Clinical profile of tuberculosis in children up to 5 years of age

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Abstract

Introduction: Tuberculosis as a disease is of great public health problem in developing countries like India. Children contribute a significant proportion of disease burden and suffer from severe form of disease, but because of difficulty in establishing an accurate diagnosis, data of disease burden in pediatric population is lacking. This study is an attempt to assess clinical profile of tuberculosis in children upto 5 years of age. **Method:** present study was conducted at Kamla Raja Hospital & Gajra Raja Medical College Gwalior over a period of six months. 77 cases up to 5 years of age were selected from in-patient department, who were diagnosed to have tuberculosis. A detailed history of epidemiological factors including past history of infectious disease, history of contact contributing to disease state was recorded on predesigned Performa. Complete clinical examination and laboratory investigation was done to confirm the diagnosis. **Result:** approximately 70 % of study group was distributed in 2- 5 years of age group. Cases of CNS tuberculosis formed the main bulk to the study contributing 70.13% followed by intrathoracic (~16.88%), disseminated (6.49%), abdominal (5.19%) & lymphoid (1.29%) tuberculosis. Severe malnutrition, low socio economic status, illiteracy of parents were the important epidemiological factor affecting the disease status of child. **Conclusion:** childhood tuberculosis remained the neglected part in NTCP until RNTCP was introduced. Childhood cases have shown increasing trends with the advent of HIV infection. Prompt suspicion and early diagnosis can be an important step in controlling this epidemic.

Keywords: clinical profile, childhood tuberculosis , Neurotuberculosis, Disseminated Koch's

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Introduction

Tuberculosis is a major public health problem worldwide especially in under-developed and developing countries, posing a challenge to the health system since ancient time. Globally, the World Health Organization (WHO) reports more than 9 million new cases of tuberculosis (TB) each year [1] and an estimated, 19-43.5% of the world's population is infected with *M tuberculosis* [2]. WHO declared it a global emergency in 1993. The problem of tuberculosis in pediatric age group represent tip of iceberg as demonstrated by P.M. Udani by the pediatric T B pyramid. In endemic areas, children contribute a significant proportion of the disease and suffer from severe tuberculosis related morbidity and mortality particularly when associated with HIV infection and severe malnutrition. Childhood tuberculosis is important

sensitive indicator of recent spread of infection from adults. Children rarely contribute to spread of tubercular infection, because childhood tuberculosis is usually extra-pulmonary and lack of adequate pulmonary force to form droplets in pulmonary tuberculosis especially less than 6 years of age.

Because of paucibacillary nature of tuberculosis, it is difficult to establish an accurate diagnosis in children. The true extent of morbidity and mortality related to tuberculosis in endemic area is lacking. Of the several components of TB control programe, case finding remains the cornerstone for effective control.

Diagnosis of tuberculosis in children is extremely challenging [3], the most important reason for this is –

- Inability to demonstrate AFB which is a gold standard, because of pausibacillary nature of infection.
- Clinical symptoms and sign of tubercular disease are non specific. No different from common childhood symptoms and signs.

- Predominantly extra-pulmonary rather than pulmonary as in adults
- Most of new techniques are costly, technically difficult and till date have unacceptable sensitivity and specificity.
- It is difficult to differentiate tubercular infection from disease by these new techniques.

Except for the study conducted at AIIMS Delhi from 1966 to 1999 from the OPD of pediatric clinic, national level data on pediatric tuberculosis is lacking hence the present study is an attempt to find out the epidemiological factors and clinical profile of tuberculosis in children below 5 years of age.

Material and method

Study design & sampling: This was a prospective study, done in department of pediatrics Kamala Raja and Gajra Raja Medical College, Gwalior. Total 77 cases were selected from the admitted patient of the pediatric wards of Kamala Raja Hospital with diagnosis of tuberculosis. Research was conducted over a period of six months with prior permission from institutional ethical committee.

Inclusion criteria:

Children age up to 5yrs, with suspected diagnosis of tuberculosis.

Exclusion criteria

- Children of more than 5 yrs
- Children with doubtful diagnosis

Question form

For every child who was included in this study a detailed clinical history to assess demographic data such as age,

sex, residence, parental occupation, parental education, family size, birth order, socio-economic status which determines disease status was recorded in detail. History of contact with tuberculosis and history of infectious disease was also recorded.

Clinical examination

A detailed head to toe clinical examination including anthropometric assessment was done. Patients were classified into different grades of malnutrition using IAP classification. Especial emphasis was given to check for BCG scar mark. A thorough examination of all the system was done to detect signs consistent with the disease.

Laboratory investigations

- Routine investigation including hemoglobin, TLC, DLC, ESR
- Tuberculin test using 0.1ml of 1 TU of PPD- RT 23 with Tween-80
- CHEST X-RAY
- CSF EXAMINATION in suspected case of CNS tuberculosis.
- Gastric aspirate in cases when required.
- FNAC in case of lymphadenopathy and confirmed by typical histopathological appearance.
- CT SCAN in all the suspected case of CNS tuberculosis except for those who were non affording.

Statistical analysis: Data was entered into SPSS version 13. Data was presented as proportions. Statistical significance of difference in proportions was tested using chi-square test and a p-value of less than 0.05 was considered as significant.

Results

Total 77 cases with diagnosis of tuberculosis were included in this study. All children included in this study were of age up to 5 yrs.

Table No 1: Age and site of involvement in Patients

S No	Age groups	Systems					Total	%
		Intra-Thoracic	CNS	Abdo-Minal	Lymph Node	Disseminated		
1	0-1 yrs (3)	1	2	0	0	0	03	03.89
2	1-2 yrs (14)	3	10	0	0	1	14	18.18
3	2-3 yrs (23)	3	19	0	0	1	23	29.87
4	3-4 yrs (13)	4	9	0	0	0	13	16.88
5	4-5 yrs (24)	2	14	4	1	3	24	31.16
	Total (77)	13	54	4	1	5	77	100
	%	16.88	70.12	5.19	01.29	06.49		

Table No-01 shows that 24 patients (31.16%) were in 4-5 year of age group followed by 23 (29.87%) in 2-3 yeas age group, 14 (18.18%) in 1-2 yrs, 13 (16.88) in 3-4 yrs and only 3 (3.89%) belong to 0-1 year age group. Male to female ratio was 1.7:1 with 63% male and 37% female. CNS tuberculosis is commonest type (70.12%), followed by intra-thoracic (16.88%), disseminated (06.49) and abdominal (5.19%). Only one case of lymph node tuberculosis and five cases of disseminated TB were seen. CNS tuberculosis was common in younger age group that is in 1-3 year age group, this difference was statically significant.

Table No 2: showing age wise distribution of children with h/o contact with TB, history of measles and nutritional status

Age Groups	No of Patients	H/O Measles	H/O Contact	PEM Grade III & IV
0-1 Yr	03	1	3	2
1-2 yr	14	0	6	7
2-3 yr	23	4	10	16
3-4 yr	13	3	7	5
4-5 yr	24	9	12	15
Total	77	17	38	45
%		22%	49%	58.4%

Table No-02 shows that most of the patients (54.4%) have grade III and grade IV malnutrition. Majority of malnourished patients belong to 2-3 years and 4-5 years of age group. 49% patients also having history of contact with Tuberculosis and 22% have h/o Measles.

Table No 03: **Distribution of cases showing H/O contact, BCG status and positive Montoux test in different type of Tuberculosis**

S. No	Type of disease	No .of cases	Positive H/o contact (%)	BCG Scar Status (Absent) (%)	Mantoux Test Positivity (%)
1.	Intra thoracic TB	13(16.8)	06	05	05
2.	CNS TB	54(70.1)	27	38	19
3.	Abdominal TB	04(05.1)	00	01	04
4.	Lymphatic TB	01(01.2)	01	00	01
5.	Disseminated TB	05(06.4)	05	04	01
	Total	77	39 (50.6%)	38 (49.5%)	30 (38.97%)

Table No 03 shows that in lymph node TB and disseminated TB, h/o contact is positive in 100% cases, where in CNS TB only 50% patients having h/o contact. Total only 50% patients, having positive contact history. There is another important interference from this table that in 49% children BCG scar was not present. Only 38.97% patients showed positive reaction to tubercular antigen.

Table No 4: Presenting symptoms in different type of Tuberculosis

S. NO	Symptoms	Type of Tuberculosis					
		INTRA-THORACIC	CNS	ABDO-MINAL	LYMPH-NODE	DISSEMINATED	TOTAL
		(13)	(54)	(04)	(01)	(05)	(77)
1	Fever	13 (100%)	53 (98.1%)	03 (75%)	00	05(100%)	74 (96.1%)
2	Cough	11 (84.6%)	12 (22.2%)	01 (25%)	00	02 (40%)	26 (33.7%)
3	Not gaining wt	04 (30.7%)	07 (12.9%)	01 (25%)	00	01 (20%)	13 (16.8%)
4	Anorexia	06 (46.1%)	37 (68.5%)	04(100%)	00	04 (80%)	51 (66.2%)
5	Altered sensorium	01 (7.6%)	35 (65.8%)	00 (00%)	00	02 (40%)	38 (49.3%)
6	Seizures	00 (00%)	40 (74.0%)	00 (00%)	00	02 (40%)	42 (54.5%)

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Table No 04 shows that fever (96.1%) was the most common presenting symptom followed by anorexia in 66.2% cases. Fever (98.1%), altered sensorium (65.8%), anorexia (68.51) and seizures (74.0%) were the presenting feature in CNS TB.

Table No 5: Radiological Evidence of Tuberculosis

		X-Ray (n=77)			CT Scan (n=36)		
S. No	Type of disease	No. of Cases	Positive Findings	%	Findings	No of Cases	%
1.	Intra thoracic TB	13	13	100	Ventricular Dilatation	22	81
2.	CNS TB	54	37	68.51	Basal Exudate	26	69
3.	Abdominal TB	4	00	00	Tuberculoma(Ring Lesion)	06	15
4.	Lymphatic TB	1	01	100	Infarct (Hyperdence)	07	22
5.	Disseminated TB	5	03	60	Normal	05	15
	Total	77	54	70.1			

Table No 05 shows that positive radiological findings were present in 70.1% cases. Intra-thoracic TB having 100% positivity whereas CNS TB have 68.5% positivity. CT scan was done in 36 patients. 81% patients have ventricular dilatation and 69% patients have basal exudates. CT scan was normal in 15% cases.

Discussion

Tuberculosis is a major health problem worldwide posing a challenge to the health system since ancient time. Pediatric tuberculosis has traditionally received a lower priority than adult TB in National TB programmes because of its considered non-infectious, is difficult to diagnose, cases have been thought to be few and it was wrongly assumed that effective control of adult TB and use of BCG by itself could prevent childhood TB[4].

Childhood TB can be considered as "the neglected rising Epidemic" despite the decrease in TB burden since 1960s resurgence was seen in nineties due to resistant (MDR, XDR and recently TDR) and HIV infection [5]. The extent of childhood TB in India is unknown due to diagnostic difficulties; it is estimated to be 10.2% of the total adult incidence [6]. The maximum risk of a child getting TB is between 1-4 years when there is an increased risk of progression from infection to disease.

Age and sex: Various studies have reported that children below five years are at increased risk as well as sufferer of severe form of disease like CNS TB. In our study 77.9% cases were found in age group between 2-5 years. Bai SS & Devi RL [7] and V. Seth et al. [8] in their study group of two months to 12 years found that 49.5% and 50% respectively of total cases were in 1- 5 year age group. G.P Mathur et al.[9] also showed similar result in their study. Male to female ratio in the present study was 1.7:1 was close to study of Bai SS & Devi RL with ratio of 1.5:1[7].

Clinical types of tuberculosis: In our study CNS form of tuberculosis was most common, 70.13 % followed by 16.88% of Pulmonary TB, Higher number of cases of CNS is cause of concern as sequel of it lead to permanent disability in child's life . Only one case in our study was of lymphatic TB. Many studies have reported increasing trend in extra pulmonary tuberculosis in children [10, 11]. V. Seth [8] at pediatric TB clinic AIIMS described 47% cases of pulmonary tuberculosis and only 26.5 % cases of CNS TB. Higher incidence of CNS TB in our study is similar to G.P. Mathur [9] who also studied the tuberculosis in under six years of age. Lower incidence of CNS TB i.e. 26.5% in V. Seth [8] and other studies may be because of inclusion of higher age groups and OPD patients. As our study was conducted in hospitalize patient and CNS tuberculosis is consider severe form of TB usually need hospitalization and being a tertiary care center, usually deal with complicated form of disease, possible explanation of higher number of CNS tuberculosis.

Contact to tuberculosis, Malnutrition, history of measles: As we know, because of pausibacillary nature of childhood tuberculosis, children do not transmit disease among themselves unlike other childhood diseases, contact with an adult case of TB is an important factor determining disease state.

 History of contact in our study was seen in 50.6% cases. P. Chandra [12] & V. Seth [8] also found contact in 52% and 33.7% of cases of their study group. This shows that

children are at increased risk, even when an obvious source is not detected. Malnourished child is more prone for TB infection, in our study 58.4% of cases were severely malnourished similar to V. Seth who also found 58% of study group to be severely malnourished. Recent combination with HIV has worsened the situation. HIV infection significantly increases severe malnutrition case death. WHO guidelines for the management of severe malnutrition in high HIV prevalence settings need modification. It should include routine HIV and TB testing and offer guidance on the criteria and timing of TB treatment and highly active antiretroviral therapy initiation [13, 14]. HIV could neither be diagnosed, nor excluded clinically in severe malnutrion. We recommend HIV testing be offered to all children with severe malnutrion where HIV is prevalent. The fact that measles by its immunosuppressive action, precipitate the subclinical form of TB, is well known and documented. In present study 22% had suffered from measles in recent past. A recent article by Kristensen et al.[15] suggested that measles vaccine and bacille Calmette–Guérin (BCG) vaccine might reduce mortality beyond what is expected simply from protection against measles and tuberculosis. Starr S et al [16] found in their study that measles in INH-treated children with tuberculosis exerted a deleterious effect on the course of the tuberculosis. The effect of measles on the tuberculosis appeared 2 weeks to 3 months after the measles, manifesting itself as an increased pulmonary infiltration or as an increased number of gastric washings positive for M. Tuberculosis.

BCG vaccination and Mantoux test: BCG vaccination of infant and children is the only available intervention to reduce the risk of primary infection progressing to disease to distant sites such as meningitis, military and bone TB. Among various studies to assess BCG vaccination status by BCG scar survey, Singh KP et al [17], in less than 5 years, Seth V [8] at AIIMS in less than 3year age group and 3-6 year age group found 41.2% & 47.2% respectively. In our study BCG scar was absent in 49.5% cases of tuberculosis, which was statically significant. Lack of BCG scar usually indicate un-vaccinated condition, common in rural areas because of lack of basic health facilities and some time reluctance of giving vaccines because of social practice. BCG vaccination is very effective and provides good immunity for extra-pulmonary tuberculosis even in puberty [18]. Roth A et al, found in their study that a BCG scar is a marker of better survival among children in countries with high child mortality. BCG vaccination may affect the response to several major infections including malaria [19].
Mantoux test is one of the important investigations used to diagnose childhood tuberculosis, but its positivity depends upon various factors. If the child is severely

malnourished, having severe and disseminated form of disease, patient suffering from viral disease (such as measles and chicken pox) and on prolonged steroids decreases the chances of it being positive. The range of tuberculin positivity is 19.3%-73.3% in childhood tuberculosis according to Udani et.al. In our study mantoux positivity was found in 38.9%. Chandra P. in his study of 0-10 year age group found positive mantoux test in 67% in BCG vaccinated group and 87% in non vaccinated group [12]. Contrary to other study the lower positivity in present study may be due to higher number of CNS cases and severely malnourished children. The new techniques have a higher specificity than Mantoux for the diagnosis of latent tuberculosis, in contacts and vaccinated in childhood with BCG. But the most cost-effective diagnostic strategy is Mantoux screening and confirmation with QFT-G [20]. Another method of tuberculin skin test, known as the "Tine Tuberculin Skin Test" (multipuncture percutaneous), demonstrated a higher positive test rate than the Mantoux [21].

Clinical presentation: Non-specific manifestations of pediatric TB could be one of the reasons for delay for admission and diagnosis of severe form of tuberculosis disease in our setup. Fever was the most common symptom in our study i.e. 96.1% in contrast to V. Seth study and Bai SS et al who found fever in only 28.6 % & 65.3 % respectively [7]. Anorexia (66.2%), cough (33.7%) and not gaining weight (16.8%) are other non-specific symptoms, but seizures (74%) and altered mental status (65.57%) with focal neurological deficit are specific symptoms and sign that indicate CNS tuberculosis. The diagnosis in most cases is still based on clinical evidence alone. The present study was designed to study clinical profile, laboratory investigations and outcome of pediatric tuberculosis. Bacteriological or histological confirmation is very difficult and a chance of positivity is very less. This study supports the use of history and clinical features to diagnose childhood tuberculosis. Shrestha S et al (2011) also support our findings [22].

Investigation: It is well known that diagnosis of childhood tuberculosis is very difficult [23]. No single diagnostic procedure can be considered as gold standard for diagnosis. Investigations in present study were carried out depending upon the necessity of the case and affordability of parents and to rule out other differential diagnosis. Pulmonary TB was diagnosed mainly based on chest radiograph, Mantoux test and ESR. Special investigations were done for Extra Pulmonary TB patients. Ultrasound, biopsies, CSF examination and CT Scan etc to corroborate with the clinical diagnosis. Chest radiograph was used for both pulmonary and extra-

pulmonary though its reliability as diagnostic tool is questionable[18] . A high proportion (100%) of chest radiographs were interpreted as positive for patients diagnosed as Pulmonary TB. Overall chest radiograph are positive in 70.1% cases. Interpretation of laboratory and radiological findings become more difficult in view of HIV pandemic.

Although tuberculosis most commonly involves the lungs, one with the involvement of the central nervous system (CNS) is the most serious type of systemic tuberculosis due to its high mortality rate, common neurological complications and sequelae. In our study 81% patients have ventricular dilation and 69% patients have basal exudates. In neuroimaging, initial investigation is CECT brain. MRI and MR spectroscopy of brain are superior to CT Scan. Together they can be used to differentiate tuberculoma from other infective lesions such as brain abscess or neuro-cysticercosis and neoplastic lesions4. In MRI brain tuberculoma, tubercular abscess, astrocytoma can usually be differentiated. CNS involvement is noted in 5-10% of extra-pulmonary cases and accounts for approximately 1% of all TB cases. Definitive diagnosis of CNS tuberculosis depends upon detection of tubercular bacilli in CSF and radiological findings give supportive evidence so every patients with CNS tuberculosis should preferably be evaluated with radio-imaging, CECT either before or within 48 hours of treatment.[25]

In our study, CSF findings suggestive of CNS tuberculosis, found in 51.9% children. CSF values became more abnormal over time, with increasing leukocyte counts and protein levels and decreasing glucose levels. The typical analysis of CSF from patients with CNS tuberculosis demonstrates a moderate lymphocytic pleocytosis, moderately elevated proteins levels and low CSF sugar level. Identification of AFB in CSF through both smear and/or culture methods remains the most important and most widely available means of diagnosis of CNS tuberculosis.[26]. Because of the infrastructure related limitation CSF culture was not done in our study.

Our study had few limitations. As this was a hospitalized based study, it gave a better picture of distribution of disease pattern in hospitalized patient not real pattern of tuberculosis in community. For better assessment of clinical profile of childhood tuberculosis, we need to include both in and out door patients.

Conclusion

1. The problem of tuberculosis in pediatric age group is like tip of iceberg.

2. CNS tuberculosis (70%) is the most common cause of admission in our setting in children up to five years.

3. In spite of the large set of various diagnostic aids, depending upon their availability, sensitivity, specificity and affordability, the clinical profile remains the corner stone for identification of the cases.

4. Hence it is recommended that all the patient coming with fever, not gaining weight, anorexia and with no obvious diagnosis should not be given therapeutic trials and tuberculosis should be considered as an important differential. All such cases should be referred to DOTS centre and should be properly investigated to break the rise of this neglected epidemic.

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