Clinical profile and outcome of children with tuberculosis in a tertiary care hospital in Mumbai, India

*Noella Maria Delia Pereira[1]

Abstract

Introduction: As children are usually infected by an adult with pulmonary tuberculosis (TB), childhood TB reflects transmission of *Mycobacterium tuberculosis* within a community

Objective: To study clinical profile and outcome of children with TB from 0 to 12 years of age in a tertiary care hospital in Mumbai, India.

Method: A prospective observational descriptive study of 30 children with TB was conducted over 18 months at a tertiary general hospital in Mumbai and followed up till recovery.

Results: Out of the 30 children with TB**,** 3 (10%) were below the age of 1 year, 8 (26.6%) were aged 1-5 years and 19 (63.3%) were above 5 years of age. Male to female ratio was 1:1.3. Extra-pulmonary TB was more common (63.3%) than pulmonary TB (36.6%). Twenty (66.6%) children had a history of previous adult contact with TB, 29 (96.6%) were vaccinated with BCG and 10 (33.3%) were malnourished. Common clinical features were cough (53.3%), fever (46.6%), weight loss (46.6%) and lymphadenopathy (33.3%). Anaemia and raised ESR were seen in 46.6% and 73.3% respectively. All 30 children were non-reactive for the HIV antibody test. Tuberculin sensitivity test was positive in 16 out of 30 children (53.3%). Drug-resistant TB was seen in 2 (6.6%) children. All 30 cases (100%) recovered completely with their primary regimen.

Conclusions: In this study, extra-pulmonary TB was found in 63.3% of children. TST positivity (>10mm) was found in only 53.3% of children with TB. Complete resolution of symptoms was seen in

all cases except the case of the Potts spine patient who had a residual spine deformity after completing treatment. A weight gain of ≥10 % of body weight at diagnosis was seen at the end of 3 months in the age groups <1 year and >5–12 years.

Introduction

As children are usually infected by an adult with pulmonary tuberculosis (TB), childhood TB is a reflection of the transmission of *Mycobacterium tuberculosis* within a community[1-3]. Mumbai is a city whose population has doubled since 1991 and where 41.3% of the residents live in the slums[4]. Rise in the urban population with consequent overcrowding and migration of families from rural areas to cities for work have led to increased poverty, malnutrition, morbidity and mortality rate of several diseases including TB[5]. Poverty has been a significant risk factor for TB in addition to severe malnutrition, illiteracy and a low socio-economic status[6,7]. Globally, TB incidence is decreasing by about 2% annually but this is not rapid enough to reach the 2020 milestones of the End TB strategy[8].

Bacillus Calmette Guerin (BCG) vaccination has always been known to protect children from the severe forms of TB especially neuro-TB and disseminated TB[9]. Its efficacy varies from 75–86% for prevention of miliary TB and TB meningitis and is around 50% for pulmonary TB[10]. The estimated national coverage for BCG vaccination in India has increased from 74% to 91% between 1999 and 2013[11]. Poor immunisation coverage with BCG vaccine has been shown to play a significant role in the higher incidence and case fatality rate of neuro-TB[12]. The diagnosis of TB in childhood is most challenging as it is a pauci-bacillary disease thus relying on both clinical and radiological features for diagnosis and management[13].

Objectives

To study the clinical profile and outcome of children with TB from 0 to 12 years of age in a tertiary care hospital in Mumbai, India.

[1]*K. J. Somaiya Medical College and Research Centre, Mumbai, India*
*Correspondence: noella_pereira@yahoo.com

Method
This is a prospective observational descriptive study carried out in a tertiary care general hospital in Mumbai from 1st February, 2017 to 31st July, 2018, a period of 18 months. Ethical Approval was obtained from the institutional ethics committee. Informed consent was obtained from the parents. All children with TB <12 years old presenting to the out-patient department as well as those admitted in the ward were included in the study. Both pulmonary and extra-pulmonary TB patients as defined by WHO criteria[13] were included in the study. Those treated outside the hospital or previously treated relapsed patients were excluded.

A detailed clinical history was obtained from the parents including a history of contact with TB and prior immunization with BCG. A thorough physical examination was carried out noting growth parameters such as weight, height, weight for height (aged 5 years or less) and body mass index aged 5 years or more). Malnutrition was defined as weight for height less than 2 standard deviations below the mean ('z' scores) for children aged 5 years or less[14] and BMI less than -2SD for age for children above 5 years of age ('z' scores)[15].

Investigations like haemogram, HIV by ELISA test, Mantoux tuberculin sensitivity test (5TU), sputum/gastric lavage for acid fast bacilli (AFB), sputum/gastric lavage for Xpert MTB/RIF and chest X-ray were carried out at the commencement of therapy. Specific investigations like body fluid analysis, CT scan/MRI, biopsy, fine needle aspiration cytology, tissue/fluid for Xpert MTB/RIF, culture and adenosine deaminase (ADA) levels were done whenever needed.

All patients were started on anti TB treatment according to the revised national TB programme guidelines[16]. Drug resistant TB was determined by Xpert MTB/RIF and drug sensitivity testing on positive TB culture tests at an RNTCP accredited laboratory. Anaemia was defined as haemoglobin <11g/dl[17]. Elevated erythrocyte sedimentation rate (ESR) done at the end of 1 hour was defined as more than 20mm by Westergren method.

Patients were followed up monthly for six months after starting therapy and their weight and height was recorded at each follow up visit. The primary outcome was the assessment of the clinical profile of these patients presenting with TB. The secondary outcome was to assess the weight gain in grams and percentage of weight gain of the body weight at diagnosis at the end of each month till six months after anti–tubercular treatment was started.

Statistical analysis
Characteristics of the children are described as numbers and percentages. For analysis of comparison of pulmonary TB and extra-pulmonary TB, all characteristics were categorical in nature. Therefore, Fischer Exact test was used. $p<0.05$ was taken as statistically significant. For the average weight gain at the end of month of therapy in the different age groups, mean weight gain in grams of the children was calculated as well as the mean percentage of weight gain of the body weight at diagnosis was calculated in each of the age groups.

Results
During the study period 30 (75%) children were treated for TB and followed up out of 40 patients. The characteristics of the children with TB are shown in Table 1.

Table 1
Characteristics of the children with TB (n=30)

Characteristic	Number (%)
Age group	
<1 year	03 (10.0)
1 - ≤ 5 years	08 (26.6)
> 5 - 12 years	19 (63.3)
Gender	
Male	13 (43.3)
Female	17 (56.6)
Symptom/Sign	
Cough	16 (53.3)
Fever	14 (46.6)
Weight loss	14 (46.6)
Lymph node swelling	10 (33.3)
Decreased appetite	03 (10.0)
Abdominal pain	02 (06.6)
Back pain	02 (06.6)
Headache	02 (06.6)
Vomiting	02 (06.6)
Wheezing	02 (06.6)
Contact with TB	20 (66.6)
Malnourished	10 (33.3)
BCG	
Vaccinated	29 (96.6)
Non vaccinated	01 (03.3)
Haemoglobin <11g/dl	14 (46.6)
Raised ESR	22 (73.3)
HIV non-reactive	30 (100)
TST positivity (> 10mm)	16 (53.3)
Drug resistant TB	02 (06.6)
Type of tuberculosis (TB)	
Pulmonary TB	11 (36.6)
Extra-pulmonary TB	19 (63.3)
Pleural effusion	05 (16.6)
Abdominal TB	02 (06.6)
Lymph node TB	09 (30.0)
Disseminated TB	02 (06.6)
Neuro TB	01 (03.3)

BCG: Bacillus Calmette Guerin ESR: Erythrocyte sedimentation rate, HIV: Human immunodeficiency virus, TST: Tuberculin sensitivity test

Two children presented with drug resistant TB and were both malnourished. One of them had disseminated TB (pleural effusion with Potts spine and paraspinal abscess) and the other child had pulmonary TB showing a cavitatory lesion on chest X-ray. Only one child was not vaccinated with BCG vaccine and she presented with disseminated TB (pleural effusion with paraspinal abscess). *Mycobacterium tuberculosis* (MTB) was isolated from the sputum/gastric lavage sample of the child with multi-drug resistant (MDR) pulmonary TB and from the pus drawn from the paraspinal abscess from the child with drug resistant TB with pleural effusion and Potts spine who was found to have Pre–XDR TB. All children completed their course of treatment and fully recovered. No child died during or after the course of treatment and none were lost to follow up. The child with drug resistant disseminated TB (pleural effusion with Potts spine and paraspinal abscess) mentioned above had a residual spine deformity at the end of treatment.

Comparison of children with pulmonary and extra-pulmonary TB is shown in Table 2.

Table 2: *Comparison of children with pulmonary and extra-pulmonary TB*

Characteristic	Pulmonary TB *(n=11)* Number (%)	Extra-pulmonary TB *(n=10)* Number (%)	p value
Age group			
<1 year	02 (18.1)	01 (5.26)	0.536
1 - ≤ 5 years	03 (27.2)	05 (26.3)	1
> 5 - 12 years	06 (54.5)	13 (68.4)	0.695
Gender			
Male	08 (72.7)	10 (52.6)	0.44
Female	03 (27.2)	09 (47.3)	
Symptom/Sign			
Cough	09 (81.8)	07 (36.8)	0.025
Fever	05 (45.4)	09 (47.3)	1
Weight loss	07 (63.6)	07 (36.8)	0.2568
Lymph node swelling	0 (0.0)	10 (52.6)	0.004
Decreased appetite	02 (18.1)	01 (05.2)	0.5367
Wheezing	02 (18.1)	0 (0.0)	0.1264
Abdominal pain	0 (0.0)	02 (10.5)	0.5195
Back pain	0 (0.0)	02 (10.5)	0.5195
Headache	0 (0.0)	02 (10.5)	0.5195
Vomiting	01 (09.1)	01 (05.2)	1
Contact with TB	10 (90.9)	10 (52.6)	0.3927
Malnourished	04 (36.3)	06 (31.5)	1
BCG			
Vaccinated	11 (100)	18 (94.7)	1
Non Vaccinated	0 (0.0)	01 (05.2)	
Haemoglobin <11g/dl	06 (54.5)	08 (42.1)	0.7065
Raised ESR	09 (81.8)	13 (68.4)	0.6722
TST positivity (> 10mm)	07 (63.6)	09 (47.3)	0.1461
Drug Resistant TB	01 (09.0)	01 (05.2)	1

TB: Tuberculosis, BCG: Bacillus Calmette Guerin ESR: Erythrocyte sedimentation rate, TST: Tuberculin sensitivity test

Cough was seen more significantly in children with pulmonary TB (*p*=0.025) and lymph node swelling was seen more significantly in children with extra-pulmonary TB (p=0.004) as seen in Table 2.

For children <1 year of age, 1- ≤ 5 years and >5-12 years, the average weight gain as well as the percentage of weight gain of body weight at diagnosis at the end of the each month after starting anti-tubercular treatment has been depicted in Table 3.

Table 3: *Average weight gain in grams and mean percentage of weight gain (of body weight at diagnosis) at the end of each month after starting anti-TB therapy*

End of month	<1 year		1- ≤ 5 years		> 5-12 years	
	Weight gain (g)	Weight gain (%)	Weight gain (g)	Weight gain (%)	Weight gain (g)	Weight gain (%)
1 month	450	9.02	385.75	3.015	1370	5.81
2 month	1113.33	24.58	636.25	5.359	2303.15	9.71
3 month	1640	38.7	860	7.53	2540	10.76
4 months	1886.66	45.7	1120	9.86	2944.21	12.38
5 months	2333.33	56.3	1367.5	12.11	3490.52	14.46
6 months	2586.66	60.8	1587.5	14.24	4004.21	16.91

The weight gain seen in the children in the age group of <1 year is more than those seen in the other two age groups. The is probably due to more rapid weight gain seen normally in the first year of life as part of their normal growth and development.

Chest x-ray findings in the 30 patients with childhood TB are shown in Table 4.

Table 4
Chest x- ray findings in children with TB (n=30)

Chest X ray findings	
Normal	10 (33.3)
Perihilar lymphadenopathy	07 (23.3)
Pleural effusion	07 (23.3)
Segmental lesion(s)	04 (13.3)
Calcification	02 (06.6)
Bronchopneumonia	01 (03.3)
Cavitation	01 (03.3)

Ten (33.3%) children had a normal chest X-ray and those were children with extra-pulmonary TB (tuberculous lymphadenitis, abdominal tuberculosis, neuro-TB, and Potts spine). The term 'segmental lesion' refers to any radiographic opacity that clearly filled a lobe or a segment of a lobe[18].

Discussion
The present study assessed the clinical profile and outcome of the children with TB. In this study, extra-pulmonary TB was found to be more common that pulmonary TB. This was similar to the findings seen in studies by Shrestha *et al*[2] and Panigatti *et al*[3]. Extra-pulmonary TB is more common in children, superficial lymphadenitis being the most common form[19]. In the present study too, we found extra-pulmonary TB to be more common, superficial lymphadenitis being the most common form, typically involving the cervical lymph nodes.

The clinical findings in this study were similar to those found by Goyal *et al*[20]. Wheezing was seen as one of the presenting complaints in two children which was also seen in the study by Donald *et al*[18].

Raised ESR was seen in 73.3% of the children with TB whilst TST positivity was seen in only 53.3%. Failure to respond to tuberculin sensitivity test may result from poor nutrition, recent measles or measles immunisation, overwhelming tuberculous infection or an inherent lack of tuberculin hypersensitivity[18]. Therefore, a negative TST test does not rule out TB[21].

The protective role of BCG vaccination is well known[22]. However TB was seen in almost all children (96.6 percent) vaccinated with BCG. Hence it can be concluded that TB can be present in children vaccinated with BCG[21]. Absent BCG vaccination was associated with disseminated TB in this study as well as in the study done by Shrestha *et al*[2].

The chest radiological findings seen mostly were perihilar lymphadenopathy and pleural effusion followed by segmental lesions, calcification, bronchopneumonia and cavitation. Segmental lesions typically involved the right lung. Similar findings were seen in studies by Donald *et al*[18] and Shrestha *et al*[2]. Cavitation was seen in one child aged 12 years. In the study by Goyal *et al*[20] older children >5 years were found to have cavitatory lesions which was also found in this study. Cavities are associated with a higher mycobacterial load and can therefore pose a transmission risk[1].

Even though 66.6% children had a known adult contact with TB, in a high burden TB setting like India, exposure from non-household sources in the community are important. Contact tracing of children of sputum-smear positive adults and chemoprophylaxis with isoniazid preventive therapy (IPT) can be an important strategy to prevent active TB[23].

A favourable response to anti–tubercular treatment (weight gain and disappearance of symptoms and signs) are known features of probable TB[24]. In the present study, weight gain was seen in each of the age groups from 0–12 years after starting anti–tubercular treatment. Marais *et al*[25] have defined good clinical response as "complete symptom resolution and weight gain of ≥10% of body weight

at diagnosis, within 3 months of starting anti-TB treatment". In the present study, complete resolution of symptoms was seen except in the case of the Potts spine patient who had a residual spine deformity after completing treatment. A weight gain of ≥10 % of body weight at diagnosis was seen at the end of 3 months in the age groups <1 year and >5–12 years. However, in the age group 1- ≤ 5 years, weight gain seen at the end of 3 months was <10% of the body weight at diagnosis. This could have been due to lack of proper nutrition and prolonged breastfeeding with improper weaning. Anaemia which was seen in 75% of the children in this age group could have also been contributory to poor weight gain.

The present study has a few limitations. The number of patients is small. Being a hospital based study, the type of patients seen may vary from those seen in the community. They may be far more critical due to delay in referral to the hospital for diagnosis and treatment. A high degree of suspicion is required to diagnose TB in a high prevalence setting and any pneumonia that does not respond to appropriate antibiotic therapy must be suspected of being tuberculous even if not confirmed bacteriologically. A positive TST along with clinical and radiological confirmation and a history of an adult contact with TB are diagnostic of TB in settings where the prevalence of malnutrition is high.

Conclusions
In this study, extra-pulmonary TB was found in 63.3% of children. TST positivity (>10mm) was found in only 53.3% of children with TB. Complete resolution of symptoms was seen in all cases except the case of the Potts spine patient who had a residual spine deformity after completing treatment. A weight gain of ≥10 % of body weight at diagnosis was seen at the end of 3 months in the age groups <1 year and >5–12 years.

References

1. Schaaf HS, Marais BJ, Whitelaw A, Hesseling AC, Eley B, Hussey GD, *et al.* Culture confirmed childhood tuberculosis in Cape Town, South Africa: a review of 596 cases. *BMC Infectious Diseases* 2007; **7**:140.
https://doi.org/10.1186/1471-2334-7-140
PMid: 18047651 PMCid: PMC2225409

2. Shrestha S, Marahatta SB, Poudyal P, Shrestha SM. Clinical profile and outcome of childhood tuberculosis at Dhulikhel Hospital. *Journal of. Nepal Paediatric. Society* 2011; **31**(1):11-6.

3. Panigatti P, Ratageri VH, Shivanand I, Madhu PK, Shepur TA. Profile and outcome of childhood tuberculosis treated with DOTS – An observational study. *Indian Journal of Pediatrics* 2014; **81**(1):9-14.
https://doi.org/10.1007/s12098-013-1175-8
PMid: 23893370

4. World Population Review. Mumbai Population 2019. 2018. Available from: http://worldpopulationreview.com/world-cities/mumbai-population/ [Accessed 11th February 2019].

5. Zombini EV, de Almeida CHD, Silva FPCV, Yamada ES, Komatsu NK, de Figueiredo SM. Clinical epidemiological profile of tuberculosis in childhood and adolescence. *Journal of Human Growth and Development* 2013; **23**(1):52-7.
https://doi.org/10.7322/jhgd.50391

6. Seddon JA, Shingadia D. Epidemiology and disease burden of tuberculosis in children: a global perspective. *Infection and Drug Resistance* 2014; **7**:153-65.
PMid: 24971023 PMCid: PMC4069045

7. Janssens JP, Rieder HL. An ecological analysis of incidence of tuberculosis and per capita gross domestic product. *European Respiratory Journal* 2008; **32**(5): 1415-6.
https://doi.org/10.1183/09031936.00078708
PMid: 18978146

8. World Health Organization. 'Global Tuberculosis Report 2018'. WHO, Geneva, 2018.. Available from: https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1 [Accessed on 11th February 2019].

9. Seth V, Kabra SK. Bacillus Calmette – Guerin (BCG). In. Seth V and Kabra SK, editors. *Essentials of Tuberculosis in Children*. 4th edition. New Delhi. Jaypee Brothers Medical Publishers; 2011:555-588.
https://doi.org/10.5005/jp/books/11309_38

10. Advisory Committee on Vaccine & Immunization Practices (ACVIP). Bacillus Calmetter Guerin (BCG) Vaccine. In. Vashishtha VM, Choudhury P, Bansal CP,

Yewale VN, Agarwal R, editors. *IAP Guidebook on Immunization 2013-14* Gwalior, National Publishing House, Indian Academy of Pediatrics;2014:111-114.

11. Bhatnagar P, Gupta S, Kumar R, Halder P, Sethi R, Bahl S. Estimation of child vaccination at state and national levels in India. *Bulletin of the World Health Organisation.* 2016; 94(10):728-34. https://doi.org/10.2471/BLT.15.167593 PMid: 27843162 PMCid: PMC5043206

12. Gupta R, Garg A, Venkateshwar V, Kanitkar M. Spectrum of childhood tuberculosis in BCG vaccinated and unvaccinated children. *Medical Journal Armed Forces India.* 2009*;* **65**:305-7. https://doi.org/10.1016/S03771237(09)80088-9

13. World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014). WHO, Geneva, 2013. Available from: https://apps.who.int/iris/bitstream/handle/10665/79199/9789241505345_eng.pdf;jsessionid=C55C0B13E5AB190B1B8037D6959B4EA4?sequence=1 [Accessed on 13th February 2019].

14. World Health Organization. WHO Child Growth Standards. Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. Methods and development. WHO, Geneva, 2006. Available from: https://www.who.int/childgrowth/standards/Technical_report.pdf?ua=1 [Accessed on 17th February 2019]

15. .De Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school – aged children and adolescents. *Bulletin of the World Health Organisation.* 2007; **85**(9):660-7. https://doi.org/10.2471/BLT.07.043497 PMCid: PMC2636412

16. Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare, New Delhi, India. Revised National TB Control Programme. Technical and Operational Guidelines for Tuberculosis Control in India. 2016.. Available from:

https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=4573&lid=3177 [Accessed on 13th February 2019].

17. World Health Organization. Haemoglobin for concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. 2011; 1-6. Available from: https://www.who.int/vmnis/indicators/haemoglobin.pdf [Accessed on 3rd March 2019].

18. Donald PR, Ball JB, Burger PJ. Bacteriologically confirmed pulmonary tuberculosis in childhood. Clinical and radiological features. *South African Medical Journal* 1985; **67**(15):588-90.

19. Shingadia D, Novelli V. Diagnosis and treatment of tuberculosis in children. *Lancet Infectious Diseases* 2003; **3**(10):624-32. https://doi.org/10.1016/S14733099(03)00771-0

20. Goyal A, Shah I, Patankar N, Chilkar S. Clinical profile of children with pulmonary tuberculosis. *Clinical Epidemiology and Global Health.*2014; **2**(1):24-7. https://doi.org/10.1016/j.cegh.2014.01.003

21. Nanavath K, Karimunnisa S. Clinical profile of paediatric cases with tuberculosis. *IOSR Journal of Dental and Medical Sciences* 2017; **16**(9):06-08.

22. Centers for Disease Control and Prevention. The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States. A Joint Statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. *MMWR Recomm Rep.* 1996; 45(RR-4):1-18. [Online]. Available online from: https://www.cdc.gov/mmwr/pdf/rr/rr4504.pdf [Accessed on 23rd February 2019].

23. Said K, Hella J, Ruzegea M, Solanki R, Chiryamkubi M, Mhimbira F, Ritz N, Schindler C, Mandalakas AM, Manji K, Tanner M, Utzinger J, Fenner L. Immunologic – Based Diagnosis of Latent Tuberculosis among Children less than 5 years of age exposed and unexposed to tuberculosis in Tanzania: Implications for

Tuberculosis Infection Screening. *Pediatr Infect Dis J.* 2018. [Epub ahead of print].

24. Osborne CM. The challenge of diagnosing childhood tuberculosis in a developing country. *Archives of Disease in Childhood.*1995; **72**(4):369-74.
https://doi.org/10.1136/adc.72.4.369
PMid: 7763076 PMCid: PMC1511255

25. Marais BJ, Gie RP, Hesseling AC, Schaaf S, Lombard C, Enarson DA, *et al.* A refined symptom –based approach to diagnose pulmonary tuberculosis in children. *Pediatrics* 2006; **118**(5):e1350–9.
https://doi.org/10.1542/peds.2006-0519
PMid: 17079536