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Research Article

Tuberculosis

A cross sectional study of in-hospital cases of Pediatric Tuberculosis detected by CBNAAT at a tertiary care teaching hospital of Central India.

Pratap Singh M.[1], Kumar Sharma P.[2*], Upadhyay P.[3], Agrawal P.[4], Kumar Gupta D.[5], Verma V.[6], Mehta A.[7], Gupta R.[8]

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[1] Munindra Pratap Singh, Demonstrator, Department of Physiology, G.R. Medical College, Gwalior, Madhya Pradesh, India.

[2*] Pawan Kumar Sharma, Associate Professor, Department of Designated, Govt. Medical College, Datia, Madhya Pradesh, India.

[3] Pradeep Upadhyay, Child Specialist, Govt. Medical College Associated District Hospital, Datia, Madhya Pradesh, India.

[4] Puneet Agrawal, Senior Resident, Department of Pediatrics, Govt. Medical College, Datia, Madhya Pradesh, India.

[5] Dinesh Kumar Gupta, Child Specialist, Govt. Medical College associated District Hospital, Datia, Madhya Pradesh, India.

[6] Vishal Verma, District Tuberculosis Officer, Datia, Madhya Pradesh, India.

[7] Abhishek Mehta, Associate Professor, Department of Microbiology, Govt. Medical College, Datia, Madhya Pradesh, India.

[8] Rajesh Gupta, Professor, Department of Pediatrics, Govt. Medical College, Datia, Madhya Pradesh, India.

Background: Childhood tuberculosis is difficult in the identification of the organism due to improper sampling as well as low sensitivity of the smear. Newer diagnostic methods like Cartridge based nucleic acid amplification tests (CBNAAT) can rapidly identify Mycobacterium tuberculosis with improved sensitivity over the smear testing. **Material & Method:** This observational record based cross-sectional study was undertaken to identify the epidemiology of tubercular infection in children diagnosed with CBNAAT. The study was carried out by analyzing the data of children from six months to 18 years who were diagnosed with Tuberculosis and treated with anti-tuberculosis therapy (ATT) from April 2018 to March 2020. **Results:** Data of a total of 166 patients was analyzed. 42% of overall collected samples were reactive to CBNAAT testing for tuberculosis. 40 gastric aspirate samples were collected and only four (10%) turned reactive for tuberculosis by CBNAAT. None of the pediatric samples was positive for MDR TB. 66% of children completed treatment and 33% were declared cured. **Conclusion:** 42% positivity after CBNAAT testing for tuberculosis infection in collected samples of sputum and gastric aspirate where only 10% yield in GA samples.

Keywords: Pediatric TB, CBNAAT, Gastric aspirate, Sputum

Corresponding Author

Pawan Kumar Sharma, Associate Professor, Department of Designated, Govt. Medical College, Datia, Madhya Pradesh, India.
Email: drpksharma1984@gmail.com

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Introduction

Globally, an estimated 10.0 million people suffered from TB in 2019. There were an estimated 1.2 million TB deaths among HIV-negative people in 2019 and an additional 208000 deaths among HIV-positive people. Children aged <15 years constituted 12% of the total cases. WHO End TB Strategy suggests an 80% reduction in the TB incidence rate and a 90% reduction in the annual number of TB deaths by 2030. [1]

Childhood tuberculosis mostly left unnoticed as there is difficulty in identification of the organism due to improper sampling as well as low sensitivity of the smear. This leads to difficulty in the detection of cases. [2]

In clinical practice, the diagnosis of Pediatric TB requires a systematic approach comprising the following fundamental steps: clinical history and detailed physical examination; imaging evaluation and identification of the pathogen. The disease has variability in clinical presentations, and symptoms are often non-specific. [3]

Newer diagnostic methods like Cartridge based nucleic acid amplification tests (CBNAAT) and line probe assays (LPA) can rapidly identify Mycobacterium tuberculosis with improved sensitivity over the smear testing and have been made available under the Revised National Tuberculosis Control Programme (RNTCP) across the country. [2]

Cartridge based nucleic acid amplification test (CB-NAAT, GeneXpert,) is an automated cartridge-based molecular technique that detects Mycobacterium Tuberculosis as well as rifampicin resistance within two hours and has been endorsed by WHO as an initial diagnostic test in suspected pulmonary and some forms of extrapulmonary tuberculosis in the pediatric population. [4]

Childhood TB represents a sentinel event within a community, usually indicating recent transmission from adult cases. Childhood TB is therefore a reflection of TB control in any population. [5]

RNTCP fact file reflects that Madhya Pradesh reported 14007 children diagnosed with tuberculosis in 2018.[6] More data is needed from children, including more evaluation of specimens other than sputum as well as operational evaluation of the role of Xpert MTB/RIF in the diagnostic evaluation of children with suspected TB. [7]

Given the scarcity of available data especially in children from resource-limited regions of the country, this cross-sectional study was undertaken to analyse the in-hospital prevalence of Pediatric tuberculosis in children up to 18 years of age.

Aims & Objective

01. To identify the epidemiology of tubercular infection in children diagnosed with the modern available modality like CBNAAT.
02. To identify different types of sampling methods used in the diagnosis of Pediatric TB.

Material and Method

Setting: Department of Pediatrics and District Tuberculosis Center (DTC) associated with Government Medical College Datia, M.P., India.

Duration and type of study: This observational record based cross-sectional study was done over two years from April 2018 to March 2020.

Sampling methods: The study was carried out by analyzing the clinical & laboratory data of 166 patients treated with ATT.

Inclusion criteria: Pediatric patients of age ranging from six months to 18 years who were diagnosed with Tuberculosis by Cartridge Based Nucleic Acid Amplification (CBNAAT) test done by GeneXpert (Cepheid-2013) and were treated with anti-tuberculosis therapy (ATT) at the study centre.

Exclusion criteria: Patients out of age criteria and not registered for ATT in DTC Datia were excluded.

Ethical consideration & permission: Study approved by the institutional ethics committee.

Statistical Analysis: Statistical analysis was done using a Microsoft Excel spreadsheet.

Results

Data of a total of 166 patients were analyzed. Male: female ratio was almost equal i.e. 1.04:1 (Male-85, Female 81). 150 patients were below the poverty line. 66% of the patients were from rural areas. 83% of patients had a tubercular contact history in the family and almost the same percentage (84%) households had a history of smoking in family members. 73% had a reactive tuberculin test. All the patients were non-reactive on HIV Screening. (Table 1)

In 24% of cases gastric aspirate was sampled and only four (10%) turned reactive for tuberculosis by CBNAAT. Out of 136 sputum samples from children more than five years of age, 65 (48%) were reactive in CBNAAT testing. 42% of overall collected samples were reactive to CBNAAT testing for tuberculosis at this centre. None of the pediatric samples was positive for MDR TB. 66% of children completed treatment and 33% were declared cured. Age-wise sampling distribution has been shown in Table-2.

S. No.	Parameters	Result	Percentage (n=166)
1	Age-wise distribution		
	6-12 months	09	05%
	1-5 years	22	13%
	5-10 years	27	16%
	10-18 years	108	65%
2	Sex wise distribution		
	Male	85	51%
	Female	81	49%
3	Cast wise distribution		
	General	12	07%
	OBC	82	49%
	SC	64	39%
	ST	09	05%
4	Religion wise distribution		
	Hindu	153	92%
	Muslim	13	08%
5	Financial condition wise distribution		
	APL	16	09%
	BPL	150	91%
6	Area wise distribution		
	Rural	110	66%
	Urban	56	34%
7	Occupation wise distribution		
	Labourer	113	68%
	Farmer	45	27%
	Service class	06	03%
	Business	02	01%
8	Status of smoking in family		
	Yes	140	84%
	No	26	16%
9	History of contact		
	Yes	137	83%
	No	29	17%
10	HIV screening	All	100%
11	Mantoux test Reactive	122	73%
12	Type of sample		
	Sputum	126	76%
	Gastric aspirate	40	24%
13	CBNAAT results		
	Reactive	69	42%
14	Test results		
	Treatment completed	97	58%
	Treatment after default	14	08%
	Cured	55	33%

Table/Figure 1: Distribution of studied cases according to general profile, sampling and results

	6 to 12 months	>1 -5 years	>5-10 years	>10-18 years
Gastric aspirate	08 (02)	21 (02)	10 (nil)	01 (nil)
Sputum	00	00	17 (09)	119 (56)

Table/Figure 2: Distribution of studied cases according to sampling results in different age groups.

Discussion

This Record based study was undertaken to identify the epidemiology of tubercular infection in children diagnosed with a modern available modality like CBNAAT in the Datia district of central India.

During the study period, total tubercular patients notified were 46,00,811 in India and 3,59,284 in Madhya Pradesh alone, including both from the public as well as the private sector. [8] This study observed that 83% of children diagnosed with TB were having contact history in the family. About the above-mentioned data, Pediatric TB may have more hidden cases which are not reaching the health facility. In a recent study, TB screening for the child contacts of adult cases is not being done in the routine as a result many of the active TB cases in children may be missed. So, timely TB screening is imperative to reduce the burden of pediatric TB in India. [9]

In a prospective study conducted on 223 Children with TB, they were found more likely to be HIV positive, TST positive, reside in rural areas, exposed to biomass cooking fuel, and have a mother with less than primary school education.[10] In our study we found none of the child with HIV infection on screening but 66% were from rural areas and 73% were tuberculin reactive. 84% of children diagnosed had exposure to smoke in the household. Other important contributing factors to the global resurgence of TB include poverty, overcrowding, increased travel, immigration, inadequate implementation of TB control programmes, multidrug-resistant TB (MDR TB) and incomplete treatment. [11]

This study revealed that more than 90% (n= 150) patients were below the poverty line suggesting a direct relationship of TB with poor financial and poor hygienic conditions of the children in such families.

The most important and revolutionary development in TB diagnostics is the Xpert MTB/RIF assay. This is a fully automated real-time DNA based test that can detect both TB and resistance to rifampicin in less than 2 hours.[7] The revised National Tuberculosis Control Programme (RNTCP) which is now renamed as National Tuberculosis Elimination Programme (NTEP) has introduced Xpert facility at every district level of the country. [8] Xpert MTB/RIF has a high sensitivity of 95.7% and specificity of 99.3% for detecting MTB in pulmonary samples of patients with TB.

The sensitivity of Xpert MTB/RIF for detecting smear-negative, culture-positive samples is 77.7%; its sensitivity for detecting smear-positive, culture-positive samples is 99.2%. The sensitivity and specificity for detecting rifampicin resistance is 94.5% and 97.7% respectively concerning culture as the reference standard.[12]

Whilst adult TB cases are often easily recognizable, due to typical radiological features and a positive sputum smear, childhood TB is frequently more difficult to diagnose. The clinical and radiological features of childhood TB are often non-specific and subject to variable interpretation.[13] In primary care settings, microbiological confirmation of PTB is still rarely attempted in children.

This is due to the incorrect perception that respiratory specimens are difficult or impossible to obtain in children, the lack of infrastructure or trained staff to obtain such specimens and the lack of policy regarding microbiological confirmation in children. However, the yield of direct acid-fast smear microscopy is also very low since the disease is typically paucibacillary[14]. A meta-analysis of 15 studies, including 3,640 children, demonstrated a sensitivity of Xpert for TB detection of 62% using expectorated or induced sputum, and a sensitivity of 66% using samples from gastric lavage. [15]

This study result shows 51% yield from sputum samples but only 10% reactive from the gastric aspirate. Proper sampling technique, sample transportation and timely processing need to be evaluated separately. A study from Brazil also pointed out the need to standardize gastric lavage protocols for the diagnosis of pulmonary tuberculosis in children. [16]

In a study carried out to assess the utility of Xpert assay, out of the 210 gastric aspirate samples, 34 (16.19%) were positive by Xpert assay. For a sample to be positive, 131 CFU/ml of bacilli is required by GeneXpert [17] There is importance of screening the samples by ZN staining and then confirming the diagnosis by culture, as GeneXpert cannot detect the Non-Tuberculous Mycobacteria (NTM) species [18] which is needed to be evaluated further at study centre as it is observed that the overall yield of tubercular infection detected by Xpert is 42% including both sputum and GA samples but rest of the children were clinically diagnosed as tubercular and were treated accordingly.

Limitations

This was a retrospective study based on patients records analysis. Sample collection and processing was out of the scope of this study.

Conclusion

This study concludes with 42% positivity after CBNAAT testing for tuberculosis infection in collected samples of sputum and gastric aspirate where only 10% yield in GA samples. Because of the WHO End TB strategy, there is a need to implement standard procedures for sampling methods to increase yield in collected samples for diagnosis of Pediatric tuberculosis and improve contact tracing with the available diagnostic tools.

What does the study add to existing knowledge?

Diagnosis of Pediatric Tuberculosis can be improved with newer technology like CBNAAT by proper utilization of sampling techniques.

Author's contribution

Gupta R: Study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Sharma PK: Data collection, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Singh MP: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Agrawal P: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Upadhyay P: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Gupta DK: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study

Verma V: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Mehta A: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study

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