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"Study of CBNAAT in diagnosis of EPTB."

Medicine

KEYWORDS: Extrapulmonary Tuberculosis, Cartridge based nucleic acid amplification test, R Resistance.

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ABSTRACT

Background:
Extrapulmonary Tuberculosis accounts for about15 to 20% of all cases of Tuberculosis in India. It is difficult to diagnose EPTB due to varied presentations and difficulty in obtaining adequate sample for investigations. Cartridge based Nucleic Acid Amplification Test (CBNAAT) also known as GeneXpert is a major advance in diagnosis of Tuberculosis (TB) in past decade.

Aims and Objectives:
To diagnose EPTB using CBNAAT.
To detect R Resistance in EPTB using CBNAAT.

Materials and methods: 212 samples from different extrapulmonary sites were sent for CBNAAT for diagnosis of EPTB and R Resistance.

Results:
51 samples were diagnosed to be EPTB maximum being lymph node TB and R Resistance was detected in five. Scrotal TB which is a rare condition was also diagnosed and was found to be R Resistant.

Conclusion: CBNAAT is a useful investigation in diagnosis of EPTB. Also R Resistant EPTB can be rapidly diagnosed with CBNAAT.

Introduction:
Extrapulmonary Tuberculosis (EPTB) accounts for about15 to 20% of all cases of Tuberculosis in India.1The percentage may be higher in children and in HIV infected individuals.2 Diagnosing EPTB is challenging as it requires a clinician to obtain adequate specimen involving the concerned organ for investigations to confirm diagnosis. Also paucibacillary nature of the disease poses difficulty in diagnosis. Cartridge based Nucleic Acid Amplification Test (CBNAAT) also known as GeneXpert is a major advance in diagnosis of Tuberculosis (TB) in past decades. It allows detection of Mycobacteria Tuberculosis bacilli as well as Rifampicin resistance (R Resistance) thus making it an important and attractive tool in diagnosis of EPTB.1 The aim of this study was to diagnose EPTB using CBNAATand to detect R Resistance in EPTB using CBNAAT.

Methods and materials:
This study was conducted in Dept. of Pulmonary medicine, Goa Medical College Hospital which is a tertiary care hospital. This was a retrospective analytical study conducted from April 2016 to January 2017.212 samples from extrapulmonary sites were sent for CBNAAT to Intermediate Reference Laboratory of Goa Medical College Hospital. The results obtained were analysed using numbers and proportions.

Results:
Total number of samples examined from various extrapulmonary sites were 212.Out of these 59 were from lymph nodes, 82 of pleural fluid, 12 from urogen ital system, 12 from abdomen ,29 of cerebrospinal fluid (CSF),8 from skin, 2 from breast and 8 from skeletal system.

Table no. 1 shows number of samples examined .

Type	Lymph Node	Pleural Fluid.	Uro-genital	Abdominal.	CSF	Skin	Breast	Bone
No.	59	82	12	12	29	8	2	8

Out of 212 samples thus examined,51 were positive for Mycobacteria Tuberculosis (MTB) by CBNAAT ie average of 24%.Out of 51positive by CBNAAT, 38 were of lymph node TB ie 64%, 6 of TB pleural effusion ie 7.3%, 2 of urogenital TB ie 16.6%,2 of abdominal TB ie16.6%,1 of CNS TB ie 3.4%,2 of TB involving the skeletal system ie 25%.

Table no.2 shows number and percentage of EPTB cases diagnosed by CBNAAT.

Total No	Lymph node	Pl. Fluid	Urog enital	Abd.	CSF (CNS)	Skin	Breast	Bone
Samples	59	82	12	12	29	8	2	8
EPTB cases	38	6	2	2	1	0	0	2
% ofEPTB cases	64	7.3	16.6	16.6	3.4	0	0	25.

Out of 51cases diagnosed as EPTB, 5 were R Resistant detected by CBNAAT. Among these 5 R Resistant cases,3 were of lymph node TB, 1 was of scrotal TB and 1 was of abdominal TB.

Table no. 3 shows no. of R Resistant cases diagnosed by CBNAAT.

Total no. of R Resistant EPTB cases	Lymph node	Urogenital	Abdominal
5	3	1	1

Discussion:
TB is a major public health problem in India and worldwide. EPTB constitutes 15 to 20% of all cases of TB. Diagnosis of EPTB poses challenge as symptoms vary depending on the organ involved. Clinicians have low level of suspicion because of varied presentations. Also many a times it is difficult to obtain adequate tissue sample for investigation to confirm the diagnosis.[3] All these factors lead to a delay in diagnosis. Accurate and rapid laboratory investigations have therefore gained importance. CBNAAT is one such useful and rapid laboratory investigation for diagnosis of TB and detection of R Resistance.

Various studies have shown sensitivity of CBNAAT for EPTB ranging from 25 to 96.6%. Lower sensitivity has been reported for CSF, pleural, pericardial, peritoneal and synovial samples.[4]

An overall sensitivity of 83.1% and a pooled specificity of 98.7% for diagnosis of EPTB was recently published in a meta-analysis by Denkinger et al.[2]

According to INDEX TB guidelines there is strong evidence for use of CBNAAT in diagnosis of lymph node TB.5In our study we found MTB detected by CBNAAT in 38 lymph node samples out of 59 investigated

ie 64%.27 samples of lymph node fine needle aspirate(FNAC) and 11 samples of lymph node biopsy were positive by CBNAAT. So the FNAC samples were found to be adequate for CBNAAT in lymph node TB. Three cases of lymph node TB were diagnosed as R resistant by CBNAAT.

There is a strong recommendation for not using CBNAAT on pleural fluid according to INDEX TB guidelines.5 Same observation was seen in our study wherein only six cases of TB pleural effusion were diagnosed by CBNAAT out of 82 cases studied ie only 7.3%.Low sensitivity of CBNAAT in pleural fluid samples is due to likely low bacillary load in pleural fluid.6 Also presence of PCR inhibitors in pleural fluid may be responsible for negative CBNAAT result.2 Sehgal et al in their systematic review had similar finding of low sensitivity of CBNAAT in the diagnosis of TB pleural effusion.[7]

According to INDEX TB guidelines, use of CBNAAT in TB Meningitis may be as an adjunctive test as it may be false negative and then one has to rely on clinical judgement and other tests to confirm diagnosis.5 In our study out of 29 samples of CSF studied only one was positive by CBNAAT. Therefore we can conclude that some of these samples might have been false negative. However we do not have clinical background of these patients as they were mainly treated in general medicine ward of the hospital.

Till date there is no study showing high level of evidence on the efficiency of CBNAAT in diagnosing urogenital TB.8Also according to INDEX TB guidelines, further research is needed to determine the efficiency of CBNAAT in diagnosing urogenital TB.5 However in our study, out of 12 suspected cases of urogenital TB, CBNAAT was positive in two cases. Out of these two cases one was TB of scrotum and second TB of prostate. TB of scrotum is rare condition and often misdiagnosed due to clinician's unawareness.9 CBNAAT helped in not only diagnosing such a rare condition but also in detecting R Resistance in this sample.

Study data are lacking regarding sensitivity and specificity of CBNAAT in diagnosis of bone and joint TB, urogenital TB and abdominal TB.5 Only two cases of abdominal TB were diagnosed by CBNAAT in our study.In both, omental biopsy was sent for CBNAAT which was proved to be tuberculous with one showing sensitivity to Rifampicin and second showing resistance. Two cases of skeletal TB were diagnosed wherein synovial fluid aspirate was positive for TB by CBNAAT both being sensitive to Rifampicin. None of the breast and skin tissue samples were diagnosed as TB by CBNAAT.

CBNAAT thus proved to be a useful investigation in diagnosis of EPTB mainly lymph node TB in our study. Also R resistance was detected rapidly in five EPTB cases out of which scrotal TB was a rare presentation. So far there was not much information available about drug resistance in EPTB precisely because of same reasons ie difficulty in obtaining adequate samples for investigation and limited availability of drug sensitivity testing facility.10 However with recent advances in diagnostic investigations of TB one of which is CBNAAT, the diagnosis of EPTB as well as R-resistant EPTB is going to be easier and faster. However clinicians will have to keep in mind EPTB while investigating patients with clinical presentation suspicious of EPTB and make use of this very important and valuable tool as it is made available through Revised National TB Control Programme (RNTCP) all over the country. Also according to the RNTCP guidelines, one indication of use of CBNAAT is for diagnosis of EPTB. This study justifies its use in some types of EPTB especially lymph node TB whereas recommendation of not using it in pleural effusion as per INDEX TB guidelines is also justified in this study. Due to less number of samples examined from other sites we are not able to give any definite conclusions regarding other types of EPTB. However CBNAAT is useful in diagnosing rare forms of EPTB like scrotal TB and even R Resistance in scrotal TB making it an important and attractive tool in diagnosis of EPTB and R Resistance in EPTB.

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