

## Original Research Article

# Effectiveness of CBNAAT in the diagnosis of extrapulmonary tuberculosis

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### ABSTRACT

**Background:** Tuberculosis is still a major health problem worldwide. It is estimated that about one-third of the world's population is infected with mycobacterium tuberculosis. While pulmonary tuberculosis is most common presentation; extrapulmonary tuberculosis is also an important clinical problem. CBNAAT is cartridge based nucleic acid amplification test with a well-established role in the diagnosis of pulmonary tuberculosis (PTB). We determined the effectiveness of CBNAAT in the diagnosis of extrapulmonary tuberculosis (EPTB) cases in comparison to AFB smear.

**Methods:** Retrospective study of suspected extrapulmonary tuberculosis patients in a tertiary care centre of the study area was conducted. The study period was from January 2017 to July 2018. Data of 166 consecutive suspected extrapulmonary tuberculosis patients was retrieved. Effectiveness of CBNAAT in the diagnosis of EPTB was assessed as compared to that of AFB smear.

**Results:** Samples collected from 166 suspected EPTB patients were subjected to AFB smear and CBNAAT. Samples collected included lymph node, pus, pleural fluid, tissue, CSF, gastric lavage, cystic fluid, peritoneal fluid, ascitic fluid, colonic fluid, synovial fluid, urine. In AFB smear results, 17 cases were positive for TB bacilli and 149 were negative for the same. In CBNAAT results, 25 cases were positive for TB bacilli and 141 cases were negative. In comparative analysis, 8 cases were AFB smear negative but CBNAAT positive.

**Conclusions:** CBNAAT is a useful tool in the diagnosis of EPTB cases because of its simplicity and rapid turnaround time. CBNAAT is more effective as compared to AFB smear in the diagnosis of EPTB cases.

**Keywords:** CBNAAT, Extrapulmonary tuberculosis, Pleural effusion, Tuberculosis

### INTRODUCTION

Tuberculosis is still a major health problem worldwide. It is estimated that about one-third of the world's population is infected with mycobacterium tuberculosis.

While pulmonary tuberculosis is most common presentation; extrapulmonary tuberculosis is also an important clinical problem. Worldwide, extrapulmonary tuberculosis (EPTB) accounts for ~25% of all TB cases.<sup>1</sup>

Tuberculosis is one of the dreaded diseases which accounts for 9.6 million cases globally as per the WHO Global TB Report 2015. Among these cases India contributes to 2.2 million incidence cases. It has not only high morbidity but also the mortality is high with 0.22 million deaths in India in 2015.<sup>2</sup> The prevalence of tuberculosis was estimated to be 10.5 million. In India alone 1.8 million new cases of TB arise annually.<sup>3,4</sup> It is estimated that about 40% of the Indian population is infected with TB bacteria.

To reduce the incidence and prevalence, India introduced National Tuberculosis Control Programme (NTP) in 1962, followed by Revised National Tuberculosis Control Programme (RNTCP) 1993-1996 and with Directly Observed Treatment Short-Course chemotherapy (DOTS) strategy in 1997. WHO released STOP TB STRATEGY in 2006. India adopted it in 2007. There are continuous efforts made to decrease the incidence and prevalence of tuberculosis, continuous change in the strategies under RNTCP are made. Further there was adoption of Goals of NSP with a vision of TB Free India in 12<sup>th</sup> five-year plan in (2012-17). The current adoption of END TB STRATEGY has a vision of WORLD FREE OF TB.<sup>5</sup>

TB affecting other sites-known as extra-pulmonary TB, is rarely smear-positive; it is generally accepted that the contagious potential of this form is negligible, and it has, therefore, never been a priority in the campaigns undertaken by national TB control programs.<sup>6,7</sup> Lymph nodes are the most common site of involvement followed by pleural effusion and virtually every site of the body can be affected.<sup>8</sup>

Extrapulmonary tuberculosis forms a significant proportion of the total TB cases and is a major health problem in both developing and developed countries. Diagnosing EPTB is challenging due to its varied clinical presentations and paucibacillary nature of the disease.<sup>9</sup> AFB smear hasn't proved to be much useful in diagnosing EPTB. CBNAAT is cartridge-based nucleic acid amplification test which detects the presence of TB bacilli and tests for resistance to Rifampicin also. CBNAAT is likely to revolutionize the diagnosis and treatment of EPTB, as it is a very cost-effective and rapid test. Hence, we performed a retrospective analysis to assess the effectiveness of CBNAAT for diagnosing EPTB as compared to that of AFB smear. Our study aimed to define the role of CBNAAT in clinical decision-making in suspected EPTB cases.

In this study, all patients suspected to have EPTB are evaluated by means of AFB smear and CBNAAT. Comparative analysis of the results of AFB smear and CBNAAT is done.

## METHODS

The study is a retrospective descriptive study conducted at MGM Hospital Aurangabad after obtaining permission of the institutional ethical committee. The study used data from January 2017 to July 2018.

All the patients who were suspected to have extrapulmonary tuberculosis and are above 18 years of age were included in the study. Patients suspected to have or those who already have pulmonary tuberculosis and are below 18 years of age were excluded from the study.

The study population consisted of all the suspected extrapulmonary tuberculosis patients visiting the OPD of

MGM Hospital Aurangabad and who were willing for AFB smear and CBNAAT investigations.

To fulfil the objectives of research, samples from all the patients suspected to have extrapulmonary tuberculosis were collected and subjected to AFB smear and CBNAAT. CBNAAT is cartridge-based nucleic acid amplification test which detects the presence of TB bacilli and tests for resistance to Rifampicin also. It is simple, rapid, cost effective and doesn't require technical expertise. It can diagnose TB within 2 hours and gives accurate results due to use of disposable closed cartridges preventing cross contamination. In settings where resources are limited for facilities like culture DST, CBNAAT is extremely useful, simple and reliable test.

Samples collected included lymph node, pus, pleural fluid, tissue, CSF, gastric lavage, cystic fluid, peritoneal fluid, ascitic fluid, colonic fluid, synovial fluid, urine. The results of both the AFB smear and CBNAAT of the samples of all the suspected extrapulmonary tuberculosis patients were compared in the study. Reports were retrieved from MGM Hospital Aurangabad. This laboratory is accredited by RNTCP for AFB smear and CBNAAT testing of samples taken both pulmonary and extrapulmonary tuberculosis patients.

It was a record-based study so consent of the patients for inclusion criteria was not taken into consideration. Confidentiality of the patients was maintained.

## RESULTS

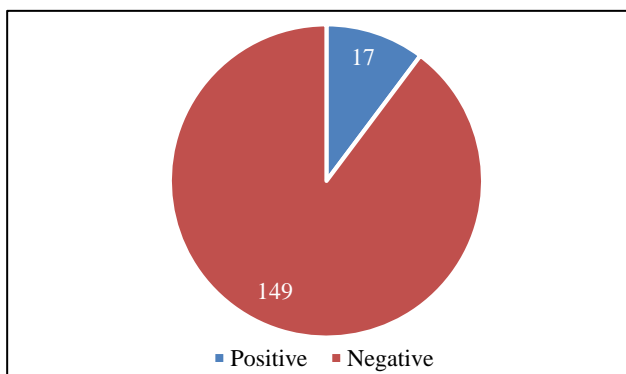
Total of 166 patients were included in the study. All the patients who were suspected to have extrapulmonary tuberculosis and are above 18 years of age were included in the study. Patients suspected to have or those who already have pulmonary tuberculosis and are below 18 years of age were excluded from the study. Samples collected included lymph node, pus, pleural fluid, tissue, CSF, gastric lavage, cystic fluid, peritoneal fluid, ascitic fluid, colonic fluid, synovial fluid, urine. Samples from all the patients suspected to have extrapulmonary tuberculosis were collected and subjected to AFB smear and CBNAAT.

Among 166 suspected extrapulmonary tuberculosis cases, 17 samples were AFB smear positive and 149 were negative for AFB smear. Figure 1 shows the distribution of patients according to diagnosis based on AFB smear.

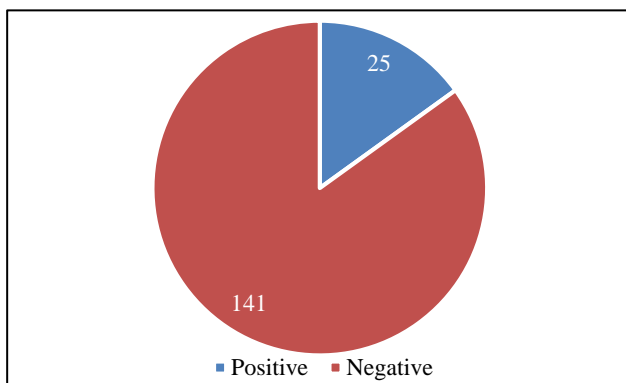
In CBNAAT results, 25 out of 166 suspected extrapulmonary tuberculosis cases were positive for TB bacilli and 141 were negative for the same. Figure 2 shows the distribution of patients according to diagnosis based on CBNAAT.

When the results of the 166 samples collected from suspected extrapulmonary tuberculosis patients subjected to AFB smear and CBNAAT were compared, 8 cases

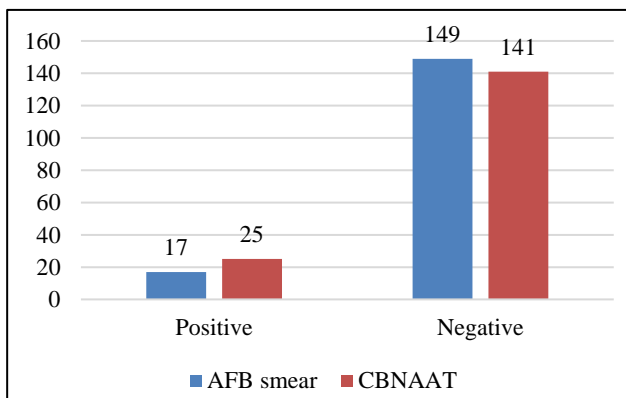
turned out to be negative for TB bacilli in AFB smear whereas the same samples positive for TB bacilli in CBNAAT i.e. 8 cases were falsely reported as negative for TB bacilli in AFB smear. As the suspected extrapulmonary tuberculosis samples included many samples other than pleural fluid and lymph node, the overall samples turning out to be positive for TB bacilli in both AFB smear and CBNAAT is less. It would have been higher if only pleural fluid and lymph node samples were included in the samples used for the study.



**Figure 1: Distribution of patients according to diagnosis based on AFB smear.**



**Figure 2: Distribution of patients according to diagnosis based on CBNAAT.**



**Figure 3: Distribution of patients according to diagnosis. A comparison between AFB smear and CBNAAT results.**

Figure 3 shows the distribution of patients according to diagnosis, a comparison between AFB smear and CBNAAT results. The above comparison of the results of AFB smear and CBNAAT examination of various samples of suspected extrapulmonary tuberculosis patients proves that CBNAAT is much better alternative to AFB smear in the diagnosis of extrapulmonary tuberculosis.

**DISCUSSION**

EPTB contributes to a significant burden of mortality and morbidity due to its complex and subclinical presentations, leading to a delay in diagnosis. The conventional methods such as culture DST are time consuming and require trained laboratory personnel.

CBNAAT is a semi-quantitative nested nucleic acid amplification test based on molecular detection of mutated gene. It is simple, rapid, cost effective and doesn't require technical expertise. It can be carried out in automated manner including bacterial lysis, nucleic acid extraction, and amplification and amplicon detection. It can diagnose TB within 2hours and gives accurate results due to use of disposable closed cartridges preventing cross contamination.<sup>10</sup> In settings where resources are limited for facilities like culture DST, CBNAAT is extremely useful, simple and reliable test. It also has a significant role to play in the diagnosis of extrapulmonary tuberculosis. Its potential in EPTB detection has been underutilized due to lack of awareness regarding the same. Hence, we conducted the study to determine effectiveness of this rapid and logistically simplified test in the diagnosis of EPTB.

The prevalence of EPTB is showing a rising trend. The heterogenous clinical presentations, paucibacillary nature and difficulty in obtaining specimens (often requiring invasive procedures) make the diagnosis of EPTB, a challenging task and hence the requirement for a rapid, simplified and cost effective diagnostic tool arises.<sup>11</sup> This is where CBNAAT plays an important role leading to early initiation of appropriate therapy, improved treatment outcomes, minimizing morbidity and mortality.

According to a metaanalysis findings of Denkinger et al, sensitivity among pleural fluid was 46% and sensitivity among lymph node specimens was 83%.<sup>12</sup> Another meta-analysis finding of Penz et al, suggested sensitivity among pleural fluid was 37% and lymph node specimen was 87%.<sup>13</sup> A recently published study by Sharma et al, regarding the utility of GeneXpert in diagnosing EPTB has shown an overall sensitivity of 71% and PPV ranging from 98 to 100%.<sup>14</sup> But direct comparisons could not be drawn with our study. In this study, we found that the results of CBNAAT were better when compared to AFB smear for EPTB samples. Although the overall positive cases of EPTB diagnosed through these tests were less as the suspected extrapulmonary tuberculosis samples included many

samples other than pleural fluid and lymph node, it is however consistent with other studies of EPTB in the literature.<sup>12-14</sup> It would have been higher if only pleural fluid and lymph node samples were included in the samples used for the study.

This findings suggest that CBNAAT plays a major and important role in the diagnosis of EPTB, particularly in places with high burden and limited availability of resources. CBNAAT could be the best aid for physicians in diagnosing EPTB if more awareness is brought among them regarding its utility. Our study highlighted that CBNAAT can be a faster alternative to time taking methods like culture DST and at the same time a more efficient alternative to other rapid methods like AFB smear examination in the diagnosis of EPTB. With our study, we conclude that CBNAAT is more effective as compared to AFB smear in the diagnosis of EPTB cases and CBNAAT should be routinely utilized for rapid diagnosis of EPTB along with other conventional methods like AFB smear examination and culture DST for better overall results in the diagnosis of EPTB.

## CONCLUSION

CBNAAT is a useful tool in the diagnosis of EPTB cases because of its simplicity and rapid turnaround time. CBNAAT is more effective as compared to AFB smear in the diagnosis of EPTB cases and CBNAAT should be routinely utilized for rapid diagnosis of EPTB along with other conventional methods like AFB smear examination and culture DST for better overall results in the diagnosis of EPTB. As the suspected extrapulmonary tuberculosis samples included many samples other than pleural fluid and lymph node, the overall samples turning out to be positive for TB bacilli in both AFB smear and CBNAAT is less. It would have been higher if only pleural fluid and lymph node samples were included in the samples used for the study.

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