e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15 (12); 202-206

Original Research Article

Evaluation of Extra Pulmonary Tuberculosis (EPTB) Cases with CBNAAT in Comparison with Cytology

Jyotirmaya Nayak[1], Sridhar Panda[2], Nagendra Kumar Rajsamant[3], Gopabandhu Patra[4]

[1]Associate Professor, Department of General Surgery, SCB Medical College, Cuttack
[2]Assistant Professor, Department of General Medicine, SCB Medical College, Cuttack
[3]Assistant Professor, Department of General Surgery, SCB Medical College, Cuttack
[4]Assistant Professor, Department of Orthopaedics, Bhima Bhoi Medical College, Balangir

Received: 25-09-2023 / Revised: 28-10-2023 / Accepted: 30-11-2023
Corresponding author: Dr. Gopabandhu Patra
Conflict of interest: Nil

Abstract:

Introduction: EPTB causes a large burden of mortality and morbidity because of its complicated and subclinical presentations, which cause a delay in diagnosis. EPTB has little infectious potential and so has never been prioritized in National TB Control Program efforts. EPTB may be detected using a variety of approaches, including microscopy, culture, and identification of the organism's DNA. CBNAAT is a newer approach. The current research was designed to compare the efficacy of CBNAAT in diagnosing EPTB to that of cytology.

Materials and Procedures: The investigation comprised 120 lymph node, pus, pleural fluid, ascitic fluid, and C.S.F. samples. Samples were collected and tested for AFB smear, FNAC, and CBNAAT all at the same time.

Result: EPTB was diagnosed by CBNAAT, FNAC, and AFB stain in 40, 71, and 18 of the 120 patients, respectively.

Conclusion: CBNAAT is a modern confirmatory test that adds the advantage of concurrent drug resistance. Even in remote locations, combining CBNAAT with other tests yields a higher diagnostic result.

Keywords: CBNAAT, extra pulmonary tuberculosis, FNAC, AFB stain.

Introduction

Despite the fact that the causal bacterium was identified more than 100 years ago and that there are several very effective medications and vaccines available, TB remains a global public health concern. Tuberculosis control began with the introduction of BCG, new medications, advances in people's living standards and quality of life, and the use of health resources.

The current research was designed to compare the efficacy of CBNAAT in diagnosing EPTB to that of cytological testing. Its goal is to establish the function of CBNAAT in clinical decision-making in suspected EPTB patients [1], as well as to determine whether CBNAAT is useful in clinically suspected tuberculosis cases when acid fast bacilli (AFB) staining is negative [2].

CBNAAT (Xpert MTB/RIF assay) is a quick and completely automated NAAT (Nucleic Acid Amplification Test). RNTCP adopted CBNAAT in India in 2012.

The Xpert MTB/RIF test uses hemi-nested real-time PCR to target the rpoB gene. Xpert MTB/RIF is suggested for the diagnosis of EPTB, suspected cases of pulmonary TB (conditional recommendations), and TB in children.

Materials and Methods

Current Study is a Prospective cross-sectional study done at Department of Medicine and Surgery, SCB medical college, cuttack for a period of 18 months from March 2021 to August 2022 on 120 cases.

Inclusion criteria: All clinically suspected cases of Extra Pulmonary Tuberculosis.

Exclusion criteria: Cases of exclusive Pulmonary Tuberculosis and Cases with inadequate aspirate.

Results were reported in a pre-designed proforma after obtaining a full history, examination findings, and available investigation. FNA was used to treat lymph nodes and cold abscesses. Two smears were prepared for the Haematoxylin and Eosin (H&E) stain, one for the May Grunwald Giemsa (MGG) stain, and one for the AFB stain. Concurrently, needle washes in 0.9% normal saline were collected for CBNAAT. If the aspirate was judged to be insufficient, the FNA was repeated. The aseptically obtained aspirate was immediately

labeled and put in a sterile container with normal saline to prevent drying of the contents. Fluid samples are similarly centrifuged and spread.

Statistical analysis

Results were tabulated and analysed using SPSS software 23 version.

Results

The majority of the patients (25%) in 120 EPTB instances were between the ages of 21 and 30. Men seem to be more afflicted, accounting for 59.2% of the patient population. The majority of the cases were lymph node (59.2%) and pleural fluid (26.7%). Cytology revealed TB in 71 instances, AFB stain in 28 cases, and CBNAAT in 40 cases. CBNAAT was somewhat more positive than AFB stain. On cytology, AFB, and CBNAAT, 14 and 10 of the 28 positive HIV patients tested positive for TB, respectively. When CBNAAT and AFB staining were compared (table 2), 18 instances were identified positive in both tests, but 22 people who were positive on CBNAAT were negative on AFB, and 6 subjects who were negative on CBNAAT were positive on AFB. CBNAAT's sensitivity, specificity, PPV, and NPV were determined to be 45%, 92.50%, 75%, and 77.08%, respectively.

Table 1: Distribution of HIV status among CBNAAT

	CBNAAT Positive		CBNAAT Negative		Total
	Cases	Percentage	Cases	Percentage	
HIV Positive	12	42.9%	16	57.1%	28
HIV Negative	28	30.4%	64	69.6%	92
Total	40		80		120

Table 2: Comparison table of CBNAAT with AFB stain

AFB staining	CBNAAT		Total
	Positive	Negative	
Positive	18	6	24
Negative	22	74	96
Total	40	80	120

Table 3: Result of CBNAAT, FNAC, AFB stain among various samples

EPTB cases	Total samples	FNAC positive	CBNAAT positive	AFB positive
Lymph node	71	51	26	16
Pleural fluid	32	12	6	2
Pus	11	7	6	6
Ascitic fluid	4	1	0	0
Cerebrospinal fluid	2	0	2	0
Total	120	71	40	24

When CBNAAT and cytology results were compared, 24 instances were found to be positive in both tests, whereas 16 cases were positive on CBNAAT but negative on cytology. 47 instances that tested negative for CBNAAT tested positive for cytology. CBNAAT's sensitivity, specificity, PPV, and NPV were determined to be 60%, 41.25%, 33.8%, and 67.35%, respectively.

Discussion

In the current investigation, the patients suspected of having EPTB ranged in age from 6 months to 80 years, with the age group of 21-30 years accounting for 25% of the total. The findings were close to those of Komanapalli SK et al. [3], who had the most patients with a broad age range of 11-30 years. K Arpitha et al. [4] studied 29.4% of the cases. According to Dronadula et al. [5], 39% of cases are observed in the age range of 20-39 years.

Male preponderance of 59.2% was seen in the present research, which is equivalent to Mukherjee et al. [6, 7], Singh KG et al. [7], K Arpitha et al. [4, 8], and Rameshbabu B et al. [9] investigations. This shows that men are more conscious than females, or that a greater number of male patients were afflicted in the research group.

The majority of cases (59.2%) came from lymph nodes, mostly in the anterior cervical group. Pleural fluids made up 26.7% of the total. Tortoli et al. [10] found 24% of instances of pleural effusion, whereas Causse et al. [11] found 19.4% of cases of pleural or other bodily fluids.

When compared to research on EPTB samples, the proportion of pleural fluid cases is higher. Ascitic fluid made up 3.3% of the samples, whereas CSF made up 1.7% of the cases. 9.2% of the patients had pus samples (cold abscess samples, swellings, subcutaneous abscesses, and a few with numerous discharging sinuses).

According to Kandi et al. [12], pulmonary samples made up 55% of the total, extrapulmonary samples made up 45%, lymph node samples made up 19%, pleural fluid and BAL fluid samples made up 10%,

and CSF samples made up 2.5%. The majority of the samples in Dronadula et al.'s [5] research are lymph node aspirates, which account for the majority of all samples and EPTB samples.

CBNAAT and FNAC positive cases are (21/82) 25.60% in our investigation of lymph node and pus sample cases. 11 instances out of 82 (13.41%) are FNAC negative and benefit from becoming positive in CBNAAT. However, in (14/82) of instances where CBNAAT failed to identify the bacilli, 17.07% of cases were discovered in FNAC, which might be owing to the last passage sample submitted for CBNAAT yielding smaller quantity of sample when sent for CBNAAT in normal saline, which could be overly diluted [13]. Extrapulmonary samples are often pauci bacillary, therefore if there is very little aspirate, the CBNAAT may be negative even if the FNAC is positive.

In the current research, both CBNAAT and FNAC negative cases (36/82) account for 43.90% of the total, indicating that the tests are more specific. The CBNAAT and FNAC demonstrated sensitivity of 65.62% and specificity of 72% among all lymph node and pus samples, accounting for 82 patients, which is equivalent to the sensitivity of Aruna L et al. [14] research.

In the current investigation, 18 patients were found to be positive in AFB and CBNAAT, whereas 6 were positive in AFB but negative in CBNAAT (shown in picture 2). This might be owing to the thick caseous material yielding fewer aspirates on FNAC, resulting in increased dilution of the sample for CBNAAT, resulting in sample negative. 22 CBNAAT positive patients tested negative for AFB. This demonstrates the efficacy of CBNAAT in paucibacillary samples. Calculating chi-square statistics between CBNAAT and AFB yields a value of 23.4375 and a p-value of 0.00001.

Mukherjee et al. [6] found AFB smear positive in lymph node FNA in 28 of 114 cases (24.6%) and five of eleven (45.5%) instances of cold abscess aspirate. Manju Kumari et al. [15] found 41% CBNAAT positive and 24% AFB positive in their research. Only 17% of TB cases were discovered with CBNAAT and were reported as negative on AFB stain. Gupta H et al. [60] found AFB positive in 14/50 patients (28%) and CBNAAT positivity in 32/50 cases (64%). According to Patil SB et al. [17], among 192 diagnosed cases of EPTB, 46.35% were positive on AFB stain and 55.20% were positive on CBNAAT. In the current research, 18 patients were positive in AFB and Cytology, with 6 instances becoming negative in cytology after being positive in AFB. On cytology, 53 patients that tested negative for AFB tested positive. When compared to cytology, the sensitivity, specificity, PPV, and NPV of AFB were determined to be 25.35%, 87.76%, 75%, and 44.79%, respectively. Gundrajakuppam et al. [18] discovered that the sensitivity, specificity, PPV, and NPV of AFB stain with FNAC were 12.5%, 97.1%, 83.3%, and 49.6%, respectively.

The sensitivity and specificity of AFB stain against composite diagnostic procedures were 23.08% and 100%, respectively, in a research conducted by Vishnu et al. [19], Tamanna et al. [20].

AFB positive is modest in epthelioid granulomas without necrosis (5.8%-30.0%), but much greater in necrotizing epithelioid granulomas (32.0%-64.7%). It is greatest (48.5%-77.4%) in necrosis without epithelioid granulomas [21]. This shows that CBNAAT positive is highest in abscess patients, with the highest bacillary burden, since most abscesses have caseous necrosis [21].

All investigations showed good specificity for detecting AFB on ZN stain, which is comparable to our current research. The low sensitivity might be attributed to the poor quality of the smear and the paucibacillary character of the fine needle aspirate, but as predicted, the specificity was the greatest.

CBNAAT positivity was identified in 42.9% of the 28 HIV positive patients (table 2). In those living with HIV, the sensitivity is about 30%. CBNAAT testing is negative in 57.1% of HIV patients. The sensitivity of Komanapalli SK et al. [3] research among EPTB with HIV patients is 78.95%, while the specificity is 50%. When compared to the present research, the sensitivity of CBNAAT among HIV patients is high. The overall number of HIV patients in the current research is large due to a high degree of clinical suspicion among them.

There are nine CBNAAT negative instances among HIV patients who tested positive on FNAC and must be validated by culture. Seven of the 12 CBNAAT positive individuals tested negative in FNAC. The investigation by Komanapalli SK et al. [3] revealed extremely few HIV positive patients. According to Kandi S et al. [12], 6% of CBNAAT positive individuals had HIV.

CBNAAT positive in lymph nodes is 36.6%, 18.7% in pleural fluid, 54.5% in pus, and 100% in CSF in the present investigation (table 1). Rameshbabu B et al. [9] discovered CBNAAT positive in lymph nodes, various swellings, pleural fluid, pus & abscesses, ascitic fluid, CSF, and others.

Dr Prayas et al. [21] found CBNAAT positive in 66.2% of cases, AFB positivity in 47.5% of cases, and FNAC positivity in 72.5% of EPTB samples. EPTB is difficult to diagnose owing to its various clinical manifestations and paucibacillary nature [2]. The AFB smear has not been shown to be very helpful in the diagnosis of EPTB. CBNAAT is a nucleic acid amplification test that identifies TB bacilli as well as Rifampicin resistance. Because it

is a low-cost and quick test, CBNAAT has the potential to change the diagnosis and treatment of EPTB.

Conclusion

CBNAAT is a confirmatory test that is highly useful in diagnosing EPTB patients since it can detect bacilli in low numbers as well as treatment resistance. CBNAAT is a more effective approach than AFB stain for detecting EPTB in fluids. The best approach in early suspicious instances of lymph node is FNAC. Incorporating CBNAAT into the initial diagnosis of EPTB patients would limit the inappropriate use of antituberculosis medicines. Thus, when CBNAAT is used in conjunction with cytological investigation, it may aid in the correct diagnosis and early treatment of EPTB.

References

1. Shivprasad Kasat, Mahendhra Biradar, et al. Effectiveness of CBNAAT in the diagnosis of extra pulmonary tuberculosis: International journal of research in medical sciences/Kasat S et al. Int J Res Med Sci. 2018 Dec; 6(12):3925-3928.
2. Maurya AK, Kant S, Nag VL, Kushwaha RA, Dhole TN. Trends of anti-tuberculosis drug resistance pattern in new cases and previously treated cases of extrapulmonary tuberculosis cases in referral hospitals in northern India. J Postgrad Med. 2012; 58(3):185-9.
3. Sunil Kumar Komanapalli, Uma Prasad, et al. Role of CB-NAAT in diagnosing extra pulmonary tuberculosis in correlation with FNA in a tertiary care center Int J Res Med Sci. 2018 Dec;6(12):4039-4045.
4. Arpitha K, et al., Comparative Study of FNAC, ZN Staining and GeneXpert in Suspected Cases of TB Lymphadenopathy National Journal of Laboratory Medicine. 2021 Jul;10(3):PO26-PO29.
5. Gayathri Dronadula, Apuroopa Murari, et al. Cytological Study of Tuberculosis in Pulmonary and Extrapulmonary Lesions in Correlation with Cartridge Based Nucleic Acid Amplification Test (CBNAAT) Annals of Pathology and Laboratory Medicine, 2020 Feb, 7(2).
6. Mukherjee S, et al., Role of Cartridge Based Nucleic Acid Amplification Testing in Diagnosis of Extrapulmonary Tuberculosis-Experience from a Teaching Institution in Eastern India Int J Cur Res Rev., 2021 March, 13(06).
7. Singh KG, Tandon S, et al. Role of CB-NAAT in diagnosing Mycobacterial tuberculosis and rifampicin resistance in tubercular peripheral lymphadenopathy international Journal of Medical Research and Review, 2017 March, 5(03).
8. Bhaskar Thakkar, Vaidehi R Patel, et al. Role of CBNAAT (Cartridge based nucleic acid amplification test) in early diagnosis of tuberculous lymphadenopathy and drug resistant tuberculous lymphadenopathy with the help of fine needle aspiration cytology International Journal of Health and Clinical Research. 2022; 5(3):442-446.
9. Vatsyayan R, et al. Extra pulmonary tuberculosis manifestation in head and neck and its diagnosis with recent tools like cartridge based nucleic acid amplification test Int J Otorhinolaryngol Head Neck Surg. 2021 May; 7(5):829-836.
10. Tortoli E, Russo C, Piersimoni C, Mazzola E, Monte PD, Pascarella M, et al. Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis. Eur Respir J. 2012; 40: 442-447.
11. Causse M, Ruiz P, Juan Bautista GA, et al. Comparison of two molecular methods for the rapid diagnosis of extrapulmonary tuberculosis. J Clin Microbiol. 2011:49(8):3065-3067.
12. Kandi S, Reddy V, et al. Diagnosis of pulmonary and extra pulmonary tuberculosis: how best is CBNAAT when compared to conventional methods of TB detection? Pulm Res Respir Med Open J. 2017;4(2):38-41.
13. Harry L Iochim, Jeffrey Medeiros L. Iochim lymph node pathology 4th edition.
14. Aruna L, Ghanshyani K, et al. Correlation of cytomorphology and cartridge based nucleic acid amplification test (CBNAAT) on fine needle aspirates in the diagnosis of tuberculous lymphadenitis. Med Pulse International Journal of Pathology. 2018; 7(3):128-32.
15. Kumari M, Khambra P, et al. Rapid diagnosis of tubercular lymphadenopathy by cartridge-based nucleic acid amplification test (CBNAAT) and its correlation with Ziehl-Neelsen staining on fine needle aspiration cytology. Int J Health Sci Res. 2020; 10(7):17-21.
16. Gupta H, Mehra V, Sharma RK, et al. To study the differentials of suppurative lymphadenitis by FNAC and their evaluation by ZN staining, CB- NAAT, fluorescent microscopy, fungal and bacterial cultures. International Journal of Clinical and Diagnostic Pathology. 2020; 3(1):235-41.
17. Patil SB, Dhage SM, et al. Cartridge based nucleic acid amplification test: A sensitive diagnostic tool for tuberculosis on fine needle aspirates samples. Int J Community Med Public Health. 2020; 7(4):1511-1515.
18. Lavanya G, Sujatha C, et al. Comparison of GeneXpert with ZN Staining FNA samples of

suspected extrapulmonary tuberculosis. IOSR J Dent Med Sci. 2019; 18(7):25-30.
19. Goyal VK, Jenaw RK, et al. Diagnostic Yield of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) In Lymph Node Tuberculosis at Institute of Respiratory Disease, SMS Medical College, Jaipur. JDMS. 2019; 18(4):63-7.
20. Nur TE, Akther S, Kamal M, et al. Diagnosis of Tuberculous Lymphadenitis Using Fine Needle Aspiration Cytology: A Comparison Between Cytomorphology and GeneXpert Mycobacterium Tuberculosis Resistant to Rifampicin (MTB/RIF) Test. Clinical Infection and Immunity. 2019 Jan; 4:6-11.
21. Marluce Bibbo. Bibbo comprehensive cytopathology 2nd edition Dr prayas, Dr Aditi Baghla et al., Cartridge Based Nucleic Acid Amplification Test (CBNAAT) in the Diagnosis of Extrapulmonary Tuberculosis International Journal of Scientific Research, 2022 April, 11(04).