Original Article

# Clinico-Epidemiological Profile of Pediatric Extrapulmonary Tuberculosis at a Tertiary Care Centre in Central India

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## Abstract

**Background:** Paediatric extra-pulmonary tuberculosis (EPTB), despite being a significant proportion of childhood tuberculosis (TB), remains difficult to diagnose. Moreover, microbiological confirmation remains challenging despite advances in molecular diagnostics. Therefore, a proper understanding of the clinico-epidemiological profile, along with the use of laboratory methods, can help in timely diagnosis and the initiation of treatment. The aim is to study the clinico-epidemiological profile of paediatric EPTB and assess the diagnostic utility of cartridge-based nucleic acid amplification test (CBNAAT) in these cases. Settings and Design is prospective observational study, conducted at a tertiary care centre between September 2023 and September 2024. **Material and Methods:** Children (≤18 years) diagnosed with EPTB per NTEP guidelines were included. Their relevant epidemiological and clinical data, as well as CBNAAT results, were analysed. **Results:** A Total of 100 children diagnosed with EPTB during this period were analysed. 60% were >10 years, with M: F = 1:2. Tubercular lymphadenopathy (47%) was most common, followed by CNS TB (23%). Contact history is positive in 28% of cases. Fifty-four children were not BCG vaccinated. Sixty-two children were undernourished. Overall, CBNAAT positivity was 20.2% (n=158), with the highest positivity (55.5%) in FNAC samples. Rifampicin resistance was detected in only 2 cases (6.25%). **Conclusion:** Tubercular lymphadenopathy and CNS tuberculosis were the two most common forms of EPTB. The overall positivity rate for CBNAAT was 20.2%.

**Keywords:** Pediatric TB , Extrapulmonary Tuberculosis , CBNAAT

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## Introduction

TB remains a major health problem in developing countries like India. The WHO Global TB Report 2024[1] identifies India as a contributor of 26% of global TB cases. Paediatric TB comprises 12% of the total burden, with 17% presenting as EPTB. Despite advancements in molecular diagnostics, EPTB in children is difficult to diagnose due to nonspecific symptoms, difficulty in obtaining samples, and the paucibacillary nature of the disease. As per National Tuberculosis Elimination Programme (NTEP) guidelines,[2] diagnosis relies on clinico-epidemiological features supported by laboratory tests. This study analyses the clinico-epidemiological profile and the utility of CBNAAT in paediatric EPTB at a tertiary care centre.

## Materials and Methods

A prospective observational study was conducted in the Department of Pediatrics at a tertiary care hospital between September 2023 and September 2024, after obtaining Institutional Ethics Committee approval (Ref. No.: EC/MGM/SEP-23/115).

After obtaining informed consent and assent (as appropriate), children aged 18 years or less diagnosed with EPTB per NTEP guidelines were included in the study. Based on available data on the prevalence of EPTB in children, a sample size of 100 was selected.

All relevant epidemiological and clinical data of patients were recorded in a pre-designed proforma, with special emphasis on the type and duration of symptoms, a history of contact with an open case of tuberculosis in the family, socioeconomic status, the child's nutritional status, and BCG vaccination status. Patients underwent relevant investigations based on their clinical status. Chest X-ray was obtained in all the cases. CBNAAT samples were obtained from appropriate extrapulmonary sites using standard techniques.

Patients were managed as per standard TB treatment protocols. The collected data were manually transferred to a Microsoft Excel worksheet. Categorical variables were described as percentages, and CBNAAT positivity was calculated. Statistical analysis was done using SPSS version 22 (IBM SPSS Statistics, IBM Corporation).

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## RESULTS

This prospective observational study included 100 paediatric patients diagnosed with EPTB. Demographic profile of patients is summarised in Table 1. The mean age was 9.22 years, with a female-to-male ratio of 2:1. 59% patients were from urban areas, and most (88%) belonged to lower socioeconomic strata. Contact history with a known TB case was reported in 28% of patients. Tubercular lymphadenopathy was the most common form of EPTB (47%), followed by CNS and pleural TB. Fever (62%) and cervical lymphadenopathy (55%) were the most common presentations. Sixteen children below 5 years had severe acute malnutrition (SAM), and 46 children older than 5 years were undernourished. BCG vaccination was documented in 46% of cases, as assessed by the presence of a BCG scar. CBNAAT samples were sent to all patients, totalling 158. The overall positivity rate of CBNAAT was 20.2%. The specimen with the highest positivity rate was the FNAC aspirate (55.5%). CBNAAT positivity in CSF and gastric aspirate was low at 17.4% and 11%, respectively. Rifampicin resistance was detected in only 2 cases (6.25%), including 1 case each of MDR and XDR TB. These children had lymph node TB. Comparison of CBNAAT results at various extra-pulmonary sites is shown in table 4. The p-value of 0.021(Fisher's exact test) indicates a statistically significant association between the site of disease and CBNAAT positivity, suggesting that CBNAAT is more likely to detect TB in lymph node specimens than in other extra-pulmonary sites.

**Table 1: Demographic profile of EPTB cases (n=100)**

| Characteristic | Numbers |
|---|---|
| Mean age | 9.22 years |
| Male to female ratio | 1:2 |
| Urban | 59 |
| Rural | 41 |
| Socioeconomic status<br>Lower class<br>Upper lower class<br>Lower middle class<br>Upper middle class | <br>26<br>28<br>34<br>12 |
| Positive history of contact | 28 |

**Table 2: Clinical profile of EPTB cases (n=100)**

| Characteristic | | Numbers |
|---|---|---|
| Presenting symptoms | Fever | 62 |
| | Lymphadenopathy | 55 |
| | Weight loss | 40 |
| | Cough | 27 |
| | Seizures | 24 |
| | Altered sensorium | 19 |
| | Abdominal pain | 6 |
| | Abdominal distension | 6 |
| Sites of EPTB | Lymph node | 47 |
| | CNS | 23 |
| | Pleural | 10 |
| | Abdominal | 9 |
| | Spine | 7 |
| | Disseminated | 2 |
| | Congenital | 1 |
| | Osteomyelitis | 1 |
| SAM/Underweight | | 62 |
| BCG vaccination received | | 46 |

**Table 3: CBNAAT results of samples**

| Speciemen | Numbers tested | Positive result |
|---|---|---|
| Gastric/sputum | 100 | 11(11%) |
| FNAC aspirate | 27 | 15(55.5%) |
| CSF | 23 | 4(17.4%) |
| Pleural fluid | 5 | 1(20%) |
| Ascitic fluid | 3 | 1(33.3%) |

**Table 4: Comparison of CBNAAT according to site**

| Site | CBNAAT | | Total | P-value |
|---|---|---|---|---|
| | Positive | Negative | | |
| CNS | 4 (17.4%) | 19 (82.6%) | 23 (100.0%) | 0.021 Sig. (Fisher's exact test) |
| Lymph node | 23 (48.9%) | 24 (51.1%) | 47 (100.0%) | |
| Pleural | 1 (10.0%) | 9 (90.0%) | 10 (100.0%) | |
| Abdominal | 2 (22.2%) | 7 (77.8%) | 9 (100.0%) | |
| Spine | 1 (14.3%) | 6 (85.7%) | 7 (100.0%) | |

| | | | | |
|---|---|---|---|---|
| Disseminated | 0 | 2 (100.0%) | 2 (100.0%) | |
| Osteomyelitis | 0 | 1 (100.0%) | 1 (100.0%) | |
| Congenital | 1 (100.0%) | 0 | 1 (100.0%) | |
| Total | 32 (32.0%) | 68 (68.0%) | 100 (100.0%) | |

## Discussion

This prospective observational study was conducted to evaluate the clinico-epidemiological profile of paediatric EPTB cases and the diagnostic utility of CBNAAT in these cases. The mean age of the 100 patients studied was 9.2 years, with 60 patients being>10 years old. A similar age distribution pattern was reported by Ramanathan et al,[3] in their study. Only 10 patients were in the infantile age group, indicating a lower prevalence of EPTB in this age group. Gosai et al,[4] reported 18 cases in children < 1 year. A female preponderance (M: F = 1:2) was observed, in contrast to studies by Gosai et al. four and Ksoo et al.[5] This discrepancy may be attributed to limited study duration and sample size, and these results cannot be generalised. Similar to a study by Kumar et al,[6] a higher proportion (59%) of cases came from urban areas, possibly due to better healthcare infrastructure and reporting in urban settings. This gap also underscores the need to strengthen further screening and diagnosis services for paediatric TB in rural areas of our region. Most of the cases belonged to low socioeconomic status, an observation similar to other studies like Ramanathan et al.[3]

A contact history was present in 28% of children, compared with 40% reported by Singh et al,[7] in their study. Lack of this history may suggest an undetected adult in the family who is an open case of TB, rather than the actual absence of any household contact. This also highlights the importance of screening all family members in such cases. Sixteen children who were below 5 years had SAM, and 46 children older than 5 years were undernourished. This was also shown by Gosai et al.4 in their study, in which the prevalence of malnutrition was 86%, highlighting that childhood malnutrition remains one of the most important risk factors for developing TB disease in children. Vaccination status of cases was assessed by looking for a BCG scar, and only 46% had a visible BCG scar. Similar studies (e.g., Gosai et al,[4]) reported higher coverage (66%) with BCG. This may be due to differences in health care-seeking behaviour and the availability of basic vaccination facilities. This also highlights the importance of promptly inoculating BCG immediately after birth using a correct technique. Measures to address malnutrition and vaccination will help tremendously in controlling paediatric TB. None of our cases was HIV-positive, which may be due to low regional prevalence (0.08% in Madhya Pradesh).[8] Hence, co-infection may not be a major concern in our geographical area, as compared to globally.

Tubercular lymphadenopathy was the most common form of EPTB observed in our study (47%), followed by CNS (23%), pleural (10%), abdominal (9%), and spinal TB (7%). Sood et al. also found lymphadenopathy and CNS TB to be the most frequent forms, while Ksoo et al,[5] reported higher rates (31.3%) of disseminated TB. Variation in the occurrence of various forms of EPTB across studies may reflect differences in study settings, study duration, and case definitions used to include cases. Fever was the most common symptom observed in our cases, along with symptoms specific to the site involved, like lymphadenopathy, seizures, altered sensorium, and abdominal pain. Similar symptom profiles were monitored by Gosai et al.[4]

CBNAAT samples were sent to all patients. In some patients, more than one sample was sent, so a total of 158 samples were sent. The overall positivity rate for CBNAAT was 20.2% (32 positive out of 158 samples).[9] Similar positivity rates were observed in a study conducted by Annamalai et al,[10] (34.5%), while other researchers reported lower rates (Sen et al., 17.6%, Das et al., 13.8%).[11,12] This low positivity rate of CBNAAT in paediatric EPTB may be due to the paucibacillary nature of the disease, difficulty in obtaining a satisfactory sample, or limitations in clinical and other laboratory diagnostic criteria. The specimen showing the highest positivity rate was the FNAC aspirate (26 samples from lymph node aspirate and one from spinal abscess), with 55.5% positivity. CBNAAT positivity in CSF and gastric aspirate was low at 17.4% and 11%, respectively. Similarly, in Annamalai et al,[10] CBNAAT positivity in CSF is low (17%). Rifampicin resistance was detected in only 2 cases, including 1 case each of MDR and XDR TB. These children had lymph node TB. This is comparable to Sen et al,[11] and Das et al,[12] where rifampicin resistance was 6.1% and 5.7% respectively. This low number suggests that resistant TB is currently not a major problem in the paediatric population in our region, but one needs to keep a close watch on this.

Other investigations that were suggestive of TB aetiology in our cases included FNAC showing caseating granulomatous (27), communicating hydrocephalus in CNS TB (15), and pleural fluid analysis (5). Given the low CBNAAT positivity rates in EPTB cases, the supporting role of these investigations cannot be underemphasised. In our study, four children died during the hospital stay; all of them had CNS TB. Limited data are available on mortality rates in paediatric EPTB and the specific forms of TB contributing to it. Therefore, meaningful comparisons or conclusions could not be drawn.

## Conclusion

This study showed that paediatric EPTB was more common in children above 10 years, with female sex, malnutrition, low socioeconomic status, and lack of BCG vaccination as important risk factors. Tubercular lymphadenopathy was the most frequent form, followed by CNS TB, the latter causing all the deaths observed. Overall, the CBNAAT positivity rate was 20.2%, with the highest yield in FNAC aspirates. Supporting investigations were useful in diagnosing EPTB.

**Limitations:** This was a single-centre study conducted at a tertiary care hospital, which may affect the extrapolation of results to the community level. Use of other methods for documenting mycobacteria, such as culture, which is considered the gold standard, was not used; hence, comparison of

CBNAAT with these standard methods could not be done. The lack of a control group precluded the calculation of statistical differences between the observations. Further larger studies with multi-centre designs and the application of multimodal diagnostics are needed to generate data with greater validity and generalisability.

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## Conflicts of interest
There are no conflicts of interest.

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