e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(12); 311-317

Original Research Article

Factors Associated with Extrapulmonary Tuberculosis with Temporal Associaton with CB-NAAT in a Tertiary Care Centre

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Received: 11-10-2025 / Revised: 16-11-2025 / Accepted: 12-12-2025
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Conflict of interest: Nil

Abstract

Introduction: Extrapulmonary tuberculosis (EPTB) contributes significantly to the global TB burden, particularly among children, posing diagnostic challenges due to its varied clinical presentations. Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) has emerged as a rapid and reliable diagnostic tool. This study aimed to evaluate factors associated with EPTB and assess the temporal association of CBNAAT positivity with symptom duration at presentation.

Material and Methods: A hospital-based prospective observational study was conducted in the Pediatric Department of Gauhati Medical College & Hospital from July 2023 to July 2024. Seventy-five children aged 1–12 years diagnosed with EPTB were included. Detailed demographic, clinical, and socioeconomic data were collected. Relevant samples from affected sites were subjected to CBNAAT testing. Associations of CBNAAT positivity with history of TB contact, nutritional status, Mantoux test, and time of presentation were statistically analyzed.

Results: The mean age of the study population was 5.2 years, with maximum cases (37.3%) in the 4–8 years age group. Slight female predominance was noted (52%). Lymph node TB and CNS TB were the most common presentations (41.3% each). CBNAAT was positive in 27 cases (36%). Significant associations were found with history of TB contact (p=0.0001), malnutrition (p=0.0001), and Mantoux positivity (p=0.0001). CBNAAT positivity showed no statistically significant relation with time of presentation (p=0.061), though higher detection rates were observed beyond two weeks of symptom onset.

Conclusion: EPTB in children predominantly involves lymph nodes and CNS. CBNAAT proves valuable in diagnosis, especially in malnourished children, those with TB contact, and Mantoux positivity. Temporal presentation did not significantly influence CBNAAT detection, underscoring the need for timely testing across all presentations.

Keywords: Extrapulmonary tuberculosis, Pediatrics, CBNAAT, Malnutrition, TB contact history.

Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, is a contagious disease that can involve almost any organ of the human body. While pulmonary TB is the most common form, extrapulmonary tuberculosis (EPTB) also contributes significantly to the global TB burden. According to estimates, nearly one-fourth of the world's population has been exposed to TB bacteria. EPTB is defined as infection of organs and tissues outside the pulmonary parenchyma and accounts for nearly one-fifth of all TB cases. It can affect the central nervous system, lymph nodes, abdomen, bones, joints, genitourinary system, skin, or present as disseminated disease. The clinical manifestations are often subtle, leading to delays in diagnosis and management [1,2]. EPTB can present in diverse forms. Tuberculous lymphadenitis commonly involves the cervical or supraclavicular lymph nodes. TB meningitis is a severe form with high mortality in children, while miliary TB occurs when bacilli spread through the bloodstream, often affecting immunocompromised individuals. Skeletal TB, including Pott's spine, affects weight-bearing joints and vertebrae, leading to complications such as spinal cord compression if untreated. The heterogeneity of presentations makes early detection challenging but vital to reduce morbidity and mortality [3]. Diagnosis of EPTB requires a combination of clinical suspicion and confirmatory investigations. Clinical presentations vary with the site involved, ranging from lymph node swellings to neurological deficits or abdominal symptoms. Imaging modalities such as X-rays, CT scans, and MRI are invaluable for identifying lesions in pleura, bones, or the central nervous system. Histopathology remains a

cornerstone, revealing granulomas characteristic of TB infection. Biopsy and culture from the affected site provide definitive confirmation but may be time-consuming [4].

Modern diagnostic approaches include nucleic acid amplification tests (NAATs), which detect TB DNA in extrapulmonary samples. Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) is particularly important as it provides rapid and accurate results, even from paucibacillary samples such as cerebrospinal or pleural fluid. Histopathology and additional specialized tests like Polymerase Chain Reaction (PCR), culture, and drug susceptibility studies may also be required, especially in suspected multidrug-resistant cases. A multidisciplinary approach involving clinicians, radiologists, pathologists, and microbiologists is often necessary to establish an accurate diagnosis [5,6].

CBNAAT has transformed the diagnostic landscape of TB by addressing the limitations of traditional methods. Its key advantages include speed, accuracy, safety, and ease of use. Results are available within two hours, allowing early initiation of therapy and preventing further transmission. It detects M. tuberculosis DNA as well as mutations associated with rifampicin resistance, which is a crucial marker of multidrug resistance. The technology is user-friendly, requires minimal training, and reduces the chances of human error through automation. Since testing is done in closed cartridges, the risk of contamination is minimized, ensuring biosafety for laboratory personnel [7].

The impact of CBNAAT on TB control is substantial. By providing quick and reliable results, it improves case detection, including drug-resistant strains, thereby facilitating prompt and effective treatment. Its global adoption, particularly in TB-endemic countries, has expanded diagnostic capacity even in resource-limited settings. This accessibility strengthens public health efforts in controlling TB [8]. Extrapulmonary TB often presents with nonspecific symptoms, making it crucial to employ multiple diagnostic modalities. CBNAAT serves as an essential tool alongside conventional tests such as PCR, culture, and histopathology. While additional investigations may be necessary in drug-resistant cases, CBNAAT provides a rapid initial diagnosis, guiding clinicians in early treatment decisions [9].

The challenge of TB control has been compounded by rising multidrug-resistant strains and HIV-associated TB. These conditions increase the complexity of management, demanding faster and more reliable diagnostic methods. CBNAAT, by combining sensitivity, specificity, and rapid turnaround, represents a major step forward in addressing these challenges [10].

Extrapulmonary tuberculosis is a significant clinical and public health concern due to its varied presentations and diagnostic challenges. CBNAAT has emerged as a breakthrough diagnostic tool, offering speed, reliability, and accessibility. Its widespread use has enhanced early detection and management of EPTB, contributing to reduced morbidity and mortality. Continued integration of CBNAAT with conventional and advanced diagnostic methods is essential to improve outcomes and strengthen global TB control strategies [11,12].

The aim of this study was to investigate the factors associated with extrapulmonary tuberculosis and to evaluate its association with Cartridge-Based Nucleic Acid Amplification Test (CBNAAT).

Material and Methods

This prospective observational study was conducted at the Department of Pediatrics, Gauhati Medical College & Hospital Guwahati from 1st July 2023 to 1st July 2024. Ethical approval has been obtained from the Ethical Approval Committee of Srimanta Sankardeva University of Health Sciences, Assam.

Study Population: The study population comprised children aged 1–12 years diagnosed with extrapulmonary tuberculosis during the study period. Participants were included if they had histopathological changes or culture-positive samples from lesion sites, positive CBNAAT results, or strong clinical evidence with favorable response to treatment, and known or pending HIV status, with parental consent. Children with pulmonary TB co-infection or those whose parents did not provide consent were excluded from the study.

Data Analysis: Data were analyzed using SPSS version 29, where descriptive statistics including mean and standard deviation were calculated for quantitative variables, while qualitative variables were expressed as numbers and percentages.

To assess associations between categorical variables, the Chi-square test was employed for comparison of proportions between groups, enabling statistical evaluation of relationships and identifying significant factors influencing extrapulmonary tuberculosis and its diagnostic association with CBNAAT in the studied pediatric population.

Results

In this study of 75 children with extrapulmonary tuberculosis, the highest number of cases (37.3%) occurred in the 4–8 years age group, with a mean age of 5.2 years. Females constituted 52% (n=39) of the cases, while males accounted for 48% (n=36). The majority of patients, 57.3% (n=43),

were from rural areas, whereas 42.7% (n=32) resided in urban settings. Socioeconomic assessment using the Modified Kuppuswamy Scale revealed that half of the patients (50.7%, n=38) belonged to the lower socioeconomic class, highlighting a significant burden among disadvantaged groups.

Table 1: Diagnosis wise frequency distribution of patients in the study population

Diagnosis	Frequency	Percentage (%)
TB meningitis	22	29.3
Tuberculoma	9	12
Lymph node TB	31	41.3
Cutaneous TB	3	4
Abdominal TB	4	5.3
Joint TB	6	8

In the study population, extrapulmonary TB was most commonly seen as lymph node TB (41.3%) and CNS TB (41.3%, including TB meningitis 29.3% and tuberculoma 12%), while abdominal (5.3%), joint (8%), and cutaneous TB (4%) were less frequent.

Among the 75 children studied, 19 (25.3%) presented with symptoms lasting less than 2 weeks, 26 (34.7%) had symptoms for 2–8 weeks, and the largest group, 30 patients (40%), experienced symptoms for more than 8 weeks before hospital presentation. Regarding BCG vaccination, 56 children (74.7%) had received the vaccine, while 19 (25.3%) were unvaccinated. These findings highlight delayed healthcare-seeking behavior in many cases and underline the protective role of BCG vaccination, although a notable proportion of patients lacked immunization.

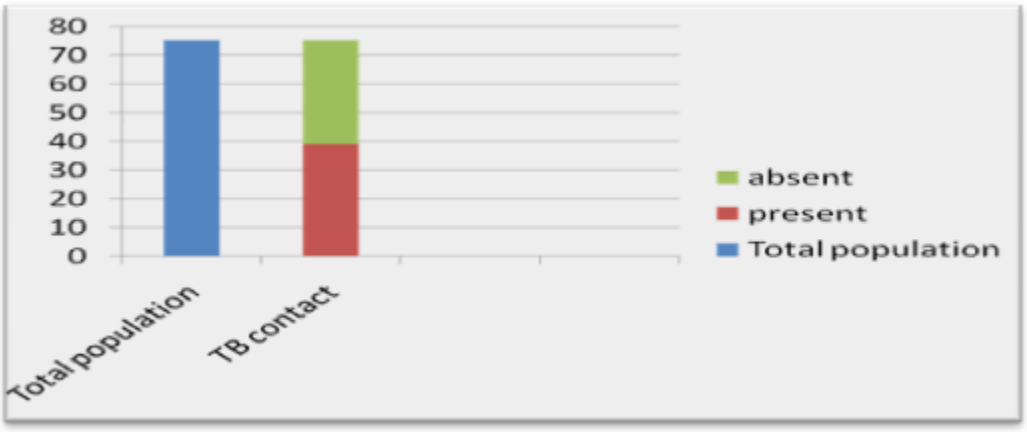

Figure 1: History of TB contact in the study population

In the study population, 52% (n=39) had a history of TB contact within the last two years, while 48% (n=36) reported no such contact. In this study, 43 children (57.3%) were malnourished, while 32 (42.6%) had normal nutritional status, highlighting the strong association between malnutrition and extrapulmonary tuberculosis. Clinical presentation varied, with the most common features being generalized weakness in 59 patients (78.6%), lymph node swelling in 37 patients (49.3%), and fever in 34 patients (45.3%). Other symptoms included significant weight loss, loss of appetite, night sweats, headache, vomiting, altered sensorium, abdominal pain, joint swelling, and skin ulceration, reflecting the diverse manifestations of the disease in children.

Table 2: Frequency of Mantoux positivity in Extrapulmonary TB study sample

Mantoux test	Frequency	Percentage
Positive	41	54.7
Negative	34	45.3

In the study sample, 54.7% (n=41) of patients with extrapulmonary TB showed Mantoux test positivity, while 45.3% (n=34) were negative. In this study, CBNAAT results showed that 27 children (36%) with extrapulmonary tuberculosis tested positive, while 48 children (64%) were negative, indicating a moderate detection rate of the test in this population.

Table 3: CBNAAT positivity in relation to CBNAAT samples

Samples	Total	CBNAAT Positive (%)	CBNAAT negative (%)
CSF	31	7 (22.5)	24 (77.4)
Lymph node aspirate	31	16 (51.6)	15 (48.3)
Ascitic fluid	4	2 (50)	2 (50)
Bone and joint fluid	6	2 (33.3)	4 (66.7)
Skin tissue aspirate	3	0	3 (100)

CBNAAT positivity was highest in lymph node aspirates (51.6%), followed by ascitic fluid (50%), bone and joint fluid (33.3%), and CSF (22.5%), while all skin tissue aspirates were negative.

Table 4: Relation of age of patient with CBNAAT positivite

	CBNAAT		
Age	CBNAAT Negative	CBNAAT Positive	Total
<=2 Y	13	8	21
2-4 Y	6	3	9
4-8 Y	20	8	28
>8 Y	9	8	17

The mean age of patients was 63.2 ± 39.2 months, and CBNAAT positivity showed no significant correlation with age (p=0.65).

Table 5: Relation of sex of patient with CBNAAT positivity

Sex		CBNAAT		
		Negative	Positive	Total
Male	N	25	11	36
	%	52.10%	40.70%	48.00%
Female	N	23	16	39
	%	47.90%	59.30%	52.00%
Total	N	48	27	75
	%	100.00%	100.00%	100.00%

CBNAAT positivity was slightly higher in females (59.3%) than males (40.7%), but the difference was not statistically significant (p=0.345).

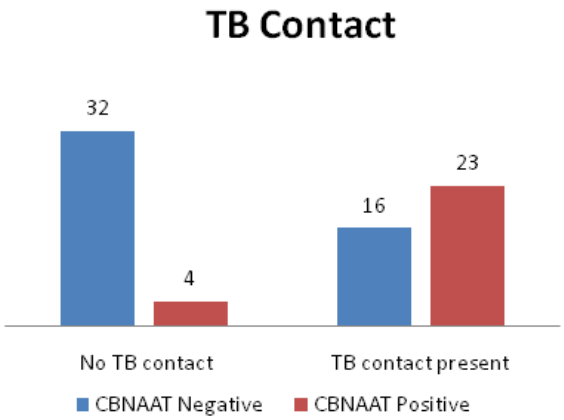

Figure 2: Relation of history of TB contact with CBNAAT positivity

CBNAAT positivity was significantly higher in patients with a history of TB contact (23/39) compared to those without (4/36), showing a strong statistical association (p=0.0001). In the study sample of extrapulmonary tuberculosis patients, CBNAAT positivity was significantly associated with malnutrition. Among 43 patients with malnutrition, 24 tested positive on CBNAAT, whereas only 3 of 32 patients without malnutrition were CBNAAT positive. Statistical analysis revealed a p-value of 0.0001, indicating that CBNAAT positivity was significantly higher in patients with malnutrition.

Table 6: CBNAAT positivity in relation to Mantoux test

Mantoux Test	CBNAAT Negative	CBNAAT Positive	Total
Mantoux Test Negative	29	5	34
Mantoux Test Positive	19	22	41
Count	48	27	75

CBNAAT positivity was significantly higher in patients with a positive Mantoux test (22/41) compared to those with a negative test (5/34), with a strong statistical association (p=0.0001).

Table 7: CBNAAT positivity in relation to time of presentation

	CBNAAT		
Onset Time	CBNAAT Negative	CBNAAT Positive	Total
<2 wk	16	3	19
2-8 wk	13	13	26
>8 wk	19	11	30

CBNAAT positivity was highest in patients presenting 2–8 weeks after symptom onset (50%) and lower in <2 weeks (15.7%) and >8 weeks (36.6%), with no statistically significant association (p=0.061).

Discussion

This study was designed to explore the association of different factors with extrapulmonary tuberculosis (EPTB) in children and to examine the positivity rate of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), particularly in relation to the duration of symptoms at presentation. A total of 75 children admitted with EPTB at Gauhati Medical College & Hospital were included.

Extrapulmonary TB can present at any age, but in this study 21 patients (28%) were below 2 years, 9 (12%) were between 2–4 years, 28 (37.3%) were between 4–8 years, and 17 (22.7%) were above 8 years. The mean age was 63.2 months ± 39.2. These findings indicate a predominance in the 4–8-year age group, which is consistent with previous studies reporting variable mean ages across populations Baghaie N, et. al; 2010 [13].

Karim MM, et. al; 2006,Gender distribution showed that 36 patients (48%) were male and 39 (52%) were female, giving a male-to-female ratio of 1:1.1. This aligns with several earlier studies that demonstrated a higher prevalence of EPTB in females compared to males [14].

Socioeconomic status was assessed using the Modified Kuppuswamy Scale. The majority of patients, 38 (50.7%), belonged to the lower class, followed by 14 (18.7%) in the upper-lower class, 11 (14.7%) in the lower-middle class, and 12 (16%) in the upper-middle class. These results are similar to other studies where the majority of patients belonged to lower socioeconomic groups Balakrishnan T, et. al; 2021[15].

History of TB contact was found in 39 patients (52%). Among these, 22 had family members with TB, while 17 had exposure to neighbors or community members. Alwani H, et. al; 2022, studies where TB contact ranged from 20–75% in pediatric EPTB cases [16].

Regarding BCG vaccination, 56 patients (74.7%) had received the vaccine while 19 (25.3%) had not. Qian X, et. al; 2018,studies also emphasized its protective role, particularly against disseminated TB, though the rates of vaccinated EPTB patients varied across studies [17].

Malnutrition was observed in 43 patients (57.3%), a significant proportion of the study group. Grønningen E. 2025, corroborated earlier studies that reported malnutrition as a common comorbidity in EPTB patients, ranging from 41–85% [18].

The distribution of EPTB types revealed lymph node TB (41.3%) and CNS TB (41.3%) as the most frequent presentations. Among CNS TB, 22 patients (29.3%) had TB meningitis, while 9 (12%) had tuberculoma. Other forms included joint TB (8%), abdominal TB (5.3%), and cutaneous TB (4%). Ravikumar P &Bai PG. 2017, results are in line with previous findings, although the proportions varied between populations [19,20].

Mantoux test was positive in 41 patients (54.6%), and among them, 22 also tested positive for CBNAAT, showing a statistically significant correlation (p = 0.0001). Asma F. 2019,reported Mantoux positivity rates between 35–76% in EPTB cases [21].

CBNAAT positivity was recorded in 27 cases (36%), with the highest yield from lymph node aspirates (51.6%), followed by ascitic fluid (50%), bone and joint fluid (33.3%), and cerebrospinal fluid (22.5%). This pattern is consistent with earlier reports showing variable positivity, with lymph node samples generally providing the highest diagnostic yield [22].

Jadhav PT, et. al;analyzed in relation to the time of presentation, CBNAAT positivity was seen in

15.7% of cases presenting within 2 weeks of symptoms, 50% of cases presenting between 2–8 weeks, and 36.6% of cases presenting after more than 8 weeks. However, this association was not statistically significant (p = 0.061). Gupta R, et. al; 2025,analyzed temporal association of CBNAAT with time of symptom onset, the present findings suggest that positivity may be higher when samples are taken after two weeks of illness, warranting further research [23,24]. Pervin R, et. al; 2024, demonstrated that extrapulmonary tuberculosis in children is associated with younger age, female predominance, lower socioeconomic status, malnutrition, and significant history of TB contact. Lymph node and CNS TB were the most frequent forms encountered. CBNAAT proved to be a valuable diagnostic tool, with higher yields from lymph node aspirates. Although no significant association was found between CBNAAT positivity and time of presentation, trends indicate higher positivity after two weeks of symptoms, highlighting the need for larger studies in this area [25].

Conclusion

This study concluded that extrapulmonary tuberculosis occurred slightly more in females, though the difference was not statistically significant. The most common presentations were CNS TB, including meningitis and tuberculoma, and lymph node TB. CBNAAT positivity was highest in lymph node aspirates and showed significant association with TB contact history, malnutrition, and Mantoux positivity. No relation was found between CBNAAT positivity and time of presentation, though higher yields were noted after two weeks, indicating the need for further research to enhance detection and reduce missed cases.

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