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Original Research Article

Clinico-epidemiological profile and diagnostic procedures of tuberculosis in children: a study from OPD of Bangabandhu Sheikh Mujib Medical University

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ABSTRACT

Background: Childhood tuberculosis (TB) is a significant cause of mortality and morbidity, contributing to a considerable TB burden in developing countries like Bangladesh. The aim of this study was to describe the clinical profile and diagnostic procedures in childhood TB cases in the outpatient department (OPD) of a tertiary care hospital.

Methods: This cross-sectional study was conducted on children aged 3 months to 18 years from July 2023 to June 2024 in the OPD of the Paediatrics Department at Bangabandhu Sheikh Mujib Medical University (BSMMU) who were diagnosed with tuberculosis according to the National Guidelines for the Management of Tuberculosis in Children, 2021. Data were collected through direct interviews and analyzed by MS Excel.

Results: Among 834 suspected patients, 139 were diagnosed with tuberculosis. Here, 47.48% cases were pulmonary TB and 52.51% were extrapulmonary TB (EPTB). Among EPTB 30.93% were TB lymphadenitis. Common symptoms like fever were present in 84.48%, weight loss in 69.78%, cough in 64.74% and lumps in the neck and axilla in 35.25% cases. Mantoux test was positive in 71.92%, abnormal chest X-ray findings in 46.76%. Fine needle aspiration cytology from lymph nodes was suggestive in 32.37%. Sputum GeneXpert and stool GeneXpert ultra tests were positive in 10.79% and 20.14% respectively.

Conclusion: This study found that cases of extrapulmonary TB were more prevalent than pulmonary TB among children. The diagnosis of tuberculosis was primarily based on clinical suspicion, supported by various investigations, especially bacteriological detection through stool and sputum GeneXpert ultra tests in children.

Keywords: Tuberculosis, Pulmonary, Extrapulmonary tuberculosis, Mantoux test, Gene Xpert

INTRODUCTION

Tuberculosis (TB) is a communicable disease that poses significant challenges to public health and is among the leading causes of mortality globally. It is caused by the bacillus Mycobacterium tuberculosis. Even though TB primarily affects the lungs, it can also attack other parts of the body.[1] Around 25% of global population has been infected with M. tuberculosis. Prior to the COVID-19 pandemic, tuberculosis was the primary cause of death from a single infectious agent, superseding HIV/AIDS.[1]

In 2020, tuberculosis (TB) unfortunately resulted in the loss of 1.5 million lives globally. It is recognized as the 13th leading cause of death worldwide and is the second leading infectious cause of mortality following COVID-19. During that year, an estimated 10 million individuals were reported to have contracted TB, which included 5.6 million men, 3.3 million women, and 1.1 million

children.[2] TB is a concern in every country and impacts people across all age groups. However, it is important to note that cases of TB in children and adolescents can sometimes be overlooked by healthcare providers, which poses challenges in terms of diagnosis and treatment within these younger demographics.

It was observed in 2020 that eight countries were responsible for approximately two-thirds of the global tuberculosis burden. India reported the highest number of cases, with China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa following closely behind. It is worth noting that one of the key health targets established within the United Nations Sustainable Development Goals (SDGs) is to effectively eliminate the TB epidemic by the year 2030.[2]

Developing countries face significant challenges, bearing 95% of the global tuberculosis (TB) burden and accounting for 99% of reported TB-related deaths.[3] It is noteworthy that approximately 9% of TB cases worldwide occur in children under the age of 15, with this figure increasing to 15% in low-income countries.[4] However, national TB control programs often prioritize adult patients with sputum smear-positive TB due to their higher level of infectiousness. Consequently, childhood TB may receive less emphasis within these programs, partly due to the complexities associated with confirming diagnoses and the tendency to overestimate the protective effects of the BCG vaccine.[5]

Diagnosing TB in children can be particularly challenging in resource-limited settings, such as Bangladesh. Concerns are growing regarding the impact of TB on HIV-positive children.[6] Research performed in Taiwan, the USA, and Saudi Arabia has shed light on the epidemiology and clinical aspects of childhood TB.[7-10] The clinical presentation of TB can vary significantly depending on the local context of TB and HIV prevalence. Furthermore, the diagnostic methods available for childhood TB often depend on the resources within healthcare systems, highlighting the need for tailored approaches in different settings.

In Nepal, it is estimated that around 45% of the population is affected by tuberculosis (TB), with approximately 20,000 new infectious cases reported annually.[11] However, there is a recognized need for more research focusing on the epidemiology, clinical profiles, and diagnostic methods related to childhood TB in low-income countries, including Nepal. Addressing this gap could significantly enhance our understanding and response to this important public health issue.

Collecting sputum samples for acid-fast bacilli (AFB) testing presents significant challenges, particularly for children under the age of seven. The bacteriological diagnosis of active tuberculosis (TB) tends to be more straightforward in adults compared to children. This difference is largely attributed to the lower bacterial load typically found in pediatric cases and the varied symptoms that can complicate the diagnostic process. Recognizing this complexity, the World Health Organization (WHO) made recommendations in 2013 to utilize the Gene Xpert MTB/RIF test for diagnosing pediatric TB and detecting rifampicin resistance. Additionally, they emphasized the importance of considering the clinical profile to enhance diagnostic accuracy.[12] In this context, we undertook a study to explore and describe the clinical and epidemiological profiles as well as the diagnostic processes utilized for pediatric TB patients.

METHODS

Study place

This cross-sectional study was conducted in the outpatient department (OPD), Department of Pediatrics at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Children of 3 months to 18 years old who presented with sign symptoms of presumptive TB and later on diagnosed as tuberculosis according to National guidelines for the management of tuberculosis in children 2021, Bangladesh came to OPD during the study period were enrolled in this study.

Exclusion criteria

Childhood TB patients with other co-morbidities like-cystic fibrosis, primary immune deficiency (PID), nutritional disorders and whose parents did not give consent to participate were excluded from the study.

Inclusion criteria

A total of 139 cases of diagnosed tuberculosis, identified between July 2023 and June 2024, were included in this study.

The study was performed following ethical standards stated in the 1964 Declaration of Helsinki and its later amendments. Informed written consent was obtained from parents and Institutional Review Board Clearance Certificate (No. BSMMU/2023/5989, Date: 11/04/2023) was taken before enrollment of the study. Appropriate statistical test was used to analyze the data of demographic, clinical, laboratory findings. Frequency distribution was calculated by percentages.

Data collection

Data were collected from OPD records to document differences in age, sex, monthly distribution of TB cases, clinical characteristics, the spectrum of different types of TB, and imaging and laboratory findings among the participants. Diagnostic evaluations based on clinical findings included chest X-rays, the Mantoux test, fine

needle aspiration cytology (FNAC) from lymph nodes, lymph node biopsy, sputum testing with Gene Xpert, stool testing with Xpert Ultra, and CT scans of the brain.

Based on the results, subjects were categorized into two groups: those with pulmonary tuberculosis (PTB) and those with extrapulmonary tuberculosis (EPTB). The EPTB group included cases of TB lymphadenitis, tubercular pleural effusion, disseminated TB, miliary TB, central nervous system TB, and abdominal TB.

Operational definition

Presumptive TB

A patient who presents with the symptoms or signs suggestive of TB

Bacteriologically confirmed case

It is a patient from whom a biological specimen is positive by WHO-approved rapid diagnostics (e.g. Xpert-MTB/RIF), smear microscopy or culture.

Clinically diagnosed TB case

In this patient who does not fulfill the criteria of bacteriological confirmation or smear not done; but diagnosed as active TB by a clinician and decided to have a full course of anti-TB treatment.

Pulmonary TB

Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.

Miliary TB is classified as PTB because there are lesions in the lungs.

Extrapulmonary TB

Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs outside the lung parenchyma and bronchial tree (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges, etc.)

Symptom criteria for PTB

Persistent, non-remitting cough for >2 weeks not responding to conventional antibiotics and/or bronchodilators and/or, Persistent documented fever (>380˚C/100.4 ºF) >2 weeks after common cases such as typhoid, malaria or pneumonia have been excluded; and/or, documented weight loss or not gaining weight during the past 3 months (especially if not responding to de-worming together with food and/or micronutrient supplementation) or severe malnutrition and/or, Fatigue, reduced playfulness, decreased activity.

RESULTS

A total of 139 patients diagnosed with tuberculosis during the study period were enrolled in this study. The age range of the study population was from 3 months to 18 years. The age distribution of cases was as follows.

A total 15 patients (10.79%) were aged between 3 months and 1 year, 36 patients (25.89%) were between 1 and 5 years, 31 patients (22.30%) were aged 6 to 10 years, and 57 patients (41%) were in the age group of more than 10 to 18 years. The highest number of cases, 41%, was found in the 10 to 18 years age group (Table 1). The gender distribution revealed that 76 patients (54.67%) were male and 63 patients (45.32%) were female (Figure 1). A total of 834 patients were advised to undergo tests, among which 139 cases were diagnosed as TB.

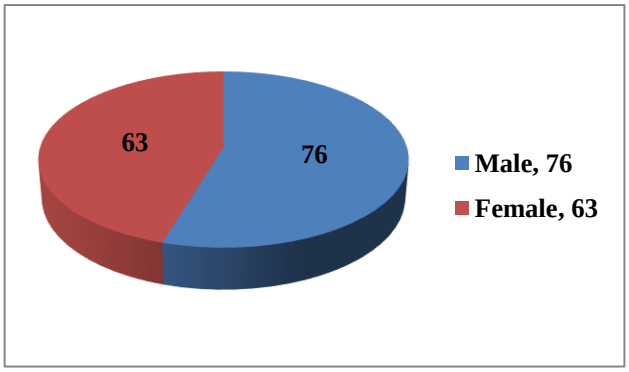

Figure 1: Gender distribution of study population (n=139).

Table 2 illustrates the age-wise distribution of pulmonary and extra-pulmonary cases. Among the 139 TB cases, 66 (47.48%) were pulmonary TB, while 73 (52.51%) were extra-pulmonary TB. In the older age group (over 10 to 18 years), the majority of cases, 36 (63.15%), were identified as extra-pulmonary TB. This category included TB lymphadenitis, tubercular pleural effusion, abdominal TB, disseminated TB, miliary TB, and CNS TB. Among the 73 extra-pulmonary TB cases, 43 (58.9%) were diagnosed with TB lymphadenitis, while tubercular pleural effusion, abdominal TB, and disseminated TB were diagnosed in 11 (15.06%), 9 (12.32%), and 7 (9.5%) cases respectively (Table 3).

Table 4 presents various clinical features observed in the study population diagnosed with tuberculosis. The observed clinical features included fever, weight loss, cough, lumps in the neck and axilla, fatigue, abdominal pain, altered bowel habits, breathlessness, and headaches. Fever was reported in 118 cases (84.48%), weight loss in 97 cases (69.78%), cough in 90 cases (64.74%), and lumps in the neck and axilla in 49 cases (35.25%). For suspected TB cases, various imaging and laboratory tests were conducted for diagnosis. The Mantoux test was administered to all cases, and positive induration was found in 100 patients (71.92%). Chest X-ray findings

revealed patchy opacity and consolidation in 65 cases (46.76%), mediastinal lymphadenopathy in 15 cases (10.79%), pleural effusion in 14 cases (10.07%), and miliary mottling in 4 cases (2.87%). Suggestive FNAC results from the lymph node were observed in 45 cases (32.37%). Among 4 lymph node biopsy cases, TB was confirmed. For bacteriological confirmation, sputum gene Xpert and stool gene Xpert Ultra tests were positive in 15 cases (10.79%) and 28 cases (20.14%) respectively, while gastric lavage was positive in 3 cases. CT scan of the brain in one case showed a tuberculoma (Table 5).

Table 1: Distribution of TB cases according to age (n=139).

Age (in year)	No. of cases	%
3 months to <1 year	15	10.79
1-5 year	36	25.89
6-10 year	31	22.30
11- 18 years	57	41

Table 2: Comparison of types of TB in different age group (n=139).

Age (in year)	Pulmonary TB (n=66)	Extra pulmonary TB (n=73)
3 months to <1 year	8	7
1-5 year	20	16
6-10 year	17	14
11-18 year	21	36

Table 3: Spectrum of different types of TB cases (n=139).

Types of TB	Frequency	%
Pulmonary TB	66	47.48
Extra pulmonary TB	73	52.51
TB lymphadenitis	43	30.93
Pleural effusion	11	7.91
Abdominal TB	9	6.47
Disseminated TB	7	5.03
Miliary TB	2	1.43
CNS TB	1	0.71

Table 4: Presenting clinical features among the study population diagnosed with tuberculosis (n=139).

Clinical features	Frequency	%
Fever	118	84.48
Weight loss	97	69.78
Cough	90	64.74
Lump in neck, axilla	49	35.25
Fatigue	28	20.14
Breathlessness	14	10.07
Abdominal pain	9	6.61
Altered bowel habit	8	5.75
Headache	1	0.71

Table 5: Imaging and laboratory findings among the study population (n=139).

Variables		Frequency	%
Mantoux test		100	71.92
Chest X-ray findings	Patchy opacity and consolidation	65	46.76
	Mediastinal lymph node	15	10.79
	Pleural effusion	14	10.07
	Military mottling	4	2.87
FNAC suggestive tuberculosis		45	32.37
Lymph node biopsy suggestive TB		4	2.87
Sputum gene Xpert		15	10.79
Gastric lavage		3	2.15
Stool Xpert ultra		28	20.14
Tuberculoma in CT brain		1	0.71

DISCUSSION

This study intended to explore the clinical profile of tuberculosis (TB) in children aged 3 months to 18 years, focusing on 139 diagnosed cases. Notably, the data revealed that the highest incidence, at 41%, was observed in the 11–18-year age group, a finding that resonates with research conducted by Kakarani et al and Pratinidhi et al.[13]

In addition, the work of Shrestha et al. highlighted a significant prevalence in the 10-15 year age group (63.4%), followed by children under 5 years (29.3%), which aligns with our findings.[14] Conversely, Ahasan et al reported in their study from Bangladesh that the majority of TB cases were found in the 1 to 5 year age group (21 cases, 41.18%), echoing similar observations made by Sancjez-Albisua et al.[15,16] It is also noteworthy that studies from tertiary care settings in India suggest that children under 5 years comprise a considerably higher proportion (18-34%) of total childhood TB cases.[17] These findings collectively contribute to a deeper understanding of TB in pediatric populations.

In our study, we observed a slight male preponderance, with 76 males (54.67%) and 63 females (45.32%). This finding aligns with the results of Ahsan et al, who reported 27 males (52.94%) and 24 females (47.06%). The male-to-female ratio of 1.12:1 is consistent with several other studies, including one conducted in Bhutan that found 57% of participants were male and 43% female.[18,19]

Conversely, Bajaj et al, identified a slight female preponderance (52.64%), which corresponds with findings from Franco et al in Brazil (51.6%) and Suryanarayana et al.[9,20] The variations in these results may reflect differing cultural preferences for male children in specific social contexts, such as in Bangladesh. Out of the 834 patients advised to undergo

testing, 139 received a diagnosis of tuberculosis (TB). Our findings indicate that extrapulmonary TB (EPTB) represented the majority of cases at 52.51%, with pulmonary TB (PTB) following closely at 47.48%.

While many studies have traditionally highlighted the predominance of pulmonary TB over EPTB, it is worth noting that Sreeramareddy et al reported that 55% of TB patients had extrapulmonary involvement. Additionally, there is growing evidence suggesting an upward trend in extrapulmonary manifestations among children.[21-24] In our study, we observed that lymph nodes were the most common site for EPTB, a finding that is consistent with other studies.

The observed higher proportion of extra-pulmonary tuberculosis (EPTB) cases may be largely due to our institution's status as a tertiary medical university hospital, which enables the diagnosis of more EPTB cases thanks to advanced investigative facilities and the expertise of our histopathologists. Among the 139 diagnosed cases, 30.93% of the EPTB group had tuberculous lymphadenopathy, a figure that exceeds the 16.7% reported by Garg et al.[25] Additionally, pleural effusion was identified in 12 cases (15.7%) within the EPTB group; this percentage is somewhat lower than the 26.1% noted by Franco et al.[9] In our findings, pleural effusion was reported in 11 cases (7.91%), which is fewer than the results documented by Garg et al and Franco et al.[9,25]

The most frequently observed symptoms in the study included fever (118 cases, 84.48%), weight loss (97 cases, 69.78%), cough (90 cases, 64.74%), and the presence of lumps in the neck or axilla (49 cases, 35.25%). Additional symptoms noted were breathlessness (14 cases, 10.07%) and abdominal pain (9 cases, 6.61%). In their research, Hatwal et al. reported comparable findings, with fever occurring in 75.6% of cases and cough noted in 63.4%.[26]

A study from Chennai, India, highlighted that fever and cough were the predominant symptoms, observed in 47% of cases, alongside visible glandular swelling in 49%.[25] Similarly, a study conducted in the Philippines revealed that fever (86.6%), cough (76.1%), and breathing difficulties (28.4%) were the most prevalent symptoms.[27]

These observations generally correlate with our findings. It is important to acknowledge that nonspecific symptoms are often prevalent among children, which can complicate the diagnostic process. This emphasizes the necessity for healthcare professionals to facilitate timely and accurate diagnosis.

The Mantoux skin test was utilized in nearly all cases of tuberculosis (TB), and it yielded positive results in approximately 71.92% of instances. While a negative Mantoux test may not definitively exclude the possibility of TB, a positive result can be an invaluable diagnostic tool, particularly in resource-limited settings. Extrapulmonary TB was mainly diagnosed through fine needle aspiration cytology (FNAC) and biopsy, with 45 cases (32.37%) of TB lymphadenitis identified via FNAC. These findings highlight the diagnostic challenges that treating physicians may face in resource-limited environments, a situation that has been corroborated by other studies.[24,26,27]

Furthermore, chest X-rays were recommended for all forms of TB, ensuring a comprehensive approach to diagnosis. Clinical features that suggest the presence of tuberculosis (TB), along with positive results from supplementary tests, assist physicians in interpreting chest X-rays as indicative of TB. Among all diagnosed TB cases, a notable 70.49% (98 cases) demonstrated positive findings. The positive chest radiograph results were primarily linked to pulmonary TB, but they also occurred in some instances of TB lymphadenitis, disseminated TB, and miliary TB.

Sreeramareddy et al noted that an impressive 94% of chest radiographs were interpreted as positive for patients diagnosed with pulmonary TB (PTB).[24] It is widely recognized that sputum testing utilizing GeneXpert or other samples, such as stool for Xpert Ultra, serves as the gold standard for TB diagnosis. Stool Xpert ultra yielded positive results in 28 cases (20.14%), which reflects a higher detection rate compared to sputum samples analyzed with Gene Xpert. This finding indicates that stool may be a valuable alternative to respiratory specimens in pediatric cases. Kabir et al and colleagues noted that while Xpert ultra on stool demonstrates greater sensitivity, it does exhibit lower specificity when compared to the traditional Xpert method.[28]

CONCLUSION

In this study, the frequency of extrapulmonary tuberculosis cases in children was greater than that of pulmonary TB. Majority of the extrapulmonary TB cases were tubercular lymphadenitis. The commonest symptom observed was fever followed by weight loss and cough. Children aged 10 to 18 years were mostly affected. The diagnosis of tuberculosis in children was principally based on clinical suspicion and was supported by various other investigations, particularly bacteriological detection of mycobacterium tuberculosis using gene Xpert Ultra of stool specimen.

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