International Journal of Infectious Diseases and Therapy
2020; 5(2): 23-28
http://www.sciencepublishinggroup.com/j/ijidt
doi: 10.11648/j.ijidt.20200502.11
ISSN: 2578-9651 (Print); ISSN: 2578-966X (Online)

Pattern of Childhood Tuberculosis in the Outpatient Department of a Tertiary Level Hospital in Dhaka City

Md. Mozammel Haque[1, *], Md. Abdullah-Al-Maruf[2], Abdullah Al Baki[1], A. Z. M. Motiur Rahman[1], Md. Arif Rabbany[3], Dhiman Chowdhury[4], Muhammad Jabed Bin Amin Chowdhury[4], Muhammad Ismail Hasan[5], Mohammad Morshad Alam[5], Jugindra Singha[6], Md. Shohidul Islam Khan[6], Md. Humayan Kabir[6], Mohammed Golam Mowla[7], Kamrunnaher Shultana[8]

[1]Department of Pediatrics, 250 Bedded Hospital, Moulvibazar, Bangladesh

[2]Department of Medicine, 250 Bedded Hospital, Moulvibazar, Bangladesh

[3]Department of Pediatrics, Upazilla Health Complex, Sreepur, Gazipur, Bangladesh

[4]Department of Pediatrics, Chattogram Medical College Hospital, Chattogram, Bangladesh

[5]Department of Pediatrics, Sadar Hospital, Laxmipur, Bangladesh

[6]Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh

[7]Department of Pediatrics, Upazilla Health Complex, Muktagacha, Mymensingh

[8]Department of Pediatrics and PICU, Square Hospitals Ltd., Dhaka, Bangladesh

Email address:

mmhaque16rmc@yahoo.com (Md. M. Haque), drmaruf58@gmail.com (Md. Abdullah-Al-Maruf), abdullahalbaki09@gmail.com (A. Al Baki), azmmotiur.rahman@gmail.com (A. Z. M. M. Rahman), arifdrmmc@gmail.com (Md. A. Rabbany), dhimanchow@gmail.com (D. Chowdhury), jabedbinamin@yahoo.com (M. J. B. A. Chowdhury), dr.ismail98@gmail.com (M. I. Hasan), dr.morshadalam36@yahoo.com (M. M. Alam), sjugindra@gmail.com (J. Singha), drsikhan49@gmail.com (Md. S. I. Khan), humayan.somc@gmail.com (Md. H. Kabir), dr.mdgmowla@gmail.com (M. G. Mowla), dina_bd2010@yahoo.com (K. Shultana)

[*]Corresponding author

To cite this article:

Md. Mozammel Haque, Md. Abdullah-Al-Maruf, Abdullah Al Baki, A. Z. M. Motiur Rahman, Md. Arif Rabbany, Dhiman Chowdhury, Muhammad Jabed Bin Amin Chowdhury, Muhammad Ismail Hasan, Mohammad Morshad Alam, Jugindra Singha, Kamrunnaher Shultana. Pattern of Childhood Tuberculosis in the Outpatient Department of a Tertiary Level Hospital in Dhaka City. *International Journal of Infectious Diseases and Therapy*. Vol. 5, No. 2, 2020, pp. 23-28. doi: 10.11648/j.ijidt.20200502.11

Received: March 22, 2020; **Accepted**: April 9, 2020; **Published**: May 15, 2020

Abstract: Introduction: Tuberculosis (TB) in children is increasingly becoming an important cause of global child morbidity and mortality. Objective: The objective of this study was to evaluate the clinical spectrum of TB in children under the age of 15 years and document any changes that occur over time. Materials & Methods: This observational study was conducted in the pediatric outpatient department (OPD) of 250 Bedded TB Hospital, Shyamoli, Dhaka, from October'2016 to January'2017. A total 71 children of both sex up to 15 years of age, who were diagnosed as having TB and attended the pediatric OPD of TB hospital during the four months study period were enrolled. The data was analyzed on the basis of patient's age, gender, socioeconomic status, mode of presentation, BCG vaccination status, history of contact with smear positive TB patient, clinical findings, investigations and associated co-morbidities. Results: This study revealed that among the 71 cases of TB, (72%) had extra-pulmonary TB (EPTB) and (28%) had pulmonary TB (PTB), the commonest age group was 6 to 15 years with male preponderance (51%). Pulmonary TB was diagnosed mostly clinically (60%) followed by positive sputum smear result (20%), gastric aspirate for acid-fast bacilli AFB (5%) and sputum for Gene Xpert (5%). Distribution of extra-pulmonary TB (EPTB) according to the organ involvement was TB lymphadenitis (49%), osteoarticular TB (19.6%) and abdominal TB (5.9%). Cervical lymphadenopathy was the commonest presentation (76%) among the EPTB cases. Tuberculin skin test (TST) was positive in (69%) cases. Among the total cases (90%) children had TB alone whereas (10%) had other co-morbid disease along with TB. Conclusion: Extra-pulmonary TB (EPTB) was more prevalent among the childhood TB cases in a tertiary level set up

where cervical TB lymphadenitis was the commonest.

Keywords: Childhood TB, Pulmonary TB, Extra-pulmonary TB

1. Introduction

Tuberculosis (TB) caused by the Mycobacterium tuberculosis remains as an infection of tremendous clinical and public health importance worldwide. Despite the accelerated efforts to control TB for decades, it remains the seventh leading cause of death globally [1]. World Health Organization (WHO) estimated that over 1.3 million cases of TB and 450000 associated deaths occur annually in children [2] which represent about (6%) of the global TB burden [3]. WHO in 2007 showed that smear-positive TB in children aged 14 years accounted for (0.6%–3.6%) of all reported cases and the majority reside in Africa and Southeast Asia [4]. This finding suggests that children in developing countries will emerge as a high risk group eventually. In 2013, WHO estimated that up to 80,000 HIV children die from TB [5]. A study estimated the incidence of TB infection and disease among children in 22 high burden countries which reveals that 53 million has latent infection, 7.6 million (14.3%) has active infection with TB and 650,000 (1.2%) developed the disease finally [5]. The annual risk of TB infection in children in developing countries is (2%-5%). About (8%-20%) of deaths due to TB occur in children [7, 8]. TB in children is increasingly becoming an important cause of global child morbidity and mortality.

In Bangladesh, child TB represents (10%) of the total TB cases and remains a major cause of morbidity and mortality [1] and the burden of TB patients is the sixth of its world burden [9]. TB in children is a direct consequence of adult TB and is a good marker of current transmission in the community. The two main factors detecting the risk of progression to disease are patient's age and immune status [10-15]. Although the pulmonary TB is the most common presentation, extra-pulmonary TB accounts for up to one third of all cases of TB [7, 16-18]. Tuberculosis involves organ other than the lungs such as serous membrane, lymphnodes, abdomen, genitourinary tract, skin, joints, bones, meninges which are included as extra-pulmonary TB. Tuberculosis in children is mostly related to primary infection and it presents with various forms of relatively less aggressive primary TB [7, 16-18]. However contrary to the common notion, aggressive forms of pulmonary TB akin to adult forms are increasingly seen in pediatric clinical practice especially in adolescents [7, 16-18].

The most common form of childhood TB, the classical primary complex consists of a focal parenchymal lesion typically seen in lungs, at mid-lower zones with enlarged draining hilar/paratracheal node. Along with pulmonary manifestations, (25% to 35%) children have an extra-pulmonary presentation [19, 20]. The most common extra-pulmonary form of TB is lymphatic which accounts for about two thirds of all cases of EPTB. The second most common form is meningeal form arising in (13%) of children with TB [19, 20].

The clinical and physical manifestations of disease tend to be different by the age of onset of disease. Neonates are at higher risk of progression of infection to disease, with higher rate of miliary TB and meningeal involvement [20]. Pre-school children and adolescents are more likely to have significant signs or symptoms, whereas school-age children often have clinically silent disease. Half of young children with radio-graphically moderate to severe pulmonary TB don't have any symptoms or physical findings and, mainly, are detected by contact tracing of an adult with pulmonary TB [11-15]. Infants also, are more likely to experience clinical manifestations of TB, may be due to small airway diameters. Non-productive cough and mild dyspnea are the most common symptoms in this age group. Systemic complaints such as anorexia, fever, and night sweats occur less commonly. Some infants have difficulty in gaining weight and growing up. Some infants and young children with bronchial obstruction show localized wheezing or decreased breath sounds that may be accompanied by tachypnea or respiratory distress [11-15]. Children between 5 to 10 years are less likely to develop disease than other age groups, and adolescent patients can present with progressive primary pulmonary TB or cavitary disease [11-15, 19, 20]. The diagnosis of childhood Tuberculosis still remains a major challenge, as it is complicated by the absence of a practical "gold standard" [21, 22]. Bacteriologic confirmation, the accepted gold standard, is of limited use in children because of the paucibacillary nature of their disease and poor bacteriologic yields. Sputum smear microscopy, often the only diagnostic test available in endemic areas, is positive in less than (10% to 15%) of children with probable TB [23] and mycobacterial culture detects the bacilli in (30%–40%) cases [22, 24]. Best specimen for diagnosis of pulmonary TB in a child is the early morning gastric lavage [25, 26]. Gastric aspirates detect Mycobacterium tuberculosis in less than (50%) of cases and a negative culture never excludes the diagnosis of PTB [27-30]. In the absence of bacteriological confirmation, the diagnosis of childhood TB in endemic countries is based on close contact with an infectious patient, presence of suggestive clinical signs and symptoms, a positive Tuberculin skin test (TST), and/or abnormalities on x-ray [31-34]. Though the chest radiograph is a valuable diagnostic tool, its findings may be normal for a significant proportion of children with confirmed pulmonary TB. Now a days, PCR is being used for species identification, molecular epidemiology and rapid detection of drug resistance [35, 36].

Over the last few years, interest of WHO in childhood TB has increased dramatically. For the first time ever, in 2012, WHO included an estimate for childhood TB in their annual

report [37] and in 2012, the focus of World TB Day was children [37]. The global TB control strategy has focused predominantly on smear-positive cases and, therefore, not on childhood TB as it is usually paucibacillary and smear negative [38]. In addition, childhood TB remains neglected for various reasons, mainly the difficulty in diagnosing pulmonary TB, the lack of scientific studies on childhood TB, the largely unknown outcomes of children with TB and the belief that childhood TB is not important for TB control [38, 39]. Further research, understanding and prevention of TB among children are urgently needed. The overall objective of this study was to evaluate the clinical spectrum of TB in children in a tertiary care hospital under the age of 15 years.

2. Materials & Methods

This study was conducted in the pediatric outpatient department (OPD) of 250 Bedded TB Hospital, Shyamoli, Dhaka, from October'2016 to January'2017. This tertiary level health care facility receives referred TB patients from the other primary, secondary or tertiary hospitals all around the country and also from the chamber of private practitioners. A total 71 children of both sex, age 0 to 15 years were enrolled in this survey. The children who were already diagnosed as TB patient in this hospital or elsewhere, already on anti-TB drugs or going to be introduced anti-TB therapy who came to the OPD of 250 Bedded TB Hospital during the four months period were sequentially enrolled. This was an observational study conducted for a pre-specified four months period and hence the statistical methods for sample size determination and randomization was not applied. For the confirmation of TB in children, case specific diagnostic modalities were used by the primary attending physician like clinical response to anti-TB therapy (who were not responded to other antibiotics previously), Tuberculin skin test (TST), smear test (sputum/gastric lavage), chest x-ray, fine needle aspiration cytology (FNAC) or biopsy etc. So, it was not considered mandatory by the primary physician doing chest x-ray or TST in all children. All the lymph node TB cases (except the mediastinal nodes) were diagnosed either by FNAC or biopsy. The data was analyzed on the basis of patient's age, gender, socioeconomic status, mode of presentation, BCG vaccination status, history of contact with smear positive TB patient, clinical findings, investigations and associated co-morbidities. Written informed consent was taken from the patients and ethical clearance was taken from the appropriate authority.

3. Result

Table 1 showed that, among the total 71 cases of childhood TB, the common age group was 6-15 years (68%) with male preponderance (51%). School going and urban children were affected more, (61%) & (79%) respectively. Prevalence of child TB was more common (42%) in upper middle income group (9000-17999 taka per month) and children of drivers (23%). Eighty three percent studied children had contact with smear positive PTB patient. Ninety six percent of the enrolled children were BCG vaccinated.

Table 1. *Socio-demographic characteristics of the studied children (n=71) Data are presented as number (%).*

Patient profile	Variables	Number (%)
Age	0-5 years	23 (32%)
	6-15 years	48 (68%)
Sex	Male	36 (51%)
	Female	35 (49%)
Education	No schooling[∞]	24 (33%)
	School student	43 (61%)
	Madrasa student	4 (6%)
Living area	Rural[¶]	16 (21%)
	Urban[¥]	55 (79%)
Socio economic status	Upper	23 (32%)
	Upper middle[Ω]	30 (42%)
	Lower middle[©]	10 (14%)
	Lower[♦]	8 (12%)
Frequency of parent's profession	Day laborers	6 (8%)
	Driver	16 (23%)
	Small traders	9 (13%)
	Garment workers	3 (4%)
	Others	37 (52%)
Contact with TB patient	Present	12 (17%)
	Absent	59 (83%)
BCG status	Vaccinated	68 (96%)
	Not vaccinated	3 (4%)

[∞]Either minor or did not go to school for some other reasons.
[¶]Living in village or upazilla (sub district) level. [¥]Living in district and/or metropolitan city.
Monthly income 18,000 taka. [Ω]Monthly income 9000-17999 taka. [©]Monthly income 6500-8999 taka. [♦]Monthly income <6500 taka.
(Source: Kuppuswamy classification of socioeconomic status-January 2015).

Table 2 shows the pattern of TB, where pulmonary TB was (28%) and extra-pulmonary TB was (72%). Among the pulmonary cases smear negative and among the extra-pulmonary cases TB lymphadenitis constituted the highest percentage, (60%) & (49%) respectively.

Table 2. *Distribution of pattern of TB among studied children (n=71) Data are presented as number (%).*

Pattern of TB No (%)	Sub category	Number (%)
Pulmonary TB 20 (28%)	Smear negative	12 (60%)
	Smear positive	08 (40%)
Extra-pulmonary TB 51 (72%)	TB lymphadenitis	25 (49%)
	Osteoarticular TB	10 (19.6%)
	Abdominal TB	03 (5.9%)
	Localized TB abscess	03 (5.9%)
	Pleural effusion	03 (5.9%)
	TB meningitis	02 (4%)
	TB osteomyelitis	02 (4%)
	Brain abscess	01 (2%)
	Pericardial TB	01 (2%)
	Disseminated TB	01 (2%)

In Table 3, involvement of different groups of lymph node is shown where the most common group of lymph node was

cervical (76%) followed by inguinal (12%), mediastinal (8%) and axillary (4%).

Table 3. *Distribution of TB lymphadenitis (n=25) Data are presented as number (%).*

Site of Involvement	Number (%)
Cervical	19 (76%)
Inguinal	03 (12%)
Mediastinal	02 (8%)
Axillary	01 (4%)

Clinical presentation of pulmonary and extra-pulmonary TB in children is shown in Tables 4 & 5 respectively. In case of pulmonary TB, most of the children presented with fever (80%), cough (75%) and anorexia (40%). In case of EPTB, most of the children (52%) presented with systemic manifestation than only lymph node presentation.

Table 4. *Clinical presentation of pulmonary TB among the studied children (n=20) Data are presented as number (%)*

Presentation	Number (%)
Fever	16 (80%)
Cough	15 (75%)
Anorexia	08 (40%)
Chest Pain	07 (35%)
Dyspnea	06 (30%)
Weight loss	05 (25%)
Not gaining weight	02 (10%)

Table 5. *Clinical presentation of TB lymphadenitis among the studied children (n=25) Data are presented as number (%).*

Presentation	Number (%)
Systemic presentation	13 (52%)
Local (only lymph node) presentation	12 (48%)

Table 6 shows the number of children having contact with smear positive pulmonary TB cases which was (14%) of the total (n=71). TST was not performed as a diagnostic tool by the primary attending physician in 42 patients, so, n=29. In this study TST ≥10 mm was considered positive which was (69%) [Table 7].

Table 6. *Distribution of studied children according to history of contact with smear positive case (n=71) Data are presented as number (%)*

Contact with smear positive case	Number (%)
Absent	61 (86%)
Present	10 (14%)

Table 7. *Status of Tuberculin skin test (TST) among studied children (n=29) Data are presented as number (%).*

Diameter of induration	Number (%)
<10 mm	09 (31%)
≥10 mm	20 (69%)

4. Discussion

According to WHO, TB is a worldwide pandemic [40]. In 2008, WHO ranked Bangladesh sixth among the world's 22 high TB burden countries [41]. The incidence of both pulmonary and extra-pulmonary TB is expected to rise [42]. In this study, EPTB constituted (72%) of all cases of TB, while about (15% to 20%) was reported by Fanning [43, 44] and (10%) by Haegi [43, 44]. Study done by Charlett, et al. [45], in the United Kingdom, showed (15%) British children presented with extra-pulmonary TB whereas in Bangladeshi, Pakistani or Indian ethnic, it was (50%) [45]. According to our national child TB guideline EPTB accounts for about (30%) of TB in children [46], as seen in high burden country. Although this study result did not represent the national incidence of child TB, this figure indicated that there was a gap between the National Tuberculosis Control Program (NTP) reported child TB and actual disease burden in the community [46].

In this study, the majority of EPTB cases presented with TB lymphadenitis (49%) and the commonest lymph node involved was the cervical group (76%). A study by Shafiullah [47] showed the lymph nodes to be the most common site of EPTB as observed in (66%) of studied cases which was consistent with this study result. In a study in Hong Kong [17], the most common site of EPTB was the pleura, followed by the lymph nodes. Another study in Holland [48] showed that the most common sites of EPTB were both pleura and lymph node (17% for each).

In this study the commonest group of lymph node involved in TB lymphadenitis was cervical (76%) followed by inguinal (12%) and mediatsinal (8%). A study by Hatwal D [49] showed that cervical lymphadenopathy was the commonest presentation followed by axillary and inguinal which was almost similar to our study.

A study by Napoleon [50] showed that fever, cough, weight loss, expectoration and hemoptysis were the commonest symptoms among the PTB cases which was consistent with this study where the most of the patient with PTB presented with fever (80%), cough (75%), anorexia (40%) and weight loss (35%). Another study by Hatwal D [51] showed that all of the EPTB cases presented with fever, anorexia, weight loss, malaise and the result was also comparable to this study.

Dhara, et al. [51] in his study showed that history of contact with smear positive TB patient was (28%) which was (17%) in this study. This can be explained by the lack of knowledge or awareness among people about TB, its clinical symptoms and the need for consultation with physician for proper diagnosis in our country which hinders the screening and identification of smear positive cases. In the same study done by Hatwal D [49] showed that positive TST was present in (70.85%) of the study cases which was also similar to our study result (69%).

5. Conclusion and Recommendation

From the present study it can be concluded that extra-pulmonary TB (EPTB) was more prevalent among childhood Tuberculosis in a tertiary level set up where cervical TB lymphadenitis was the commonest. This short duration study

involved a small number of patients, so, further large scale multi-center study is recommended to delineate the original TB scenario in the country.

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