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TRUENAT: AN INDIGENOUS TOOL FOR DIAGNOSIS OF PULMONARY AND EXTRA-PULMONARY TUBERCULOSIS

Pulmonary Medicine

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ABSTRACT

Early and accurate diagnosis followed by rapid treatment is very important for breaking the cycle of disease transmission in tuberculosis. TrueNAT assays are newer and indigenous molecular diagnostic test for the diagnosis of tuberculosis and detection of rifampicin resistance. A prospective single centre based study was conducted among 1083 presumptive TB patients in a tertiary care centre during the year 2020 to 2021. Liquid culture was used as a reference standard. Out of the different specimens tested, 419 (38.6%) were positive with TrueNAT MTB. The overall sensitivity, specificity, NPV, PPV of TrueNAT with culture were 78.01%, 96.8%, 82.98% and 95.7%, respectively. Whereas sensitivity and specificity for PTB and EPTB specimens were 80.84% and 98%, 67.85% and 95.63%, respectively.Our study showed that the TrueNAT assay allows rapid detection of TB and can be utilized in resource limited settings to provide quick and accurate diagnosis. TrueNAT is more cost-effective and feasible option for peripheral healthcare facilities due to portability and requirement of less sophisticated infrastructure.

KEYWORDS

Mycobacterium, TrueNAT, Tuberculosis.

INTRODUCTION

Tuberculosis, caused by Mycobacterium tuberculosis (Mtb), is the leading cause of death by an infectious disease.[1] It remains a serious public health problem in India, accounting for nearly one-fourth of global burden.[2] Globally, each year an estimated 4.1 million TB cases go undiagnosed leading to prolonged transmission.[3]

Conventional diagnostic methods like smear microscopy and solid/ liquid culture have many limitations. Nucleic Acid Amplification Test (NAAT) is faster than culture and known to have good sensitivity and specificity. GeneXpert detects mycobacterium tuberculosis and also drug resistance to rifampicin. But due to high cost and need for uninterrupted power supply, its use is limited to district and sub-district levels in India.[4]

Bigtec laboratories, India developed an indigenous, portable version of CBNAAT, known as TrueNAT, a novel, cost effective and rapid diagnostic method. It is a point of care, battery operated and chip based RTPCR for detection of TB and rifampicin resistance in <2hours and can be easily used even in rural areas.[5] TrueNAT MTB amplifies a portion of nrdB gene and has limit of detection of about 100CFU/ml sputum sample.[6] This study is aimed to evaluate the diagnostic accuracy of TrueNAT assays in both pulmonary (PTB) and extra-pulmonary tuberculosis (EPTB).

METHODS

This is a hospital based, prospective study carried out on 1083 patients in a tertiary care centre, Jaipur during the year 2020-21. Presumptive cases of PTB and EPTB who gave informed consent and willing to provide specimen at enrolment were included and patients who took ATT within last 60days and microbiological evidence of NTM were excluded from the study.

After recruitment, patients were interviewed for demographic and clinical history. Specimens collected on the same visit depending on the site of involvement. In suspected PTB, specimens like sputum, gastric lavage, or broncho-alveolar lavage (BAL) and in suspected EPTB, specimens from lymph node tissue/ pus, pleural fluid/ tissue, cerebrospinal fluid (CSF), ascitic fluid, synovial fluid, urine, endometrial tissue/ aspirate or pericardial fluid were collected in a sterile container, under aseptic conditions depending on the site of infection.

TrueNAT MTB assay involve two steps: DNA extraction and detection of Mtb. 2-5 ml of the sample collected was mixed with liquefaction buffer and then lysis buffer. It was transferred to cartridge and loaded in the DNA extraction device (20mins) for automated extraction and purification. 6µL of DNA elute is put on TrueNAT chip and loaded into PCR analyser. After 35mins, result screen will indicate as either MTB-detected or not. For MTB positive results, another aliquot of the same DNA extracted is transferred to the Truenat MTB-RIF-Dx chip (60mins) for detection of rifampicin resistance.

RESULTS

Majority of the study subjects were males (63.5%) and most belonged to the age groups 21-40 years (48.3%). From 433 EPTB samples collected, most common were lymph node (43.6%), pleural (25.8%) and CSF (13.4%). Out of 433 EPTB samples, around three fourth (79.2%) were TrueNAT negative and of 90 TrueNAT positive samples, 72 were rifampicin sensitive and 18 were rifampicin resistant.

Among 650 PTB samples, majority were sputum samples (77%). Half (50.6%) of PTB samples were TrueNAT positive. All sputum smear positive samples were detected positive by TrueNAT also. Out of 329 positive samples, 86% were rifampicin sensitive and remaining (14%) were rifampicin resistant. TrueNAT and liquid culture results of various specimens analysed are summarized in table-1. The efficacy of TrueNAT in diagnosing TB was assessed by comparing results with liquid culture as gold standard. The sensitivity, specificity, positive and negative predictive value of TrueNAT are summarized in table-2

Table-1: Distribution of specimen types and its TrueNAT and liquid culture results

Specimen	Total no.	TrueNAT negative	TrueNAT positive			Liquid culture positive
			Rif sensitive	Rif resistant	Total	
EPTB						
1.Lymphnode tissue/ pus	189 (43.6%)	149	25	15	40	59
2.Pleural Fluid/ tissue	112 (25.8%)	77	34	1	35	38
3.Cerebro-Spinal Fluid	58 (13.4%)	49	7	2	9	13
4.Ascitic Fluid	29 (6.7%)	27	2	0	2	1
5.Endometrial aspirate/tissue	17 (3.9%)	13	4	0	4	1
6.Urine	16 (3.7%)	16	0	0	0	0
7.Pericardial Fluid	10 (2.4%)	10	0	0	0	0
8.Synovial fluid	2 (0.5%)	2	0	0	0	0

Total EPTB specimen	433	343	72	18	90	112
PTB						
1.Sputum Smear Positive	250 (38.5%)	0	217	33	250	250
2.Sputum Smear Negative	250 (38.5%)	205	38	7	45	102
3.Broncho-Alveolar Lavage	100 (15.3%)	78	18	4	22	33
4.Gastric Lavage	50 (7.7%)	38	12	0	12	17
Total PTB specimen	650	321	285	44	329	402

Table-2: Comparison of TrueNAT with liquid culture

	PTB samples		**EPTB samples**		**Total**	
	TrueNAT positive	**TrueNAT negative**	**TrueNAT positive**	**TrueNAT negative**	**TrueNAT positive**	**TrueNAT negative**
Liquid culture positive	325	77	76	36	401	113
Liquid culture negative	4	244	14	307	18	551
Sensitivity	80.84%		67.85%		78.01%	
Specificity	98%		95.63%		96.8%	
PPV	98.7%		84.44%		95.7%	
NPV	76%		89.5%		82.98%	

DISCUSSION

This prospective study shows that TrueNAT assays have an overall good performance in rapid diagnosis of TB. In this study, we compared the performance of the TrueNAT assay with the MGIT960 liquid culture for detecting TB in pulmonary and extra-pulmonary clinical specimens. This is one of the very few studies including both PTB and EPTB together in TrueNAT analysis.[7]

In the present study, 1083 patients were included (650 PTB and 433 EPTB). Tuberculosis was seen more in males (63.5%) in the present study which are in par with the global reports on TB by WHO.[1] Similar to other studies[8,9] among EPTB specimen, lymph node TB (43.6%) was the predominant followed by pleural TB (25.8%).

Our study findings showed that on comparison with liquid culture, TrueNAT has higher sensitivity (80.84%) for detecting PTB than EPTB clinical specimens (67.85%), with an overall sensitivity of 78.01%. Study by Tripathi et al[10], reported a sensitivity of 84.1% for TrueNat in pulmonary specimen. Reena et al study[11] showed in extra-pulmonary TB, TrueNAT had a sensitivity of 100%, which is very high compared to the present study.

TrueNAT has higher specificity in both pulmonary and EPTB specimens (98%, 95.63% respectively). A prospective study by Penn-Nicholson et al[12] showed the specificity of TrueNAT MTB as 97.2% in pulmonary TB. Similarly, a study[11] on EPTB showed TrueNAT specificity of 95.1%.

It is evident from the study results that TrueNAT is more sensitive to Mtb in pulmonary specimens than EPTB specimens. This might be due to use of culture as standard for comparison. Sensitivity can be increased by including more than one sample, which is practically difficult in EPTB cases.

CONCLUSION

Our study showed that the TrueNAT assays are good diagnostic tools for MTB detection. TrueNAT satisfy most of the requirements in WHO's target product profile (TPP) of smear replacement test like battery powered operation and less than 2hours to result. TrueNAT, being cost effective and portable, if deployed at peripheral centres can improve the overall case detection and early diagnosis in high burden countries like India. Hence, it has the potential to be used as a point of care TB diagnostic tool.

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