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ASSESSING CARTRIDGE BASED NUCLEIC ACID AMPLIFICATION TEST (CBNAAT) IN DIAGNOSIS OF EXTRA PULMONARY TUBERCULOSIS.

Pulmonary Medicine

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ABSTRACT

BACKGROUND: Diagnosis of extra-pulmonary TB is still more challenging as the numbers of TB bacilli present at the tissue site of disease are less in number and it's not easy to obtain clinical specimens from deep seated organs. Thus now Cartridge based nucleic acid amplification (CBNAAT) test is recommended by WHO for diagnosis of extra-pulmonary TB. Present study was done with the objective to identifying the roles of CBNAAT in the diagnosis of extra-pulmonary tuberculosis. **MATERIALS & METHODS:** The present hospital based cross sectional study was done in Dr. Panjabrao Deshmukh Memorial Medical College & Hospital on 561 extra pulmonary presumptive TB cases during period Jan 2020-June 2020. **RESULTS:** Out of the total 561 samples tested, 65 (11.59%) were CBNAAT positive, of which 60(92%) were rifampicin sensitive and 5(8%) rifampicin resistant for mycobacterium tuberculosis. **CONCLUSION:** The study concludes that CBNAAT is an effective and robust method which provides early diagnosis of extra-pulmonary tuberculosis over other diagnosis methods.

KEYWORDS

Extra pulmonary Tuberculosis, CBNAAT, Rifampicin resistant.

INTRODUCTION:

Globally, an estimated 10.0 million people fell ill with TB in 2019; India has the highest number of Tuberculosis (TB) cases in the world (26%), with over two million TB cases every year. Annually, one fourth of the global incident TB cases occur in India [(1)]. Early and accurate diagnosis is the first critical step in controlling TB. The control of TB is hampered by diagnostic methods with sub-optimal sensitivity, particularly for the detection of drug resistant forms and in patients with human immunodeficiency virus (HIV) infection [(2)]. Early detection is essential to interrupt transmission and reduce the death rate. Although pulmonary TB is the most common presentation, extra pulmonary TB is also an important clinical condition.

Worldwide, EPTB accounts for approximately 25% of all TB cases and even higher percentages in HIV-infected individuals and children [(3)]. In India extra-pulmonary tuberculosis constitute 10-15% of total TB cases which involves pleural, lymph node gastrointestinal tract and other organs. [(4)]

The diagnosis of extrapulmonary tuberculosis is challenging because of the paucibacillary nature ,lack of specific signs and symptoms and often negative acid fast bacilli smear of biological specimens. Besides the technical expertise's and the bio safety concerns ,Culture on LJ (LOWENSTEIN JENSEN) medium is the gold standard which takes 2-8 weeks to produce growth causing delay in starting the treatment[(5)].

To overcome this problem WHO strongly recommends widespread use of CBNAAT for diagnosis of extra-pulmonary tuberculosis. The CBNAAT assay consist of a closed system that is based on real time polymerase chain reaction (PCR), which requires minimal technical expertise in diagnosis of tuberculosis and rifampicin resistance and the results are obtained within 2hours [(6)]. Therefore CBNAAT can serve as a promising tool to aid in achievement of global objective of early detection of TB and can improve TB care. The evidences for its use in investigation of EPTB remains comparatively weak, many more studies are needed for assessing its role in variety of clinical sample other than sputum.

MATERIALS & METHODS:

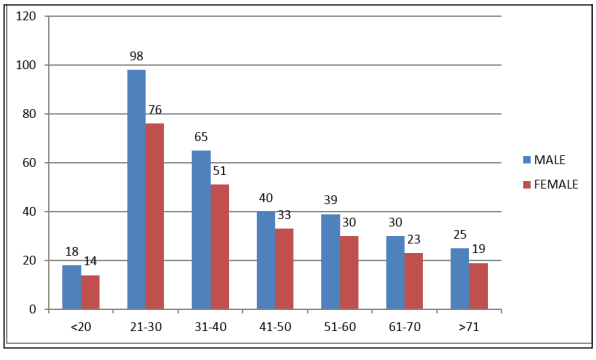
The present hospital based cross sectional observation study was done in Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, tertiary care teaching hospital. The study was carried on total 561 patients, to Assess Cartridge Based Nucleic Acid Amplification Test (CBNAAT) in Diagnosis of Extra Pulmonary Tuberculosis. The study was conducted between Periods Jan 2020-June 2020.

In the present study, 561 patients suspected of having EPTB attending OPD & IPD of hospital during above mentioned study period were selected on the basis of inclusion and exclusion criteria and were subjected to further investigation by using CBNAAT. Patients above 18 years of age with clinically suspected to have EPTB were included in the study.

Patients already having pulmonary tuberculosis, Patients with a history of lung malignancy or fungal infection & Patients with previous history of extra-pulmonary or pulmonary tuberculosis or on TB treatment were excluded from study.

TB detection was done using CBNAAT. All specimens were processed according to Genexpert system operating manual given by central TB Division, government of India[(6)].

RESULTS:



Bar diag.1: Age wise distribution of study subjects

In this study it was found that among 561 study subjects, majority were young adults i.e. from age group 21-30 years (31%), followed by 31-40 years (20%). Very few were from age group < 20 years (5.7%) (Bar diag.1)

Table no. 1: Distribution of EP samples based on gender

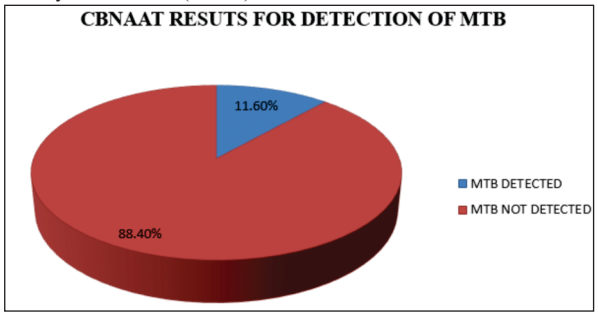
GENDER	FREQUENCY	PERCENTAGE
MALE	315	56.15
FEMALE	246	43.85
TOTAL	**561**	**100**

A total of 561 specimens were collected during the study period. Amongst the samples received 315 (56%) were males and 246 (43.8%) were females.

Table no. 2: Extra-pulmonary samples distribution & their sensitivity to Rifampicin.

TYPE OF SAMPLES	NOS OF SAMPLES	CBNAAT POSITIVE FORMTB (%)	RIF-SENSITIVE	RIF-RESISTANCE
FNAC	143	21(14.68)	19	2
PLEURAL FLUID	169	24(14.20)	23	1
CSF	41	4(9.75)	3	1
ASCITIC FLUID	88	3(3.40)	3	0
PUS	97	11(11.34)	10	1
PERINEAL ABSCESS	10	0(0)	0	0
SYNOVIAL FLUID	2	1(50)	1	0
BREAST TISSUE	8	1(12.5)	1	0
FOREARM SWELLING	1	0(0)	0	0
LEG SWELLING	2	0(0)	0	0
TOTAL	**561**	**65 (11.60)**	**60 (92)**	**5(8)**

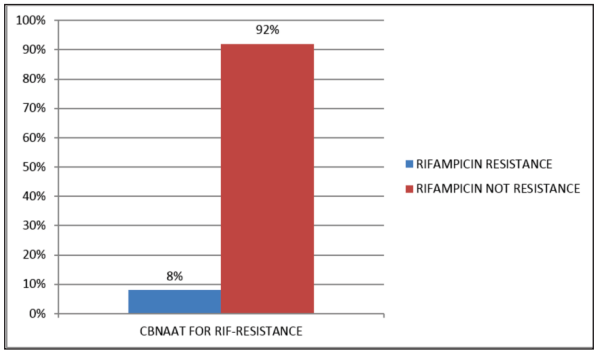
Out of the 561 samples that were examined the majority were pleural fluid 169 (30.1%) followed by FNAC143 (25.4%), Pus 97(17.3%) and the rest of extrapulmonary samples Ascitic Fluid 88(15.6%), CSF 41(7.3%), Perianal Abscess 10(1.78), Breast Tissue Aspirate 8(1.42%) and Synovial Fluid 2(0.35%) etc.



Pie Diag. 1: Distribution according to CBNAAT results for MTB detection

In this study it was found that, out of 561 study samples, 65 (11.60%) study samples were positive for Tuberculosis (Pie Diag. 1).

Out of this 65 MTB detected samples, Rifampicin resistance was found in 5 (8%) study samples (Bar diag.2)



Bar diag.2: Distribution of study samples according to CBNAAT results for Rifampicine resistance.

DISCUSSION:

Tuberculosis is a major cause of morbidity and mortality in our country. Early diagnosis of tuberculosis along with accurate detection of drug resistance is critical for prevention of tuberculosis transmission and development of resistant cases. Diagnosis of extra pulmonary TB (EPTB) remains especially challenging since the number of Mycobacterium tuberculosis (MTB) bacilli present in tissues at sites of disease is often low and clinical specimens from deep-seated organs may be difficult to obtain[7].

Nucleic acid amplification tests for rapid TB diagnosis are increasingly being used. In resource limited settings the adoption of newer techniques remains challenging due to involvement of start up and training cost. However CBNAAT has been reported to be cost effective even in these settings. [8,9]

CBNAAT is capable of detecting both live and dead bacteria and has better sensitivity and specificity than smear microscopy and culture. [10] Numerous studies have assessed the yield of CBNAAT for extra-pulmonary diagnosis.

The total sample positivity by CBNAAT in our study was 11.59%. A study conducted by Yadav K et al on extra-pulmonary tuberculosis using CBNAAT found 23% positivity [11]. Saurab Jain et al in his study on rapid diagnosis of pulmonary and extra-pulmonary tuberculosis by cartridge Based nucleic acid amplification test found 41.87% of sample positivity[5]. Gour Sanjay M et al found 17.6% sample positivity in their study. [12] Rifampicin resistance by CBNAAT was low in our study (8%). Very similar observation was found by Gour Sanjay M et al.[12] and 6.47% in Saurab Jain et al [5]. A Similar Study conducted by Dr Pragati Rao et al detected Rifampicin resistance 13.55% [13].

In present study maximum sample positivity was found in FNAC 21(14.68%) followed by plural fluid (14.2%). Similarly Yadav K .et al found maximum cases of FNAC with MTB detected in 47.9 % [11]. Molecular techniques have changed the field of Tuberculosis diagnosis in both pulmonary and extra-pulmonary cases as they yield rapid results.

CONCLUSION:

The study concludes that CBNAAT is an effective and robust method which provides early diagnosis of extra-pulmonary tuberculosis over other diagnostic methods.

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