Infection in Children Journal
Volume: 1, Issue 1: 1-5
DOI:

CASE SERIES

DIAGNOSTIC DIFFICULTIES AND CHALLENGES OF PEDIATRIC TUBERCULOSIS – REVIEW THROUGH A CASE SERIES

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ABSTRACT

Background: The incidence of childhood DSTB as well as DRTB is on rise. Extra-pulmonary TB equally contributes to pulmonary TB with highest mortality of neurological TB in children. Despite the very high disease burden, there are very few studies on tuberculosis among Paediatric population. In this case series we wish to discuss the difficulties in diagnosis of Paediatric TB along with clinical presentation, microbiological, radiological reports, treatment given and outcome.

Clinical Description: Total 24 Paediatric patients (Age range 5months to 12 years) with diagnosis of tuberculosis (from March 2024 to December2024) were included in this case series. Patients were categorised as per age, sex, nutritional status, pulmonary/extra-pulmonary TB and DSTB/DRTB (as per The National Tuberculosis Elimination Programme guidelines). Pulmonary Tuberculosis was most common form followed by neurological TB. Malnutrition was contributory factor in 58.3% cases.

Management & Outcome: Treatment was given as per NTEP guidelines. The outcome was recorded as discharge, death and lost to follow up.

Microbiological confirmation was reported to be more than 30%.The mortality was 12.5% and was highest in CNS TB (28.5%). The rate of MDR TB was 8.3 %.

Conclusion: Despite increasing incidence of childhood TB, poor microbiological yield of tubercular bacilli in children poses difficulty and delays the diagnosis. Increasing awareness about timely screening and evaluation of all children with suspected TB infection with due emphasis on microbiological evidence/ supportive radiological investigations may help in bridging this gap and can improve the outcome. Multidisciplinary team approach is need of the hour.

ARTICLE HISTORY
Received 16 October 2025
Accepted 26 August 2026

KEYWORDS
Childhood TB burden, Diagnostic Difficulties, Childhood TB outcome.

Introduction

A global total of 8.2 million people were reported as newly diagnosed TB in 2023, India accounts for 26% of global TB burden.[1] The actual burden of paediatric TB is not known due to diagnostic difficulties but has been assumed that 10% of total TB load; with more than 100,000 estimated deaths every year, it is one of the top 10 causes of childhood mortality.[2]

In India, approximately 3.42 lakh children (0-14 years of age) are estimated to get TB every year and account for about 6% of total TB cases reported to NTEP in 2020-21.[3] Nearly a third of the children with TB globally are from India, despite an estimated detection gap of about 56%. [4]

Pulmonary TB is the most common form of TB in children; however, extra-pulmonary TB (EPTB) in children also forms a significant proportion of cases than adults.[3]

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Despite the very high disease burden, there are very few studies on Paediatric tuberculosis. This case series highlights the clinical presentation, diagnostic challenges, microbiological & radiological reports, treatment and outcome.

Clinical Description

Total 24 tuberculosis diagnosed Paediatric patients (March 2024 to December 2024) both outdoor and indoor were included in this case series.

They were categorised as per age, sex, nutritional status (using WHO charts & IAP BMI charts). Their HIV status, BCG vaccination status, Mantoux reaction, TB contact history, prior treatment, GeneXpert, MGIT and radiological reports were recorded. They were categorised into pulmonary/extra-pulmonary TB and DSTB/DRTB (as per NTEP guidelines). Treatment was given as per NTEP guidelines. The outcome was recorded as discharge, death and lost to follow up.

Clinical profile is mentioned here in the following tables.

Table 1. Demographic Profile and Clinical Details of the cases

Age /Sex wise distribution of patients (n=24)			**Nutritional Status (Normal in 10 children)**		
Age	0 to 5 years	>5years	**FTT (below 6mo)** 01	**SAM /MAM (6mo to 5 yrs)** 04	**Undernourished as per BMI (children >5yrs)** 09
Male	5	6	00	01(Moderate Acute Malnutrition)	04 underweight
Female	3	10	01	03(Severe Acute Malnutrition)	2 Underweight, 03 (severe thin)

Clinical Details									
HIV Status		**BCG vaccinated**		**History of contact**		**Prior treatment with antibiotics**		**Mantoux Test**	
Positive	Negative	Yes	No	Yes	No	Yes	No	Positive	Negative
0	24 (100%)	24 (100%)	0	8 (33%)	16 (66%)	16 (66%)	8 (33%)	10 (41.6%)	14 (64.4%)

Table 2. Presenting symptoms and Distribution of Pulmonary / Extra-pulmonary TB

Presenting symptoms	
Symptom	**Present**
Fever	19 (79%)
Cough	10 (41%)
Vomiting	13 (54%)
Headache	04 (16.6%)
Lymph node swelling	3 (12.5%)
Abdominal pain	7 (29.1%)

Distribution of Pulmonary / Extra-pulmonary TB						
Type of TB	**Distribution**	**No**	**Total cases**	**Clinical Diagnosis**	**Abnormal Chest/ spinal/bone Radiology/ Neuroradiology**	**GeneXpert/MGIT Positive**
Respiratory	Pulmonary	4	10	Yes	All 10	03
	Pleural	1				
	Pulmonary + Pleural	2				
	Pulmonary with lymph nodal	3				
Disse-minated		2	02	Yes	02	01(sputum sample positive)
Lymph Nodal	Isolated lymph nodal	3	03	Yes	02	***01 (FNACs/o caseous necrosis)**
Skeletal	Mastoiditis	1	03	Yes	00	***01 Rifa Resistance sample -pus from chest wall abscess**
	Ribs with chest wall abscess	1				
	C1,C2 Vertebra Pott's Spine	1				
Abdominal system	Lymph nodal Intestinal	1 1	02	Yes	02	00
Central Nervous System	Tuberculoma	5	07	Yes	07	03 ***1 Rifa Resistance sample was CSF (MGIT positive)**
	TBM	2				

**Two Rifampicin resistance Tuberculosis among 24 patients (8.3%)*

Most common presenting symptom was fever present in 79 percent of patients (19 out of 24).

Drug Sensitive and Drug Resistance TB - 2 out of 24 cases tested positive for Rifampicin resistance on GeneXpert (1st was Chest wall abscess, 2nd was TB Meningitis). MGIT was positive only in one Rifa resistance case of TB Meningitis.

Management and Outcome

22 patients received first line Anti Tubercular Treatment at our institute as per NTEP guidelines. While other two patients diagnosed with Rifampicin resistance were referred & treated at JJ Hospital which is Nodal DR-TB treatment centre.

21 out of 24 patients were discharged. All of them are cured and doing well on follow up. 3 patients out of 24 cases expired. Two patients expired in the hospital, both had CNS TB (TB Meningitis), one was DSTB and other was Rifa resistance TB.

Other one patient a 5 months female with FTT with disseminated drug sensitive tuberculosis, parents were non-compliant had lost to follow up and brought child dead to hospital within one month of starting 1st line AKT.

Diagnostic Difficulties & Challenges

Pulmonary TB:10 out of 24 patients had pulmonary TB.

Nine patients received prior antibiotics for fever and pneumonia. Because of no response to antibiotic therapy they were referred to tertiary centre for further management. This caused delay in diagnosis & treatment. Patients presenting with pneumonia and pleural effusion are invariably treated with antibiotics first when there is no clue towards tuberculosis.

One such case of Pneumonia with pleural effusion 8years female child with no improvement even after 2 weeks of antibiotics. 1st Sputum geneXpert was negative, in view of persistent symptoms HRCT chest was done which showed mediastinal lymphadenopathy. Repeat sputum for GeneXpert was indeterminate. Thus third time gene expert was sent for confirmation which came negative. During the course of admission the patient developed seizures and CT Brain revealed multiple granulomas which confirmed our suspicion of Tuberculosis. She was started on first line ATT, child improved clinically and got completely cured.

Another case of pleural effusion 6years Male child not responding to medical treatment, with initial TB work-up negative underwent surgical intervention for VATS & decortication. The pleural biopsy revealed tubercular granuloma, treatment and outcome.

A case of AGE with MAM, 1 year male child was incidentally diagnosed with pulmonary TB, while under treatment. TB screening was done because of malnutrition. Chest X-Ray was abnormal & GL gene expert came positive. Later mother gave history of active TB in grandfather. Child was started on first line ATT along with nutritional rehabilitation and improved on follow up.

This emphasizes the importance of sending correct sample for microbiological testing i.e Gastric Lavage, induced sputum, Broncho alveolar Lavage, Lymph node aspirate or biopasy etc, so as to help confirmation and timely treatment of such cases. Mediastinal lymphadenopathy needs CT guided biopsy and histopathology to confirm the diagnosis of TB when repeated sputum gene expert samples are negative without any other clues for TB. Non availability of facilities like bronchoscopy and interventional radiology could delay the diagnosis of of tuberculosis in those patients in whom sputum/gastric lavage samples are negative.

Central nervous system (CNS) TB –

There were 7cases of CNS TB out of which 2 were meningitis and 5 patients had tuberculoma.

A case of CNS TB 5years Male presented with only two days of high grade fever without focus. During further 3 days of ward stay child was worked up and started on antibiotics. Due to persistence of fever and deteriorating sensorium lumbar puncture was done which was suggestive of tubercular meningitis. His CSF geneXpert revealed Rifa Resistance. Patient was transferred to JJ hospital for MDR TB management where he succumbed during the treatment.

A five month old baby initially presented like bronchiolitis at 2 months of age. Later she developed sepsis with septic ileus for which she was treated with Meropenem, Child responded well and got discharged after 2 weeks. At 5 months of age she was readmitted with third nerve palsy and MRI brain suggestive of tuberculoma with TB Meningitis, X-ray chest during this admission showed miliary TB. Later on mother revealed that father was on ATT and was noncompliant to treatment. Child was started on first line AKT. Parents had taken Discharge against medical advice. She was brought dead a month after the diagnosis.

A 6year old female child admitted with fever, focal seizures and otitis media. Her neuroimaging revealed tubercular granuloma with mastoiditis of temporal bone. Pus from ear was negative for geneXpert. She responded to first line ATT.

Skeletal TB-

There were two cases of skeletal TB.

One was 10 year female child presented with fever and neck stiffness. CSF was done for suspected meningitis which later on turned out to be positive for MTB with Rifa sensitivity. Neuroimaging with spinal screening was suggestive of tuberculomas, tubercular Meningitis, Pott's spine (Cervical vertebra) with para pharyngeal abscess.

The child was started on first line ATT. During the course of stay the child succumbed.

Second was 9 years old female presented with fever and soft tissue swelling on right infrascapular area. HRCT Chest was suggestive of abscess involving subcutaneous tissue, muscles underlying ribs. USG guided pus aspiration was done which detected MTB with Rifa Resistance. Patient was referred to JJ hospital and was started on MDR TB treatment. She responded to Drug Resistant TB Regimen.

Abdominal TB-

There were 2 cases of Abdominal TB. Managing one of them was a challenge. 9 years male child with subacute intestinal obstruction. CT abdomen was suggestive of ascites, intestinal obstruction and omental thickening.

Ascitis tap fluid was negative for MTB. Giving ATT to a child with continuous vomiting was a challenge as no injectable alternative is available in first line drugs. Hence ATT was given through Ryle's tube. Gradually the child improved and started tolerating ATT orally so was discharged. On follow up after 2 months the child presented with fever and there was right sided pleural effusion on chest Xray.There was also history of TB in elder sibling and she was a treatment defaulter which raised the suspicion of MDR TB in our case. However there was improvement of appetite and weight so Immune Reconstitution Inflammatory Syndrome was also considered as differential. To confirm the diagnosis cervical lymph node biopsy was done, which was negative for MTB. Later on he responded to first line ATT.

Lymph node TB-

There were 2 cases of lymph nodal TB one was 6 years old male with bilateral cervical lymphadenopathy without any constitutional symptoms. Diagnosis was confirmed by FNAC, child responded to first line ATT even though microbiologically negative.

Second case was 10 years female having constitutional symptoms of fever more than 1 month, weight loss, anorexia. Sputum microbiologically was negative but chest Xray showed hilar lymphadenopathy and HRCT chest revealed multiple necrotic mediastinal lymphnodes. Child responded to first line ATT.

Discussion & Review of Literature

The diagnosis of TB in children is difficult and challenging task requiring not only knowledge but also coordination & multidisciplinary team approach. In our case series many cases (more than 50%) geneXpert was negative even on repeat sampling. All that helped us in diagnosis was high index of suspicion and supportive investigations like histopathology/ radiology. In this case series culture was positive only in one case of chest wall abscess (< 1%) with Rifa resistance in geneXpert report. Similar difficulties were mentioned in the study by Jain SK et al from Pune; with only 3% culture positive (may be due to high rates of extra-pulmonary TB).[5]

GeneXpert Assays was the first point-of-care assay for TB and was endorsed by the WHO in 2010, GeneXpert has demonstrated improved efficacy in detecting intrapulmonary and extrapulmonary TB.[6] However, as per Kay et al., 2020 the sensitivity of geneXpert has been found to vary depending on the specimens used for analysis, namely sputum, stool, bronchoalveolar lavage fluid (BALF), gastric juice, interstitial fluid and biopsies. GeneXpert's estimated specificity among all specimens is generally higher than 98%.[7]

We did not do GeneXpert ultra for our patients because of unavailability of test, however as per the available literature it is more sensitive. GeneXpert Assays limit of Detection is 112.6 bacterial colony forming units/L and it has poor sensitivity in detecting paucibacillary cases. GeneXpert Ultra has a limit of detection of 15 CFU/L and thus is recommended by WHO to be used in children as well adults to increase the overall sensitivity of MTB detection. However the increase in sensitivity is accompanied by a slight decrease in specificity leading to higher number of false positive results. Thus, the results of GeneXpert Ultra require clinical correlation in culture negative specimens.[8]

In this case series we had 10 pulmonary TB & 7 CNS TB cases among total 24 patients. Pulmonary tuberculosis was most common form followed by neurological TB in the study reported by Kumar A, which is similar to above cases. [9]

Malnutrition was potent contributory factor (91.8%) in the study by Kumar A. while it was 58.3% in above case series.[9] Microbiological confirmation was reported to be more than 30% in our case series, while it was 8.8% in the study by Tripathi BB. [10]

The mortality rate in the above case series was 12.5% (Age was 5 month, 5years and 10years,with 2 females, 1 male), similar mortality rate (13.8%) was reported by Tripathi BB,10 while mortality rate of 9.5% was reported by Kumar A.[9] The mortality was highest in CNS TB (70%) in the study by Tripathi BB,10 which is similar to the present case series where all 3 patients died of tubercular meningitis, one being disseminated TB with CNS involvement.

The rate of MDR TB was 8.3 % in the current study, it was reported to be 7.3% in the study by Mauskar et al[11] ; 7% in the study by Shah and Chilkar,[12] and was less than 2% in the study by Jain SK.[5]

Conclusion

The incidence of childhood DSTB as well as DRTB is on rise. Extra-pulmonary TB equally contributes to pulmonary TB with highest mortality of neurological TB in children. Microbiological yield of tubercular bacilli is very poor in children which poses difficulty and delays in the diagnosis. Detailed clinical evaluation, screening of all high risk cases, emphasis on microbiological evidence, appropriate sample selection and supportive radiological investigations if clinically indicated can help in early diagnosis, treatment and improve outcome. Availability of facilities like bronchoscopy, interventional radiology & multidisciplinary approach involving other specialities plays vital role in early diagnosis and management of such challenging cases.

Compliance with Ethical Standards
Funding: None
Conflict of Interest: None

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