Original Article

Clinical profile of different type of tuberculosis in hospitalized children in tertiary care center

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ABSTRACT

Background: Since the implementation of directly observed treatment short (DOTS) program, the prevalence, clinical profile, and risk factors of pulmonary and non-pulmonary tuberculosis (TB) necessitating hospitalization in pediatric patients are not evaluated extensively. **Materials and Methods:** We designed a prospective observational study to evaluate the clinical profile of different types of TB in hospitalized children <12 years old. Different types of TB in children hospitalized from 1st January 2013 to 30th June 2014 were recorded. Detailed clinical history, clinical examination findings, diagnostic methods, and treatment of these cases were analyzed by age groups and types of TB. **Results:** During the study period, 150 (2.8% of total admission) patients with TB were admitted in our institute. 87 (58%) patients were <5 years old, and 92 (61.33%) children were male. 140 (93.33%) children were malnourished. The clinical profile of TB included neuro TB in 78 (37.32%), pulmonary in 67 (32.05), abdominal in 27 (12.91%), and disseminated in 27 (12.91%) patients. Less than half of children with neuro TB and disseminated TB were immunized with *Bacillus* calmette-guerin (BCG). **Conclusion:** Despite aggressive DOTS implementation, the prevalence of TB, particularly, non-pulmonary TB in children is quite alarming. All the variants of TB are prevalent in the children. The neuro TB and the pulmonary TB dominate in the hospitalized cases. Younger age, lack of protection of BCG vaccination, and malnutrition are the main risk factors in childhood TB.

Key words: *Bacillus calmette-guerin vaccination, Childhood tuberculosis, Malnutrition*

Despite recent progresses, tuberculosis (TB) remains a global public health problem. Each year, about 8 million people worldwide develop TB. Of these, 95% occur in developing countries, and India accounts for about 20% of the global burden of the TB [1]. Childhood TB has been neglected in the global efforts to control TB [2,3] because it is considered to be rarely contagious and difficult to diagnose due to less sputum production and low acid fast *Bacilli* positivity in children. This is further compounded by the inherent problem of bacteriological examination of sputum, notably if only microscopy is available [4]. The WHO estimated that 11% of the all new TB cases diagnosed in 2000 were children [1]. The proportion is higher in high TB-burden countries, reflecting that childhood TB represents active TB transmission within a community. Similar to other high burden countries, India faces challenges in capturing childhood TB cases to be treated under the National TB program (NTP). Despite implementation of directly observed treatment short course (DOTS) program in public and private hospitals in India since 2000, the burden of childhood TB in hospitals seems to be increasing. The goals of this study were to document the profile of childhood TB cases and to determine the risk factors in the 0–12 years age groups diagnosed with TB at tertiary care center.

MATERIALS AND METHODS

This prospective study was done on the hospitalized cases of childhood TB at a tertiary care hospital of Ahmedabad city in Western India over 18 months from 1st January 2013 to 30th June 2014. All the children admitted with a clinical diagnosis of childhood TB were included in the study. The research protocol has been reviewed and approved by the institutional review board as a postgraduate research study, and the informed consent has been taken from each participant.

Inclusion Criteria

1. All children up to 12 years of age admitted with clinically suspected TB.
2. Any evidence of TB infection such as positive tuberculin skin test (TST), radiological evidence, cerebrospinal fluid examination, or fine-needle aspiration cytology (FNAC) suggesting TB.

Exclusion Criteria

1. More than 12 years of age.
2. Patients with empirical antitubercular treatment without supporting diagnostic evidence.

A detailed clinical history, family history of contact with Koch's disease, and physical examination of each child were recorded in a standardized predesigned pro forma. Complete blood count, TST, and chest skiagram were advised in all patients. Interpretation of TST and chest skiagram was done using the standardized methods [5-7]. FNAC, abdominal ultrasound, hip and spine skiagrams, abdominal paracentesis, computed tomography of relevant systems, lumbar puncture, and other relevant investigations were done to substantiate the diagnosis of TB. Sputum and gastric aspirate for acid-fast *Bacilli* (AFB) staining and culture of FNAC for AFB were also processed whenever possible.

Collected data were tabulated on the MicroSoft Excel worksheet (Microsoft, Redwoods, WA, USA). Data analyses were done using MicroSoft Excel 2007. Categorical data were expressed in proportions. In contingency tables, the significance of association between categorical data was analyzed using Chi-square test. Software phstat 2.3.5 was used for statistical analysis. A $p<0.05$ was considered statistically significant.

RESULTS

Of the total pediatric admission of 7187 during the study period, 150 were admitted with a clinical diagnosis of TB. Of these, 92 (61.33%) were males, and 58 (38.66%) were females. Maximum number of children was seen in the age group of 1–5 years, i.e., 73 (48.66%) followed by age group of 5–12 years (63, 42%) and least in infancy (14, 9.33%). We were able to trace the positive history of contact with the family member in only 54 (36%) children. 91 (60.66%) children were vaccinated with *Bacillus* calmette-guerin (BCG) at birth. The TST was positive in 68 (45.23%) children. The spectrum of TB in the different age group with BCG vaccination status is depicted in Table 1. One forty (93.33%) children were malnourished including 86 (57.33%) children with grade 1 and 2 malnutrition and 54 (36%) children with grade 3–4 malnutrition. There is a significant relationship between the malnutrition in children and occurrence of TB ($p<0.05$).

Fig. 1 shows the different presentations of TB in children. Fever, weight loss and anorexia were the three main presenting symptoms. Only 15 (10%) children were HIV positive and 2 (13.33%) of them expired. While out of 135 (90%) HIV-negative children, 16 (11.85%) children expired. There was no significant relationship between HIV status of child and mortality ($p>0.05$).

At the time of discharge from hospital, 124 (82.66%) children improved symptomatically, 5 (3.33%) were discharged against advice, 3 (2%) absconded, and 18 (12%) expired despite ongoing treatment. The leading causes of death were neuro TB in 12 (66.66%) cases and disseminated TB in 6 (33.33%) cases. Case fatality rate was low in BCG vaccinated children −4 (22.22%). There was a significant relationship between the occurrence of different types of TB and BCG vaccination status in children ($p<0.05$).

DISCUSSION

TB in children poses major challenges in diagnosis, a collection of epidemiological data, and serious implications in children <5 years by affecting their growth potential and associated significant morbidity [8-10]. Diagnosis of TB in children presents special problems as the sputum is generally not available for examination. Diagnostic algorithms include scoring system utilizing clinical parameters and results of investigations. The prevalence of TB varied from 1.5% to 3.5% [11,12] and male:female ratio varied from 0.81:1 to 3.42:1 [12,13] in different studies. In our study, the prevalence was 2.08%, and male:female ratio was 1.58:1 which correlates with the different studies. The higher prevalence in the current study may be because the hospital is a tertiary care center and caters to predominant lower socioeconomic classes where the prevalence of TB is known to be higher [14].

Consistent with the findings from other studies [15-19], more than half of childhood TB cases occurred in the age group of 0–5 years (i.e., 58% in the inpatient). High incidence of TB among children under 5 years of age indicates ongoing disease transmission in the household [20]. This can be prevented with the provision of isoniazid prophylaxis therapy (IPT) in approximately 60% of at-risk individuals [21]. According to the

Table 1: Spectrum of TB

Type of TB	Number of patients in different age groups (%)			Total number of patients (%)	BCG vaccination status (%)
	0–1 year	1–5 year	5–12 year		
Neuro TB	9 (11.53)	40 (51.28)	29 (37.17)	78 (37.32)	38 (48.71)
Pulmonary TB	6 (8.95)	34 (50.74)	27 (40.29)	67 (32.05)	45 (67.16)
Abdominal TB	2 (7.40)	12 (44.44)	13 (48.14)	27 (12.91)	18 (66.66)
Disseminated TB	3 (11.11)	14 (51.85)	10 (37.03)	27 (12.91)	12 (44.44)
Osteoarticular TB	0	1 (25)	3 (75)	4 (1.91)	0
Milliary TB	1 (25)	2 (50)	1 (25)	4 (1.91)	2 (50)
TB lymphadenitis	0	2 (100)	0	2 (0.95)	2 (100)

TB: Tuberculosis, BCG: *Bacillus* calmette-guerin

WHO recommendation, IPT should be given for 6 months to children aged <6 years who are household contacts of infectious cases [5,22]. In India, however, contact tracing and provision of TB prophylaxis to high-risk children are still difficult because of the non-acceptance by the family members due to social stigma and fear associated with the disease in illiterate and low socioeconomic group.

Clinical presentations of TB have been compared among different studies in Table 2. Unlike the adult population where cough, expectoration, and chest pain are more common, fever is the most common presenting symptom in childhood TB, followed by anorexia and weight loss or not gaining weight. Our findings are also well supported by the other studies done on childhood TB. As the children are many times fussier about their food habits, anorexia and not gaining weight are often found in children without TB, and fever is a common clinical presentation of various etiological diseases in this age. Thus, non-specific nature of clinical presentation adds in the diagnostic difficulties. Many children having cough are not able to expectorate and so the sputum is not available for the diagnostic confirmation. All these factors lead to delay in the diagnosis and initiation of the treatment probably contributing to the presentation of children with more serious forms of TB.

TB meningitis is the most common TB lesion in our study. It is worth noting that it is the most common form of TB observed in children which carries a very high mortality of more than 65% of the overall mortality due to TB. This is a serious form of TB in children in hospital practice. In addition, it is often associated with a squeal. Tuberculomas are often found in children with TB presenting as hemiparesis. Malnourished and HIV-infected children often have multiple tuberculomas in brain parenchyma. The second most common type is the pulmonary TB. Different variety of pulmonary TB including enlarged hilar lymph nodes, TB pleural effusion, TB bronchopneumonia, and TB cavity formation are seen in children. The comparison of different studies in the spectrum of TB has been described in Table 3.

An Indian study by Kabra et al. from a tertiary care referral center in North India suggests an increase in the proportion of cases of extrapulmonary TB over the past three decades [23]. The increase was predominantly due to increase in lymph node TB. The severe form of tubercular meningitis decreased over the past three decades. The community-based studies also had a low prevalence of neuro TB. In contrast to this, our center being tertiary care noted a high prevalence of neuro TB. The published studies in recent year's show that the neuro TB and the pulmonary TB are the two major types of TB in hospital-based environment. The overall case fatality rate was 12% in the study.

Status of BCG vaccination in children with different type of TB comparison with other studies has been shown in Table 4.

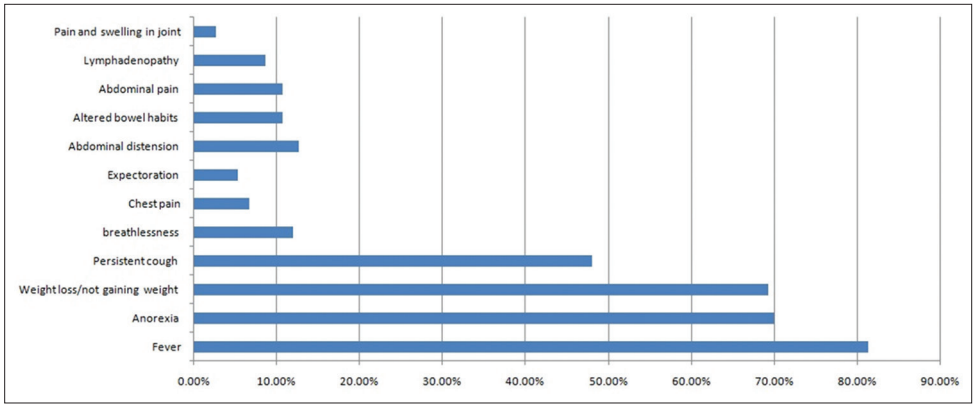

Figure 1: Clinical presentation of the study subjects

Table 2: Clinical presentations of TB - comparison with different studies

Presenting signs and symptoms	Present study (%)	Garg [12] (%)	Vishwanath et al. [25] (%)	Sushamabai and Devi [24] (%)	Swaminathan et al. [11] (%)
Fever	122 (81.33)	84	78.5	65.3	49
Anorexia	105 (70)	95	34.82	-	-
Weight loss/not gaining weight	104 (69.33)	63	23.21	33.33	47
Persistent cough	72 (48)	44	50.89	62.2	47
breathlessness	18 (12)	4.8	-	-	-
Chest pain	10 (6.66)	-	-	-	-
Expectoration	8 (5.33)	-	-	-	-
Abdominal distension	19 (12.66)	5.9	-	-	-
Altered bowel habits	16 (10.66)	5.9	3.57	-	-
Abdominal pain	16 (10.66)	18	8.92	-	-
Lymphadenopathy	13 (8.66)	16.7	24.10	11.6	47
Joint pain and swelling	4 (2.66)	2.5	-	-	-

TB: Tuberculosis

Table 3: Spectrum of TB in different studies

Type of TB	Present study	Vishwanath et al. [25] (%)	Garg [12] (%)	Sushamabai and Devi [24] (%)	Vijayasekaran et al. [28] (%)	Kabra et al. (2002) [23] (%)	Sharada and Nelliyanil [29] (%)
Neuro TB	37.32	13.39	5.9	6.32	40.4	2.6	23.2
Pulmonary	32.05	49.10	52.4	72.6	20	59	10
Abdominal	12.91	2.67	5.95	1.05	3.6	2.1	6.5
Disseminated	12.91	2.67	7.1	4.22	-	5	2.2
Osteoarticular	1.91	3.57	7.1	-	16.4	2.6	2.1
Milliary TB	1.91	0.89	2.4	1.05	-	1.7	-
Lympha-denitis	0.95	15.17	16.7	6.32	19.3	26.5	55

TB: Tuberculosis

Table 4: BCG vaccination in different types of TB - comparison with different studies

Type of TB	Present study (%)	Vishwanath et al. [25] (%)	Udani and Somu [5] (%)	Somu et al. [30] (%)	Verma et al. [26] (%)
Neuro TB	48.71	73.33	38.5	28	62
Pulmonary TB	67.16	80	37	40	95
Abdominal TB	66.66	100	80	38	99
Disseminated TB	44.44	66.66	13.9	-	96
Osteoarticular TB	0	75	-	31	-
Milliary TB	50	0	16.7	25	-
TB lymphadenitis	100	82.35	-	48	100

TB: Tuberculosis, BCG: *Bacillus* calmette-guerin

It has been suggested that BCG vaccination is responsible for the decrease in the occurrence of disseminated and severe disease. Localized forms of illness, for example, intrathoracic lymphadenopathy and localized CNS disease have been reported to occur with greater frequency in vaccinated children. This study also reveals that BCG vaccination was <50% in all the three serious forms of TB (disseminated TB, neuro TB, and disseminated TB) while other less severe forms (pulmonary TB, abdominal TB, and TB lymphadenitis) reflect the good BCG vaccination coverage. Thus, neuro TB occurs more commonly in the non-BCG vaccinated group supporting the view that BCG has a protective value against it. This can be compared with other work which showed that although BCG has low overall protection, it has good protection against neuro TB and disseminated TB. However, it is important to observe that neuro TB does occur in a significant proportion of patients even in the BCG vaccinated group. Case fatality rate was also high in the BCG-unvaccinated group (77.77%), which also supports the protection offered by BCG in overall mortality by childhood TB. Similar findings were also noted by other studies [13,24,25] except by the study of Verma et al. [26] which showed good BCG vaccination ratio in all types of TB patients.

It is a proven fact that TB is more prevalent in malnourished children. There is a significant burden of malnutrition and TB in children worldwide, especially in developing countries. It appears that malnutrition serves as the favorable environment for the TB and is associated with the worse outcomes. There are numerous evidences about malnutrition's effect on immune development and respiratory infection. The prevalence of TB was also high in malnourished children in our study.

The study by Kasai et al. [27] showed TST sensitivity of 78.3%. About 38.5% of children were diagnosed of having TB only on basis of TST. In our study, also there was a high positivity of about 45.23% of TST. Thus, TST remains the faster and more accessible test to diagnose TB in highly endemic area and should be freely available.

CONCLUSION

The prevalence of childhood TB is still very high and not decreasing even after implementation of the DOTS for more than 10 years. The rates of extrapulmonary and neuro TB are also very high in this vulnerable population. BCG vaccination has its definite protective role in preventing TB. In response to the high caseload and gross under-reporting of childhood TB cases, the NTB Program should give higher priority for childhood TB case management in designated DOTS hospitals.

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