Proportion and Factors Associated with Presumptive Tuberculosis among Suspected Pediatric TB Patients

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Abstract—The study addresses the increasing challenge of pediatric presumptive tuberculosis, emphasizing the need to understand the factors associated with it. The research aims to determine the proportion of presumptive TB and factors associated with it among suspected pediatric tuberculosis patients. A cross-sectional study was conducted at ICDDR-Bangladesh, collecting specimens from suspected pediatric patients and using logistic regression for data analysis. The study found a high proportion of presumptive TB (85.7%) but no statistically significant differences between presumptive and non-presumptive TB. Theoretical importance of the study highlights the importance of identifying factors associated with presumptive TB for better control and management strategies. Specimens were collected from 84 suspected pediatric patients diagnosed with TB based on clinical symptoms/radiological findings. Microbiological tests like smear-microscopy, culture, and GeneXpert were used to isolate presumptive TB and confirmed TB. The proportion of presumptive TB was 85.7% among suspected pediatric TB patients. Among various factors that were not found to be associated with the presumptive TB. The study concludes that despite a high proportion of presumptive TB, no significant differences were found between presumptive and non-presumptive TB cases.

Keywords—Presumptive tuberculosis, confirmed tuberculosis, patient's characteristics, diagnosis.

I. INTRODUCTION

NOT only confirmed TB but also presumptive TB is a severe public health issue. Bangladesh ranks seventh among countries with high TB incidence globally [1]. WHO recommends considering surveys in nations with a predictable TB incidence of 150 per 0.1 million people per year [9]. TB bacilli can remain latent for several years, but 5% to 10% of infected individuals face a lifetime risk of acquiring the illness [1]. Annually, 10.4 million children develop TB while 1.8 million die worldwide, and more than 95% of TB deaths occur in low and middle-income nations. The Bangladesh National Tuberculosis Control Program (BNTP) reported that in 2007, the TB incidence of children was 9/1,00,000, and the TB prevalence was 52/100000 in 2008-2009 [2].

Diagnosis of TB in children is very challenging; most receive anti-TB treatment without bacteriological confirmation [3], which is difficult due to the low bacterial load, the difficulty obtaining high-quality specimens, and the paucibacillary nature of childhood TB with 10-15% positive rate when smear-microscopy is used, and 30-40% when culture is used [4]-[6]. Previously, Islam et al. [4] and Wobudeya et al. [7] reported that specimen collection and testing are further constrained by a lack of skilled healthcare employees, sophisticated mycobacterial-laboratory and equipment facilities, as well as in-patient facilities in resource-limited countries like Bangladesh. Clinical specimens such as sputum, gastric lavage, and pleural fluid, which were known as pulmonary specimens, and cerebrospinal fluid which was known as extra-pulmonary specimens in the pediatric-TB (P-TB) [8].

Despite challenges in finding microbiological confirmation, the microbiological investigation remains very important for numerous reasons: (i) to support the diagnosis and management of complicated cases, mainly when the differential may be broad; (ii) to allow the rapid start of appropriate TB treatment through detecting TB and drug profiles. Culture techniques have the limitation of a long turnaround time of several weeks, while smear-microscopy has poor sensitivity and issues related to quality control [9]. The WHO recommended that Xpert MTB/RIF, a rapid molecular test, may be used as the initial diagnostic test in all children with presumptive pediatric TB [10].

In Bangladesh, Kamruzzaman et al. [11], Shruthi et al. [12], and Haque et al. [13] reported that the proportion of confirmed TB was 15.25%, 10.3%, and 12.95%, respectively, among the presumptive TB. In our country, however, based on the literature review, we obtained limited to no data on associated factors of presumptive TB patients. Therefore, we conducted this study to explore the presumptive TB proportion and determine their socio-demographic characteristics.

II. MATERIALS AND METHODS:

Study Design, Sample Size, and Participants

This cross-sectional study was conducted between March and November 2013 at the International Centre for Diarrhoeal Disease Research (ICDDR)-Bangladesh. A total of 212 clinical specimens such as respiratory specimens (induced sputum n = 20 and expectorated sputum n = 80), pleural fluid (n = 12), gastric lavage (n = 90), and cerebrospinal fluid (CSF) {n = 10} were collected from 34, 10, 30, and 10 patients, respectively, who were recruited based on clinical symptoms and radiological findings. After that, specimens with presumptive TB and confirmed TB were isolated by microbiological tests such as smear-microscopy, culture, and GeneXpert, and they were considered presumptive TB and non-presumptive TB. Data were collected through structured questionnaires and face-to-face interviews with their guardians.

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Laboratory Testing

Specimens were decontaminated and isolated by conventional culture on the Lowenstein-Jansen slant following Petroff's method [14]. Processed specimens were prepared and stained by auramine-stained smear microscopy - fluorescence microscopy, and GeneXpert MTB assays [10].

Statistical Analysis

Descriptive analysis was carried out using frequency and percentage. The Chi-square test was used to examine background traits between non-presumptive TB patients and presumptive TB patients. Logistic regression models were utilized to identify the associated factors related to the patients. P-values less than 0.05 were considered statistically significant. A 95% confidence interval was reported where appropriate. Data analysis was performed using STATA statistical software (version 16.0).

Ethics Statement

The Ethics Committee of ICDDR, B approved the present study. The participants were enrolled in the study only after receiving informed written permission from their parents/ guardians.

III. RESULTS

84 participants, including presumptive TB (n = 72) and non-presumptive TB (n = 12) pediatric pulmonary TB patients from all over Bangladesh, were interviewed during the study period. The overall culture-positive rate, which was the strains of Mycobacterium tuberculosis (Mtb), was 14.3% (12 out of 84), the smear microscopy-positive rate was 4.7% (4 out of 84), and the Xpert MTB/RIF-positive rate was 9.5% (8 out of 84). The proportion of non-presumptive TB, which was bacteriologically confirmed TB, was 14.3%, and presumptive TB, which was not bacteriologically confirmed TB, was 85.7%. In presumptive TB, vaccine scars, family TB history, and school-going children were observed at 16.67%, 33.3%, and 56.94%, respectively. In non-presumptive TB, 8.3% of BCG vaccine scars and family TB history were present, and 58.3% were school-going children. However, there was no statistically significant difference between the characteristics of non-presumptive TB patients and presumptive TB patients, as illustrated in Table I.

TABLE I
THE ASSOCIATION BETWEEN THE CASES AND THEIR ASSOCIATED FACTORS

Characteristics		Non-Presumptive TB patients (n = 12) frequency (%)	Presumptive TB patients (n = 72) frequency (%)	Total patients frequency (%)	P-value (chi-square)
Categories	Subcategories				
Gender	Male	6 (50)	30 (41.7)	36(42.86)	0.589
	Female	6 (50)	42 (58.3)	48(57.14)	
Age	58 days -1 year	2 (16.7)	14 (19.4)	16(19.05)	0.640
	(2-5) year	2 (16.7)	22 (30.6)	24(28.57)	
	(6-10) year	4 (33.3)	14 (19.4)	18(21.43)	
	(11-14) year	4 (33.3)	22 (30.6)	26(30.95)	
Family history	No	11 (91.67)	48 (66.7)	59(70.24)	0.079
	Yes	1 (8.33)	24 (33.3)	25(29.76)	
BCG vaccine scars	Presence	1 (8.33)	12 (16.67)	13(15.48)	0.460
	Absence	11 (91.67)	60 (83.33)	71(84.52)	
Type of specimens	P specimens	10 (83.33)	64 (88.89)	74(88.10)	0.582
	EP specimens	2 (16.67)	8 (11.11)	10(11.90)	
Education	No schooling	5 (41.67)	31 (43.06)	36(42.86)	0.928
	School student	7 (58.33)	41 (56.94)	48(57.14)	

TABLE II
LOGISTIC REGRESSION MODEL TO IDENTIFY FACTORS THAT ARE ASSOCIATED WITH PRESUMPTIVE TB AND NON-PRESUMPTIVE TB

Characteristics	Subcategories	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Gender	Female	Ref.	Ref.
	Male	1.4 (0.41 4.76)	1.46 (0.36 5.83)
Age	58 days -1 year	Ref.	Ref.
	(2-5) year	0.63 (0.08 5.04)	0.66 (0.07 6.25)
	(6-10) year	2.0 (0.31 12.75)	1.26 (0.12 13.88)
	(11-14) year	1.27 (0.21 7.89)	0.92 (0.04 21.14)
Family history	No	Ref.	Ref.
	Yes	0.18 (0.02 1.49)	0.17 (0.02 1.64)
BCG vaccine scars	Absence	Ref.	Ref.
	Presence	0.45 (0.05 3.86)	0 .67 (.05 8.44)
Type of specimens	P specimens	Ref.	Ref.
	EP specimens	1.60 (0.30 8.64)	0 .81 (0.12 5.46)
Education	No schooling	Ref.	Ref.
	School student	1.4 (0.41 4.76)	1.63 (0.14 18.59)

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Among various factors that were not found to be associated with the presumptive TB. Sociodemographic factors like family TB history with an adjusted odds ratio (AOR) of 0.17, 95% Confidence Interval (CI) of 0.02-1.64, vaccine scars (AOR: 0.67, 95% CI: 0.05-8.44), and school-going children (AOR: 1.63, 95% CI: 0.14-18.59). In logistic regression analysis, factors did not appear statistically significant in the bi-variable analysis and the multivariable model (Table II).

IV. DISCUSSION

According to the literature review, this is the first cross-sectional study that examined presumptive TB and its associated factors among the suspected pediatric TB patients of Bangladesh. It was observed that the proportion of presumptive TB was higher, almost three-quarters, than non-presumptive TB. However, no statistical significance was observed between their socio-demographic parameters. Most studies conducted have focused on non-presumptive TB, which is confirmed TB. In our country, Kamruzzaman et al. [11], Shruthi et al. [12], and Haque et al. [13] reported that the proportion of confirmed TB among the presumptive TB. However, no significant study was found on presumptive TB.

Regarding gender, males and females were equally affected by non-presumptive TB, but females were more likely to have presumptive TB. It was close to non-presumptive TB observed in another study [15], but other studies found that males were higher than females [16]-[18], and the opposite scenario was observed as well [11], [19]. Our data showed that, similar to Alavi et al. [19] most non-presumptive TB patients were 6-14 years old. Nevertheless, a previous study by Ahsan et al. [15] mentioned that most non-presumptive TB are between 1 and 5 years old. On the other hand, younger children are more affected than infants with presumptive TB. School-going children were more in presumptive TB and non-presumptive TB. The non-presumptive TB had less family TB history and BCG vaccine scar than those with presumptive TB. Neither the non-presumptive TB patient's mother nor the presumptive TB patient's mother had TB during pregnancy and breastfeeding. It was observed that the majority of the patients' parents worked in menial employment. However, no statistical significance was found between their socio-demographic parameters.

Our findings indicate the warrant for special attention to pediatric TB, both non-presumptive TB and presumptive TB. They should focus on establishing a healthcare organization, developing sophisticated mycobacterial laboratory capacity for early diagnosis and treatment, growing skilled healthcare employees, monitoring individuals with TB symptoms, and more interventions on cases. Moreover, nationwide and longitudinal studies need to be further elucidated with more patients to realize the proportion of presumptive TB and its associated factors in Bangladesh. Although the BNTP is implementing its nationwide TB control strategies, the high proportion of pediatric TB is an alarming issue. The magnitude of the presumptive TB burden has remained an unfamiliar territory for worldwide health policymakers [20]. Providers, investigators, policymakers, and advocates should all be aware that children must be involved in the discussion about how to halt the toll of presumptive TB. Consequently, the BNTP should concertedly capture pediatric TB, both presumptive TB and non-presumptive TB with associated factors.

This study had several strengths. This is the first study to systematically assess the factors associated with presumptive TB patients in Bangladesh. Moreover, the conventional culture, gold standard test method, and GeneXpert were performed to identify presumptive TB. We believe that our study provides a significant vision to the key facilitators of pediatric TB diagnosis and treatment in Bangladesh. This study had a few limitations. For example, the sample size was small, which might not reflect the scenarios of the whole country.

V. CONCLUSION

The current study's findings indicated that the proportion of presumptive TB was an alarming issue. It was higher than non-presumptive TB, but no significant differences existed between them. Presumptive TB patients are an effective measure that may be critical in determining the characteristics of patients suffering from chronic illness.

AUTHOR CONTRIBUTIONS

Conceptualization: Naima Nur
Investigation: Naima Nur
Laboratory work & report: Naima Nur
Data entry & analysis: Naima Nur
Writing – original draft: Naima Nur
Writing – review & editing: Naima Nur, Safa Islam, Md. Faridul Alam, Saeema Islam

REFERENCES

[1] Nur N., Sharif A. B. and Mitra D. K. (2023). Stress resilience in patients with drug-resistant TB. The International Journal of Tuberculosis and Lung Disease 27(7):551-556. https://doi.org/10.5588/ijtld.22.0648

[2] Talukder K., Salim M. A. H., Jerin I., et al. (2012) Intervention to increase detection of childhood tuberculosis in Bangladesh. Int J Tuberc Lung Dis. 16(1):70–75; 16(January 2011): 70–75. http://dx.doi.org/10.5588/ijtld.11.0060.

[3] Hailu D., Abegaz W. E., Belay M. (2014) Childhood tuberculosis and its treatment outcomes in Addis Ababa: a 5-year retrospective study. BMC Pediatr; 14(61). http://www.biomedcentral.com/1471-2431/14/61.

[4] Islam Z., Sanin K. I., Ahmed T. (2017). Improving case detection of tuberculosis among children in Bangladesh: lessons learned through an implementation. BMC Public Health 17(131); 1-9. https://doi.org/10.1186/s12889-017-4062-9

World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:18, No:7, 2024

[5] Sanchini, A., Fiebig, L., Drobniewski. F. et al. (2014). Laboratory diagnosis of paediatric tuberculosis in the European Union/European Economic Area: analysis of routine laboratory data, 2007 to 2011. Euro Surveill. 2014;19(11). http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId = 20744.

[6] Chisti M. J., Graham S. M., Duke T. et al. (2014). A Prospective Study of the Prevalence of Tuberculosis and Bacteraemia in Bangladeshi Children with Severe Malnutrition and Pneumonia Including an Evaluation of Xpert MTB/RIF Assay. PLoS One; 9(4): e93776. http://doi: 10.1371/journal.pone.0093776.

[7] Wobudeya E., Bonnet M., Walters E. G., et al. (2022). Diagnostic Advances in Childhood Tuberculosis-Improving Specimen Collection and Yield of Microbiological Diagnosis for Intrathoracic Tuberculosis. Pathogens; 11(4): 389. https://doi.org/10.3390/pathogens11040389.

[8] Zar. H. J., Hanslo. D., Apolles. P., et al. (2005). Induced sputum versus gastric lavage for microbiological confirmation of pulmonary tuberculosis in infants and young children: a prospective study. Lancet; 365: 130–34.

[9] Sharma S. K., Kohli M., Yadav R. N., et al. (2015). Evaluating the diagnostic accuracy of xpert MTB/RIF assay in pulmonary tuberculosis. PLoS One; 10(10): 1-9. https://doi.org/10.1371/journal.pone.0141011

[10] World Health Organization (WHO) (2014). Xpert MTB_RIF implementation manual_ technical and operational 'how-to'; practical considerations. https://www.ncbi.nlm.nih.gov/books/NBK254323/

[11] Kamruzzaman M., Hossain M., Islam A., et al. (2019). Clinical Profile of Tuberculosis: A Study in a Tertiary Care Paediatric Hospital, Dhaka, Bangladesh. Journal of Dental and Medical Sciences; 18(5): 34-39. https://doi.org/10.9790/0853-1805143439

[12] Shruthi S., Ratageri V. H., Shivananda I., et al. (2019). Pulmonary Tuberculosis in Children with Severe Acute Malnutrition: A Prospective Hospital-based Study. Pediatric Infectious Disease; 1(1): 1-3. https://doi.org/10.5005/jp-journals-10081-1101

[13] Haque M., Supti S. H., Jahan et al. (2023). Clinico-Epidemiological Profile and Diagnostic Procedures of Tuberculosis in Children: A Retrospective Study from OPD of Tertiary Care Center in Bangladesh. Journal of Tuberculosis Research; 11(1): 1-11. https://doi.org/10.4236/jtr.2023.111001

[14] Petroff S. A. (1915). A new and rapid method for isolation and culture of tubercle bacilli directly from the sputum and faece. J Exp Med; 21 (1): 38-42. https://doi.org/10.1084/jem.21.1.38.

[15] Ahsan M. R., Hussain M., Makbul S., et al. (2019). Clinical Pattern of Pediatric Tuberculosis in a Tertiary Care Hospital in Bangladesh. Dhaka Shishu (Children). Hospital Journal; 35(1): 9-13.

[16] Guo Q., Pan Y., Yang Z., et al. (2016). Epidemiology and clinical characteristics of pediatric drug-resistant tuberculosis in chongqing, China. PLoS One; 11(3): 1-12. https://doi.org/10.1371/journal.pone.0151303

[17] Satana D., Genc G. E., Tamay Z. et al. (2014). Prevalence and drug resistance of mycobacteria in Turkish cystic fibrosis patients. Annals of Clinical Microbiology and Antimicrobials; 13:28. http://www.ann-clinmicrob.com/content/13/1/28.

[18] Kabir S., Uddin M. K. M., Chisti M. J., et al. (2018). Role of PCR method using IS6110 primer in detecting Mycobacterium tuberculosis among the clinically diagnosed childhood tuberculosis patients at an urban hospital in Dhaka, Bangladesh. Int J Infect Dis; 68: 108–114. https://doi.org/10.1016/j.ijid.2018.01.015.

[19] Alavi S. M., Salmanzadeh S., Bakhtiyariniya P., et al. (2015). Prevalence and treatment outcome of pulmonary and extra-pulmonary pediatric tuberculosis in southwestern Iran. Casp J Intern Med; 6(4): 213-219. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4649270/pdf/cjim-6-213.pdf.

[20] World Health Organization (WHO) (2022). Global Tuberculosis Control. Global TB Programme. Geneva, Switzerland. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022.