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Respiratory Medicine

STUDY OF AWARENESS AND UTILITY OF CARTRIDGE BASED NUCLEIC ACID AMPLIFICATION TEST (CBNAAT) AMONGST DOCTORS

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ABSTRACT **Introduction:** CBNAAT is one of the most useful investigations in detecting tuberculosis and drug resistance. It is now included in new RNTCP guidelines. Majority of patients with tuberculosis receive care from a primary care physician such as general practitioners and the rest obtain treatment from specialists including respiratory physicians. This study aims to explore the awareness and utility of CBNAAT amongst general practitioners and specialists other than respiratory physicians.

Aim: To obtain data regarding awareness and utility of the CBNAAT amongst the doctors.

Methodology: A survey was carried out amongst the general practitioners including AYUSH doctors and specialists other than Respiratory physicians in the vicinity of our hospital regarding the awareness and utility of CBNAAT.

Results: The awareness amongst surveyed population showed partial awareness regarding the CBNAAT and its utility is thus inadequate.

Conclusion: It was concluded that many aspects of CBNAAT is not known to general practitioners.

KEYWORDS : CBNAAT, Tuberculosis, awareness, utility.

INTRODUCTION:

The global burden of tuberculosis (TB) is enormous. More than 9 million new Mycobacterium tuberculosis (MTB) cases and 1.7 million deaths occur annually worldwide[1]. Most of them occur in resource-limited settings. The incidence of TB in underdeveloped countries is increasing, and this is thought to be because of associated poor hygiene conditions and the greater prevalence of AIDS.

Tuberculosis remains the most common opportunistic infection among PLHIV, and HIV-TB co-infected individuals are at high-risk of death [2]. Standard sputum based methods to detect pulmonary tuberculosis include sputum microscopy and culture. However, sometimes there is scanty sputum production and in PLHIV there is lack of caseous necrosis leading to decreased number of bacilli in sputum, and high incidence of non-tubercular mycobacterial infection. These factors decrease the sensitivity and specificity of sputum microscopy as a diagnostic tool.

To overcome these shortcomings, sputum culture and sensitivity for mycobacteria can be used. But it is a slow test usually taking 4 - 8 weeks, not widely standardised, and not economical for screening purposes. This delays initiation of anti-tubercular treatment especially for drug-resistant forms of TB, also increases risk of transmission of (drug-resistant) TB in the community and increases the risk of spread to extra-pulmonary sites within the patient [3].

Cartridge-based nucleic acid amplification test (CBNAAT) or GeneXpert is a recently introduced polymerase chain reaction (PCR) based method for detection of TB. It also detects rifampicin resistance as it targets the rpoB (RNA Polymerase B) gene of mycobacteria. CBNAAT (GeneXpert) is a *Mycobacterium tuberculosis*-specific automated, cartridge based nucleic acid amplification assay, having fully integrated and automated amplification and detection using real-time PCR, providing results within 100 minutes. It is a highly specific test as it uses 3 specific primers and 5 unique molecular probes to target the rpoB gene of *M. tuberculosis*, which is the critical gene associated with rifampicin resistance. No cross-reactions have been observed with many other bacterial species tested, including a comprehensive panel of mycobacteria, thereby excluding non-tubercular mycobacteria (NTM). Being a PCR based method, clinical validation trials done in four distinctly diverse settings have shown that 92.2 per cent of culture-positive patients were detected by a single CBNAAT test with a specificity of 99 per cent as compared to the sensitivity of a single direct sputum smear of 59.5% [4].

As general physicians, AYUSH practitioners diagnose and treat large number of pulmonary and extra pulmonary tuberculosis patients, but awareness and use of CBNAAT (GeneXpert) for detection of drug resistance is very less and inadequate amongst them. This study aims to obtain the data regarding awareness of the CBNAAT amongst the general practitioners. To improve its awareness, utility and importance in confirmation of diagnosis and detecting drug resistance.

Aim:

To obtain the statistical data regarding awareness and utility of the CBNAAT amongst the general practitioners.

MATERIALS AND METHODS:

A survey was carried out amongst practitioners other than respiratory physicians to assess the awareness and utility of CBNAAT by means of a questionnaire. Data collected was compiled and analysis was done.

Questionnaire used for analysis:

1. Are you aware of an investigation known as CBNAAT (GeneXpert)?
2. Can CBNAAT (GeneXpert) be used in diagnosing tuberculosis?
3. Can CBNAAT (GeneXpert) detect rifampicin resistance?
4. Can CBNAAT (GeneXpert) alone be used to detect MDR TB?
5. Have you ever prescribed CBNAAT (GeneXpert) to your patients?
6. Can CBNAAT (GeneXpert) detect isoniazid resistance?
7. Can CBNAAT (GeneXpert) detect extrapulmonary tuberculosis?
8. Can CBNAAT (GeneXpert) replace AFB culture?
9. Does CBNAAT (GeneXpert) involve microscopic examination?

All the above questions were analysed on the answers given by them as: YES/NO/DON'T KNOW

Inclusion Criteria:

General practitioners around the vicinity of our hospital, including AYUSH doctors.

Exclusion Criteria:

Practitioners not willing to participate in the survey

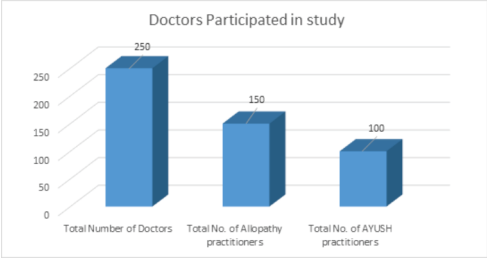
Sample Size: 250 General practitioners in total were included in the study.

Type of study: Cross Sectional survey based study.

Data Collection Technique: Survey questionnaire The data was then tabulated, interpreted and conclusions drawn.

RESULTS:
The data obtained from patients was tabulated as under:

Chart no. 1 : Number of doctors participated in study



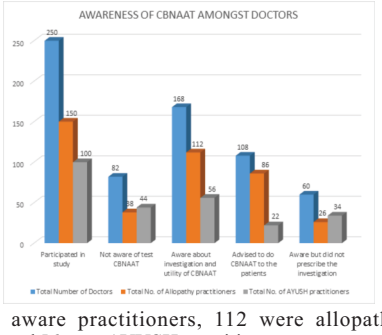
Total 250 doctors participated in the study. Out of 250, 150 doctors were allopathy general practitioners and 100 doctors were AYUSH practitioners.

It was observed that, only 168 doctors out of total 250 have ever heard the term CBNAAT and aware of the investigation and its utility.

Table No. 1 Master table

S. NO.	Total number of doctors who	Total Number of Doctors	Total No. of Allopathy practitioners	Total No. of AYUSH practitioners
1	Participated in study	250	150	100
2	Not aware of test CBNAAT	82	38	44
3	Aware about investigation and utility of CBNAAT	168	112	56
4	Aware and advised to do CBNAAT to the patients	108	86	22
5	Aware but did not prescribe the investigation	60	26	34

Chart No. 2 AWARENESS OF CBNAAT AMONGST DOCTORS



Out of the aware practitioners, 112 were allopathy general practitioners and 56 were AYUSH practitioners.

Out of 168 aware general practitioners only 108 practitioners had ever prescribed the investigation to the patient, which includes 86 allopathy and 22 AYUSH practitioners.

60 doctor have heard about CBNAAT but they did not prescribe the test because of not having any knowledge about its utility, specificity and sensitivity.

82 doctors were totally unaware of the investigation and utility of the CBNAAT, which included 38 allopathy general practitioners and 44 were AYUSH practitioners.

From above results it was concluded that there is partial awareness of CBNAAT amongst doctors. Utility of the investigation is also very less even after few doctors are aware of the investigation.

DISCUSSION:
CBNAAT purifies, concentrates, amplifies by rapid real time PCR and identifies targeted nucleic acid in TB genome and provides results from unprocessed samples in less than 2 hours with minimal hands on technical time. [5]

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 2 hours and gives accurate results due to use of disposable closed cartridges preventing cross contamination.[6] 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 extra pulmonary tuberculosis. CBNAAT allows the rapid detection of TB and Rifampicin resistance in a single test. It has a sensitivity superior to that of conventional microscopy and culture on solid media.

DIAGNOSTIC ALGORITHM OF TUBERCULOSIS:
All presumptive TB will undergo sputum smear examination (spot–early morning or spot sample). If the first sputum is positive, it is categorized as microbiologically confirmed TB

Smear-positive and presumptive multi-drug resistance TB (MDR TB): A Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) will be performed to rule out Rifampicin resistance and categorized as microbiologically confirmed drug-sensitive TB or Rifampicin resistant TB.

If the first smear is negative and chest X-ray (CXR) is suggestive of TB, 2nd sample will be subjected to smear and CBNAAT simultaneously.

On the basis of the CBNAAT result, patients will be categorized as microbiologically confirmed drug-sensitive TB or Rifmpicin resistant TB.

A Rifampicin indeterminate result will get an additional CBNAAT to get a valid result and in case of indeterminate on second occasion, the specimen will be sent to the Intermediate Reference Laboratory (IRL) or Culture and Drug Sensitivity Test (C and DST) centre for Line Probe Assay (LPA) or Liquid Culture and Drug Sensitivity Test (LC and DST)

Whenever facilities are available, effort should be made to obtain DST results of all drugs. If both the sputum smear and CXR are negative, the patient should be referred to a pulmonologist. All key population (PLHIV, children, EPTB, etc.) will preferentially get a CBNAAT done.[8][9][10]

The WHO policy guidance on the use of CBNAAT was issued in December 2010. The recommendations were that it should be used as the initial diagnostic test in individuals at risk of having MDR-TB or HIV-associated TB (strong recommendation), and that it could be used as a follow-on test to microscopy in settings where MDR and/ or HIV is of lesser concern, especially in smear-negative specimens (this was a conditional recommendation, recognising major resource implications). This recommendation applied to the use of CBNAAT in sputum specimens only, as data on its performance (sensitivity and specificity) for testing of extra pulmonary specimens at that time were limited.[11]

RNTCP adopted CBNAAT in India in April 2012. In the government set up, CBNAAT was launched in 2012 as a pilot project in Maharashtra by the State tuberculosis department. By the end of 2012, under EXPANDx-TB project, 12 CBNAAT labs were established all over India across different states14. CBNAAT is currently being made available at more centres with the aim to establish it at every hospital associated with a medical college throughout the country and also in private institutions [12][13].

As Majority of patients with pulmonary and extra pulmonary tuberculosis receive care from a primary care physician such as general practitioners (GPs) including AYUSH practitioners and specialists, it was observed from the results that, there is lack of awareness and proper knowledge about utility, sensitivity, specificity of the CBNAAT investigation in general practitioners. It is very much necessary to raise awareness about the investigation CBNAAT amongst the all doctors, so that its utility can be increased in diagnosis of MDR tuberculosis.

CONCLUSION:

It was concluded that certain aspects of CBNAAT (GeneXpert) though an important investigation in diagnosis of Tuberculosis is not known to many primary care physicians, AYUSH doctors and specialists. There is great need to raise awareness and utility of CBNAAT investigation to improve diagnosis of tuberculosis and to detect drug resistance. This data can help to increase awareness about investigation and its importance in detecting MDR tuberculosis patients. Thus ensuring maximal utility of the CBNAAT, ultimately attributing to better detection rate of Tuberculosis and drug resistance.

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