



Research Article

ROLE OF CBNAAT IN DIAGNOSIS OF EXTRA PULMONARY TUBERCULOSIS:
A PROSPECTIVE OBSERVATIONAL STUDY

Venkata Manohar K¹, Vijaya kumari Sathri², Shantha kumari kummari³, K Prasanna purna⁴,
Sahasini Vasireddy⁵ and K V Subba Naidu⁶

Assistant professor¹, Associate professor², Assistant professor³, Professor⁴, Professor⁵ and Professor⁶

¹Dept of Respiratory Medicine, Santiram Medical College, Nandyal, Andhra Pradesh

²Dept of community Medicine, Govt Medical College, Nandyal, Andhra Pradesh

³Dept of community Medicine, Govt Medical College, Nandyal, Andhra Pradesh

⁴Dept of Respiratory Medicine, Narayana Medical College, Nellore, Andhra Pradesh

⁵Dept of community Medicine, Govt Medical College, Nandyal, Andhra Pradesh

⁶Dept of Respiratory Medicine, Narayana Medical College, Nellore, Andhra Pradesh

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ABSTRACT

Background: Tuberculosis (TB) remains a major infectious disease in developing countries, with the diagnosis of extra pulmonary TB (EPTB) posing significant challenges. In recent years, cartridgebased nucleic acid amplification test (CBNAAT) has emerged as an important diagnostic tool since the diagnostic yield is higher. This study aims to evaluate the diagnostic accuracy of the CBNAAT in EPTB, and to assess the CBNAAT performance in detecting Rifampicin resistance among the patients studied. Methodology: An institutional-based observational prospective study was conducted at Department of Respiratory Medicine, Narayana Medical College & Hospital, Nellore during period from January 2019 to November 2020. 25 patients with presumptive extra pulmonary TB were taken as study participants. Results: The most common age group of patients in this study was 41-60 years (48%). In the present study, the Sensitivity of CBNAAT in diagnosing extra pulmonary TB was 93.33%, specificity was 40% and positive predictive value of 70%.

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INTRODUCTION

Worldwide, Tuberculosis continues to be the most important cause of death from a single infectious microorganism.¹ Alarming rise in the global incidence of TB and the development of drug resistance, it is needed to develop a rapid diagnostic technique for the diagnosis of tuberculosis.² Tuberculosis is a significant health problem globally, with estimated new cases and deaths; every year is 8.7 million and 1.4 million, respectively.³ According to the WHO, India has the highest number of TB cases and the highest TB burden in the world.⁴ The available techniques for the diagnosis of tuberculosis are time-taking and also have variable sensitivity and specificity. This results in increased mortality, morbidity, and the development of drug resistance (MDR, XDR) in TB patients.^{5,6} The gold standard technique for diagnosing tuberculosis is culture. But culture is a slow process, and it may take 2-8 weeks for positive reports. Besides this, Mycobacterium culture is a complicated procedure, and it requires BSL II/III that is not affordable in everywhere.^{7,8}

Microscopic examination of smear for Acid Fast Bacilli is a fast method, but its sensitivity is low. WHO has recommended the implementation of Cartridgebased nucleic acid amplification test (CBNAAT) in the National Tuberculosis program in the developing countries.⁹ The CBNAAT is a modern diagnostic technique which is automated, easy to operate, and based on real-time PCR analysis; perform sample processing and rapid diagnosis of Rifampicin resistance in a single setting in clinical specimen.^{9,10} With the advent of the End TB Strategy, for the rapid diagnosis of Rifampicin Resistance, CBNAAT/ Genexpert test is used. Gene Xpert MTB/RIF (Xpert) is a fully automated real-time hemi-nested PCR system implementing molecular beacon technology for the diagnosis of TB infection. Moreover, CBNAAT simultaneously detects TB bacilli and Rifampicin drug resistance, providing an accurate result in less than two hours. This helps the patient to be initiated on treatment on the same day, thereby reducing the initial loss to follow up. It has minimum bio safety requirements, training needs and can be housed in non-conventional laboratories. We undertook this

*Corresponding author: Shantha Kumari Kummari

Dept of community Medicine, Govt Medical College, Nandyal, Andhra Pradesh

study to see the role of CBNAAT among extra pulmonary TB, along with its added advantage of upfront Drug Sensitivity testing (DST) for the diagnosed TB cases. This may help policy and practice to use only CBNAAT instead of LED-FM in routine programmatic settings.¹¹

OBJECTIVE

To identify the Role of CBNAAT in detection of MTB (Mycobacterium tuberculosis) and Rifampicin sensitivity in extra pulmonary Tuberculosis

MATERIALS & METHODS

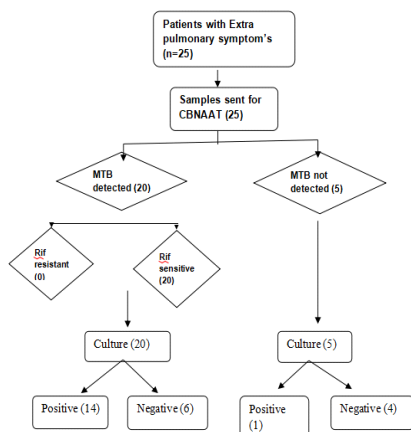
This was a prospective observational study conducted in a tertiary care hospital in the Department of Respiratory Medicine, Narayana Medical College & Hospital, Nellore, Andhra Pradesh from January 2019 to November 2020. All patients who were diagnosed with EPTB, aged 18 years and above and who were willing to give consent were included in the study. Patients who were not willing to participate in the study, who are known or suspected case of HIV infection. those on anti-tubercular therapy (ATT) for more than one month and not fitting into inclusion criteria were excluded.

Sample Size

25 patients with presumptive extra pulmonary TB were taken as study participants consulted during study period.

Sampling procedure: After taking the informed consent, a detailed history was taken from the patients and recorded. Provisional diagnosis of extra pulmonary TB¹² was made as per WHO Criteria, (Presence of organ specific symptoms and signs like swelling of lymph node, pain and swelling in joints, neck stiffness, disorientation and/or constitutional symptoms’ like significant weight loss, persistent fever for more than 2weeks, night sweats).For the Extra pulmonary TB, samples from Pleural tissue was taken by **Thoracoscopy**,¹³ pus from the pleural cavity, Pleural fluid samples were taken by **Thoracentesis**,¹⁴ Pus from Cervical lymph node, Pus from Mediastinal lymph node were taken by **FNAC**,¹⁵ and pus from Psoas abscess was collected .These collected samples were sent for CBNAAT for detection of MTB and Rifampicin sensitivity. Extra pulmonary CBNAAT both positive and negative samples were sent for the culture, done in the Microbiology Department. As culture test is the gold standard to diagnose TB, CBNAAT results were compared with culture result to the sensitivity and specificity of CBNAAT.

Figure 1: Flowchart explaining the patient flow in the study



Statistical Analysis

Data collected was tabulated using Microsoft Excel and analysed using Statistical Package for the Social Sciences version 20. Results were represented using frequencies and percentages. Sensitivity, specificity, Likelihood ratios, predictive values and 95% confidence interval (CI) were estimated.

Ethical committee approval

The study was approved by the institutional ethical committee.

RESULTS

Table 1: Socio Demographic profile of the study participants

Parameter	Number	Percentage (%)
Age		
18-40	10	40
41-60	12	48
>60	3	12
Total	25	100
sex		
Males	13	52
Females	12	48
Total	25	100
Literacy		
Illiterate	9	36
literate	16	64
Total	25	100
Occupation		
Unemployed	9	36
Employed	16	64
Total	25	100
Personal history		
H/O Smoking	8	32
H/O Alcohol	6	24
H/O Tobacco chewing	2	8

The study included a sample of 25 patients. Most of the patients in this study was 41-60 years (48%), followed by 18-40 years (40%) and in the age group of above 60years were only 3(12%). out of 25 participants males were 52% , and females were 48%. In the present study illiterates were 36%, literates were 64% and unemployed were 36%, employed were 64%.Out of the 25 patients in the study, 32% had h/o smoking, and 24% had a history of alcohol intake, and 8% had a history of tobacco chewing.(Table 1)

Table 2 Co morbidities among study participants

Co morbidities	Number	Percentage
Diabetes Mellitus	8	32
Hypertension	2	8
Asthma	3	12
COPD	6	24
Past H/O TB	1	4

Among the patients in the study, the most common co morbid condition is Diabetes mellitus (32%), COPD(24%) followed by Asthma (12%), Hypertension(8%), and with a past history of TB was 4%.(Table 2)

Table 3 Type of Extra pulmonary specimen sent for CBNAAT

Extra pulmonary specimen	Number	percentage
Pleural tissue	10	40
Pleural fluid	2	8
Pus from the pleural cavity	5	4
Pus from Cervical lymph node	6	12
Pus from Mediastinal lymph node	1	4
Pus from Psoas abscess	1	4
Total	25	100%

Among the 25 extra pulmonary cases, samples were sent for CBNAAT from pleural tissue (40%), pus from cervical lymph node (12%), pleural fluid (8%), pus from the pleural cavity (4%) and pus from Psoas abscess(4%).(Table 3)

Table 4 Result of CBNAAT among extra pulmonary cases

CBNAAT result	Number	Percentage
MTB detected	20	80%
MTB not detected	5	20%
Total	25	100%

(n=25)

Mycobacterium Tuberculosis detected in CBNAAT was 80%

Table 5 Effectiveness of CBNAAT in diagnosing extra pulmonary TB

Result	Culture positive	Culture negative	Total
CBNAAT Positive	14(True positives)	6 (false positives)	20
CBNAAT Negative	1 (false negatives)	4(True negatives)	5
Total	15	10	25

Statistic	Value	95% ci
Sensitivity	93.33%	68.05% - 99.83%
Specificity	40%	12.16% - 73.76%
Positive Likelihood Ratio	1.56	0.92 -2.63
Negative Likelihood Ratio	0.17	0.02 - 1.28
Positive Predictive Value	70%	58.02% - 79.76%
Negative Predictive Value	80%	34.21% - 96.85%
Accuracy	72%	50.61% - 87.93%

The effectiveness of CBNAAT is known by comparing the results with culture, as it is the gold standard to diagnose TB. In the present study, the Sensitivity of CBNAAT in diagnosing extra pulmonary TB was 93.33% (68.05% -

99.83%), specificity was 40% (12.16% - 73.76%) and Accuracy was 72%(50.61% -87.93%).

Table 6 Rifampicin sensitivity status in CBNAAT

Rifampicin sensitivity/Resistance	Number	Percentage
Rifampicine resistant	0	0
Rifampicine sensitive	20	100
Total	20	100

There was no Rifampicine resistance noted among 20 MTB detected samples. (Table 6)

DISCUSSION

In the present study The most common age group of patients in this study was 41-60 years (48%), followed by 18-40 years (40%), age group of >60years were only 12%.In the study done by Sharma Shubhkaran *et al.*,¹⁶The majority of patients (87.7%) belong to the age group of 21 to 60 years, which is almost similar to this study.In the study done by R Dewan *et al.*,¹⁷ The most common age group is 41 – 60years. Almost similar to this study.Variation in the most common age group affected with some studies is may be due to variation in sample size.In this study, out of 25, males were 13 in number, and females were 12. In the study done by Sharma Shubhkaran *et al.*,¹⁶ There were 50 male and seven female patients in the study group. It is almost similar to the present study.In the study by Swetha madas *et al.*,¹⁸ Among the 50 patients studied, 37 were males, and 13 were females. In the present study, Among the study participants illiterates are 36%, literates are 64%.In the study done by Vandana Bhoi *et al* ¹⁹ illiterates are 23.1% .which is almost similar to present study .literates are more in number may be due to seeking of health care behaviour.

In the present study unemployed are 36%, Employed are 64%. In the study done by Vandana Bhoi *et al.*,¹⁹ un employed are 29.6%. Out of the 25 patients in the study, 32% had h/o smoking, and 24% had a history of alcohol intake, and 8% had a history of tobacco chewing. In the study done by Sharma Shubhkaran *et al.*,¹⁶ Out of 57 patients, 33% were a smoker, and 31.5% of patients were alcoholic.Among the patients in the study, the most common co morbid condition is Diabetes mellitus (32%), COPD(24%) followed by Asthma(12), Hypertension(8%), and with a past history of TB was 4%. In the study done by Bhavanarushi sreekanth *et al.*²⁰ · Diabetes Mellitus (n=35) was a common co morbid condition in this study population.In the present study, among the 25 extrapulmonary samples, MTB was detected among 20 samples and not detected among the five samples. No rifampicin resistance was noted among CBNAAT positive extrapulmonary samples. In the present study, the Sensitivity of CBNAAT in diagnosing extrapulmonary TB was 93.33, and specificity was 40%, Positive predictive value is 70%, Negative predictive value is 80%. In the study done by Sunil Kumar *et al.*,²¹ CBNAAT positives are 31(18.6%) among 166 extrapulmonary specimens. 01 are rifampicin resistant. The sensitivity and specificity of CBNAAT in extrapulmonary TB are 86.9% and 99.7%, respectively. In the study done by Sunil Kumar Komanapalli.,²² the most common presentations are Lymph nodes and cervical swellings. Among 298 respiratory samples, 105/114 (92.1%) sputum samples, 148/169 (87.6%) bronchoalveolar lavage specimens, and 8/15 (53.3%) gastric aspirates were Xpert-positive. Among 128 non-respiratory

MTB samples, 50/56 (89.3%) lymph node specimens, 18/23 (78.3%) bone samples, 12/16 (75.0%) pus, 9/12 (75.0%) cavitory fluids, 6/7 (85.7%) urine samples were Xpert-positive.²³

CONCLUSION

The performance of CBNAAT observed in this study aligns with findings from other researchers, who have also established its efficacy in diagnosing a significant proportion of cases. Additionally, the increased case detection facilitated by Xpert suggests it should be employed as the initial diagnostic test to reduce workload. The high sensitivity of the CBNAAT detected in this study ensures that the disease can be ruled out with a high degree of confidence.

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CONFLICT OF INTEREST: None

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