Original Research Article

Evaluation of the clinico-radiological profile and its therapeutic implications in childhood tuberculosis: a prospective study

Vinod Kumar Mishra[1], Shobha Kant Chaudhary[2], Tushar Kumar[3*]

[1]Associate Professor, Department of Paediatrics, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

[2]Associate Professor, Department of Paediatrics, Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

[3]M.D. (Radiodiagnosis), Fellowship (contd) in Vascular and Interventional Radiology, Manipal Hospital, Banglore, Karnataka,India

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Abstract

Aim: to evaluate the clinico-radiological profile in childhood tuberculosis related to its diagnostic, prognostic and therapeutic implications at tertiary health care centre. **Material and methods:** This was a prospective study was done in the Department of Paediatric, Vardhman Institute of Medical Science (VIMS) Pawapuri, Nalanda, Bihar, India for 14 months. Total 100 children's with age up to 5yrs and suspected diagnosis of tuberculosis were included in this study. 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. Especial emphasis was given to check for BCG scar mark. Laboratory investigations were done for all the children. **Results:** Out of 100 cases 32 patients (32%) were in 4-5 year of age group followed by 30(30%) in 2-3 yeas age group, 18(18%) in 1-2 yrs, 16 (16) in 3-4 yrs and only 4 (4%) belong to 0-1 year age group. Male to female ratio was 1.8:1 with 65% male and 35% female. CNS tuberculosis is commonest type (67%), followed by intra-thoracic (18%), disseminated (8) and abdominal (6%). Only one case of lymph node tuberculosis. Most of the patients (60%) have grade III and grade IV malnutrition. Majority of malnourished patients belong to 2-3 years and 4-5 years of age group. 52% patients also having history of contact with Tuberculosis and 24% have h/o Measles. lymph node TB and disseminated TB, h/o contact is positive in 100% cases, where in CNS TB only 50.75% patients having h/o contact. Total only 52% patients, having positive contact history. There is another important interference from this table that in 50% children BCG scar was not present. **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

Introduction

An estimated one million children were diagnosed with tuberculosis (TB) in 2016, according to World Health Organization (WHO) data.[1] In the European WHO region, the European Centre for Disease Prevention and Control (ECDC) estimated that Spain, the United Kingdom, Romania, and France contributed 62% of pediatric TB cases occurring in the European Union/European Economic Area countries.[2] However, the true global incidence and prevalence of childhood TB remains uncertain due to lack of microbiological confirmation of active TB in the majority of children.[3] Children typically have a paucibacillary disease, which hinders the detection of Mycobacterium tuberculosis in biological samples. Also, respiratory specimens (i.e., sputum) are difficult to obtain in young children and, consequently most children with active TB worldwide are started on treatment based solely on clinical history, clinical symptoms, and radiological signs.[4] Microscopic examination of sputum smears is the key to diagnosis in most countries, but its usefulness is limited in young children with paucibacillary disease who are also unable to expectorate.[4] Children in whom M. tuberculosis infection is detected, young children and those with recent exposure are at increased risk for progression to disease.[4] Knowledge of the child's status regarding exposure intensity to the index case modifies the pre-test probability of disease and the positive predictive value of subsequent investigations.[4] In fact, children under two account for the major part of the elevated morbidity and mortality associated with TB.[5] Moreover, the diversity of the clinical presentation in infants and young children and the non-specific nature of most signs and symptoms complicate TB diagnosis at this age. Constitutional symptoms often include failure to thrive and reduced playfulness.[4] Non-specific clinical manifestations, particularly in meningeal forms, further complicate early recognition of the disease in these infants.[6,7] Finally, the recognition of cellular immune response against M. tuberculosis is based on two main tests, the tuberculin skin test (TST) and the interferon-γ release assays (IGRAs). However, these tests fail to differentiate M. tuberculosis infection from active disease, and their sensitivity is lower in this age group than in older children, making it more difficult to establish diagnosis of infection.[4] The contribution of all these factors leads to delay in diagnosis that can be crucial for the patient's clinical outcome and complication occurrence.[6,7] Literature is scarce on treatment outcome, complications and sequelae occurring in TB diagnosed in children under two. Wiseman

**Correspondence*

Dr. Tushar Kumar

M.D. (Radiodiagnosis), Fellowship (contd) in Vascular and Interventional Radiology, Manipal Hospital, Banglore, Karnataka, India.

E-mail: tusharkumar.1191@gmail.com

et al.[6] described complications as any infiltration or compression of anatomical structures adjacent to the affected site (i.e., neurologic, vascular, bronchial, cardiac, and bone complications), with the potential to cause a functional deficit.

Material and methods

This was a prospective study was done in the Department of Paediatric, Vardhman Institute of Medical Science (VIMS) Pawapuri, Nalanda, Bihar, India for 14 months. Total 100 children's with age up to 5yrs and suspected diagnosis of tuberculosis were included in this study. Children of more than 5 yrs and with doubtful diagnosis were excluded from the study.

Methodology

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. 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.

Investigations

Laboratory investigations were done for all the children such as 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 and CT scan in all the suspected case of CNS tuberculosis except for those who were non affording.

Results

Total 100 cases with diagnosis of tuberculosis were included in this study. All children included in this study were of age up to 5 yrs.

Table 1: Age and site of involvement in Patients

Age groups	Systems						
	Intra- Thoracic	CNS	Abdo- Minal	Lymph Node	Dissemina ted	Total	%
0-1 yrs	2	2	0	0	0	4	4
1-2 yrs	3	13	0	0	2	18	18
2-3 yrs	4	24	0	0	2	30	30
3-4 yrs	6	10	0	0	0	16	16
4-5 yrs	3	18	6	1	4	32	32
Total	18	67	6	1	8	100	100
%	18	67	6	1	8	100	100

Table 1 shows that 32 patients (32%) were in 4-5 year of age group followed by 30(30%) in 2-3 yeas age group, 18(18%) in 1-2 yrs, 16 (16) in 3-4 yrs and only 4 (4%) belong to 0-1 year age group. Male to female ratio was 1.8:1 with 65% male and 35% female. CNS tuberculosis is commonest type (67%), followed by intra-thoracic (18%), disseminated (8) and abdominal (6%). Only one case of lymph node tuberculosis. CNS tuberculosis was common in younger age group that is in 1-3 year age group, this difference was statically significant.

Table 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	4	1	4	2
1-2 yr	18	0	9	13
2-3 yr	30	6	15	20
3-4 yr	16	3	10	9
4-5 yr	32	14	14	16
Total	100	24	52	60
%		24	52	60

Table.2 shows that most of the patients (60%) have grade III and grade IV malnutrition. Majority of malnourished patients belong to 2-3 years and 4-5 years of age group. 52% patients also having history of contact with Tuberculosis and 24% have h/o Measles.

Table 3: Distribution of cases showing H/O contact, BCG status and positive Montoux test in different type of Tuberculosis

Type of disease	No .of cases	Positive H/o contact (%)	BCG Scar Status (Absent) (%)	Mantoux Test Positivity (%)
Intra thoracic TB	18	9	8	7
CNS TB	67	34	33	25
Abdominal TB	6	00	2	6
Lymphatic TB	1	1	00	0
Disseminated TB	8	8	7	2
Total	100	52	50	40

Table 3 shows that in lymph node TB and disseminated TB, h/o contact is positive in 100% cases, where in CNS TB only 50.75% patients having h/o contact. Total only 52% patients, having positive contact history. There is another important interference from this table that in 50% children BCG scar was not present. Only 40% patients showed positive reaction to tubercular antigen.

Table 4: Presenting symptoms in different type of Tuberculosis

Symptoms	Type of Tuberculosis					
	INTRA-THORACIC	CNS	ABDO-MINAL	LYMPH-NODE	DISSEMI NATED	TOTAL
	(18)	(67)	(6)	(01)	(8)	(100)
Fever	18(100%)	65 (97.01%)	04(66.67%)	00	8(100%)	95(95%)
Cough	16 (88.89%)	14(20.89%)	2(33.33%)	00	4(500%)	36 (36%)
Not gaining wt	5(27.78%)	8 (11.94%)	2(33.33%)	00	2 (25%)	17 (17%)
Anorexia	9 (50%)	45(67.16%)	6(100%)	00	6 (75%)	66 (66%)
Altered sensorium	01 (5.56%)	43 (64.18%)	00 (00%)	00	4(50%)	48 (48%)
Seizures	00 (00%)	49 (73.13%)	00 (00%)	00	4 (50%)	53 (53%)

Table 04 shows that fever (95%) was the most common presenting symptom followed by anorexia in 66% cases. Fever (97.01%), altered sensorium (64.18%), anorexia (67.16) and seizures (73.13%) were the presenting feature in CNS TB.

Table 5: Radiological Evidence of Tuberculosis

X-Ray (n=100)				CT Scan (n=50)		
Type of disease	No. of Cases	Positive Findings	%	Findings	No of Cases	%
Intra thoracic TB	18	18	100	Ventricular Dilatation	40	80
CNS TB	67	47	70.15	Basal Exudate	36	72
Abdominal TB	6	00	00	Tuberculoma (Rin g Lesion)	8	16
Lymphatic TB	1	01	100	Infarct (Hyperdence)	12	24
Disseminated TB	8	5	62.5	Normal	8	16
Total	100	71	71			

Table 5 shows that positive radiological findings were present in 71% cases. Intra-thoracic TB having 100% positivity whereas CNS TB have 70.15% positivity. CT scan was done in 50 patients. 80% patients have ventricular dilatation and 72% patients have basal exudates. CT scan was normal in 16% 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.[8]

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.[9] 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.[10] 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.

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 78% cases were found in age group between 2-5 years. Bai SS & Devi RL[11] and V. Seth et al.[12] 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.[13] also showed similar result in their study. Male to female ratio in the present study was 1.8:1 was close to study of Bai SS & Devi RL with ratio of 1.5:1.[11]

In our study CNS form of tuberculosis was most common, (67%), followed by intra-thoracic (18%), disseminated (8) and abdominal (6%). Only one case of lymph node tuberculosis.Many studies have reported increasing trend in extra pulmonary tuberculosis in children.[14,15] V. Seth[12] 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[13] who also studied the tuberculosis in under six years of age. Lower incidence of CNS TB i.e. 26.5% in V. Seth[12] 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.

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 52% cases.

P. Chandra[16] & V. Seth[12] 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[17,18]. 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 24% had suffered from measles in recent past. A recent article by Kristensen et al.[19] 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[20] 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 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[21] in less than 5 years, Seth V [12] 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 50% 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 .[22]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.[23] 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 40%. 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.[16] 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.[24] Another method of tuberculin skin test, known as the "Tine Tuberculin Skin Test" (multipuncture percutaneous), demonstrated a higher positive test rate than the Mantoux.[25]

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. 95% in contrast to V. Seth study and Bai SS et al who found fever in only 28.6 % & % respectively.[11] Anorexia (66%), cough (36%) and not gaining weight (17%) are other non- specific symptoms, but seizures (73.13%) and altered mental status (64.18%) 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.[26]

It is well known that diagnosis of childhood tuberculosis is very difficult.[27] 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.[22]A high proportion (100%) of chest radiographs were interpreted as positive for patients diagnosed as Pulmonary TB. Overall chest radiograph are positive in 71% 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 80% patients have ventricular dilation and 72% 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 lesions.[28] 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 patient with CNS tuberculosis should preferably be evaluated with radio-imaging, CECT either before or within 48 hours of treatment.[29]

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.

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