ISSN: 0975-1556

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2021; 13(3); 95-101

Original Research Article

A Prospective Observational Study to Assess the Clinico-Microbiological Profile of Children Suspected with Pulmonary Tuberculosis

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Received: 12-04-2021 / Revised: 03-05-2021 / Accepted: 23-06-2021
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Conflict of interest: Nil

Abstract

Aim: To evaluate the relation of clinical features with microbiological findings in children of suspected pulmonary tuberculosis. **Methods:** The prospective observational study was conducted in the Upgraded Department of Paediatrics, Patna Medical College and Hospital, Patna, Bihar, India for 13 months 80 children aged between 6 months to 18 years presenting with constitutional symptoms like persistent fever >2 weeks without a known cause and/or unremitting cough for >2weeks and/or weight loss of 5% in three months or no weight gain in past three months along with any one of the following findings i.e., history of contact or Mantoux positive. Chest X-ray was done and reported by the radiology department and findings suggestive of TB like hilar and paratracheal lymphadenopathy, parenchymal lesions, cavitatory lesions were included in this study. **Results:** A total of 80 paediatric inpatients with mean age of 11.24±5.01 years were included in the study. The median age was found to be higher (12.5 years). A total of 58.75% subjects in the study belonged to more than 12 years of age. There was a female preponderance in the study. Only 35 (43.75%) male patients were present in the study compared to 45(56.25%) female patients. Fever 67 (83.75%) was found to be the most common complaint followed by cough 61(76.25 %). Other prominent symptoms, in the beginning of the illness, consisted of weight loss (87.5%), loss of appetite (86.25%), and breathlessness (16.25%). Haemoptysis, chest pain and breathlessness were relatively less prevalent. Out of 80 subjects, 20% of the patients tested positive for Mycobacterium tuberculosis and remaining 80% tested negative both by ZN staining and CBNAAT. The proportion of CBNAAT positive patients with cavitation on chest X-ray were 65% and were significantly higher (p-0.0022). **Conclusion:** Females were more likely to suffer from TB disease as compared to the males. The study also found out that the patients with clinical finding suggestive of pulmonary Koch's do not always have sputum CBNAAT positivity.

Keywords: Microbiology, CBNAAT, Pulmonary Tuberculosis

Introduction

Microbiological confirmation of pulmonary tuberculosis (TB) in children remains challenging despite recent advances.[1] Collection of specimens for testing, such as induced sputum (IS) or gastric aspirate, is perceived to be invasive and complex. Even when such specimens are obtained and tested, the diagnostic yield can be suboptimal, with microbiological confirmation achieved in only half of children diagnosed with pulmonary TB, even in well-resourced research studies.[2] Improved microbiological confirmation is important, not only for clinical care but also because assessment of novel diagnostic biomarkers for TB in children is severely constrained by the lack of a sensitive reference standard test.

Mycobacterium tuberculosis is a non-motile, non-spore-forming, obligate aerobe, acid-fast bacillus that often appears beaded or unstained using Gram stain. Like all mycobacteria, it is distinguished by its ability to form stable mycolate complexes with aryl methane dyes (carbolfuchsin, auramine, and rhodamine). In 98% of cases, M. tuberculosis is transmitted through the air when a person with pulmonary disease coughs.[3] Once the infected droplet nuclei are inhaled, M. tuberculosis bacilli land in the alveoli where they are consumed by alveolar macrophages. In some individuals, the immune system is able to clear the infection without treatment. In others, M. tuberculosis subverts the alveolar macrophages' attempts at its degradation and instead replicates inside the macrophages for several weeks.[3] As the bacilli multiply, they are frequently carried into regional lymph nodes by alveolar macrophages and can spread hematogenously to other sites, including but not limited to the lung apices, vertebrae, peritoneum, meninges, liver, spleen, lymph nodes, and genitourinary tract. Most patients are asymptomatic during this time and usually have no radiologic evidence of disease, but around this time, they develop cell-mediated immunity, and tests of tuberculosis (TB) infection—the tuberculin skin test and the interferon gamma (IFN-) release assays (IGRAs)— become positive. In the majority of individuals, the pathogenesis ceases at this point, and the person remains asymptomatic and is said to have tuberculosis infection.[3] However, in some individuals, tuberculosis infection progresses to tuberculosis disease. While healthy adults infected with M. tuberculosis have a 5% to 10% chance of developing TB disease within their lifetime, and the majority who do so develop disease within the first 1 to 2 years after infection, infants and toddlers who are infected but untreated have a 40% to 50% chance of developing disease within 6 to 9 months; beyond these early years, the rate of progression to disease decreases significantly with increasing age.[4] Any condition or treatment that depresses cellmediated immunity (such as HIV infection, diabetes mellitus, poor nutritional status, or tumor-necrosis factor alpha inhibitors) increases the risk of progression from infection to disease in adults and children. In young children, the organisms tend to spread from the original lung focus to the regional hilar and mediastinal lymph nodes, which then enlarge if inflammation is intense. The lymph nodes can compress or erode into the bronchi, which frequently results in a distal atelectasis or parenchymal infection, causing the socalled "collapse-consolidation" lung lesion. However, the hallmark of childhood TB is intrathoracic lymphadenopathy with or without subsequent parenchymal disease. The number of organisms involved in this process tends to be small; hence, childhood TB is often called paucibacillary. As a result, finding direct evidence of the organism in body fluids and tissues is difficult, and in most case

series, fewer than 40% of childhood TB cases can be microbiologically confirmed.[5-7]

Material and methods

The prospective observational study was conducted in the Upgraded Department of Paediatrics, Patna Medical College and Hospital, Patna, Bihar, India for 13 months, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

Inclusion Criteria

80 patients were included in this study. In accordance with the Revised National TB Control Program (RNTCP) guidelines issued in the Technical and Operational Guidelines for TB Control in India 2016[8], children aged between 6 months to 18 years presenting with constitutional symptoms like persistent fever >2 weeks without a known cause and/or unremitting cough for >2weeks and/or weight loss of 5% in three months or no weight gain in past three months along with any one of the following findings i.e., history of contact or Mantoux positive. Chest X-ray was done and reported by the radiology department and findings suggestive of TB like hilar and paratracheal lymphadenopathy, parenchymal lesions, cavitatory lesions were noted.

Exclusion Criteria

Children who were already on Antitubercular Therapy (ATT) had any unexplained illness; were asthmatic; had possibility of foreign body aspiration leading to non-resolving pneumonia or HIV positive cases.

A detailed history was taken and general examination was done to see for lymphadenopathy, cutaneous TB markers, anthropometry, respiratory system findings and organomegaly. Mantoux test was carried out in every child (suspected to be suffering from TB) by injecting 5TU of tuberculin intradermally into the anterior aspect of left forearm. The result was read between 48-72 hours of injection. An induration of less than 5 mm around the injected site was taken as negative and 10 mm or more was taken as positive.[9] On the basis of the history, clinical examination and investigations, a diagnosis of pulmonary TB was made.

Two sputum samples were collected from each patient. One in a sterile specimen cup with a tight-fitting cap was sent for Ziehl-Neelsen (ZN) staining and the other one in a falcon tube to be sent for CBNAAT to TB hospital Ambala and report were collected. CBNAAT is a Polymerase Chain Reaction (PCR) based method which can detect the presence of Mycobacterium tuberculosis and provide results within 100 minutes.[10]

Statistical analysis

The data recorded from the study was tabulated into a master chart. Results were expressed as number and percentage. The data was analysed using Microsoft SPSS version 21.0 and along with graph pad prism software. Chi-square test was used for comparison between attributes. The p-value <0.05 was considered significant.

Results

A total of 80 paediatric in patients with mean age of 11.24±5.01 years were included in the study. The median age was found to be higher (12.5 years). A total of 58.75% subjects in the study belonged to more than 12 years of age. There was a female preponderance in the study. Only 35 (43.75%) male patients were present in the study compared to 45(56.25%) female patients. table 1

Table 1: Gender and age distribution of patients

Gender	Number of patients	Percentage
Male	35	43.75
Female	45	56.25
Age		
Below 6 years	9	11.25
6-12 years	24	30
12-18 years	47	58.75
Age mean	11.24±5.01years	

Fever 67 (83.75%) was found to be the most common complaint followedby cough 61(76.25 %) [Table 2]. Other prominent symptoms, in the beginning of the illness, consisted of weight loss (87.5%), loss of appetite (86.25%), and breathlessness (16.25%). Haemoptysis, chest pain andbreathlessness were relatively less prevalent. Table 2.

Table 2: Clinical symptoms

symptoms	Number of patients	Percentage
Fever	67	83.75
cough	61	76.25
weight loss	70	87.5
loss of appetite	69	86.25
Haemoptysis	3	3.75
chest pain	7	8.75
breathlessness	13	16.25

Out of 80 subjects, 20% of the patients tested positive for Mycobacterium tuberculosis and remaining 80% tested negative both by ZN staining and CBNAAT. Table 3. The proportion of CBNAAT positive patients with cavitation on chest X-ray were 65% and were significantly higher (p-0.0022). Table 4

Table 3: Sputum positivity by ZN staining and CBNAAT inoverall population.

Sputum Result (ZN staining)	Total Number of patient's n (%)
Positive	16 (20%)
Negative	64 (80%)
Sputum Result (CBNAAT)	
Positive	16 (20%)
Negative	64 (80%)

Table 4: Comparison between cavitation and sputum positivity.

	Sputum positivepatients	Sputum negativepatients	p-value
Cavitation present	12	12	0.0022
Cavitation absent	4	52	

Discussion

This study was conducted to evaluate the clinico-radiological features in children suspected of pulmonary TB and to compare them with the sputum results. in this study there was a female preponderance in the study. Only 35 (43.75%) male patients were present in the study compared to 45(56.25%) female patients There exists no valid proof that pulmonary TB has any sexual

predominance, however in the results obtained in the present study and as described by majority of authors, pulmonary TB was found to be more prevalent among females as compared to males.[11-13]

In the present study, 87.5% of the females were found to be undernourished. Henceforth, it is possible to hypothesise that higher frequency of disease in the females can be attributed to neglect of the girl child in the region leading to poor nutritional status, making them more vulnerable to the disease. The most common presentations in symptomatic children suspected of pulmonary TB are fever, cough and weight loss. In the present study, Fever 67 (83.75%) was found to be the most common complaint followed by cough 61(76.25 %). The results were similar to as described by majority of the authors showing fever being the most common presentation.[14-16] Other prominent symptoms, in the beginning of the illness, consisted of weight loss (87.5%), loss of appetite (86.25%), and breathlessness (16.25%). Early diagnosis and treatment is critical to reduce transmission of TB. Sputum microscopy for AFB using ZN staining is a simple easy and economical test for diagnosing pulmonary TB. CBNAAT has been endorsed by WHO in the recent past for diagnosis of TB as it is not only more sensitive but also tells about the resistance to rifampicin. The present study provided comparison between the sputum results obtained via ZN staining and CBNAAT. In the present study, out of 80 subjects suspected of having pulmonary TB, only 16 subjects (20%) showed positive for the presence AFB by ZN staining as well as CBNAAT. Remaining 64 subjects (80%) tested negative both by ZN staining as well as by CBNAAT. The results obtained in the present study were different from the observations made by other authors. Alvarez-Uria G et al., concluded smear positivity in 69% patients against CBNAAT which showed positivity in 75% patients.[17] In a similar study conducted by Dewan R et al., sputum positivity by ZN staining was seen in 11% patients against CBNAAT which showed sputum positivity in 40% patients.[10] The differences are more likely related to the fact that the adequacy of the sputum samples were not taken into consideration during sample collection. Moreover, the paucibacillary nature of the tuberculous bacilli in the sputum samples giving false negative results, as is clearly evident in the literature.[18] In the present study, it was also observed that sputum positivity was significantly higher among patients with history of contact or exposure. Significant association between history of contact and sputum positivity was seen in studies conducted by Sekadde MP et al., and Arora A et al., respectively.[19,20] Cavitatory lesion on chest X-ray is a hallmark finding and marks the presence of progressive primary disease or adult onset TB in children. In the present study, it was found that proportion of sputum positive patients with cavitation was significantly higher (p-0.0022). The importance of cavitation in TB is that it provides communication to the bacteria with the environment leading to a oxygenated environment inside the cavitation resulting in bacterial proliferation.[21] Hence children with cavitary lesion in chest X-ray or adult type of TB have a greater chance of having sputum positivity.

Conclusion

The present study concluded that females were more likely to suffer from TB disease as compared to the males. The study also found out that the patients with clinical finding suggestive of pulmonary Koch's do not always have sputum CBNAAT positivity. Sputum positivity was significantly associated with cavitatory lesion on chest X-ray.

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