Content available at: iponlinejournal.com

IP Indian Journal of Immunology and Respiratory Medicine

Journal homepage: www.innovativepublication.com

Original Research Article

Role of CBNAAT in diagnosis of new pulmonary TB cases under RNTCP: A Retrospective analysis from Ahmedabad, India

Meghna Patel[1], Kaushal Bhavsar[1,*], Kiran Rami[1], Arvind Vala[1], Kalpita Shringarpure[2]

[1]*Dept. of Pulmonary Medicine, GMERS Medical College, Sola, Ahmedabad, Gujarat, India*
[2]*PSM Medical College, Vadodara, Gujarat, India*

ARTICLE INFO

Article history:
Received 23-10-2019
Accepted 16-11-2019
Available online 09-12-2019

Keywords:
New Pulmonary TB
Sputum Microscopy
CBNAAT
Drug Resistant TB

ABSTRACT

Introduction and Aim: The World Health Organisation (WHO) TB statistics for India for 2016 give an estimated incidence of 2.79 million cases. CBNAAT (Cartridge based nucleic acid amplification Test) helps to diagnose upfront drug resistance within two hours of sample submission.

Materials and Methods: We collected data from RNTCP laboratory for all newly diagnosed cases of Pulmonary TB registered from December 2018 to July 2019 who underwent sputum microscopy by LED FM and CBNAAT testing.

Result: Out of 333 patients, 241 (72%) were sputum microscopy positive while CBNAAT detected Mycobacterium TB (MTB) in 289 (86.8%) patients of whom Rifampicin resistance was detected among 15 patients (4.5%). This included 12/240 sputum positive patients in whom MTB was detected by CBNAAT and 3/49 sputum negative patients in whom MTB was detected by CBNAAT. There is moderate agreement for diagnosis of MTB by CBNAAT and sputum microscopy (Kappa = 0.55, CI: 0.449 to 0.655).

Conclusion: Universal upfront sputum CBNAAT in all new suspected cases of pulmonary TB according to current guidelines of RNTCP shows moderate agreement with LED-FM and yields a elevated percentage of patients being diagnosed with pulmonary sputum positive TB.

1. Introduction

India is the chief tuberculosis (TB) load country in the world. The World Health Organisation (WHO) TB statistics for India for 2016 give an estimated incidence of 2.79 million cases.[1] Incidence of MDRTB/RR cases is 1,47,000 (11/lakh population) as per Global Tuberculosis Report 2017.[2] For finding of TB patients under RNTCP programme, sputum microscopy is the initial diagnostic test in suspected cases of tuberculosis. In 2011, WHO released a new policy on LED-FM (Light Emitted Diode- Fluorescent Microscopy) for analysis of TB. FM is equally accurate, at least 10% more sensitive and has qualitative, operational, cost and workload advantages for all laboratories performing sputum smear microscopy.[3] Majority of the Designated Microscopy Centers (DMCs) under RNTCP programme have facility of LED-FM to diagnose TB patients. With the advent of the End TB Strategy, for the rapid diagnosis of Rifampicin Resistance CBNAAT/ Genexperttest is used.[4] Genexpert MTB/RIF (Xpert) is a fully automated real time heminescested PCR system implementing molecular beacon technology for diagnosis of TB infection. Moreover, CBNAAT simultaneously detects TB bacilli and Rifampicin drug resistance, providing an accurate result in less than two hours.[4] This helps the patient to be initiated on treatment on the same day thereby reducing the initial loss to follow up. It has minimum bio safety requirement, training needs and can be housed in non-conventional laboratories. We undertook this study to see if CBNAAT is equally sensitive as LED-FM to diagnose pulmonary TB; along with its added advantage of upfront Drug Sensitivity testing (DST) for diagnosed pulmonary TB cases. This may help policy and practice to use only CBNAAT instead of both LED-FM and CBNAAT in routine programmatic settings.

* *Corresponding author*.
E-mail address: drkaushal85@gmail.com (K. Bhavsar).

https://doi.org/10.18231/j.ijirm.2019.051

2. Materials and Methods

This was a retrospective record review of 333 newly diagnosed pulmonary TB patients who underwent sputum microscopy and CBNAAT as per RNTCP guidelines from December 2018 to July 2019. All newly diagnosed patients higher than 11 years of age were incorporated in the study.

Under the RNTCP Gujarat, LED-FM has been introduced since 2016 while CBNAAT was initially used to diagnose Drug Resistant TB. In LED FM, time required per sample to prepare and read slide is approximate one hour while sample processing for CBNAAT takes 20-30 minutes. So CBNAAT is less time consuming as compared to LED FM with added advantage of detecting rifampicin resistance in same process.

2.1. Statistical analysis

The number of patients being diagnosed as sputum positive or negative as well as those diagnosed as having Rifampicin resistant has been reported as percentage and proportions. Agreement in diagnosis of sputum positivity and negativity by both LED-FM and CBNAAT has been reported by Kappa statistic for agreement between two methods. The data were analyzed using SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

3. Results

In the study group, there were 223(66.9%) males. More than half of the patients (187/333, 56%) were in the age group 18-40 years, followed by 103(30%) patients in the age group 41-56 years. Seventeen (5%) of the patients were between 11-17 years of age (Table 1).

Out of 333 patients, 241(72%) were sputum microscopy positive and 92 patients (28%) were sputum microscopy negative, while CBNAAT detected MTB in 289(86.8%) patients. Rifampicin resistance was detected among 15 patients (4.5%). This included 12/240 sputum positive patients in whom MTB was detected by CBNAAT and 3/49 sputum negative patients in whom MTB was detected by CBNAAT. The agreement for diagnosis of MTB by CBNAAT and sputum microscopy is moderate (Kappa = 0.55, CI: 0.449 to 0.655). (Table 2).

Out of 333, the 274(94.8%) patients in whom Rifampicin resistance was not detected were put on Category 1 (one) as per RNTCP guidelines and 15 patients (4.5%) in whom CBNAAT report showed Rifampicin resistance detected were put on short course MDR TB regimen as per new PMDT guidelines.

4. Discussion

The RNTCP in Gujarat has initiated upfront Drug Sensitivity testing in lieu with achieving the targets of End TB Strategy by 2025. This study was undertaken to look for the conformity in the analysis of pulmonary TB patients by LED-FM and CBNAAT. This is the primary research of this type to observe if this approach would really help in the precise diagnosis of pulmonary TB by CBNAAT along with its added advantage of upfront DST testing.

Table 1: Age wise Distribution of patients diagnosed as pulmonary TB

Age (years)	Total N (%)	Male N (%)	Female N (%)
11 – 17	17(5%)	5	12
18 – 40	187(56%)	122	65
41 – 64	103(30%)	80	23
≥ 65	26(7.8%)	16	10
Total	333	223	110

Literature search shows a systematic review that studied the cost effectiveness of LED-FM and CBNAAT[5] and a study that evaluates the sensitivity and specificity of LED-FM and CBNAAT in Extra-pulmonary TB patients.[6] However, this study will help us understand if CBNAAT can be initiated without LED-FM for the finding of pulmonary TB in addition to drug resistance; consequently saving duplication and thereby, time and manpower.

Under RNTCP, for analysis of Pulmonary TB, each presumptive TB patients should undergo sputum microscopy testing. As per guideline of RNTCP two sputum samples (one is spot and one is early morning) of patient taken for microscopy examination.[7] Majority of the DMCs have a facility for LED-FM due to it's equally accurate and more sensitive result as compared to Zeil -Nelson (ZN) staining method.[2] Culture, although extremely sensitive and specific system for TB diagnosis, needs two to eight - weeks to yield results and therefore alone does not assist in early diagnosis.[8] CBNAAT is a molecular method of culture of Mycobacterium tuberculosis which also gives Rifampicin drug resistance in same sitting. It gives result within two hours.[4] Unlike conventional nucleic acid amplification tests (NAATs), CBNAAT MTB/RIF is unique because sample processing and PCR amplification and detection are integrated into a single self-enclosed test unit, the CBNAAT cartridge.[9] For early and rapid diagnosis of Rifampicin resistance cases, CBNAAT (CBNAAT) method is used under RNTCP; especially in a high TB burden country like India.

In our study, CBNAAT detected MTB in 87% patients, while 72% were sputum microscopy positive. There was moderate agreement between the CBNAAT and LED-FM sputum positivity. Thus, CBNAAT detected more number of sputum positive TB patients than LED-FM. The yield of CBNAAT was therefore more.

Twelve primary resistance cases in sputum positive cases and three in sputum negative cases were detected ; thus giving an incidence of 4.5% for primary drug resistance.

Table 2: Agreement between diagnoses of pulmonary TB patients using upfront CBNAAT and sputum microscopy correlation

	CBNAAT Positive	CBNAAT Negative	Total	Kappa statistic
Sputum microscopy positive	240	01	241	Kappa= 0.552, SE of kappa = 0.053, 95% CI: 0.449 to 0.655
Sputum microscopy negative	49	43	92	
Total	289	44	333	

(Number of observed agreements: 283 (84.98% of the observations) Number of agreements expected by chance: 221.3 (66.46% of the observations) Kappa = 0.552, SE of kappa = 0.053, 95% confidence interval: From 0.449 to 0.655, The strength of agreement is considered to be 'moderate')

This proportion was higher than the study done by Sharma et al in 2008-09 and Virupakashapp et al in 2017 as well as the drug resistant National and sub-national TB surveys conducted in India[10–13] Furthermore, sputum microscopy requires examination of two sample per patients; thereby increasing laboratory workload and requiring trained and experienced laboratory staff in staining and diagnosing microscopically. The process of making samples ready for CBNAAT test requires minimum training and infrastructure. CBNAAT is proved to be cost effective in high burden TB settings.[14] Introducing early treatment of DRTB in patients also decreases rate of infection to community and decreased morbidity and mortality due to MDRTB.

This study was conducted on patients having pulmonary TB. A larger cohort including Paediatric cases as well as extra-pulmonary cases and further multi-centric studies may help to confirm our findings, thereby informing further policy and practice regarding exclusive upfront DST testing by CBNAAT.

5. Conclusion

Universal upfront sputum CBNAAT in all new suspected cases of pulmonary TB according to current guidelines of RNTCP shows moderate agreement with LED-FM and yields a higher proportion of patients being diagnosed with pulmonary sputum positive TB.

6. Conflict of interest

None.

Acknowledgment

The authors are thankful to laboratory staff of DMC of GMERS Medical College, Sola, Ahmedabad for their proper reporting and recording of data of all patient s in laboratory register. We thank our residents involved in data collection.

References

1. Available from: https://www.tbfacts.org/tb-statistics-india (accessed on 2019 on October 1st).
2. India TB report ; 2018,. Available from: https://tbcindia.gov.in.
3. 3.Laboratory diagnosis of tuberculosis by sputum microscopy, the handbook, Global edition, Publication of the Global laboratory initiative, working group of STOP TB Partnership; 2013.
4. Available from: https://tbfacts.org/CBNAAT/ (accessed on 2019 on October 1st).
5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30372436, (accessed on 2019 on October 1st).
6. Available from: https://nrhm.gujarat.gov.in/images/pdf/3-diagnosis-of-smear-positive-pulmonary-tb.pdf.
7. Diagnosis of smear positive pulmonary TB , effective from 1st April 2009. Available from: https://nrhm.gujarat.gov.in/images/pdf/3-diagnosis-of-smear-positive-pulmonary-tb.pdf.
8. RNTCP Technical and Operational Guidelines for Tuberculosis Control in India-2016.P-14. ;.
9. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults Cochrane Infectious Diseases Group. 2014;(1). Available from: https://www.ncbi.nlm.nih.gov/pubmed/24448973.
10. Sharma SK, Kaushik G, Jha BD, George N, Arora SK, Gupta D. Prevalence of mdr-tb among new pulmonary tb cases. *Indian J Med Res*. 2011;133(3):308–319.
11. Virupakashapp V, Ranganath M, Manjunath MP, Mahendra M. Utility of CBNAAT in diagnosis of mycobacterium tuberculosis in tertiary care teaching hospital in South India. *IP Indian J Immunol Respir Med*. 2018;3(1):3–6.
12. RNTCP Technical and Operational Guidelines for Tuberculosis Control in India-2016, Central TB Devision, Ministry of Health and Family Welfare, New Delhi, India, P-1.
13. Guidelines on programmatic management of drug resistant TB in India 2017, Revised National Tuberculosis Control Programme, Central TB Division, Ministry of Health and Family Welfare, Nirman Bhavan, New Delhi p 3.
14. Sagili DK, Muniyandi M, Nilgiriwala KS, Shringarpure KS, Kalpita S, et al. Cost effectiveness of CBNAAT and LED FM for diagnosis of pulmonary tuberculosis: a systemic review ; 2018,. Available from: https://journals.plos.org.

Author biography

Meghna Patel Associate Professor

Kaushal Bhavsar Assistant Professor

Kiran Rami Professor

Arvind Vala Second Year Resident

Kalpita Shringarpure Tutor

Cite this article: Patel M, Bhavsar K, Rami K, Vala A, Shringarpure K. Role of CBNAAT in diagnosis of new pulmonary TB cases under RNTCP: A Retrospective analysis from Ahmedabad, India. *Indian J Immunol Respir Med* 2019;4(4):221-223.