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# Clinico-Epidemiological Profile and Diagnostic Procedures of Tuberculosis in Children: A Retrospective Study from OPD of Tertiary Care Center in Bangladesh

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## Abstract

**Background:** Childhood Tuberculosis (TB) is an important cause of mortality and morbidity, which causes a significant TB burden in developing countries. **Objectives:** The aim of this study was to describe clinical profile and diagnostic procedures used in outpatient department (OPD) of a tertiary care hospital. **Methods:** It was a retrospective study conducted in OPD of Paediatrics Department, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh. Age range of studied populations, 3 months to 18 years who presented with clinical features of TB and were later diagnosed with tuberculosis according to national guidelines for the management of tuberculosis in children, 2021 were enrolled in this study. A total of 108 diagnosed cases of Tuberculosis between August 2021 and July 2022 were enrolled in this study. Data were collected from OPD records and transferred into MS excel sheet for data processing & analysis. **Results:** Among 834 suspected patients, 108 patients aged 3 months to 18 years were diagnosed with tuberculosis. The highest number of cases 47 (43.51%) were found in 11 - 18 years age group. Gender distribution of the patient showed 58 (53.70%) were male and 50 (46.29%) were female. Among 108 TB cases, 44 (40.74%) were pulmonary TB and 64 (59.25%) were extrapulmonary Tb. Among 64 extrapulmonary TB cases 38 (59.37%) cases were diagnosed as TB lymphadenitis. Fever 83 (76.85%), weight loss 62 (57.4%), cough 50 (46.29%), lump in neck and axilla 38 (35.18%) were found in most of the cases. A positive Mantoux test was found in 68 (62.96%) patients. Chest x-ray findings showed patchy opacity and consolidation in 46 (42.59%) cases. Suggestive FNAC from lymph node was observed among 35 (32.4%) cases. For bacteriological confirmation sputum gene Xpert and stool xpert ultra were positive among 10 (9.25%) and 23

(21.29%) cases. **Conclusion:** In this study, extrapulmonary TB (EPTB) cases were more than pulmonary TB (PTB) in children. Diagnosis of tuberculosis was based on clinical suspicion supported by various investigations especially bacteriological detection with stool X pert ultra in children.

## Keywords

Tuberculosis, Pulmonary, Extrapulmonary, Mantoux

## 1. Introduction

Tuberculosis (TB) is a communicable disease that is a major cause of morbidity and one of the leading causes of death worldwide. TB is caused by the bacillus Mycobacterium tuberculosis (*M Tuberculosis*). The disease typically affects the lungs (pulmonary TB) but can affect other sites also [1]. About a quarter of the world's population has been infected with M. tuberculosis. Until the coronavirus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS [1].

A total of 1.5 million people died from TB in 2020. Worldwide, TB is the 13$^{th}$ leading cause of death and the second leading infectious killer after COVID-19. In 2020, an estimated 10 million people fell ill with TB worldwide, 5.6 million men, 3.3 million women and 1.1 million children [2]. TB is present in all countries and age groups. Child and adolescent TB are often overlooked by health care providers and can be difficult to diagnose and treat.

In 2020, eight countries accounted for two-thirds of the total TB burden, with India leading the count, followed by China, Indonesia, Phillippines, Pakistan, Nigeria, Bangladesh and South Africa. Ending the TB epidemic by 2030 is among the health targets of the United Nations Sustainable Development Goals (SDGs) [2].

Developing countries account for 95% of the burden of tuberculosis (TB) and 99% of the TB mortality reported worldwide [3]. It is estimated that about 9% of TB cases globally occur among children less than 15 years of age. The same proportion in low-income countries is 15% [4]. However, the national TB control programs lay more emphasis on sputum smear-positive adult TB cases since they are highly infectious. As a result childhood TB is often neglected by TB control programs due to the difficulties in confirming diagnosis, and over estimating the protective efficacy of BCG vaccine [5]. Moreover, diagnosis of TB among children may be more challenging in resource-poor settings like Bangladesh. There has been an increasing concern about TB among children who are HIV seropositive [6]. Studies from Taiwan, USA and Saudi Arabia have reported about epidemiology and clinical features of childhood TB [7] [8] [9] [10]. Clinical presentation may depend on the epidemiological situation of TB and HIV in that country. Diagnostic methods followed for childhood TB may vary depending on the available resources in the health-care setting. In Nepal, about 45% of

the total population is infected with TB and an estimated 20,000 new infectious cases of TB are reported each year [11]. However, studies on epidemiology, clinical profile and diagnostic methods of childhood TB from low-income countries like Nepal are lacking.

It's difficult for children to produce sputum and especially in < 7 years old children, it is a challenge to obtain good smear samples for AFB. The bacteriological diagnosis of active TB in adults is comparatively easier when compared to children due to its paucibacillary nature and symptoms in both differ creating difficulty in diagnosis. In 2013, WHO recommended the use of Gene Xpert MTB/RIF to diagnose Pediatric TB and Rifampicin resistance along with clinical profile for ease of diagnosis [12]. Therefore, we carried out this study to describe the clinico-epidemiological profile and diagnostic processes of pediatric TB patients.

## 2. Materials and Methods

It was a retrospective study conducted in outpatient department (OPD) of Paediatrics Department, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh. Age range of studied population was 3 months to 18 years. Those 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 were enrolled in this study. Total 108 diagnosed cases of Tuberculosis in between August 2021 to July 2022 were enrolled in this study. Data were collected from OPD records for documentation of differences in age, sex, monthly distribution of TB cases, clinical characteristics, spectrum of different types of TB cases, imaging and laboratory findings among the study populations.

Based on clinical findings, chest Xray, montoux test, FNAC from lymph node, lymph node biopsy, sputum for gene xpert, stool for xpert ultra, CT scan of brain were advised. Based on the results, subjects were divided into PTB and EPTB group. EPTB group included TB lymphadenitis, tubercular pleural effusion, disseminated TB, military TB, CNS TB, abdominal TB.

### 2.1. Working Definition

**Presumptive TB:** a patient who presents with the symptoms or signs suggestive of TB

**Bacteriologically confirmed case:** is a patient from whom a biological specimen is positive by WHO-approved rapid diagnostics (eg. Xpert-MTB/RIF), smear microscopy or culture.

**Clinically diagnosed TB case:** is a 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 (PTB):** refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lungparenchyma or the tracheobronchial tree. Miliary TB is classified as PTB because there are lesions inthe lungs.

**Extrapulmonary TB (EPTB)** 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.)

### 2.2. Symptom Criteria for PTB

Persistent, non-remitting cough for > 2 weeks not responding to conventional antibiotics and/or bronchodilators:

**and/or** Persistent documented fever (>380C/100.40F) > 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.

### 2.3. Statistical Analysis

For purpose of analysis collected data in this study was transferred into MS excel sheet for further processing and analysis.

## 3. Results

During the study period, 108 patients diagnosed as tuberculosis were enrolled in this study. Age range of study population was 3 months to 18 years. Age distribution of cases, 11 (10.18%) were within 3 months to 1 year, 22 (20.37%) were in between 1 - 5 years, 28 (25.92%) were between 6 - 10 years, 47 (43.51 %) cases were between more than 10 to 18 years age group. Highest number of cases, near about fifty percent found in 11 - 18 years age group (Table 1). Gender distribution of the patient showed 58 (53.70%) were male and 50 (46.29%) were female (Figure 1). Figure 2 showed month wise distribution of number of presumptive TB tested and diagnosed TB cases from august 2021to july 2022. Total 834 patients were advised for tests, among them 108 cases were diagnosed as TB cases. Most of the cases, 91 (84.25%) were diagnosed during the last 7 months of study period that means from January to July 2022. Due to pandemic situation of Covid-19 infection less number of patients visited during months of year 2021 at outpatient department.

Table 2 shows age wise distribution of pulmonary and extrapulmonary cases. Among 108 TB cases 44 (40.74%) were pulmonary TB and 64 (59.25%) were extrapulmonary Tb. With older age group (11 to18 years) most of the cases 32 (68.08%) were extrapulmonary TB. Extrapulmonary TB included TB lymphadenitis, tubercular pleural effusion, abdominal TB, disseminated TB, miliary TB, CNS TB. Among 64 extrapulmonary TBcases 38 (59.37%) cases were diagnosed as TB lymphadenitis. Tubercular pleural effusion, abdominal TB and disseminated TB was diagnosed in 9 (14.06%), 8 (12.5%) and 6 (9.375%) cases respectively (Table 3).

**Table 1.** Distribution of TB cases according to age (n = 108).

| Age in year | Number of cases | Percentage |
|---|---|---|
| 3 months to < 1 year | 11 | 10.18 |
| 1 - 5 year | 22 | 20.37 |
| 6 - 10 year | 28 | 25.92 |
| 11 - 18 years | 47 | 43.51 |

**Table 2.** Comparison of types of TB in different age group (n = 108).

| Age in year | Pulmonary TB (n = 44) | Extrapulmonary TB (n = 64) |
|---|---|---|
| 3 months to < 1 year | 4 | 6 |
| 1 - 5 year | 11 | 12 |
| 6 - 10 year | 14 | 14 |
| 11 - 18 year | 15 | 32 |

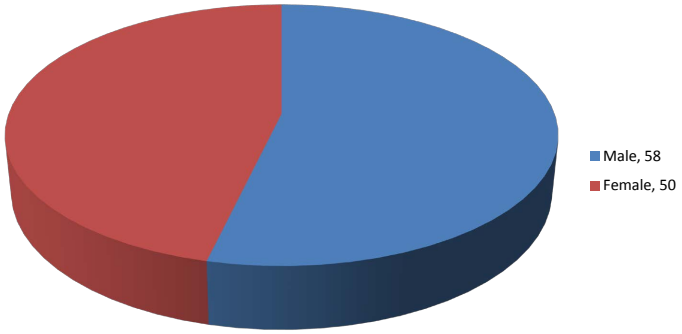


**Figure 1.** Pie chart showing gender distribution of study population (n = 108).

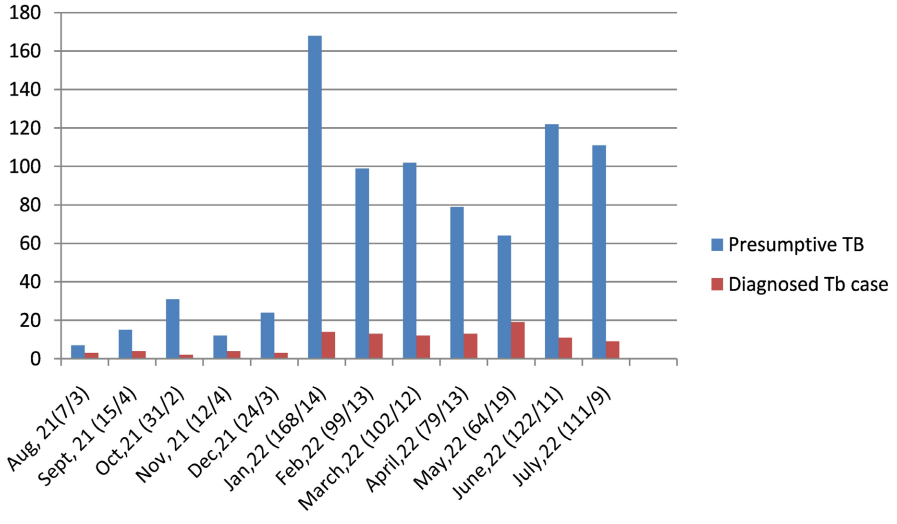


**Figure 2.** Month wise distribution of presumptive TB cases and all forms of diagnosed TB cases.

**Table 3.** Spectrum of different types of TB cases (n = 108).

| Types of TB | Frequency | Percentage |
|---|---|---|
| Pulmonary TB | 44 | 40.74 |
| Extrapulmonary TB | 64 | 59.25 |
| TB lymphadenitis | 38 | 59.37 |
| Pleural effusion | 9 | 14.06 |
| Abdominal TB | 8 | 12.5 |
| Disseminated TB | 6 | 9.37 |
| Miliary TB | 2 | 3.12 |
| CNS TB | 1 | 1.56 |

Table 4 shows different clinical features among study populations diagnosed with tuberculosis. Observed clinical features in this study were fever, weight loss, cough, lump in neck and axilla, fatigability, abdominal pain, altered bowel habit, breathlessness and headache. Fever 83 (76.85%), weight loss 62 (57.4%), cough 50 (46.29%), lump in neck and axilla 38 (35.18%) were found in most of the cases.

In suspected TB cases, to diagnose different imaging and laboratory tests were advised. Mantoux test was advised in all cases, positive induration was found in 68 (62.96%) patients. Chest X-ray findings showed patchy opacity and consolidation in 46 (42.59%) cases, mediastinal lymph node 10 (9.25%), pleural effusion 9 (8.33%) and miliary mottling in 2 (1.85%) cases. Suggestive FNAC from lymph node was observed among 35 (32.4 %) cases. Lymph node biopsy suggestive TB was found in 3 cases. For bacteriological confirmation sputum gene Xpert and stool xpert ultra were positive among 10 (9.25%)and 23 (21.29%) cases. Gastric lavage was positive in 2 cases. CT brain in one case showed tuberculoma (Table 5).

## 4. Discussion

This study was carried out to study the clinicoepidemiological profile of TB in children age ranged from 3months to 18years, of 108 diagnosed tuberculosis cases. In this study Highest number of cases, forty three percent cases found in 11 - 18 years age group which is similar to a study by Kakarani and Pratinidhi *et al.* [13]. Shrestha *et al.* also had maximum patients in age group of 10 - 15 years (63.4%) followed by age group of < 5 years (29.3%) which is similar to our study findings [14]. But Ahasan *et al.*, a study from Bangladesh found most cases of TB presented in the age between 1 to 5 years 21 (41.18%). This is similar to a study done by Sancjez-Albisua *et al.* [15] [16]. Similarly, studies from the tertiary care setting in India have previously shown that patients aged less than 5 years constituted a much higher proportion (18% - 34%) of total childhood TB cases [17].

This study had slight male preponderance (53.7%). Ahsan *et al.* found preponderance of males 27 (52.94%) in their study population as compared to females 24 (47.06%). The male to female ratio was 1.12:1, which was also found in

**Table 4.** Presenting clinical features among the study population diagnosed with tuberculosis (n = 108).

| Clinical features | Frequency | Percentage |
|---|---|---|
| Fever | 83 | 76.85 |
| Weight loss | 62 | 57.40 |
| Cough | 50 | 46.29 |
| Lump in neck, axilla | 38 | 35.18 |
| Fatigue | 18 | 16.66 |
| Abdominal pain | 10 | 9.25 |
| Breathlessness | 5 | 4.62 |
| Altered bowel habit | 8 | 7.47 |
| Headache | 1 | 0.925 |

**Table 5.** Imaging and laboratory findings among the study population (n = 108).

| Variables | | Frequency | Percentage |
|---|---|---|---|
| Chest x-ray findings | Mantoux Test | 68 | 62.96 |
| | Patchy opacity and consolidation | 46 | 42.59 |
| | Mediastinal lymph node | 10 | 9.25 |
| | Pleural effusion | 9 | 8.33 |
| | Military mottling | 2 | 1.85 |
| FNAC suggestive tuberculosis | | 35 | 32.40 |
| Lymph node biopsy suggestive TB | | 3 | 2.77 |
| Sputum gene Xpert | | 10 | 9.25 |
| Gastric lavage | | 2 | 1.85 |
| Stool Xpert Ultra | | 23 | 21.29 |
| Tuberculoma in CT brain | | 1 | 0.92 |

several other studies [18]. This distribution was similar to study done in Bhutan which had 57% males and 43% females [19]. Bajaj *et al.* found a slight female preponderance (52.64%) in their study which is in similar to studies by Franco *et al.* in Brazil (51.6%) [9] and Suryanarayana *et al.* [20]. Their findings are not consistent with ours, probably male child get more preference in our social context like Bangladesh.

Total 834 patients were advised for tests, among them 108 cases were diagnosed as TB cases. Most of the cases, 91 (84.25%) were diagnosed during the last 7 months of study period that means from January to July 2022. Due to pandemic situation of Covid-19 infection less number of patients visited during months of year 2021 at outpatient department. In the current study, EPTB constituted the major group (59.25.4%), followed by PTB (40.74%), where most of

the studies had found preponderance of pulmonary TB followed by EPTB. Sreeramareddy *et al.* found 55% of all TB patients had extrapulmonary involvement. Few studies have suggested about increasing trends of extra-pulmonary manifestations among children [21] [22]. Most common extra-pulmonary site in our setting was lymph node similar to studies reported from elsewhere [22] [23] [24]. Higherproportion of EPTB can be attributed to the issue that being a tertiary medical university hospital most of the cases of EPTB are diagnosed due to available investigation facilities and expert histopathologist. Among 108 diagnosed cases, in EPTB group, tubercular Lymphadenopathy was observed in 35.18% cases which is higher than a study done by Garg P *et al.* [25] which documented 16.7% cases of tuberculous lymphadenitis, followed by Pleural Effusion in 12 (15.7%) cases which is lesser than a study done by Franco *et al.* (26.1%) [9]. In our study, pleural effusion was found in 9 (8.33%) cases which is less in number than study findings of Garg P and Franco *et al.* [13].

Present study showed most common symptoms were fever 83 (76.85%), weight loss 62 (57.4%), cough 50 (46.29%), lump in neck, axilla 38 (35.18%), abdominal pain 10 (9.25%), breathlessness 5 (4.62%). Hatwal *et al.* found symptoms like fever (75.6%), cough (63.4%) [26]. Another study from Chennai, India had predominant symptoms as fever, cough (47%) and a visible glandular swelling (49%) [25] Also, in a study done at Philippines, most frequent symptoms were fever (86.6%), cough (76.1%) and breathing difficulty (28.4%) [27]. These study findings are almost similar to our findings. These nonspecific symptoms are mostly found in children, which makes the diagnosis difficult in children. So, physician needs higher degree of suspicion for early diagnosis.

Mantoux (skin) test was done in almost all forms of TB and about 62.96 % tested were positive. Though negative Mantoux test does not rule out TB, a positive test may be a useful diagnostic tool in a resource-limited setting like ours. EPTB was diagnosed mainly by FNAC and biopsy. 35 (32.4%) cases of TB lymphadenitis were diagnosed with the help of FNAC. These findings emphasize about the diagnostic difficulties observed by treating physicians in resource-limited settings. Such findings have been reported from other countries as well. [24] [26] [27]. Chest X ray was advised for all forms of TB. Clinical feature suggestive of TB and positive results of other tests guided physicians to interpret the chest X-ray as positive. Among all forms of TB in 62.02% (67) cases there were positive findings. Positive chest radiographs findings were mostly associated with pulmonary TB, also some cases of TB lymphadenitis, disseminated and miliary TB. Sreeramareddy *et al.* found 94% of chest radiographs were interpreted as positive for patients diagnosed as PTB [24]. Sputum for gene Xpert or other specimens like stool for Xpert Ultra for presence of acid fast bacilli are gold standard for diagnosis. Stool Xpert Ultra was positive for 23 (21.29%) cases, detection rate is more than sputum for gene Xpert. So, Stool is a alternative to respiratory specimens among children. Senjuti kabir *et al.* in a study concluded that Xpert ultra on stool has better sensitivity and lesser specificity than Xpert.

## 5. Conclusion

In this study, EPTB cases were more than PTB in children. The most common extra-pulmonary site was lymph nodes. Fever was the commonest presentation, followed by weight loss and cough. Children 11 to 18 years were most commonly affected. Diagnosis of tuberculosis was based on clinical suspicion supported by various investigations, especially bacteriological detection with stool X pert ultra in children.

## 6. Recommendation

All patients presented with fever, weight loss, anorexia and cough, tuberculosis should be kept in mind as an important differentials and every effort should be made with modern investigation facilities to confirm diagnosis in developing country like us.

## 7. Limitations

This study had a few limitations. Some important clinical and demographic information were incomplete due to suboptimal record keeping.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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