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Clinical Profile of Pediatric Tuberculosis and MGIT sensitivity: A Prospective Study from a Tertiary care Institute

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ABSTRACT
Introduction: *Tuberculosis (TB) is a major global health problem. Childhood tuberculosis (TB) is common in our community but it is relatively neglected, due to greater challenges in diagnosis. Clinical manifestations of childhood TB differ from adults. The diagnosis in most cases is based on clinical evidence but chest X-ray, Mantoux test and sputum/gastric sample microscopy are important supporting investigations.*
Objective
1) To study the clinical profile of TB.
2) To determine incidence of extra-pulmonary TB in children.
3) To know MGIT sensitivity in diagnosis of Tuberculosis.
Methods: *This prospective study was conducted among admitted and OPD patients in the department of Pediatrics over a period of 1 year. Clinically suspected cases of TB in the age group 0-14 years who met the diagnostic criteria made the study group. Refusal of consent by parent and children already on TB treatment were excluded from this study. Investigations like chest X-ray, Mantoux test, sputum/gastric aspirate microscopy and MGIT were done to confirm the clinical diagnosis.*
Results: *The incidence of tuberculosis was found 36/10000. Pulmonary tuberculosis was more common (53.9%) than extra pulmonary (35.3%) tuberculosis. BCG scar was present in 87.42%. History of contact was present in 41.2% and Mantoux test was positive in 51.98%. MGIT sensitivity was 30% in our study. The most common symptoms were fever (79.4%), anorexia (61%) and cough (59%).*
Conclusion: *This study supports that detailed history, clinical evaluation and active investigative workup has a major role in diagnosing childhood tuberculosis.*
Keywords: *Tuberculosis, Children, Mantoux, BCG, MGIT.*

Introduction

Tuberculosis (TB) is a major global health problem. It causes ill health among millions of people each year and ranks alongside the human immunodeficiency (HIV) as a leading cause of death worldwide.[1] Childhood tuberculosis remains an important cause of morbidity and mortality in developing countries. [2] Although data on childhood TB is scarce, tuberculin surveys conducted in children suggest a high rate of infection in the community with annual risk of TB infection is about 1.5%.[3] The high prevalence and incidence of TB in developing countries is probably due to a high prevalence of TB in adults acting as contacts, poor socioeconomic condition, malnutrition, overcrowding and HIV co-infections. [4,5,6]

Since the declaration by WHO of a 'Global TB emergency' in 1993, a wealth of publications have addressed important aspects of the burden, management and control of tuberculosis. In general, however, the emphasis has been on adult disease. By contrast, the pediatric TB has been relatively neglected, mainly by the challenges in the diagnosis and the lower priority by TB control programs. While the burden of TB in India is not known, regional data from WHO indicate that the sputum smear positive TB in children < 14 years old accounts for 0.6% to 3.6% of all reported cases. However, because the majority of children are sputum smear negative, this data underestimate the true burden of childhood TB. It is estimated that childhood TB constitutes 10-20% of all TB in high burden countries and accounts for 8-10% TB related deaths.[7] Literature on tuberculosis in children is scarce in the developing countries including India. Further, no such study has been done earlier in Himachal Pradesh, so our aim was to determine the clinical profile of TB in children between 0-14 years of age.

Aims and Objectives

1. To study the clinical profile of TB in children 0-14 years age group.
2. To determines the incidence of extra pulmonary TB in children.
3. To study MGIT sensitivity in diagnosis of tuberculosis.

Material and Methods

It is a prospective observational type of study carried out over a period of one year in both outpatient and inpatient population in department of pediatrics. All patients in 0-14 year age group with features of tuberculosis on history and physical examination, patients with strong history of contact with tuberculosis were included in this study. Informed consent was taken from all patients. Cases were assessed clinically by taking relevant history and doing physical examination. Specific investigations were undertaken to establish the diagnosis of tuberculosis. Categorization of patients was done in two groups, pulmonary TB and extra pulmonary TB based on criteria described below.

For pulmonary tuberculosis:

1. Sputum or gastric aspirate positive for AFB my Zeihl-Neelsen method
   Or
2. Two or more of the following:
- History of contact with a TB patient
- Cough lasting longer than 2 weeks
- Reactive tuberculin skin test
- Radiographic findings compatible with TB
- Response to anti-TB therapy (increased bodyweight by 10% after 2 months, decrease in symptoms)

For extrapulmonary TB:

o Fine needle aspiration cytology (FNAC)/ Histopathological evidence of TB in biopsy from lymph nodes, synovium or as relevant, or

o Bacteriological evidence of TB on microscopy or culture of serous fluids including pleural, pericardial, ascitic, synovial fluid and CSF, or

o History suggestive of TB including positive contact history, past history of TB or of anti-tubercular treatment, with

clinical signs suggestive of TB on examination with strong corroborative investigative evidence in the form of 1 or more of the following

- A reactive tuberculin test
- Radiographic findings compatible with TB
- Lymphocytosis in cytology of serous fluids including pleural, pericardial, ascitic, synovial fluid and CSF.
- Adenosine deaminase levels suggestive of TB in serous fluids including pleural, pericardial, ascitic, synovial fluid and CSF.
- CT/ MRI suggestive of tuberculoma or tuberculous meningitis.
- Ultrasound abdomen suggestive of abdominal TB, Or,
- Response to anti-TB therapy (increased body weight by 10% after 2 months, decrease in symptoms).

After the clinical diagnosis, the disease was classified as per the system involved. Investigations like tuberculin skin test, sputum/gastric aspirate for AFB and MGIT-960 were done for confirmation of clinical diagnosis. Radiological investigations like chest X-ray, USG abdomen (for abdominal TB) and CT/MRI were performed in relevant cases. Specific condition like lymphadenitis required FNAC, for pleural, pericardial and peritoneal effusions, fluid aspiration studies were done and samples were sent for bacteriological confirmation and biochemical profile. In meningitis lumbar puncture was done and CSF was sent for bacteriological confirmation and biochemical profile. CT/MRI was done in cases of suspected tuberculoma.

Observations

During one-year study period, 28200 children visited our hospital including both outdoor and indoor patients, of theses 102 were diagnosed as TB. Incidence of TB was calculated as 36 per 10000 children.

Out of 102 cases, 50.9% were males and 49.1% were females. Male to female ratio was 1.04.
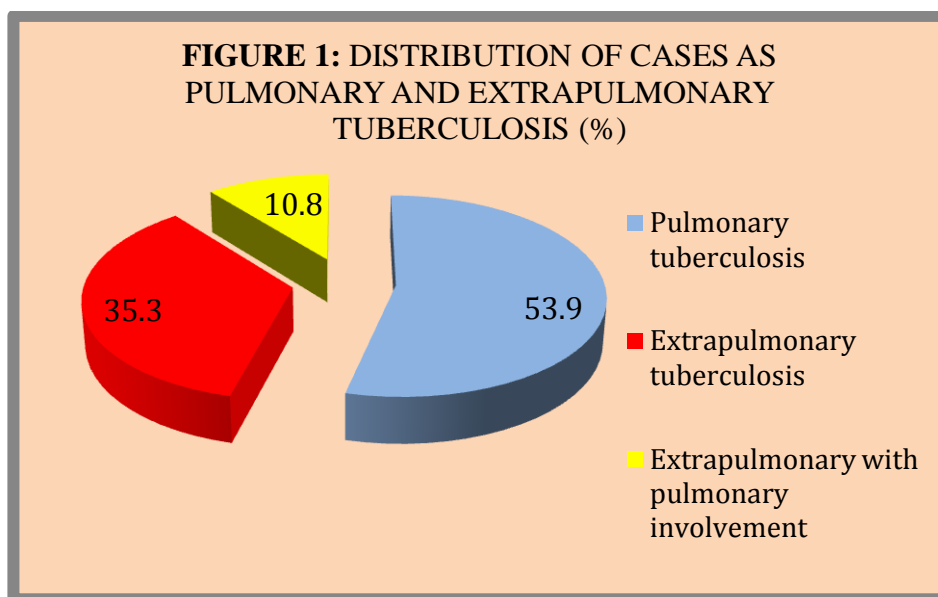

FIGURE 1: DISTRIBUTION OF CASES AS PULMONARY AND EXTRAPULMONARY TUBERCULOSIS (%)

Table 1: Demographical profile of children

Age group	Male (%age)	Female(%age)	Total(%age)
0-5	13(54.2)	11(45.8)	24(100)
6-10	10(55.6)	8(44.4)	18(100)
11-14	29(48.3)	31(51.7)	60(100)
total	52(50.9)	50(49.1)	102(100)

Mean age of TB affected children was 10.3 years. Most cases belonged to socioeconomic class IV and V (50%) followed by middle class (44.1%) and least number of cases were of upper class (3.9%).

Positive family history of contact was found in 42 patients (41.2%), whereas no history of contact was found in 60 patients (58.8%). Most of cases 18 (14.2%) with history of contact were found in age group 0-5 years followed by 15 (35.7%) cases in age group 11-14 years. Least number of cases 9 (21.4%) were found in age group 6-10 years.

Table 2: Presenting symptoms in TB patients

Serial number	Symptoms	No of cases	Percentage
1	Fever	81	79.4
2	Anorexia	63	61.7
3	Cough	59	57.8
4	Weight loss	41	40
5	Headache	17	16.6
6	Vomiting	13	12.7
7	Chest pain	11	10.7
8	Abdominal pain	10	9.8
9	Dyspnea	9	8.8
10	Seizure	9	8.8
11	Neurological deficit	2	1.9

Table 3: Clinical signs in TB patients

S.no	Clinical signs	Number	%
1.	Pallor	31	30.4
2.	Lymphadenopathy	23	22.5
3.	Pleural effusion	15	14.7
4.	Meningeal signs	9	8.8
5.	Signs of raised ICT	7	6.9
6.	Hepatosplenomegaly	5	4.9
7.	Doughy abdomen	5	4.9
8.	Neurological deficit	2	1.9
9	Respiratory distress	2	1.9
10.	Ascites	2	1.9
11.	Pericarditis	1	0.9
12.	Arthritis	0	0

In relation to sex wise distribution, pulmonary tuberculosis was found in 29.4% males in comparison to 24.5% females. Extrapulmonary tuberculosis affected 14.7% males and 20.6% in females.

Amongst extra pulmonary TB, abdominal TB was most common type accounting for 11.8% cases, whereas pericardial TB was least common variant in 0.9% cases.

Amongst investigations, AFB positivity in sputum/gastric aspirate was detected in 31(30.4%) cases, while it was negative in 71 cases (69.6%). Maximum AFB positive cases were found in age group 11-14 years (25.5%) followed by 25.5% cases in 6-10 years age group.

Chest x-rays of 102 cases were done, out of them 69.6% showed lesion on X ray film. Primary complex was most common finding observed in 35.4% cases, pleural effusion was seen in 14.7%, infiltrates in 9.8%, miliary and cavitary pattern were appreciated in 3.9% cases for each.

BCG vaccination was given in 87.42% cases (88 out of 102 cases) and 13.56% (14 out of 88) of those vaccinated did not have a BCG scar on examination.

Mantoux test was positive in 53 (51.98%) cases and 48.02% were negative. Maximum positive cases were in pulmonary TB (30.4%), followed by pleural effusion (10.8%). Abdominal TB, CNS TB, Disseminated TB each accounted for 2.94%.

MGIT was done in 30 patients, 9 patients were MGIT positive while 21 being MGIT negative. Sensitivity of MGIT was found to be 30%. Maximum positive cases of MGIT were found in pulmonary TB followed by Disseminated TB.

Discussion

The incidence of tuberculosis was 36 cases per 10000 patients. Incidence of pulmonary and extra pulmonary TB was 19 and 13 per 10000 patients. The incidence of TB in India in year 2014 was 12.6/10000. As diagnosis of childhood TB is very challenging in community, so most cases of suspected TB are referred to tertiary care centre. This can be the reason to explain the higher incidence of tuberculosis in our study than the actual incidence in India. Sex wise distribution of cases showed a slight male preponderance (50.9%), which is similar to study by Franco Et al in Brazil which showed a male preponderance of 51.6%. [8] Sivanandan S [9] and Xi-Rong Wu et al [10] also observed a male preponderance of 63% and 58% respectively.

Majority of cases in our study belonged to age group 11-14 years of age which is in accordance to study by Kakarani with 54% cases in age group 6-12 years. [11] Analyzing and comparing the above studies with the present study, it may be concluded than in early adolescence there is a slight female preponderance. The increased risk may be due to combination of increased biological susceptibility, immunological response following puberty or difference in socialization patterns of male compared to female adolescents. Most of cases belonged to lower (50%) and middle (44.1%) class. A study on children from south India showed similar results with 55.8% belonging to lower class, 38.9% middle class, and 5.3% to high socioeconomic group. [12]

The frequency of clinical symptoms was observed as fever in 79.4%, anorexia 63%, cough 57.8% and weight loss in 40%. Similar observations were reported in a study from north India by Garg P with fever and anorexia being commonest symptoms followed by weight loss and cough. [13]

In a study by Franco et al [8] fever was documented in 73.1% cases and weight loss in 53.1%. Positive family history of contact was found in 42 patients (41.2%), most number of cases 18(42.9%) were in age group 0-5 years. This was similar to various Indian studies done in children under 15 years of age showing positive history of contact in 33-52% cases. [12,13,14] Study by Franco et al [8] reported a recent contact in age group 1-5 years.

In our study pulmonary TB constituted the major group (53.9%), followed by extra pulmonary TB (35.3%). Our results are consistent with the various studies described in literature [8,9,11,13,15]

In our study CNS tuberculosis accounted for 11.8% cases, this was comparable with study of Pontual et al [16] where 16.67% cases were had isolated CNS tuberculosis. Lymphadenopathy was seen in 23.5% and isolated lymphadenopathy was seen in 1.96% cases. This was comparable to study done by Garg P, which showed 16.7% cases of tubercular lymphadenopathy [13]. Franco et al [8] showed 21.5% cases of tubercular lymphadenopathy.

Primary complex was most common finding on X ray accounting for 36(50.7%) cases and 15(21.1%) cases showed pleural effusion. Similar to study by Franco et al [8] observed primary complex in 44.3% cases.

History of BCG vaccination was positive in 87.42% cases and 13.72% of those vaccinated did not have a BCG mark on examination. Higher vaccination coverage in our study in comparison to others indicates effective implementation of National Immunization Programme.

Table 4: Studies showing BCG coverage

Serial no	Study	Year	No of cases	%vaccinated
1.	Somu et al [15]	1977-92	11568	37.82
2.	Garg p [13]	1991	170	55.2
3.	Sivanandan et al [9]	2008	541	76
4.	Present study	2014-2015	102	87.42

Out of 102 cases, Mantoux test was positive in 53(51.98%) cases. Maximum positivity was seen in pulmonary TB (30.4%) and least was in disseminated TB, which accounted for 2.94%. Sivanandan et al [9] reported Mantoux positivity in 66% cases which is similar as to our study.

In present study, sputum/gastric aspirate microscopy was positive for AFB in 31(30.4%) cases. This was in accordance to study done by Franco et al, [8] which showed sputum positivity in 32.8% cases, and frequency of sputum positivity was higher in individual aged 11-15 years. Maximum sputum positivity i.e 25.5% was seen in age group 11-14 years followed by 4.9% in 6-10 years. This finding emphasizes that as age increases percentage of sputum positivity increases and hence bacteriological sputum examination is a useful method above 10 years.

The reported sensitivity of MGIT is upto 90% and most of these studies were done in adults. The sensitivity of MGIT in our study was 30%, which was in accordance to various studies showing sensitivity of 48.5% [17], 21.9% [18] and 15%. [19] The reason low sensitivity of MGIT in children was attributed to following factors- as children less than 8 years could not expectorate so we used gastric lavage, pleural fluid, CSF and these samples have low bacterial counts. Other factors like delay in transportation, storage and neutralization of sample would have inactivated tubercle bacilli. (as MGIT detects live bacteria)

Conclusion

Tuberculosis is a major global health problem. Most of work is done in the field of adult TB. Pediatric TB has been relatively neglected mainly due to greater challenges in diagnosis and lower priority tradionally afforded to children by TB control programmes. Detailed clinical evaluation, refinement of existing investigations and development/testing of new methods like MGIT are promptly required to improve diagnosis and treatment of TB in children.

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