Original Research Article

Clinical profile of childhood tuberculosis and diagnostic efficacy of CBNAAT in tertiary care hospital

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Abstract

Background: Tuberculosis is the major problem of public health with high morbidity and mortality, a continuing scourge of India. The DOTS strategy of the national program targeted on identifying and treating smear +ve cases, which focus on infectious cases and preventing the transmission. Thus the children are ignored as a hidden epidemic since smear-positive cases are focused on diagnosis which is much less in children when compared to adults, thus the prevalence and morbidity of disease in children is not available mainly from developed countries.
Aim and objective: To study the clinical profile of childhood tuberculosis, to compare the efficacy of CBNAAT as a diagnosis tool between pulmonary and extrapulmonary TB.
Materials and methods: In the prospective study, in the Department of Pediatrics and Chest Medicine in our tertiary care hospital, Salem in the year 2018 January to December. Informed consent was obtained from parents and caregivers before including the children in the study. There was no risk to the children due to the study. A data collection sheet (proforma) was filled for each child based on the inclusion criteria that were suspected presumptive TB after obtaining informed consent.
Results: Among 100 samples collected, 69 children had extrapulmonary symptoms and signs; when compared to 31 had pulmonary symptoms and signs. Among 31 presumptive TB cases, the gold standard microbiologically confirmed TB was 2 as compared to 6 cases which were detected by CBNAAT results that were not detected by sputum examination. This was found to be statistically significant (P=0.017). Thus CBNAAT increases the detection rate of pulmonary TB thrice. Thus Sensitivity of the CBNAAT was 94%, Specificity was 86.67, PPV 33.33, NPV 95.12; Accuracy

73.33. This was highly significant at p<0.1. Among 100 presumptive TB cases, CBNAAT was positive in 10, it also detects cases that were negative by conventional laboratory methods.
Conclusion: When compared to the efficacy of CBNAAT with gold standard microbiological confirmation, CBNAAT detects thrice the caseload in pulmonary TB in the community. Thereby increasing the case detection rate and preventing the complication. In the case of extrapulmonary TB, CBNAAT detects 30% of pathologically confirmed TB lymphadenitis and 33% CNS TB among pediatric TB.

Key words

Tuberculosis, CBNAAT, Efficacy.

Introduction

Tuberculosis is the major problem of public health with high morbidity and mortality, the continuing scourge of India. The DOTS strategy of the national program targeted on identifying and treating smear +ve cases which focus on infectious cases and preventing the transmission. Thus the children are ignored as a hidden epidemic since smear-positive cases are focused on diagnosis which is much less in children when compared to adults, thus the prevalence and morbidity of disease in children is not available mainly from developed countries [1]. In industrialized countries Migration plays an important role in the increase in the incidence of TB and whereas HIV leads to the TB epidemic in developing countries like India because of poor resource availability [2]. Thus through national surveillance, only a few childhood TB are identified, most of them are missed and presenting with complications thereby leading to a massive rise in morbidity. TB within the community represents a sentinel marker for active transmission. Mycobacterium tuberculosis is the most common organism causing tuberculosis to a lesser extent by *M. africanum* and *M. bovis.* The mode of transmission is mostly from smear-positive adults. Smear -positivity is rare in Children, hence transmission from them is rare although community outbreaks can occur. Children's mostly develop extrapulmonary TB compared to pulmonary TB. They may also present as a disseminated disease more as compared to adults [3]. These represent immaturity in immune systems in children. The risk factors for developing the disease in children include malnutrition, immune suppression like measles or HIV, younger age. The incubation time is from one to six months [4]. Children who were infected and do not develop disease become a source of future adult TB case. The incubation time varies between 1-6 months. About 95 percent of children <12 years with TB are smear-negative, due to gastric aspirates low specificity; positive smear only in 20% cases and on culture in 50 % These features leads to under diagnosis of TB in children [5]. Correct cases load cannot be obtained since outside diagnosed cases are not reported. After exposure Ghon focus that is primary parenchymal lesion involvement of lung with local spread to lymph nodes, which is due to cell-mediated immunity occurs [6].

Materials and methods

In the prospective study in the Department of Pediatrics and Chest Medicine in our tertiary care hospital, Salem in the year 2018 January to December. Informed consent was obtained from parents and caregivers before including the children in the study. There was no risk to the children due to the study. A data collection sheet (proforma) was filled for each child based on the inclusion criteria that were suspected presumptive TB after obtaining informed consent.

Inclusion criteria

Children with age group less than 12 years attending the OPD in our GH with the following symptoms: Fever for more than 2 weeks, Cough more than 2 weeks, Loss of weight more than 5%

within 3 months, Swelling over the neck, Seizures, or altered level of consciousness.

Exclusion criteria

Age group for more than 12 years, Children age less than 12 years who are on ATT, Children on ART, Not giving consent for the study, Not giving consent for HIV screening.

A detailed history and physical examination were performed on each child with features of presumptive TB. Weight for age was taken to assess the nutritional status with malnutrition defined as weight for age for ≤ 2 SD. After consent, blood was drawn for HIV screening for children <18 months (considered as positive if two separate HIV ELISA tests or HIV DNA PCR were positive). Contact history with a newly diagnosed case of TB disease within the last 2 years was also used to define a suspect TB. A standard tuberculin skin test (TST) using 2 TU in 0.1mL was given, during the initial visit and read at 48–72 hours. Results were said to be positive children if induration in a TST ≥ 10 mm. Resting gastric aspirates of 3 sample on 3 consecutive days were taken by placing a nasogastric tube in situ after 10 pm and gastric juices were aspirated before the peristalsis begins in the morning, that is before the child gets up from the bed. RGJ samples were sent for the CBNAAT study. Other clinical samples like lymph nodes, cerebrospinal fluid (CSF), pleural fluid, etc. were obtained and send for CBNAAT. Chest radiographs were performed on each child with features of pulmonary symptoms. Computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US) were done when indicated.

Results

Around 100 children, suspected tuberculosis children were included in the study. Samples were collected from children after obtaining their parent's or guardian's consent. Specimens included gastric aspirates, induced sputum, sputum, lymph node aspirates, and CSF. All the specimens processed; results were obtained.

A total of 21 samples was collected from children age <5 years and 5 children (27.8%) were found to be positive for tuberculosis. Among the children in the 6-10 years group (n=54), 10 children were positive (55.6%). Among the group (above 10 years), about 25 samples were collected; 3 children turned out to be positive (16.7%) for tuberculosis. The male to female ratio of the children participated in our study was 1:1.2. A total of 45 samples were collected from male children, out of which 11 tested positive (24%), and about 55 samples were collected from female children, out of which, 7 tested positive (14%) for tuberculosis. In gender-wise scrutiny; on the application of the Chi-Square test, the difference in detection rates among male and female children was not found to be statistically significant (P=0.129) as per **Table – 1**.

Among 100 samples collected, 69 children had extrapulmonary symptoms and signs; when compared to 31 had pulmonary symptoms and signs (**Table – 2**).

Among 31 presumptive TB cases, the gold standard microbiologically confirmed TB was 2 as compared to 6 cases which were detected by CBNAAT results that were not detected by sputum examination. This was found to be statistically significant (P=0.017). Among 69 presumptive extrapulmonary TB, TB lymphadenitis positive were 11, of which CBNAAT detected in 3 cases and CNS TB was found to be positive in 3; CBNAAT detected 1 positives. This was found to be statistically significant (P=0.005) as per **Table – 3**.

Sensitivity of the CBNAAT was 94%, Specificity was 86.67, PPV 33.33, NPV 95.12; Accuracy 73.33. This was highly significant at p<0.1. Among 100 presumptive TB cases, CBNAAT was positive in 10, it also detected cases that were negative by conventional laboratory methods (**Table – 4**).

Table – 1: Age wise distribution and association with positive results.

Age	Lab results		Total
	Negative	Positive	
<5 years	16	5	21
6-10 years	44	10	54
>10 years	22	3	25
Total	82	18	100

Table – 2: Clinical profile of childhood tuberculosis.

Clinical profile	Frequency	Percent
Pulmonary TB	31	31.0
Extrapulmonary- CNS TB	24	24.0
Ex-pul/TB lymphadenitis	45	45.0
Total	100	100.0

Table – 3: Lab results versus CBNAAT results.

Lab results	CBNAAT results		Total
	Positive	Negative	
Positive	2	0	2
Negative	4	25	29
Total	6	25	31

Table – 4: CBNAAT results.

		CBNAAT results		Total
		A	B	
Lab Results	Positive	6	12	18
	Negative	4	78	82
Total		10	90	100

Discussion

Extrapulmonary TB contributes to about 70%, of which most common is TB lymphadenitis accounting for about 62% which is compared with 46% extrapulmonary TB Sanjay et al study done in Pune. This rise in part of extrathoracic TB in our study is likely to be due to children have been referred to our centers from various areas [7]. The usage of molecular testing is in add-on to the conventional laboratory methods; so that it increased mycobacterial confirmation mainly to pulmonary tuberculosis in children, in whom paucibacillary is the main drawback that has been identified by CBNAAT [8]. There are fewer details regarding the bacteriological confirmation in other pediatric studies; that explains the spectrum of TB disease [9]. Clinical skill is most important when compared to the accessibility of Xpert in high TB burden settings. The rapid turn time for the Xpert is a great advantage as compared to other conventional methods to achieve a definite diagnosis of TB. The overall detection rate in our study is 18% among 100 presumptive pediatric population. These fewer notification rates in developing countries are misleading. This is mainly due to the under-reporting of symptomatic children [10] due to low clinical suspicion and lack of techniques for the diagnosis. Age, a crucial factor in pediatric tuberculosis has contributed to the risk of transforming the infection to disease. Thus in preschool children (3-5 years), the risk is 5% and in primary school children (5-9 years), it falls to 2%. This risk again increases during early

adolescence (10-14 years) to 5% [11]. Pediatric tuberculosis, due to its paucibacillary nature and difficulty in sample collections makes the diagnosis difficult by these conventional methods. Culture, although the gold standard is not used routinely; due to delay in results. In our study, a comparison was made between the sensitivity and specificity of CBNAAT with conventional methods like acid-fast staining. The sensitivity of CBNAAT, acid-fast method, was found to be 94% and 33% respectively. The specificity of CBNAAT, acid-fast method, was found to be 90% and 84% respectively [12]. Researchers from various parts of the country reported sensitivities of CBNAAT to be 86%-100% and specificity to be 72%-99%. Thus CBNAAT can be recommended best investigation in diagnosing tuberculosis in the pediatric population, particularly in high prevalence countries like India [13]. In our study, CBNAAT has detected four positives TB cases (40%) more than the microscopy. This is similar to a study from Miller F, et al. reported that the detection rate was increased by 50% by using CBNAAT when compared to microscopy. This study explains the diagnostic performance of CBNAAT as compared with conventional methods to bring the burden of tuberculosis in children in the community [14]. The CBNAAT has a greater AUC (94) that is positive predictivity, which indicates that the test is of greater clinical utility. Hence, the CBNAAT which has increased sensitivity, specificity, and clinical utility may be used as an initial diagnostic test in the detection of pediatric tuberculosis [15].

Conclusion

Extrapulmonary TB is most common among childhood TB, of which most common is TB lymphadenitis accounting for 60%. When compared to the efficacy of CBNAAT with gold standard microbiological confirmation, CBNAAT detects thrice the caseload in pulmonary TB in the community. Thereby increasing the case detection rate and preventing the complication. In the case of extrapulmonary TB, CBNAAT detects 30% of pathologically confirmed TB lymphadenitis and 33% CNS TB among pediatric TB.

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