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Clinico-laboratory Profile of Childhood Tuberculosis Admitted at a Tertiary Hospital in Nepal

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: To describe the clinical and laboratory profile of children admitted with Tuberculosis at a tertiary care hospital in Nepal.
Study Design: Retrospective study.
Place and Duration of Study: Department of Pediatrics, Patan Academy of Health Sciences, between April 2013 and April 2018.
Methodology: All childhood TB patients (age 0-15 years) admitted to Patan Hospital from April 2013 to April 2018 (5 years) were included in the study. Medical record files of the eligible patients were retrieved from the medical records section. Medical record files, reports of chest x-rays and laboratory investigations were reviewed and information regarding diagnosis and treatment of TB was filled in a pre-designed proforma. Collected data were entered and analysed in Statistical Package for Social Sciences (SPSS version 25.0) software.
Results: A total of 64 patients were admitted with the diagnosis of TB in the Department of Paediatrics at Patan Hospital from April 2013 to April 2018. The median age of the patients was 7.8 years, age ranging from 4 months to 15 years. Male to female ratio was 1.56:1. Extra-pulmonary TB (59.38%) was more common than pulmonary TB (40.62%). Fever (79.68%) was the most common presenting symptoms. Among extra-pulmonary TB, pleural effusion (39.47%) and abdominal TB (26.31%) were the most common diseases. TB meningitis was the least common disease, seen in only 3 patients.

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Conclusion: Childhood TB is prevalent but underdiagnosed disease our setting. Extrapulmonary TB is more common in children, pleura and abdomen being the most common sites. Microbiological confirmation of TB in children is very low, so the diagnosis of TB in children largely depends upon clinical signs and symptoms along with supportive laboratory investigations.

Keywords: Tuberculosis; pediatric TB; infectious disease; global health.

1. INTRODUCTION

It has been estimated that about a quarter of the world's population is infected with *Mycobacterium tuberculosis* [1]. World Health Organization reports about 1.6 million deaths worldwide due to tuberculosis (TB) in 2017 [1]. About 95% of TB burden and 99% of TB related mortality occurs in developing countries [2]. It is estimated children less than 15 years account for about 10% of the global TB cases. This percentage may be as high as 22% in developing countries [3]. Childhood TB is an important public health issue because it acts as an indicator of recent transmission of TB in a population. Contact tracing and investigations of childhood TB patients may result in improved case-finding rates among adults [4]. Most of the national TB control programs emphasise more smear positive adult TB cases because they are highly infectious, as a result, pediatric TB receives less importance by TB control programs because of the difficulties in confirming the diagnosis and overestimating the protection rate of BCG vaccine [5]. Diagnosing TB in children remains a challenging issue in resource-limited countries like Nepal. Protocols for diagnosing TB in children may vary in different healthcare settings depending upon the availability of resources.

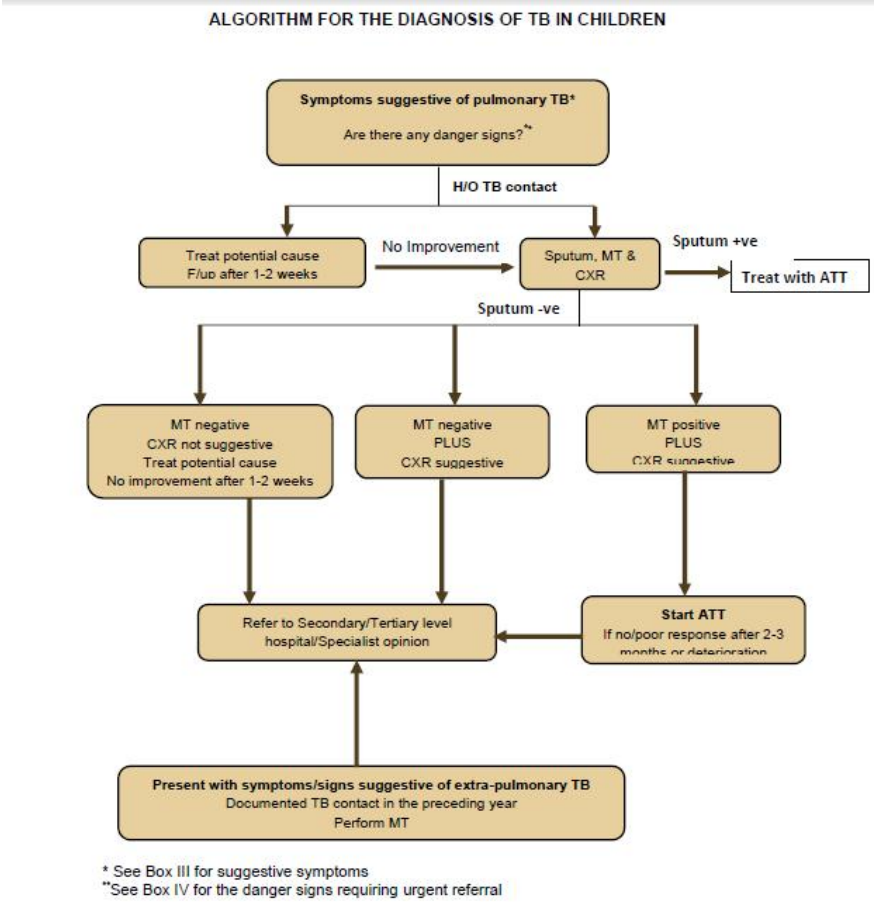

Fig. 1. Algorithm for TB diagnosis in children
(Source: Nepal Tuberculosis Program)

Around forty-five percent of the total population of Nepal is infected with *Mycobacterium tuberculosis* [6]. Current case detection rate of childhood TB in Nepal is 7%, which is less than the WHO estimate of 10% [7]. Despite the high burden of childhood TB in developing countries, reliable data on this disease is scanty, in both global and local contexts. There are very few published researches on clinical profile of TB in Nepalese children. In these contexts, this study was carried out to describe the clinic-laboratory profile of childhood TB patients admitted to a tertiary care hospital in Nepal.

2. METHODOLOGY

2.1 Study Setting

Patan Hospital (PH) is a tertiary care teaching hospital affiliated to Patan Academy of Health Sciences (PAHS). PH serves patients from Kathmandu valley and other places of Nepal. Guidelines issued by the National TB Program (NTP) of Nepal are followed for diagnosing and treating TB at PH. Children were evaluated, diagnosed and managed according to the National Childhood TB Management Guideline (Fig. 1). All the patients diagnosed with TB in various departments of PH are referred to the nearby Directly Observed Treatment, short course (DOTS) clinic from where they receive anti-tuberculosis treatment according to the NTP guidelines.

2.2 Data Collection

Ethical clearance was obtained from the Institutional Review Committee of PAHS. All childhood TB patients (age 0-15 years) admitted to Patan Hospital from 15th April 2013 to 14th April 2018 (5 years) were included in the study. Medical record files of the eligible patients were retrieved from the medical records section. Medical record files, reports of chest x-rays and laboratory investigations were reviewed and information regarding diagnosis and treatment of TB was filled in a pre-designed proforma. Collected data were entered and analysed in Statistical Package for Social Sciences (SPSS version 25.0) software.

3. RESULTS

A total of 64 patients were admitted with the diagnosis of TB in the Department of Paediatrics at Patan Hospital from April 2013 to April 2018 (5 years). Age and gender distribution of the patients is shown in Table 1. The median age of the patients was 7.8 years, age ranging from 4 months to 15 years. Male to female ratio was 1.56:1. Extra-pulmonary TB (59.38%) was more common than pulmonary TB (40.62%). Among extra-pulmonary TB, pleural effusion (39.47%) and abdominal TB (26.31%) were the most common diseases. TB meningitis was the least common disease, seen in only 3 patients.

Table 1. Age and gender distribution

Age	Male (n)	Female (n)	Total (%)
0 < 5 years	6	3	9 (14.06)
5 < 10 years	18	10	28 (43.75)
10 < 15 years	15	12	27 (42.18)
Total	39	25	64 (100)

Table 2. Spectrum of childhood TB

Site of tuberculosis	n (%)
Pulmonary	26 (40.62)
Extrapulmonary	38 (59.38)
1. Pleural effusion	15 (39.47)
2. Abdominal	10 (26.31)
3. Disseminated	5 (13.15)
4. Lymph nodes	5 (13.14)
5. Central nervous system	3 (7.89)
Total	**64 (100)**

Fever (79.68%), anorexia (73.43%), cough (64.06%) and weight loss (46.87%) were the most common presenting symptoms as shown in Table 3. Seizure was present in all 3 patients with TB meningitis. Most common signs included respiratory system findings (decreased breath sounds, bronchial sounds, crackles, wheeze, dull on percussion) followed by malnutrition and pallor in 28, 26 and 17 patients respectively. Splenomegaly and neck stiffness were the least common signs. BCG scar was seen in 51 (79.68%) patients.

Table 3. Presenting symptoms

Symptoms	n (%)
Fever	51 (79.68)
Anorexia	47 (73.43)
Cough	41 (64.06)
Weight loss	30 (46.87)
Abdominal pain	21 (32.81)
Chest pain	18 (28.12)
Breathlessness	14 (21.87)
Vomiting	7 (10.93)
Seizure	3 (4.68)

Table 4. Physical examination findings

Signs	n (%)
Chest signs*	28 (43.75)
Malnutrition	26 (40.62)
Pallor	17 (26.56)
Ascites	14 (21.87)
Lymphadenopathy	9 (14.06)
Splenomegaly	4 (6.25)
Neck stiffness	2 (3.12)

Table 5 shows different investigations carried out for the diagnosis of TB. Chest X-ray was abnormal in a relatively higher proportion of patients (62.29%). Mantoux test was positive (induration of 10 mm or more) in less than half of TB patients (42.37%) [8]. Gene Xpert and microscopy for Acid-Fast Bacillus (AFB) was carried out on samples of gastric lavage, sputum, ascitic fluid or cerebrospinal fluid (CSF) depending upon the type of TB, however, both these tests had low diagnostic yield. Gene Xpert was positive in 11 (29.72%) patients and AFB microscopy was positive only in 6 (15.38%) patients. There were 5 children with lymph node TB and FNAC was diagnostic in all of them. CSF was abnormal and suggestive of TB in all the 3 cases of TB meningitis, however, they were all negative for AFB microscopy.

Table 5. Investigations with a positivity rate

Investigation	Number of positive or abnormal investigation results/number of investigation done
Chest X-ray	38/61 (62.29)
Mantoux test	25/59 (42.37)
ESR	23/54 (42.59)
Acid Fast Bacilli stain	6/39 (15.38)
GeneXpert	11/37 (29.72)
FNAC/Biopsy	5/5 (100)
Cerebrospinal fluid analysis	3/3 (100)

4. DISCUSSION

In this retrospective study, TB was more common in children above 5 years of age compared to younger children. There were more male children with TB compared to female. Extrapulmonary TB was more common in this study. The most common extrapulmonary site of TB was pleura, followed by abdomen.

Pediatric TB remains a neglected public health issue in developing countries. Children are thought to suffer from TB less severely and less often than the adults [9]. However, in resource-limited developing countries, a significant proportion of tuberculosis patients are children, with high related mortality and morbidity [10]. Although there was a decrease in the burden of TB since the 1960s, a resurgence was seen during the 1990s due to the epidemic of HIV [11]. Two Taiwanese studies have reported a bimodal distribution of TB incidence according to age [12,13]. However, we did not find such a pattern in our study. In our study, 59.38% of patients had extra-pulmonary TB and 4 out of 5 patients with disseminated TB were of age less than 10 years. There is a possibility that BCG vaccination might have a protective role against severe forms of extrapulmonary TB [14]. This may be supported by data in this study where nearly 80% of the children received BCG vaccine. There are some studies which report that BCG vaccine may provide protection to children from M. tuberculosis infection [15,16]. Different studies have shown that young children are more likely to develop extrapulmonary TB compared to older children or adults [17,18]. There are few studies which have described increasing trends of extrapulmonary tuberculosis in children as well adults [17,18]. Pleura was the most common site of extrapulmonary involvement in our hospital, however other authors have reported lymph node as the most common extrapulmonary site of involvement [18-20]. The abdomen was the second most common site in this study. Nepal is an agrarian country when contact of a human with livestock is very common; this may be the reason for the higher frequency of extrapulmonary tuberculosis due to transmission of bovine tuberculosis. This might be the reason for abdomen being the second common site of extrapulmonary TB. However, we do not have robust evidence to support this hypothesis.

In this study, 5 (13.15%) of patients had disseminated TB, which was comparable to a similar study from western Nepal. Delayed suspicion of TB by healthcare workers, non-specific signs and symptoms of childhood TB and lack of resources might be the reasons children to arrive at the tertiary hospital at advanced stages of TB.

It is a known fact that it is difficult to diagnose TB in children [21]. In our hospital, pulmonary TB was diagnosed mainly on the basis of chest x-ray, ESR, Mantoux test, AFB microscopy and Gene Xpert. Some other investigations were done for patients with extrapulmonary TB which included ultrasonography, FNAC/Biopsy, CSF analysis etc. Chest Xray was commonly done for

both pulmonary and extrapulmonary TB patients despite its questionable reliability as a diagnostic tool as reported by some studies [22]. ESR was found to be elevated in 42.59% of children in this study whereas a study from Qatar had elevated ESR 67% of children with TB [23]. Theoretically, ESR should have a good prognostic and diagnostic value in childhood TB as other illnesses causing high ESR like rheumatoid arthritis, spondylitis, etc. are less common in children. However, some studies have found ESR to be less useful in childhood TB [23]. Microscopy of the specimen for AFB, which is considered a gold standard test in the adult population, was done in 39 patients but it was positive in only 15.38% of tested TB cases. Mantoux test was done in more than 90% of patients and around 42% of those tested had a positive result. Although the Mantoux test does not have a high sensitivity and specificity, it may be used in conjunction with other investigations in resource-limited countries.

GeneXpert was positive only in 29.72% of the children. A study by Reechaipichitkul W et al. reported a specificity of 92.1%, the sensitivity of 83.9%, the positive predictive value of 81.3% and a negative predictive value 93.3% of genexpert for detecting TB [24]. Low positivity of geneXpert and AFB demonstration in childhood TB compared to adult TB could be due to the paucibacillary nature of TB disease in children. In our study, genexpert was not done in all cases of TB and the low positivity could be due to technical issues associated with the collection, storage, processing and transportation of samples.

Above described findings emphasise regarding the diagnostic challenges faced by healthcare workers in resource-limited countries. Similar reports have been published by other authors as well [22,25,26].

5. CONCLUSION

Childhood TB is prevalent but underdiagnosed disease our setting. Extrapulmonary TB is more common in children, pleura and abdomen being the most common sites. Microbiological confirmation of TB in children is very low, so the diagnosis of TB in children largely depends upon clinical signs and symptoms along with supportive laboratory investigations.

CONSENT

As per international standard or university standard, parent's consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Ethical approval for the study was taken from IRC-PAHS.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. WHO Report: WHO Fact Sheet on Tuberculosis; 2018. Available:http://www.who.int/news-room/fact-sheets/detail/tuberculosis/
2. Dolin PJ, Raviglione MC, Kochi A: Global tuberculosis incidence and mortality during 1990-2000. Bull World Health Organ. 1994;72:213-20.
3. Heymann SJ, Brewer TF, Wilson ME, Colditz GA, Fineberg HV: Pediatric tuberculosis: What needs to be done to decrease morbidity and mortality. Pediatrics. 2000;106:E1.
4. Nelson LJ, Wells CD. Global epidemiology of childhood tuberculosis. Int J Tuberc Lung Dis. 2004;8(5):636-47.
5. Donald PR. Childhood tuberculosis: Out of control? Curr Opin Pulm Med. 2002;8:178-82.
6. Lin YS, Huang YC, Chang LY, Lin TY, Wong KS. Clinical characteristics of tuberculosis in children in the north of Taiwan. J Microbiol Immunol Infect. 2005; 38:41-6.
7. Wong KS, Chiu CH, Huang YC, Lin TY. Childhood and adolescent tuberculosis in northern Taiwan: An institutional experience during 1994-1999. Acta Paediatr. 2001;90:943-7.
8. Nelson LJ, Schneider E, Wells CD, Moore M. Epidemiology of childhood tuberculosis in the United States, 1993-2001: the need for continued vigilance. Pediatrics. 2004; 114:333-41.
9. Uysal G, Gursoy T, Guven A, Gunindi F, Cuhaci B. Clinical features of extrapulmonary tuberculosis in children. Saudi Med J. 2005;26:750-3.

10. National Tuberculosis Centre: Annual report of national tuberculosis control programme. Ministry of Health, Kathmandu, Nepal; 2006.
11. Udani PM. BCG test in the diagnosis of tuberculosis in children. Indian Pediatr. 1982;19:563-81.
12. American Thoracic Society: Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med. 2000;161:S221-S247.
13. Marais BJ, Gie RP, Schaaf HS, Beyers N, Donald PR, Starke JR. Childhood pulmonary tuberculosis: Old wisdom and new challenges. Am J Respir Crit Care Med. 2006;173:1078-90.
14. Marais BJ, Hesseling AC, Gie RP, Schaaf HS, Beyers N. The burden of childhood tuberculosis and the accuracy of community-based surveillance data. Int J Tuberc Lung Dis. 2006;10:259-63.
15. Starke JR, Jacobs RF, Jereb J. Resurgence of tuberculosis in children. J Pediatr. 1992;120:839-55.
16. Bonifachich E, Chort M, Astigarraga A, Diaz N, Brunet B, Pezzotto SM, Bottasso O. Protective effect of Bacillus Calmette-Guerin (BCG) vaccination in children with extra-pulmonary tuberculosis, but not the pulmonary disease. A case-control study in Rosario, Argentina. Vaccine. 2006; 24:2894-9.
17. Soysal A, Millington KA, Bakir M, Dosanjh D, Aslan Y, Deeks JJ, Efe S, Staveley I, Ewer K, Lalvani A. Effect of BCG vaccination on risk of *Mycobacterium tuberculosis* infection in children with household tuberculosis contact: A prospective community-based study. Lancet. 2005;366:1443-51.
18. Eisenhut M, Paranjothy S, Abubakar I, Bracebridge S, Lilley M, Mulla R, Lack K, Chalkley D, McEvoy M. BCG vaccination reduces risk of infection with Mycobacterium tuberculosis as detected by gamma interferon release assay. Vaccine. 2009;27:6116-20.
19. Phongsamart W, Kitai I, Gardam M, Wang J, Khan K. A population-based study of tuberculosis in children and adolescents in Ontario. Pediatr Infect Dis J. 2009; 28(5):416-9.
20. Maltezou HC, Spyridis P, Kafetzis DA. Extrapulmonary tuberculosis in children. Arch Dis Child. 2000;83:342-46.
21. Peto HM, Pratt RH, Harrington TA, LoBue PA, Armstrong LR. Epidemiology of extrapulmonary tuberculosis in the United States, 1993-2006. Clin Infect Dis. 2009; 49:1350-7.
22. Sreeramareddy CT, Panduru KV, Verma SC, Joshi HS, Bates MN: Comparison of pulmonary and extrapulmonary tuberculosis in Nepal-a hospitalbased retrospective study. BMC Infect Dis. 2008, 8:8.
23. Al-Marri MR, Kirkpatrick MB. Erythrocyte sedimentation rate in childhood tuberculosis: Is it still worthwhile? Int J Tuberc Lung Dis. 2000;4(3):237-9.
24. Reechaipichitkul W, Phetsuriyawong A, Chaimanee P, Ananta P. Diagnostic test of sputum genexpert MTB/RIF for smear negative pulmonary tuberculosis. Southeast Asian J Trop Med Public Health. 2016;4:457-66.
25. Graham SM, Gie RP, Schaaf HS, Coulter JB, Espinal MA, Beyers N. Childhood tuberculosis: Clinical research needs. Int J Tuberc Lung Dis. 2004;8:648-57.
26. De Villiers RV, Andronikou S, Van de Westhuizen S. Specificity and sensitivity of chest radiographs in the diagnosis of paediatric pulmonary tuberculosis and the value of additional high-kilovolt radiographs. Australas Radiol. 2004;48: 148-53.

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