www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i8.117

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

Clinical Profile of Tuberculosis in Children: A Prospective Study from Tertiary Care Institute in Sub Himalayan Region

Authors
Dr Mohit Bajaj[1], Dr Ashwani Kr Sood[2], Dr Swati Mahajan[3], Dr Ashok Garg[4]
[1]Junior Resident, Pediatrics, Indira Gandhi Medical College, Shimla, HP
[2]Prof. & Head, Pediatrics, Indira Gandhi Medical College, Shimla, HP
[3]Junior Resident, Medicine, Indira Gandhi Medical College, Shimla, HP
[4]Pediatrician, MGMSC Khaneri, Rampur, Shimla
Corresponding Author
Dr Ashok Garg
Address: House No.-35, Ward no.-2, Village-Anu Kalan, P.O. & Distt.- Hamirpur (H.P.), India
Email: *ashokgarg44@gmail.com*

Abstract
Background: *Tuberculosis has the dubious distinction of being the most persistent scourge of humankind. Childhood tuberculosis remains an important cause of morbidity and mortality in the developing countries despite the advances in diagnostic tests .TB in children is difficult to confirm and remains under diagnosed due to lack of specific diagnostic tools and most of the children present with non-specific signs and symptoms which are overlooked. The present study was planned to study the clinical profile and diagnosis of Pediatric Tuberculosis in a tertiary care teaching institute of Northern India.*
Aims and Objectives: *To study the clinico-epidemiological profile of Tuberculosis in children aged 3 months to 18 years.*
Methods: *This was a prospective cross sectional study conducted in a tertiary care teaching institute of Northern India over a period of one year. After approval from IEC and obtaining consent from parents, presumptive TB cases in the age group of 3 months to 18 years who met the inclusion criteria were recruited, additional investigations like chest X-ray, Mantoux test were ordered and CBNAAT, MGIT culture were done to confirm the diagnosis. Data collected in study tool was transferred into MS excel sheet for further processing and analysis by SPSS version 22.*
Results: *Out of 128 presumptive TB subjects, 46 had extra pulmonary TB and 30 had pulmonary TB. 47.36% were male with a male: female ratio of 0.9:1, with majority (76.32%) in the age group 11-18 years. The commonest presenting symptoms were fever (71.05%) followed by cough (61.84%) and weight loss (39.47%). Family history of contact could only be obtained in 20 patients (26.31%). Pallor was the most common sign observed in 32(42.10%). All the subjects had received BCG vaccine and most of the subjects 58(76.3%) belonged to middle socio economic group.*
Conclusion: *Childhood Tuberculosis presents with non-specific signs and symptoms in the pediatric age group and diagnosis of childhood tuberculosis requires a detailed history, good clinical examination and thorough investigative workup as well.*
Keywords: *Tuberculosis, Childhood, Mantoux, CBNAAT.*

Introduction

Tuberculosis is an infectious disease that has plagued humans since the Neolithic times with the earliest reported case dating back to5000 B.C. [1] In the year 2016, there were an estimated 10.4 million new cases of TB which included 5.9 million men and 3.5 million women and 1.0 million children with an estimated 14 lakh TB deaths. [2] In developing communities with a large proportion of the population younger than 15 years of age, a high disease incidence is observed in young children. In a study conducted at Tuberculosis Research Centre, Chennai over a 15 year period the annual risk of TB infection was seen to be 2%. [3] With an annual risk of infection of 2–3%, close to 40% of the population may be infected by the age of fifteen. [4] Children are poor producers of sputum and in children especially <7 years old, it is a challenge to obtain good smear samples for AFB. The co-infection of HIV and TB is difficult to treat and has high mortality and morbidity. 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. [5]

Aims and Objective

To study the clinico-epidemiological profile of Tuberculosis in children in age group 3 months to 18 years.

Material and Methods

This was a prospective cross sectional single centre study carried out in a teaching tertiary care institute in North India for one year from 1st august, 2016 onwards. Children in the age group of 3months-18 years presenting with symptoms of presumptive TB were recruited based on RNTCP 2017 guidelines after approval from IEC. [6] Written informed consent was obtained from the parents. After recording the demographic profile of recruited subjects and after performing standard investigations like Mantoux test and chest X-ray, fasting gastric lavage, sputum/Induced sputum samples were collected according to RNCTP guidelines and sent for Gene Xpert and MGIT culture. TST was performed using 2 TU PPD injected intradermally and the test positivity was defined according to RNTCP guidelines. Chest X-ray changes such as hilar/lymphadenitis with or without parenchymal lesion, miliary shadows and fibrocavitary pneumonia were considered highly suggestive of PTB. In suspected TB meningitis patients, two cerebrospinal fluid samples were collected and one sample was subjected to CBNAAT and other sample was subjected for MGIT culture. In pleural effusion, USG chest guided pleural tap was done and pleural fluid samples were analysed by CBNAAT and MGIT culture along with cytological examination. In patients with suspected TB lymphadenitis, two samples of FNAC / biopsy specimen were taken and analysed by CBNAAT and MGIT culture respectively.

CT and MRI brain were done in suspected CNS meningitis and USG abdomen in suspected abdominal tuberculosis. First sample was subjected to Gene Xpert as per manufacturer's instructions [7] given by Central TB Division Govt. of India and result was available within 2 hours. Second sample was inoculated into MGIT 960 tube as per manufacturer's instructions [8] and AFB positive was reported and culture were labeled as "out of protocol negatives" after 56 days if no growth was seen.

Diagnosis and Management

Based on clinical findings, CXR, TST, sputum/IS microscopy and GLA, children were classified as microbiologically confirmed TB (positive for acid-fast bacilli) and clinically diagnosed TB (negative for AFB but with highly suggestive CXR, CECT or MRI or reactive mantoux test) and not having TB and started on FDC protocol while waiting for culture reports. Based on the results, subjects were divided into PTB and EPTB

group. EPTB group [Pleural effusion, Tubercular lymphadenitis, CNS tuberculosis – tubercular meningitis / tuberculoma, abdominal tuberculosis, disseminated tuberculosis, musculoskeletal tuberculosis, renal tuberculosis and tubercular pericarditis]. All the recruited children were followed up during the study period and for the next six months after completion of study period. All samples were checked for Rifampicin resistance by CBNAAT and every subject underwent HIV screening.

Statistical analysis

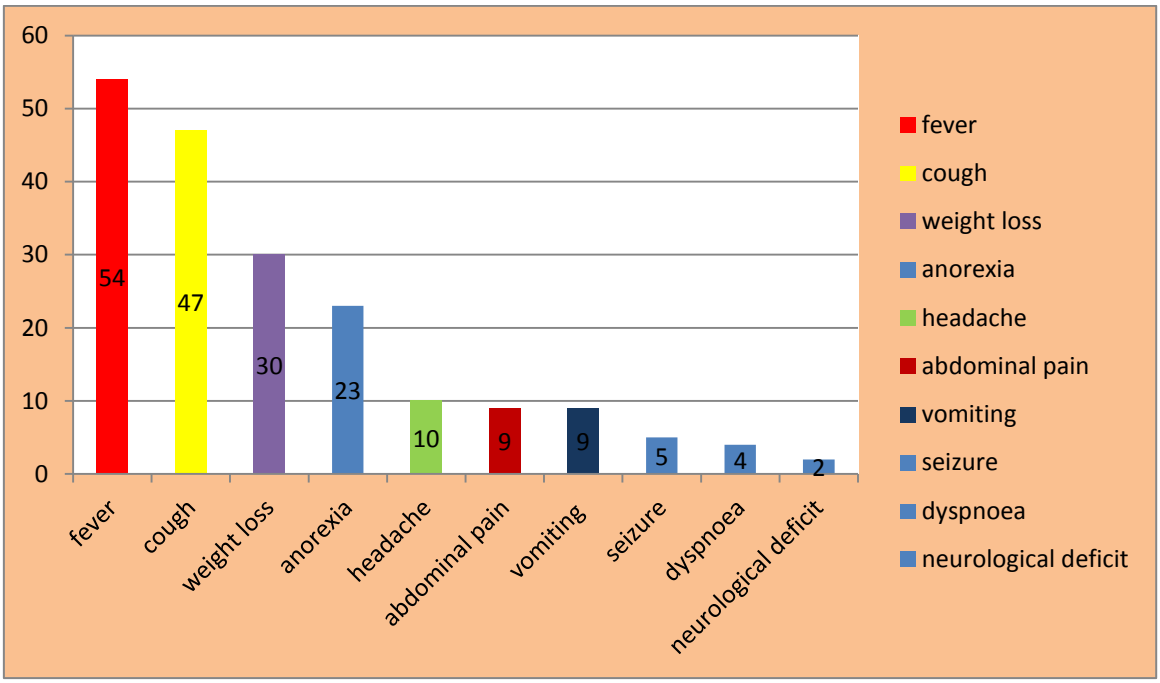
Data collected in study tool was transferred into MS excel sheet for further processing and analysis. SPSS version 22(American) and epi info version 7 software has been used for further analysis.

Observations

During the one year study period, 41200 children (0-18 years) visited our hospital as in-patients and out-patients and 128 qualified for study out of which 76 were diagnosed to have TB, 30 had PTB and 46 had EPTB with 47.36% (n-36) male subjects with male:female ratio of 0.9:1. Majority 58(76.32%) of the children were in the age group 11-18 years followed by 7 (9.21%) in age group of 6-10 years. Mean age of study group was 10.3 +/- 4.5 years. Majority of the subjects belonged to upper middle and lower middle class 58(76.3%).

The common presenting symptoms were fever (71.05%), dry cough (61.84%), weight loss (39.47%), loss of appetite (30.26%), headache (13.15%), abdominal pain (11.84%), vomiting (11.84%), seizure (6.41%), dyspnoea (5.26%) and neurological deficit (3.84%) at the time of presentation.

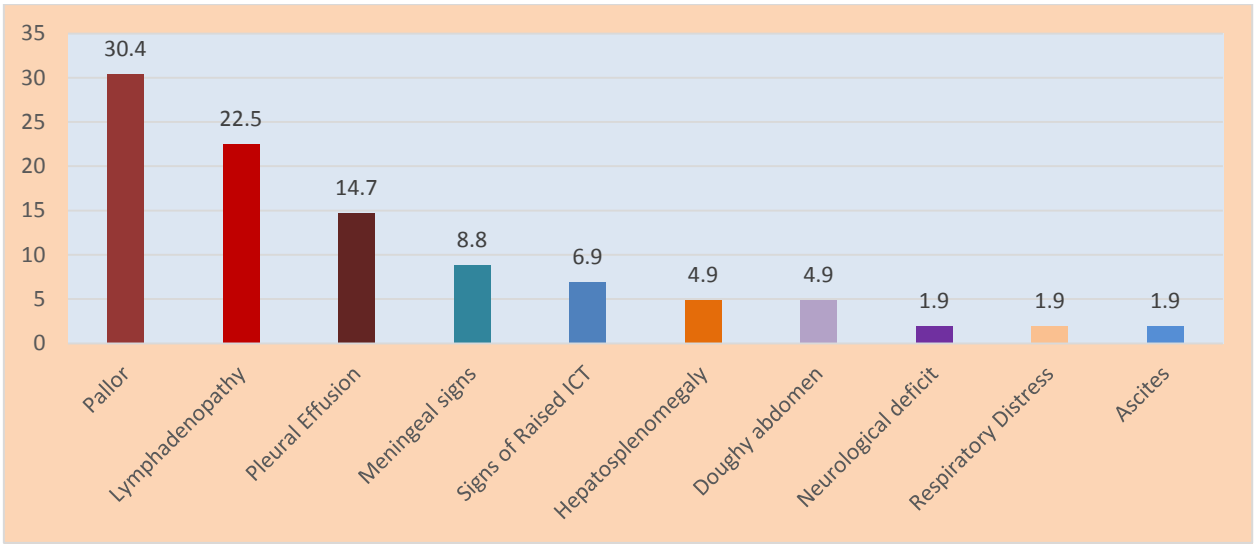
Figure1: Symptom profile of children



In this study, duration of symptoms ranged from 3 days to as long as one year with 47(62.5%) subjects symptomatic for one week to one month followed by 20 (25.8%) subjects with duration of 1 month to 3 months. Family history of contact was documented in 20 patients and majority of subjects 11(14.4%) were in age group 11-18years.

All the recruited subjects had received BCG vaccine and 44 (57.89%) had visible BCG scar mark documented. Mantoux test was reactive in 42 (55.26%) cases and in only 2.7% subjects with CNS TB Mantoux test was reactive.

Figure 2: Clinical signs in tuberculosis cases (%)



In this study, EPTB subjects constituted the major group 35.9% (n-46) followed by Pulmonary TB 23.4% (n-30). In EPTB, TB lymphadenitis and pleural effusion were observed in 22.36% (n-17) and 15.78% (n-12) subjects followed by CNS tuberculosis 11.84% (n-9).

Figure 3: Distribution of Extrapulmonary cases (%)

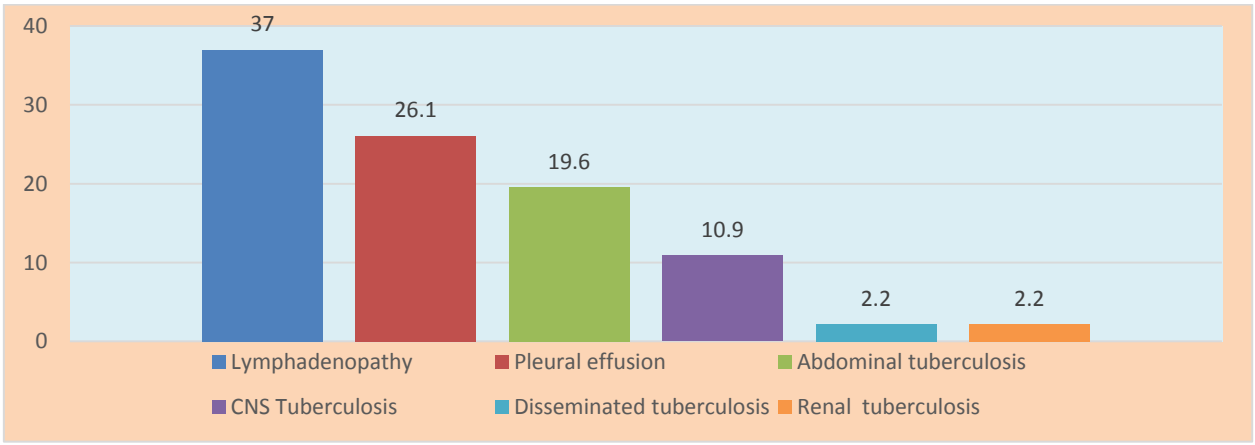


Table 1: CBNAAT and MGIT positivity according to different types of TB

S. N.	Type of TB		CB NAAT positive	MGIT positive
1	Pulmonary TB (n-30)		20 (66.67%)	21 (70%)
2	Extra-pulmonary TB (n-46)	Pleural effusion (n-12)	0	2 (16.7%)
		Abdominal TB (n-5)	1 (20%)	2 (40%)
		CNS TB (n-9)	5 (55.6%)	4 (44.4%)
		Lymph Node TB (n-17)	8 (47.1%)	12 (70.6%)
		Disseminated TB (n-2)	1 (50%)	2 (100%)
3	Total (n-76)		35 (46.05%)	43 (56.57%)

43 subjects were microbiologically confirmed and 33 subjects were confirmed clinically diagnosed based on demographic profile. All the children were Rifampicin sensitive and HIV negative**.**

Discussion

The present study was carried out to study the clinical profile of TB in children aged 3month-18 years, of 128 presumptive tuberculosis cases, 78 were diagnosed to have tuberculosis. The incidence of tuberculosis was observed to be 1.89 % which is marginally less to national data on TB (2.1%). We had a slight female preponderance (52.64%) in our study which is in consonance to studies by Franco et al in Brazil (51.6%) [9] and Suryanarayana et al [10] (51%) from AIIMS, Delhi.

In the study, maximum number of cases were in the age group of 11-18 years with markedly high female: male ratio (1:0.6) which is similar to a study by Kakarani and Pratinidhi et al. [11]

Fever was most commonly observed symptom (71.05%) followed by cough (61.84%) and weight loss (39.84%) which were similar to the observations made by Garg et al[13] and Franco et al[9] in their studies. Most of the recruited cases were from middle 58 (76.3%) socio economic groups which is similar to a study from South India. [12]

Duration of symptoms ranged from 3 days to as long as 1year prior to seeking medical treatment and in most of the cases duration was for 1 week to 1 month 47(62.5%) followed by 1 month to 3 months 20 (25.8%) which is in similarity to the study done by Xi-Rong Wu et al [14] which reported 54.7% cases with symptoms of duration 0-30 days and 28.1% had symptoms for duration of 31-90 days. Family history of contact was obtained in 20(26.31%) with majority of subjects 55%(n-11) in the age group of 11-18 years which is lower in comparison to the Indian studies documenting positive history of contact in 33-52% of the newly diagnosed case of tuberculosis under 15 years of age. [11,13] In the present study, EPTB constituted the major group (35.4%), followed by PTB (23.4%), where most of the studies had documented preponderance of pulmonary TB followed by EPTB. Higher proportion of EPTB can be attributed to the fact that being a tertiary health care institute most of the cases of EPTB are diagnosed due to free availability of CBNAAT and MGIT Culture and expert histopathologist.

In EPTB, Lymphadenopathy was observed in 22.36% (n-17)cases which is higher than a study done by Garg P[15] which documented 16.7% cases of tuberculous lymphadenitis , followed by Pleural Effusion in 12 (15.7%) subjects in EPTB which is on a lower scale to a study done by Franco et al (26.1%). [9] In our study, there were 9 (11.84%) cases of CNS tuberculosis which were on lower scale when compared to a study done by Pontual et al [15] documenting 16.67% cases with CNS tuberculosis. Out of 76 cases, 32 (42.1%) had abnormal x-ray chest with primary complex being the most common finding in 24(31.6%) cases followed by pleural effusion in12 (15.7%) cases, which is less in comparison to a study done by Franco et al[9] showing primary complex in 44.3% cases. Mantoux test was reactive in 42(55.25%) cases which is on a lower scale when compared to a study by Sivanandan et al[16] showing 66% of subjects with reactive TST. All the subjects had received BCG vaccination as per National Immunization Schedule and BCG scar was present in 26 (34.9%) subjects.

In our study, the sensitivity of the symptom-based approach in detecting TB was around 59.3% (76/128) which is similar to a study by Marais et al [17] which reported a sensitivity of 62.6% in detecting childhood TB with symptom based approach suggesting that this approach can help make the diagnosis of tuberculosis and is very useful in detection of TB in resource-limited settings such as India and justifies the algorithmic approach advocated by RNTCP.

There was no significant association with history of contact and childhood TB which can be explained by the endemicity of the disease as expected in countries such as India where a history of contact may not always be present. Mantoux test reactivity was significantly higher in the group with TB than not having TB (56.2%vs 23%) which supports the fact that a reactive Mantoux does not differentiate infection from disease and it should be considered valuable only along with symptomatology suggestive of TB and abnormal chest x ray in young children and is a useful tool for identifying the infected population in the pediatric age group, where the risk of disease is much higher than in adults.

Conclusion

Tuberculosis is a major cause of childhood mortality and morbidity despite the recent advances in diagnosis. Pediatric TB presents with certain non specific clinical features making its

diagnosis difficult suggesting that a detailed history and thorough clinical examination are of utmost importance for the diagnosis. So in all the patients presenting with fever, weight loss, and anorexia, tuberculosis should be kept as an important differential diagnosis and every effort should be made to confirm the diagnosis of TB by the use of new investigations like CBNAAT and MGIT culture along with supportive investigations.

Conflict of interest: Nil

References

1. Narain JP. Tuberculosis – epidemiology and control. World Health Organization, Regional Office for South East Asia, New Delhi, India, 2002; SEA/TB/2002.248:15-18.
2. GlobalTuberculosisReport2016, WHO Report 2014. http://www.who.int/tb/publications/global_report/2017/en/index.html.accessed 31 October, 2017.
3. Radhakrishna S, Frieden TR, Subramani R, Kumaran PP. Trends in the prevalence and incidence of tuberculosis in south India. Int J Tuberc Lung Dis 2001;5:142-57.
4. Donald PR. Children and tuberculosis: protecting the next generation. Lancet 1999;353:1001-02.
5. World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulm-onary TB in adults and children: policy update. Geneva, Switzerland: WHO, 2013.
6. 4. Sager P, Schalimtzek M, Moller-Christensen V. A case of spondylitis tuberculosa in the Danish Neolithic Age. Dan Med Bull 1972;19:176-80.
7. Global Tuberculosis Report 2016, WHO Report 2014http://www.who.int/tb/publications/global_report/2017/en/index.html.accessed 31 October, 2017).
8. National Guidelines on diagnosis and treatment of Pediatric Tuberculosis 2017, https://tbcindia.gov.in/showfile.php?lid=2904 page 8-15.
9. Guidance document for use of Catridge Based-Nucleic Acid Amplification Test (CB-NAAT) under Revised National TB Control Programme (RNTCP) issued central TB division, directorate general of health services september 2013.
10. Global laboratory initiative advancing TB diagnosis mycobacteriology laboratory manual April 2014. http://www.who.int/tb/laboratory/mycobacteriology-laboratory-manual.pdf accessed august 2017.
11. Franco R, Santana M. Clinical and Radiological Analysis of Children and Adolescents With Tuberculosis in Bahia, Brazil .The Brazilian Journal of Infectious Diseases 2003;7:73-81.
12. Sivanandan S, Walia M, Lodha R, Kabra SK. Factors Associated with Treatment Failure in Childhood Tuberculosis. Indian Pediatr 2008;45:769-71.
13. Kakarani VA, Pratinidhi AK. A study of childhood tuberculosis. Ind J Tub 1992;39:177-80.
14. Bai SS, Devi RL. Clinical spectrum of tuberculosis in BCG vaccinated children. Indian Pediatr2002;39:458-62.
15. Garg P. Childhood tuberculosis in a community hospital from a region of high environmental exposure in north India. Journal of clinical and diagnostic research 2008:2:634-38.
16. 14.Wu XR, Yin QQ, Jiao AX, Xu BP, Sun L, Jiao WW, *et al*. Pediatric Tuberculosis at Beijing Children's Hospital:2002-2010. *Pediatrics*;2012:130.

17. de Pontual L, Balu L, Ovetchkine P, Maury-Tisseron B, Lachassinne E, Cruaud P, et al. Tuberculosis in adolescents: a French retrospective study of 52 cases. Pediatr Infect Dis J 2006;25:930-32.
18. Sivanandan S, Walia M, Lodha R, Kabra SK. Factors Associated with Treatment Failure in Childhood Tuberculosis. Indian Pediatr 2008;45:769-71.
19. Marais B J, Gie RP, Hesseling AC. A refined symptom based approach to diagnose pulmonary tuberculosis in children. Pediatrics 2006; 118: e1350-59.