



CLINICAL SPECTRUM OF PEDIATRIC TUBERCULOSIS, EARLY DIAGNOSIS BY CLINICAL, RADIOLOGICAL, AND CBNAAT IN TERTIARY CARE HOSPITAL BIDAR

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ABSTRACT **Background:** Global TB report 2018 reports that in India, an estimated 2.2 lakh children become ill with tuberculosis (TB) each year. In spite of new rapid diagnostic methods, lack of gold standard test for confirming childhood tuberculosis remains an obstacle for the effective reporting of childhood TB and hence these cases often remain under diagnosed. The main objective was to study the clinical profile of childhood tuberculosis with relevant laboratory investigations aiding in early diagnosis. **Methods:** A prospective observational hospital-based study was conducted. From (October 2019 –October 2021). Children less than 18 years of age with tuberculosis were included in the study. Demographic details, presenting symptoms, family history of TB contact, nutritional status and clinical examination findings were documented. Complete blood count, ESR, Mantoux test, chest X-ray and sputum analyses for AFB were done for all patients. Either sputum or resting gastric juice was taken for detecting acid fast bacilli and CBNAAT in relevant patients. **Results:** Out of the total 54 children studied, the most common age of presentation of tuberculosis was >10 years of age (n=28, (51.3%) There was a male preponderance (n=29 (53.3%) The predominant type of diagnosis was pulmonary tuberculosis in 24 (44.4%) patients, followed by extra pulmonary in 30(55.5) and disseminated type was noticed in 1 (1.85%) Among the 30 cases with extra pulmonary TB, pleural TB (n=12, 40%) was the most common manifestation. followed by Central nervous system (n=10, 33.3%), lymph node TB (n=4,.) Overall, fever (n=50, 60.5%) were the predominant symptoms noted followed by cough (n=53, 42.7%). Whereas, lymph node swelling in 4 patients was the predominant symptom in extra pulmonary form of tuberculosis patients the Mantoux screening test was reactive in 22 (40.7%) patients and two-thirds of the undernourished children were Mantoux positive Chest radiograph findings suggestive of tuberculosis were noted in 93.25% pulmonary tuberculosis patients, out of 54 cases in TB group x-pert MTB show positive result in 10 cases the sensitivity of X-pert was 18.8% compared to clinical diagnosis of TB and Specificity was 81.25%. **Conclusions:** Diagnosis of TB in children is often challenging this study reinforces that the diagnosis of childhood tuberculosis is based on the constellation of symptom evaluation, contact history, clinical examination, with relevant laboratory investigations. Although more rapid and sensitive laboratory testing, in molecular biology, immunology, and chromatography is being developed, although a negative CBNAAT does not rule out TB, Hence This study supports that detailed history, clinical evaluation and active investigative workup has a major role in diagnosing childhood tuberculosis.

KEYWORDS : Children, Clinical profile, Tuberculosis, CBNAAT

INTRODUCTION:

Tuberculosis is one of the most widespread infections and affects almost one-third of the world's population. It is the first infectious disease to be declared a global health emergency.¹ Global TB report 2018 reports that in India, an estimated 2.2 lakh children become ill with tuberculosis (TB) each year (22% of global TB burden), with a slightly higher burden among males.¹ Pulmonary TB is the most common form in children but the extra-pulmonary TB forms a larger proportion of cases than in adults. It is also known that about 10% of the cases reported to RNTCP are from children under 14 years of age.

In children with presumptive pediatric TB, every attempt must be made to microbiologically prove diagnosis through examination of appropriate respiratory/non-respiratory specimens with quality assured diagnostic tests. The program is usually the adult oriented and hence the diagnostic strategies of the children and adults antithesis to each other i.e. smear to radiology Vs radiology to smear. Lack of standard definitions, absence of simple/reliable diagnostic test and more extra pulmonary TB cases add to lack of data on pediatric TB. There is also gross under estimation of magnitude of problem².

The major challenge of childhood Tuberculosis is establishing an accurate and early diagnosis, as children are rarely smear positive.³ 95% of cases in children less than 12 years are smear negative Smear positive cases in <14 years accounted 0.6 to 3.6% of reported cases.³ Collecting an adequate sample for microbiological diagnosis also presents a significant challenge particularly for small children who cannot provide a good sputum specimen.³ Early diagnosis and successful treatment is the most effective means to protect children from infection with tuberculosis.

Cartridge based nucleic acid amplification test (CB NAAT - Gene X-pert) is a new test for tuberculosis. It uses real time polymerase chain reaction to detect mycobacterium tuberculosis and rifampicin resistance in samples in only 2 hours.⁴ The gene x-pert integrates sample processing, nucleic acid amplification and detection of target sequence. The reactions take place in a single use cartridge. The PCR target, an 81 base pair region of rpoB gene, contains a signature sequence for

identification of tuberculosis and involves the locus where majority of mutations associated with rifampicin resistance occur.⁵ It has high sensitivity and specificity, also easy and safe to perform.¹¹

OBJECTIVES:

1. To study the clinical spectrum and disease burden of pediatric Tuberculosis in bidar
2. Early diagnosis by clinical manifestation, radiological and special emphasis of sensitivity of CB-NAAT.

MATERIALS AND METHODS

Source of Data: Bidar institute of medical sciences,

Study Design: Prospective Observational Study.

Study period: 1 year July 2022-september -2023

Sample size: 54

Method of Collection of Data (Including Sampling Procedures if any)

Informed Consent will be taken from parents of all children included in the study. Children between the age group of 6 months to 18 years admitted with presumptive tuberculosis as per criteria of Pediatric Revised National Tuberculosis Control Program 2019, shall form the study group. These children's detailed history and examination findings are recorded in a predefined, structured, standard Performa. Children less than 18 years of age with tuberculosis were included in the study. Demographic details, presenting symptoms, family history of TB contact, nutritional status and clinical examination findings were documented. Complete blood count, ESR, Mantoux test, chest X-ray and sputum analyses for AFB were done for all patients. Either sputum or resting gastric juice was taken for detecting acid fast bacilli in relevant patients for CBNAAT.

Inclusion Criteria:

Children between the age group of 6 months to 18 years admitted with symptoms suggestive of presumptive tuberculosis (pulmonary and / extra pulmonary) as per criteria of Revised National Tuberculosis Control program guidelines 2019.

Exclusion Criteria:

Children who are presently on anti tubercular therapy and who have received the same in the past.

RESULTS

A total of 54 children, diagnosed with tuberculosis in our hospital during the study period of 2 years and satisfying the inclusion and exclusion criteria were recruited for the study. Among the study population, children between 1-5 years of age 13(24.15%), between 6-10 years were 13(24.1%) and more than 10 years were 28 (51.6%). There were an increased number of childhood tuberculosis patients in more than 10 years of age. The total number of males were 29 (53.73%) and females were 25 (46.29) male preponderance was seen in all age groups (Table1)

Table 1: Socio Demographic Profile Of TB Cases In Study

Demographic profile	Frequency	Percent
Sex		
male	29	53.7
Female	25	46.4
Age group(years)		
1-5	13	24.1
6-10	13	24.1
11-15	17	31.5
16-18	11	20.4
Economic class		
Lower class	14	25.9
Lower middle	15	27.8
Upper class	3	5.6
Upper lower	12	22.2
Upper middle	10	18.5
Contact history		
Present	28	51.9
Absent	26	48.1
BCG vaccination status		
Present	49	90.7

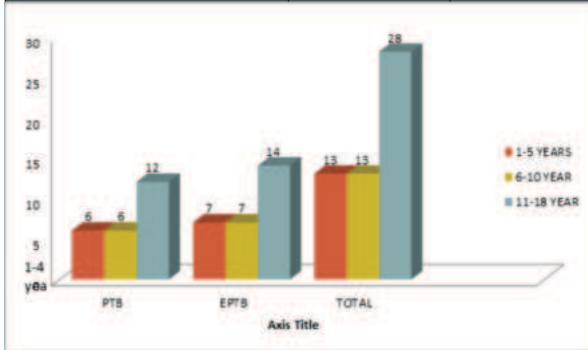


Figure 1: Age wise distribution of PTB and EPTB cases in the study

The predominant type of diagnosis was pulmonary tuberculosis in 24 (44.4%) patients, followed by extra pulmonary in 30(55.5) and disseminated type was noticed in 1 (1.85%) Among the 30 cases with extra pulmonary TB, pleural TB (n=12, 40%) was the most common manifestation. Central nervous system (n=10, 33.3%), lymph node TB (n=4, 13.3%) and abdominal TB (n=4 7.4%).

Table 2: Distribution Of Different Forms Of TB In The Study

Pediatric tuberculosis	Frequency	Percent
Pulmonary TB	24	44.4
Pleural TB	12	22.2
TB meningitis	10	18.5
Lymph node TB	4	7.4
Abdominal TB	4	7.4
Disseminated TB	1	1.9

Overall, fever (n=50, 60.5%) were the predominant symptoms noted followed by cough (n=53, 42.7%). Whereas, lymph node swelling in 4 patients was the predominant symptom in extra pulmonary form of tuberculosis patients. There were an increased number of undernourished patients in pulmonary, BCG scar was seen in the majority of patients,47 patients), extra There were 4 HIV positive patients (7.4%), belonging to the pulmonary group. Around 20 (37%) pulmonary tuberculosis patients had a positive contact history with

known tuberculosis patients. Patients diagnosed with extra pulmonary TB (n=6, 40.6%) and disseminated type (n=1, 20%) had a positive contact history.

Erythrocyte sedimentation rate (ESR) was done in all the patients in the study.

High ESR (>20mm) was noted in 13 (24.07%) patients in pulmonary group and 4 (7.40%) patients in extra pulmonary group.

Table 3: Clinical Signs And Symptoms Of TB Cases

Signs and symptoms	Frequency	Percent
Fever	52	96.29
Cough	15	27.7
Loss of appetite and weight	52	96.3
Lymphadenopathy	18	33.3
Convulsions	8	14.8
Pain abdomen	3	5.55
Diarrhea	2	3.7
Right hemiplegia	1	1.9
Chest pain	2	3.7
Breathlessness	18	33.3

Overall, the Mantoux screening test was reactive in 22 (40.7%) patients and two-thirds of the undernourished children were Mantoux positive.

Either sputum or resting gastric juice was taken for detecting acid fast bacilli in relevant patients, AFB was positive in 4 (7.40.5%) patients in pulmonary group and 1 (1.9%) among disseminated TB patients

Table 4: Distribution Of Investigations (high ESR, Mantoux Positivity, AFB Smear Positivity, Positive Radiological Findings And CBNAAT In Pediatric TB In Study

Tests	Frequency	Percent
ESR High	7	13
ESR Normal	47	47
Montoux positive	22	40.7%
Montoux Negative	32	59.2%
AFB smear positive	5	9.25%
AFB smear Negative	37	68%
AFB smear Not done	12	22.2%
Radiological findings Suggestive of TB CXR	26	48.1%
CBNAAT Positive	10	18.51%
CBNAAT Negative	44	81.48%
HIV Positive	4	16.6%
HIV Negative	20	
HIV Not done	30	

Chest radiograph findings suggestive of tuberculosis were noted in 93.25% pulmonary tuberculosis patients and all the disseminated tuberculosis patients Non- homogenous opacities (patchy infiltrations) in lung fields were the most common.

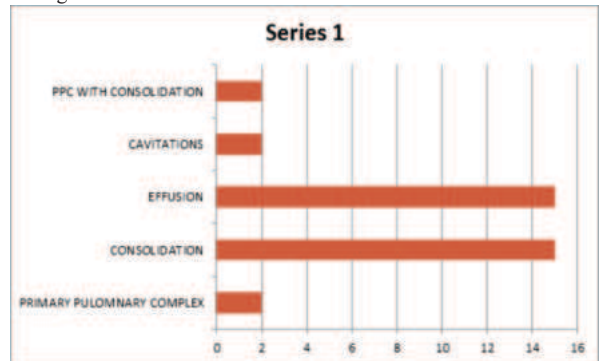


Figure 2: Radiological Findings Of Chest X-ray Of Positive Cases In Study Out of 54 cases in TB group x-pert MTB show positive result in 10 cases.

The sensitivity of X-pert was 18.8% compared to clinical diagnosis of TB. Specificity was 81.25%

The diagnostic significance of CBNAAT in various TB has been given in table 5

Table 5: Diagnostic Significance Of CBNAAT In Various Types Of TB

Type of TB	CBNAAT		Total
	Positive	Negative	
Pulmonary TB	7 (70%)	17(38.6%)	24(44.4%)
TB meningitis	0 (0%)	10(22.7%)	10(18.5%)
Pleural TB	2 (20%)	10(22.7%)	12(22.7%)
Abdominal TB	1 (10%)	3(6.7%)	4(5.6%)
Lymph node TB	0		4(7.4%)

DISCUSSION

There was a higher prevalence of tuberculosis in >10 years age group than younger kids in present study. This may be due to the inclusion of children till 18 years of age. This finding was similar to the study conducted on childhood tuberculosis by Shrestha S et al, in NepaL²

Pulmonary tuberculosis was the most common form of tuberculosis in present study than extra pulmonary and disseminated TB. This was the similar finding in a study conducted by Goyal A et al⁶, on childhood tuberculosis, pleural TB, CNS TB were the predominant manifestation among extra pulmonary forms of tuberculosis in present study.

Cough and sputum production are the most common symptoms noticed in pulmonary tuberculosis patients followed by fever. Pama CP et al⁷, in their study of tuberculosis, found that the frequent symptoms were fever (86.6%), cough (76.1%), malnutrition (52.3%), weight loss (50.7%), anorexia (44.8%), breathing difficulty 18%) and convulsions (8%).

Lymph node swelling (33%) was the predominant symptom in extra pulmonary form of tuberculosis patients.

About 65.5% of pulmonary TB children were undernourished in present study.

Swaminathan S et al, documented 62% of TB patients with grade III and IV malnutrition in their study³ Majority of patients had BCG scar in present study (87%).

Mantoux reactivity was noted in (33.3%) children with pulmonary TB (30.7%) , 75% of extra pulmonary TB, Sreeramareddy CT et al⁸, in their study on tuberculosis had a Mantoux positivity of 66% in pulmonary group with higher Mantoux positivity of 71% in extra pulmonary form of tuberculosis⁸

Most common chest X ray finding was pleural effusion in 15 cases (57%) consolidation in 11 (42%) followed by non specific finding Consolidation finding(4), Hazy densities (6). Cavitation (2)

Microbiological confirmation is the gold standard for the diagnosis of TB. It also helps identify drug-resistant TB Microbiological confirmation is not always possible in children due to the pauci bacillary nature of pediatric TB¹ and difficulty in acquiring the sample. However, we were able to make microbiological confirmation by Gene X-pert in our study was positive in 10 cases (18.5%) , 7 were of PTB patients(70%) compared to (30%) of patients of EPTB. Only one PTB patient was found to be rifampicin resistant in our study; the culture and sensitivity detected resistance to both isoniazid and rifampicin. the development of nucleic acid amplification tests (NAATs) holds promise. However, although several studies on diagnostic accuracy of (commercial) NAATs in adults were published with considerably heterogeneous, very few data are available on children¹¹

In December 2010, the X-pert MTB/RIF assay the X-pert was evaluated in clinical trials in adults, and most recently also in children with suspected tuberculosis, and showed good sensitivity and specificity in smear-positive and culture-positive and reasonable accuracy in smear-negative but culture-positive sputum samples¹³.

Looking at these data, as well as the excellent technical characteristics, in our study the sensitivity of CBNAAT was being 18.8%, and specificity being 81.25% with CI (63.56-92.79).

The assay might be considered a promising diagnostic test in childhood tuberculosis that is simple enough to be used outside central laboratories.

Smear positive cases in present study was 9.3% with both pulmonary tuberculosis and in cases of TB lymphadenitis histopathological specimen was positive for Zn staining.

CONCLUSION

Diagnosis of TB in children is often challenging this study reinforces that the diagnosis of childhood tuberculosis is based on the constellation of symptom evaluation, contact history, clinical examination, with relevant laboratory investigations. Although more rapid and sensitive laboratory testing, in molecular biology, immunology, and chromatography is being developed, Although a negative CBNAAT does not rule out TB, Hence This study supports that detailed history, clinical evaluation and active investigative workup has a major role in diagnosing childhood tuberculosis.

REFERENCES

- Anuradha G et al. Clinical profile of children with tuberculosis from a semi urban referral centre in South India: a prospective observational study. Int J Contemp Pediatr. 2019 Jul;6(4):1450-1455.
- Shrestha S et al. Clinical profile of tuberculosis in children, Nepal Med Coll J 2011; 13(2): 119-122.
- Ashok G et al Clinical Profile of Pediatric Tuberculosis and MGIT sensitivity: A Prospective Study from a Tertiary care Institute. JMSCR 2017 May;5(05).
- Andrea Rachow, Petra Clowes, Elmar Saathoff, Bariki Mtafya, Epiphania Michael, Elias Ntinginya, Dickens Kowour et al. Increased and expedited case detection by Xpert MTB/RIF assay in childhood tuberculosis: a prospective cohort study. Clinical Infectious Diseases 2012;54(10):1388-96.
- Kalpana N, et al. Clinical Profile of Paediatric Cases with Tuberculosis. IOSR-JDMS, 2017 Sept;16(Issue 9) Ver. XI: 06-08.
- Goyal A, Shah I, Patankar N, Chilkar S. Clinical profile of children with pulmonary Tuberculosis. Clinic Epidemiol Global Health. 2014;2(1):24-7.
- Pama CP, Gatchalian SR. Clinical profile of culture proven tuberculosis cases among Filipino children aged 3 months to 18 years. PIDSP. 2002;5(1):13-23.
- Sreeramareddy CT, Ramakrishnareddy N, Shah RK, Banिया R, Swain PK. Clinico-epidemiological profile and diagnostic procedures of pediatric tuberculosis in a tertiary care hospital of western Nepal-a case-series analysis. BMC Pediatr. 2010;10:57.
- Gosai DK, et al. Study of clinical profile of childhood extra pulmonary tuberculosis Int J Res Med Sci. 2014 May;2(2):501-505.
- A Parthasarathy, Piyush Gupta, MKC Nair, Rohitagarwal, IAP Textbook Of Pediatrics, 5th edition, Tuberculosis in children, pulmonary tuberculosis; 2013.p. 263.
- Vimlesh Seth, SK Kabra, Essentials Of Tuberculosis In Children, 3rd edition, 2006, Global epidemiology of pediatric tuberculosis. Pulmonary tuberculosis; 2006 .p.117..p.12.13.
- Kliegman, Stanton, St Geme, Schor, Nelson Textbook Of Pediatrics, 20th edition, Vol.2, Tuberculosis; .p.1445.
- RNTCP Updated Pediatric TB Guidelines 2019 Bates M, O'Grady J, Maeurer M, Tembo J, Chilukutu L, Chabala C, et al. Assessment of the Xpert MTB/RIF assay for diagnosis of tuberculosis with gastric lavage aspirates in children in sub-Saharan Africa: a prospective descriptive study. Lancet Infect Dis 2013;13(1):36-42. Tenali R et al. Risk factors, clinico-epidemiological profile of tuberculosis among children attending a tertiary care hospital Int J Contemp Pediatr. 2018 May;5(3):851-856. Zar HJ, Workman L, Isaacs W, Dheda K, Zemanay W, Nicol MP. Rapid diagnosis of pulmonary tuberculosis in African children in a primary care setting by use of Xpert MTB/RIF on respiratory specimens: a prospective study. Lancet Global Health. 2013;1(2):e97-104.