB in 4 (8.9%) patients. Miliary TB and Endobronchial TB comprised 1 (2.2%) each. Factors associated with different types of tuberculosis are depicted in Table 2. On statistical analysis, it was found out that anemia ($p = 0.006$) and thrombocytosis ($p = 0.024$) were most common in cavitary TB. Children ≤ 5 years of age are more commonly associated with primary complex followed by primary progressive and then by cavitary lesion (Odd's ratio: between primary complex vs primary progressive: 1.56 [95% CI = 0.43 to 5.65]; primary complex vs cavitary: 15.35 [95% CI = 0.73 to 321.60]; primary progressive vs cavitary: 10.06 [95% CI = 0.47 to 215.57]). In children > 5 years of age, it was found that cavitary lesions was more commonly seen followed by primary progressive and then by primary complex (Odd's ratio

Table 1 – Clinical and biochemical parameters of patients.

Criteria	N (%)	Mean $\pm$ SD	Median
Fever (days)	36 (80%)	37.3 $\pm$ 62.9	21
Cough (days)	30 (66.7%)	51.9 $\pm$ 88	30
Loss of appetite (days)	18 (40%)	44.7 $\pm$ 69.5	30
Respiratory distress (days)	2 (4.4%)	6.5 $\pm$ 2.1	6.5
Chest pain (days)	2 (4.4%)	21.7 $\pm$ 7.6	20
Hemoglobin (g/dl)	40	10.8 $\pm$ 1.8	11.2
Platelet count (10^5 /cumm)	31	3.7 $\pm$ 1.8	2.92
ESR (mm at end of 1 hour)	35	42.7 $\pm$ 32.5	30
White cell count (10^3 /cumm)	39	12.1 $\pm$ 4.4	10.9
Lymphocyte %	39	42.8 $\pm$ 18.6	44
TST positive (%)	38	18.1 $\pm$ 5.5	16
(values not known in 7 patients)			

Table 2 – Factors associated with Type of Pulmonary TB.

	Primary complex (%) (N = 22)	Primary progressive (%) (N = 17)	Cavitatory (%) (N = 4)	P value
Age ≤5 years	14 (63.6%)	9 (52.9%)	0	0.06
Age >5 years	8 (36.4%)	8 (47.1%)	4 (100%)	
Male	18 (81.8%)	9 (52.9%)	3 (75%)	0.169
Female	4 (18.2%)	8 (47.1%)	1 (25%)	
Fever	15 (68.2%)	15 (88.2%)	4 (100%)	0.276
Cough	14 (63.6%)	10 (58.8%)	4 (100%)	0.413
Loss of appetite	8 (36.4%)	7 (41.2%)	1 (25%)	1
Respiratory distress	0	2 (11.8%)	0	0.33
Chest pain	2 (9.1%)	0	0	0.59
Anemia (Hemoglobin <10 g/dl)	2/20 (10%)	7/15 (46.7%)	3 (75%)	0.006
Thrombocytosis (Platelet count > 4,50,000 cells/cumm)	2/20 (10%)	4/15 (26.7%)	3 (75%)	0.024
Raised ESR (>20 mm at end of 1 h)	13/19 (68.4%)	13/14 (92.9%)	1/1 (100%)	0.361
Lymphocytosis (>6500 cells/cumm)	10/20 (50%)	4/14 (28.6%)	1 (25%)	0.44
Raised SGPT (>25 IU/L)	8/16 (50%)	4/11 (36.4%)	3 (75%)	0.481
TST positivity (>10 mm)	13/21 (61.9%)	9/12 (75%)	0	0.027

between cavitatory and primary progressive: 10.06 [95% CI = 0.47 to 215.57]; cavitatory vs primary complex: 15.35 [95% CI = 0.73 to 321.60]; primary progressive vs primary complex: 1.56 [95% CI = 0.43 to 5.65].

Sixteen children (35.6%) had contact with an adult suffering from TB while only 1 (2.2%) of them had a previous history of TB. There was a single (2.2%) child with relapse and another (2.2%) child who was a defaulter.

Complications were observed in 3 (6.7%) patients with hepatitis being the most common as seen in 2 (66.7%) of these cases, followed by middle lobe syndrome seen in 1 of the case (33.3%).

4. Discussion

As per the global review of Tuberculosis by World Health Organization, India comes under a group of high prevalence countries with an annual risk between 1 and 2.5%. India accounts for 26% of total global cases.⁷

Usually children <5 years of age, and those who are malnourished are found to be more frequently affected.⁸ But, our study shows that pulmonary TB affects all age groups with a mean age of 5.4 years. The reason behind this slightly older age group may be due to inability to get tissue cultures in younger children. Also, malnutrition was found in only 40% of the patients.

Diagnosis of TB in children usually follows discovery of a case in an adult, and needs to be confirmed by tuberculin skin testing, chest radiograph, and clinical signs and symptoms.⁹ Fever, cough and loss of appetite were the most common symptoms in our patients which was similar to that reported by Swaminathan et al.¹⁰

In our study, Pulmonary TB was more commonly found in children less than 5 years of age. This is similar to a study done by Sanchez-Albisua et al.³ We found that primary complex was more common in children < years of age whereas cavitatory TB was more common in children above 5 years of age. However no such differentiation has been reported in literature.

Our study showed a male predominance. A similar study by Shrestha et al showed more males being more affected.¹¹ The male predominance in the study may be due to their ambulatory nature, which make them more exposed to the TB infected cases. It could also be due to a referral bias due to better care seeking for males due to preference for boys in Indian families.

The protective efficacy of BCG vaccination is known¹² but in the present study pulmonary TB was seen in children who had received BCG immunization. This indicates that there is still a significant chance of developing pulmonary TB even in the presence of BCG vaccination.

A positive Mantoux test also supports diagnosis of TB and has been used for circumstantial evidence for diagnosis of TB. However, a negative mantoux test does not rule out diagnosis of TB.¹³ Mantoux test was found to be positive in more than half the patients in our study.

One of the main reasons of children developing tuberculosis is through contacts but in our study only 35.5% patients gave a history of TB contact. This may be because of the family members not giving true history due to the social stigma attached to this disease¹¹ and also the adult source case may not be identified in the areas endemic for TB.

Diagnosis of tuberculosis is difficult in children and hematological parameters usually aid in the diagnosis. Raised ESR was seen in most types of TB in our patients, which is similar to a study done by Aziz et al who found a high ESR in most patients with pulmonary Tuberculosis.¹⁴ However, on statistical analysis, it was found out that anemia was most commonly seen in patients of pulmonary TB with cavitatory lesions (p value: 0.006). We found out that only 32.5% of our patients had anemia on diagnosis. This is similar to a study done by Lee SW who had anemia on diagnosis of TB in 32% of his study population.¹⁵ Other studies have showed anemia in 16–94% in patients with pulmonary TB.^{16,17} Anemia in TB develops due to suppression of erythropoietin production due to tumor necrosis factor α and other cytokines released by activated monocytes.^{16,17}

We found out that 29% of our patients had thrombocytosis on diagnosis. This is similar to a bone marrow study on

patients with pulmonary tuberculosis by Singh et al who found a statistical significance between thrombocytosis and pulmonary tuberculosis (p value: <0.04).¹⁸ This is similar to a study done by Yaranal PJ who found 26% of his study population with thrombocytosis on diagnosis.¹⁹ In our patients, thrombocytosis was seen more frequently in patients with cavitary TB. Thrombocytosis can be related to release on Interleukin-6 in case of pulmonary tuberculosis, which causes increased platelet production.¹⁹

Chest X-ray is routinely done to aid the diagnosis of TB in children. The most common chest X-ray findings in our patients were primary complex, primary progressive and cavitary type. This is similar to the findings in other study done by Krysl et al, where primary complex in 70% of the children, followed by cavitation in 10–30% and pleural effusion in 5–10% of the pediatric cases.²⁰ HRCT scan helped in diagnosis of mediastinal adenopathy in our patients, which could not be identified on Chest X-ray suggestive of a role of HRCT chest in these patients. In our study since, the chest X-rays were reported by different radiologists, there could be a misclassification bias which is also a limitation of the study.

Our study has a limitation as it has small number of patients. Moreover, since this is a hospital-based study, we may have noted a different pattern in the clinical features and preponderance of the disease.

5. Conclusion

Primary complex is the commonest presentation of pulmonary TB in children. Fever is the most common symptom of followed by cough and loss of appetite. TST is positive in more than half of the children. Similarly raised ESR is common feature. Anemia and thrombocytosis is seen more commonly among cavitary lesions. Children <5 years of age are more commonly affected with primary complex while cavitary lesions are more commonly seen in children >5 years of age.

Conflicts of interest

All authors have none to declare.

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