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Research Article

CLINICAL PROFILE AND OUTCOME OF PEDIATRIC TUBERCULOSIS IN A TERTIARY CARE SETTING IN CENTRAL INDIA

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ABSTRACT

Objective: To study the clinical profile and outcome of tuberculosis (TB) in children under 14 years of age.

Methods: It is a hospital-based cross-sectional study done in a tertiary referral center in Central India from July 2017 to June 2019. After ethical approval, 80 children (under 14 years of age) diagnosed with presumptive TB were enrolled. Those already on TB treatment or prophylaxis for more than 7 days were excluded from the study. Relevant patient details were noted on a predesigned pro forma. Routine first-line investigations for TB were done in all cases. Histopathological and specific radiology tests were done as per the site involved. Microbiological confirmation was done using microscopy, and molecular diagnosis was done by a cartridge-based nucleic acid amplification test (CBNAAT).

Results: Overall mortality was 13.8%, and 82% of them were children below 5 years of age. As per WHO criteria, 52.5% and 20% of children below 5 years of age were severely and moderately undernourished, respectively. History of contact was present in 66%; BCG scar in 91.3%; and tuberculin sensitivity test positivity in 56% of cases. Fever, cough, and weight loss were the most common presenting complaints. The majority had extrapulmonary involvement (75%), with neurotuberculosis being the most common and with the highest mortality (70%). Microbiological confirmation was possible in only 8.8% of cases.

Conclusion: It is still challenging to diagnose pediatric TB. Though newer diagnostics are now available, clinical suspicion is a valuable tool. The diagnosis of pediatric TB should thus be based on a combination of epidemiological variables, clinical suspicion, and supported by various laboratory investigations.

Keywords: Pediatric Tuberculosis, Central India, Clinical profile, TST, BCG, CBNAAT.

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INTRODUCTION

The National Strategic Plan for Tuberculosis (TB) Elimination in India sets a goal to achieve a rapid decline in the burden of TB, mortality, and morbidity while working towards the elimination of TB in India by 2025 [1]. The India TB Report (2018) observed approximately 14.5 lakh TB notifications, of which 6% were pediatric cases [2]. As pediatric TB is paucibacillary and bacteriological confirmation is not possible in the majority of cases, the available data underestimates the true burden. It is estimated that in high-TB burden settings like India, underlying undiagnosed TB may cause 20% of deaths due to pneumonia of unknown cause in children aged under-five [3]. TB in children is a direct consequence of adult TB and is a good marker of current transmission in the community. Over the years, there has been a marked increase in the incidence and a decrease in the peak age prevalence of infectious TB, and most cases now occur in young adults, who are often parents to young children. This suggests that children in developing countries will emerge very soon as a high-risk group [4]. The pool of latent infection in childhood TB is large, and for adequate TB control, shrinking the magnitude of this pool is also required. If detection and control of TB have to be brought under systematic management, childhood TB also needs to be kept under close clinical scrutiny [5]. As per the TB statistics of India, a total of 14007 pediatric TB patients were notified from the state of Madhya Pradesh in the year 2018, showing an overall high contribution to pediatric TB cases in India [6]. Keeping the above facts in mind, we intend to study the clinical profile, outcome, and diagnostic scarcity of pediatric TB in a tertiary referral center of care in Madhya Pradesh.

Objectives

To study the clinical profile and outcome of TB in children under 14 years of age.

METHODS

The present hospital-based cross-sectional study was conducted on children under 14 years of age admitted with presumptive TB between July 2017 and June 2019 in the department of pediatrics at Kamla Nehru Hospital, Gandhi Medical College, Bhopal, Madhya Pradesh. Out of 120 patients who presented with features of presumptive TB, 80 were enrolled (3 didn't consent) and 37 had already started antitubercular therapy. The study was approved by the institutional ethics committee on February 20, 2017. Written and informed consent was obtained by the parents or legal guardians prior to the study.

Inclusion criteria

Children under 14 years of age admitted with a provisional diagnosis of presumptive TB*, i.e., Organ-specific symptoms and signs with or without constitutional symptoms of persistent fever and weight loss, were considered for diagnosing extrapulmonary TB.

*Presumptive TB is defined as: persistent fever and/or cough for ≥2 weeks and/or weight loss >5% of body weight or no weight gain in the past 3 months and/or history of contact with infectious TB cases within the last 2 years.

Exclusion criteria

Children who were already on TB treatment or prophylaxis for ≥7 days.

A detailed history, demographic profile, presenting complaints, vitals assessment, and clinical manifestations were noted on the proforma. Basic laboratory investigations (complete blood counts, liver and renal function tests, serum electrolyte status, etc.), retroviral status using enzyme-linked immunoassay for >18 months and polymerase chain reaction for <18 months, and digital chest radiography with both posteroanterior and lateral views were done for all patients on admission. As per the guidelines of the Indian Academy of Pediatrics working group on TB, a tuberculin sensitivity test (TST) using 2 tuberculin units and 10 mm induration as the cutoff was used. Organ-specific specimens were sent for microbiological confirmation, like sputum/induced sputum/gastric aspirates for pulmonary TB, gastric aspirates and ascitic fluid for abdominal TB, cerebrospinal fluid cartridge-based nucleic acid amplification (CBNAAT) for CNS TB, pleural aspirates for pleural effusions and empyema, joint aspirates for TB of bones and joints, and fine needle aspiration cytology for lymphadenitis. Histopathological assessment for tuberculoid granulomas for lymph node TB was also done in the required cases. Organ-specific imaging was done in some cases to aid the diagnosis. Microbiological confirmation was done using acid fast bacilli (AFB) microscopy and molecular diagnosis by CBNAAT as first-line diagnostics. Diagnostic algorithms by the Revised National TB Control Program, India (RNTCP) (now termed the National TB Elimination Program, India) were followed for both pulmonary and extrapulmonary TB [7,8]. Children fitting into both the categories of pulmonary as well as extrapulmonary were classified as having disseminated TB, involving ≥2 organ systems. Quantitative variables were compared using the mean, qualitative variables using proportions, and p was fixed at <0.05. Results were statistically analyzed using SPSS Version 22, Chicago, Inc., USA.

OBSERVATION AND RESULTS

A total of 80 presumptive TB patients were enrolled, of which 33 (41.2%) were male and 47 (58.7%) were females, 46 (57.5%) were residents of rural areas, and 34 (42.5%) were of urban areas; 40 (50%) were below 5 years of age; and 67 (83%) belonged to lower socioeconomic class on the basis of classification as per the modified Kuppuswamy scale. Only 8 (20%) out of 40 children below 5 years of age were appropriately nourished, and 80% (p<0.05) were malnourished as per their age and gender on the basis of WHO criteria. Only one patient had a positive HIV status. 73 children (91.3%, p=0.034) had BCG scars, and 53 (66.25%, p=0.12) had a positive history of contact with an infectious case within the last 2 years. TST was done in all 80 patients and showed positive results (>10 mm induration) in 56.3%. (p=0.191).

Out of 80 patients, 80% were successfully discharged, 13.8% was the mortality, and 6.2% were left against medical advice. Both morbidity (prolonged duration of hospitalization) and mortality were highest in the children below 5 years of age, whereas 95% of the children above 10 years of age were successfully discharged on advice (p=0.029) (Table 1).

Out of 29 pulmonary TB cases, 7 (24%) had severe pneumonia and 22 (75.87%) had pneumonia (classified as per the WHO classification of pneumonia). Out of these 29 cases, 17 (58.6%) showed only areas of parenchymal consolidation on chest x-rays, 6 (20.6%) showed pleural effusion, 3 (10.3%) showed miliary shadows, and 3 (10.3%) developed pneumothorax (Table 2). In 14 patients, ultrasonography of the chest was done for confirmation, which confirmed findings of pleural effusion in 4, empyema in 2, and consolidation in 8 patients (Table 2).

Neurotuberculosis was the most common presentation and also the major cause of mortality. Out of 29 cases, 20 were finally diagnosed as pulmonary TB, with a mortality rate of 5% in one patient. In the remaining 9 patients, 6 had pleural and 3 had disseminated TB. 60 patients, out of total study subjects, were diagnosed with extrapulmonary TB [CNS TB in 23 (28.7%), abdominal TB in 17 (21.3%), pleural TB in 6 (7.5%), TB of lymph nodes in 5 (6.3%), TB of bone and joint in 3 (3.8%), and disseminated TB in 6 (7.5%). Overall mortality in the extrapulmonary group was 16.6% (10 out of 60 patients). 90% (10 out of 11) (p=0.012) of the deaths during the study period were because of extrapulmonary TB, and 70% (p=0.05) of deaths in the extrapulmonary group were contributed by CNS TB. Almost 1/4th of the patients with CNS TB died (Tables 2 and 3).

The CNS examination was abnormal in 25 children. 13 (52%) had signs of increased intracranial pressure (suggested by any of the following features of encephalopathy: altered sensorium, fundus changes, altered patterns of breathing), 6 (24%) had signs of meningeal irritation, and 6 (24%) had a neurological deficit. Abdominal examinations were abnormal in 23 children. Nine had ascites, eight had hepatosplenomegaly, and six patients complained of abdominal pain and tenderness on examination. 2 patients had joint effusion, 1 had gibbus, and 5 had only enlarged cervical lymph nodes (Table 4).

On microbiological testing, CBNAAT was found positive in 4 pulmonary and 1 extra pulmonary patient. AFB staining was found positive only in two extra pulmonary TB cases. 80% (p=0.03) of the patients who showed positive results on CBNAAT were cases of pulmonary TB

Table 1: Age wise classification of pediatric tuberculosis

Outcome	Age groups (in years)			
	0–5	6–10	>10	Total
Discharge	27 (67.5%)	19 (90.4%)	18 (94.8%)	64 (80.0%)
Death	9 (22.5%)	1 (4.8%)	1 (5.3%)	11 (13.8%)
LAMA	4 (10%)	1 (4.8%)	0	5 (6.25%)
Total	40 (50%)	21 (26.25%)	19 (23.7%)	80

p=0.029

Table 2: Age-wise classification of chest imaging findings in pediatric tuberculosis

Radio imaging	Age groups				
		0–5 year	6–10 year	>10 year	Total
CHEST XRAY	Normal	25 (67.5%)	6 (16.21%)	6 (16.21%)	37 (46.2%)
	Hilar Lymphadenopathy	4 (28.5%)	4 (28.5%)	6 (42.8%)	14 (17.5%)
	Bilateral Consolidation	6 (35.3%)	6 (35.3%)	5 (29.4%)	17 (21.25%)
	Miliary TB	1 (33.3%)	0 (0.0%)	2 (66.6%)	3 (3.8%)
	Pleural Effusion	2 (33.3%)	4 (66.6%)	0 (0.0%)	6 (7.5%)
	Pneumothorax	2 (66.6%)	1 (33.3%)	0 (0.0%)	3 (3.8%)
Total		40 (50%)	21 (26.25%)	19 (23.8%)	80
USG CHEST	Not Done	35 (53%)	17 (25.8%)	14 (21.21%)	66 (78.8%)
	Pleural Effusion	2 (50%)	2 (50%)	0 (0%)	4 (5%)
	Empyema	0 (0%)	2 (100%)	0 (0.0%)	2 (2.5%)
	Consolidation	3 (37.5%)	0 (0.0%)	5 (62.5%)	8 (10%)
Total		40 (50%)	21 (26.25%)	19 (23.8%)	80

(4 out of 5), and all patients showed Rifampicin sensitivity and were treated with first-line drugs. Thus, 7 (8.8%) patients were treated as microbiologically confirmed TB, and 73 cases were treated as clinically diagnosed TB (Table 5).

DISCUSSION

Out of the total 80 patients enrolled in this study, 50% were <5 years of age. Garg [9] did a study in Northern India, Uttar Pradesh, on 78 patients with presumptive pediatric TB and also found the maximum number of patients in the age group of 3–5 years. Jain *et al*. [10] did a 2-year study on 223 enrolled children below 5 years of age in the west part of India and found the median age to be 31 months, showing children below 5 years to be more susceptible. The probable reasons for this may be low resistance, increased prevalence of malnutrition, and close contact with infected adults in a younger age group. 80% of the children <5 years of age were malnourished ($p<0.05$), and 84% of the children belonged to lower socioeconomic status. Jain *et al*. [10] in their study also found 57% of their patients to be malnourished, and Gupta *et al*. [11] found 62% to be belonging to a lower socioeconomic class. A probable reason may be that these studies were done in government medical college hospitals, serving poor and underprivileged populations. 91.3% ($p=0.034$) had a BCG scar, showing positive immunization status meeting national standards, and 66.25% had a positive history of contact with a person with TB within the last 2 years. These rates are higher than those found in other studies by Gupta *et al*. [11] (77% and 41%) and Jain *et al*. [10] (86% and 46%), respectively. TST positivity was seen in 56% of our enrolled patients. Studies done by Kabra *et al*. [12], Vijaysekaran *et al*. [13], and Gupta *et al*. [11] showed positivity rates in the range of 30–50%. However, no significant association was found between TST positivity and mortality, similar to the studies done by Jain *et al*. [10]. The clinical spectrum of TB, with fever being the most common presentation (85%), followed by cough and weight loss, correlates with studies by Shrestha *et al*. [14] and Muley *et al*. [15], where fever was seen in 75.6% and 55% of the study subjects, respectively. This shows nonspecific symptoms are the most common presenting features of TB in children, which makes early diagnosis difficult, thus requiring a high degree of suspicion for proper workup. The spectrum of TB was similar to studies from other tertiary centers, with a significant proportion (46–70%) of children presenting with extra-pulmonary TB [10,12,16]. The increase in contribution from extrapulmonary TB in our study is likely to be because of the patients getting referred to our center for an unknown diagnosis. Out of this group, CNS TB was the most common form and correlates with the findings of Gupta *et al*. [11] and Muley *et al*. [15], contrasting other studies by Rebecca *et al*. [16] and Garg [9], where tuberculous lymphadenitis was the most common. This is likely because of the higher prevalence of CNS TB (17 out of 25) seen in <5 years of study patients where significant malnutrition was found. Overall mortality was also high in this group. Signs of increased ICT, like features of encephalopathy, altered sensorium, fundus changes, and altered patterns of breathing, were the commonest symptoms seen in cases of CNS TB, correlating with other studies. [17] The maximum number of patients in this study with abdominal involvement had ascites and visceromegaly. Basu *et al*. [18], in their study, also found abdominal distention, organomegaly, and ascites as common findings in children with abdominal TB. Despite an overall high BCG immunization rate, a higher number of cases of CNS TB were seen, which is in contrast to the effects of the BCG vaccine determined in various previous studies claiming beneficial effects on CNS and disseminated TB in children [19]. Jain *et al*. [10] also found higher (88%) coverage of BCG vaccination in their study population of children with TB. This can be attributed to the variable efficacy of BCG and has been explained in terms of genetic variations, interference of environmental mycobacteria, age at vaccination, time since vaccination, poor nutrition status, method of BCG administration, and use of different BCG strains [20,21].

In this study, microbiological confirmation was possible in 8.8% of cases. Mycobacterium culture (solid or liquid) was not done. Garg [9] used both microscopy and culture simultaneously, and Jain *et al*. [10] used mycobacterial culture first, followed by Gene Xpert to look for drug sensitivity, but only in culture-positive cases. They found microbiological confirmation in a relatively lesser number of patients

Table 3: Final diagnosis and outcome

Type of TB	Total cases number (%)	Death number (%)
Pulmonary TB	20 (25%)	1 (5%)
CNS TB	23 (28.7)	7 (30.4%)
Abdominal TB	17 (21.25%)	0 (0%)
Pleural TB	6 (7.5%)	0 (0%)
TB Lymph node	5 (6.3%)	0 (0%)
TB Bone and Joints	3 (3.8%)	0 (0%)
Disseminated TB	6 (7.5%)	3 (50%)
Total	80	11

Table 4: Systemic examination findings among study subjects according to age groups

Systemic examination	Age groups			Total
	0–5 year	6–10 year	>10 year	
CNS				
Meningeal Signs	2 (33%)	2 (33%)	2 (33%)	6 (24%)
Signs of Increased ICT	10 (77%)	1 (7.8%)	2 (15.4%)	13 (52%)
Neurological Deficit	5 (83.3%)	0 (0.0%)	1 (16.6%)	6 (24%)
Total	17	3	5	25
Abdominal				
Ascites	5 (55.6%)	2 (22.2%)	2 (22.2%)	9 (39%)
Hepatosplenomegaly	4 (50%)	2 (25%)	2 (25%)	8 (35%)
Tenderness	0 (0.0%)	6 (100%)	0 (0.0%)	6 (26%)
Total	9	10	4	23
Respiratory				
No Pneumonia	28 (55%)	11 (21.6%)	12 (23.5%)	51 (68%)
Pneumonia	9 (40.9%)	8 (36.3%)	5 (22.7%)	22 (27.5%)
Severe Pneumonia	3 (42.8%)	2 (28.5%)	2 (28.5%)	7 (8.8%)
Total	40	21	19	80
Locomotor system				
Gibbus	0	0	1 (100%)	1 (33.3%)
Joint effusion	2 (100%)	0	0	2 (66.6%)
Total	2	0	1	3
Lymphadenopathy only				
Cervical lymphadenopathy	0	2	3	5

Table 5: Result of smear AFB and CBNAAT test according to type of tuberculosis

Type of TB	AFB		CBNAAT	
	Negative	Positive	Negative	Positive
Pulmonary TB	20	0	16	4
CNS TB	23	0	23	0
Abdominal TB	17	0	17	0
Pleural TB	6	0	5	1
TB Lymph node	4	1	5	0
TB Bone and Joints	3	0	3	0
Disseminated TB	5	1	6	0
TOTAL	78	2	75	5
Chi Square Value	12.991		11.164	

(3.8%, 4.8%), respectively as they did not use Gene Xpert as first-line diagnostics. Also, in our study, the proportion of extrapulmonary TB cases was higher. However, Rebecca *et al*. [16], found 31% positivity in samples by Gene Xpert. This shows the importance of clinical expertise despite the availability of newer diagnostics in centers with a high TB burden.

CONCLUSION

Pediatric TB differs from adult TB in being more extrapulmonary and more severe in the younger population. Delay in diagnosis due to diagnostic challenges, especially in EPTB, variable clinical presentation, and the rapid progression from infection to clinical disease may be the reasons for more deaths in young children with TB. To achieve the global goal of eliminating TB by 2025, treatment and prevention of TB in children need as much attention as that in adults. Screening children with positive household contacts and the early start of preventive therapy should be given priority. The approach should be family-centric than patient-centric.

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AUTHOR'S CONTRIBUTION

Bharat Bhushan Tripathi: concept and design of the study, aims and objectives, reviewed the literature, prepared the first draft of the manuscript, arranged all the references, and this is his own dissertation work; Deepak Kumar Patel: contributed regarding the conception or design of the study, developing the consent form; Devpriya Shukla: concept, coordination, interpretation of the results, and manuscript preparation; Anurag Jain contributed regarding the conception or design of the study and developing the consent form.

CONFLICT OF INTEREST

None declared.

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