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Original Research Article

Rapid Diagnosis of Pulmonary and Extrapulmonary Tuberculosis by Cartridge-Based Nucleic Acid Amplification Test (CBNAAT)

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ABSTRACT

Introduction: Tuberculosis incidence in India is 2.74 million including 0.13 million drug resistant cases. According to WHO 0.41 million death in India due to tuberculosis in 2017. Sputum smear microscopy is facing variable sensitivity issue particularly in patients with sputum smear-negative and/or extrapulmonary disease, and drug-resistant Tuberculosis. To overcome this problem, WHO's current policies and guidance recommend to use Xpert MTB/RIF as an initial diagnostic test.

Materials and Methods: This study done at RNTCP lab, Microbiology Dept., Govt. Medical College Khandwa, M.P., India, is a Retrospective observational record based analysis from 01 January 2018 to 31 May 2019 (1 year 5 months) on 1993 samples.

Results: Out of 1736 samples, 1537 were pulmonary & 199 Extrapulmonary included in this study. Samples positivity rate were (727) 41.87 %, of which (680) 39.17% Rifampicin sensitive & (47) 2.7% resistant for Mycobacterium tuberculosis. Pleural fluid 43.7%, Pus 27% & cervical lymph node 16.6% were most common extrapulmonary sample. 37 extrapulmonary samples were positive for Mycobacterium tuberculosis, out of this 33 sensitive & 4 were resistant to Rifampicin.

Discussion: Rifampicin resistance by CBNAAT was found to be 6.47% in our study. Gour Sanjay M et al found this 6.38%, 13.55% by D. Pragati Rao et al, 25% by R Dewan et al & very high (53%) by R Tripathi et al in their study. Pleural fluid (43.7%) was the most common extrapulmonary samples followed by Pus (27%) & lymph node (16.6%). Gour Sanjay M et al also found Pleural fluid 49.81% as most common sample followed by lymph node. 40%, Pus 37.73%. Extrapulmonary sample distribution pattern like our study.

Conclusion: Rifampicin resistant Mycobacterium tuberculosis is low in our area as compare to other part of India.

1. Introduction

Tuberculosis is one of the top 10 causes of death worldwide.[1] It is the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance.[1] India is the country with the highest burden (27% of global) of Tuberculosis cases.[1] According to Global Tuberculosis Report 2018, Tuberculosis incidence in India is 2.74 million including 0.13 million drug resistant cases, According to WHO 0.41 million death in India due to tuberculosis 2017.[2]

Most easily available diagnostic method i.e. Sputum smear microscopy is facing variable sensitivity issue particularly in patients with sputum smear-negative and/or extrapulmonary disease, and drug-resistant Tuberculosis.[3–5] With the help of microscopy only 49% of cases can be detected in Madhya Pradesh, India.[6] Besides technical expertise and biosafety concerns, Culture on Lowenstein-Jensen (LJ) medium, "the gold standard test", takes 2-8 weeks to produce growth causing delayed onset of treatment.[5] New generation liquid culture diagnostics and molecular line probe assays are costly and needed biosafety measures and specialised staff.[3]

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To overcome this problem, WHO's current policies and guidance recommend that Xpert MTB/RIF be used as an initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (strong recommendation, moderate quality of evidence).[7] The guidance also provides a conditional recommendation that Xpert MTB/RIF be used as a follow-up test to smear microscopy in settings where MDR-TB or HIV are of lesser concern, especially for further testing of smear-negative specimens.[7]

2. Materials and Methods

This study done at RNTCP lab, Microbiology Dept., Govt. Medical College Khandwa, M.P., India, is a Retrospective observational record based analysis. The study period is from 01 January 2018 to 31 May 2019 (1 year 5 months). A total of 1993 samples according to inclusion & exclusion criteria mention below were included in this study.

2.1. *Inclusion criteria*

1. All adult patients above 13 years of age & both sexes.
2. All clinically suspected cases of pulmonary & extrapulmonary Tuberculosis.
3. All new & old (including treatment failure, defaulters & relapse) cases of pulmonary & extrapulmonary Tuberculosis.
4. All pulmonary & extrapulmonary samples received in CBNAAT lab.

2.2. *Exclusion criteria*

1. All patients below 13 years of age.
2. Patient of HIV/AIDS.

TB detection was done by Xpert MTB/ RiF assay, made by Cepheid (Sunnyvale, CA, United States).[6] All specimens were processed according to the GeneXpert system operator manual given by Central TB division, Government of India.[6] The assay is designed for extraction, amplification and identification of rpoB gene of M. tuberculosis as it accounts for more than 95% of mutations associated with rifampicin resistance.[6,7] Xpert MTB/RIF cartridge is a disposable, single self-enclosed test unit in which all steps of NAAT i.e. Sample processing, PCR amplification and detection are automated and integrated.

3. Results

During study period from 01 January 2018 to 31 May 2019, 1993 samples were received. Out of this, 116 PLHIV samples & 103 pediatrics age group patients samples & 38 invalid test result samples were excluded from our study. So 1736 samples were included in this study. 1537 samples were pulmonary & 199 Extrapulmonary. Sample positivity rate was (727) 41.87%, of which (680) 39.17% Rifampicin sensitive & (47) 2.7% resistant for Mycobacterium tuberculosis as shown in Figure 1. Rifampicin sensitivity in newly treated patient (96.9%) was little high as compare to previously treated patient (89.2%). Rifampicin resistance was high in previously treated patient (10.4%) as compare to newly treated patient (3.1%) as shown in Figure 2.

199 extrapulmonary samples were received during study period. 37 were positive for Mycobacterium tuberculosis, out of this 33 s ensitive & 4 were resistant to Rifampicin. All the four resistant to Rifampicin were found only sensitive to fluoroquinolones. Sample vise distribution is shown in Table 1 but the most common samples were Pleural fluid 43.7%, Pus 27% & cervical lymph node 16.6%.

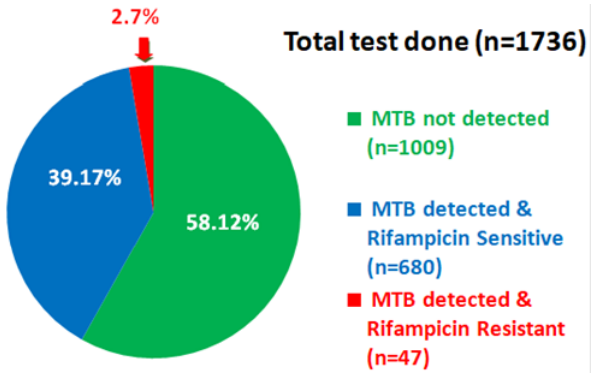

Fig. 1: Percentage distribution of test in accordance to positivity as well as Rifampicin susceptibility

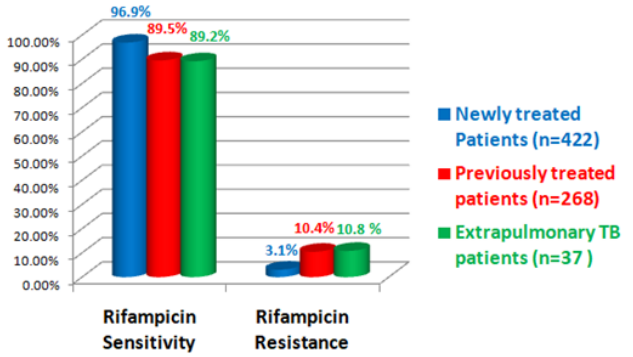

Fig. 2: Rifampicin susceptibility pattern for tuberculer patients

4. Discussion

Tuberculosis is the major cause of mortality & morbidity in our country.[1] CBNAAT shows its utility in paucibacillary Pulmonary & Extrapulmonary MTB infection, where microscopy may be compromised as well as simultaneously Rifampicin resistance detection ability make this test very useful in routine practices.

Total sample positivity by CBNAAT In our study was 41.87%. Gour Sanjay M et al found 17.6% sample positivity

Table 1: Extrapulmonary samples distribution & their sensitivity to Rifampicin

S.No.	Type of samples	Total no. of samples	Percentage vise samples distribution	Rifampicin Sensitive	Rifampicin Resistant
1	Pleural fluid	87	43.72	11	02
2	Pus	54	27.13	07	00
3	Cervical lymph node	33	16.59	08	02
4	Ascitic fluid	11	5.53	01	00
5	CSF	09	4.52	00	00
6	Synovial fluid	03	1.51	00	00
7	Gastric lavage	02	1	00	00
	Grand total no. of samples	**199**	-	**27**	**04**

in their study.[8] Rifampicin resistance by CBNAAT was low 6.47% in our study. Very similar observation (6.38%) found by Gour Sanjay M et al.[8] Rifampicin resistance also found 13.55% by D. Pragati Rao et al,[9] 25% by R Dewan et al[10] & very high (53%) by R Tripathi et al[11] in their study. Rifampicin sensitivity for positive samples by CBNAAT was 93.53% in our study. Similar observation (93.6%) also found by Gour Sanjay M et al.[8] 75% sample shown Rifampicin sensitivity in the study done by R Dewan et al[10] but R Tripathi et al[11] found only 35.8%.

Extrapulmonary samples found to be positive by CBNAAT were 18.59% in our study. Shivprasad Kasat et al also found 15.06% Extrapulmonary samples positivity in their study.[12] Pleural fluid (43.7%) was most common extrapulmonary samples followed by Pus (27%) & lymph node (16.6%). Gour Sanjay M et al also found Pleural fluid 49.81% most common sample followed by lymph node 40%, Pus 37.73%.[8] Subhakar Kandi et al found lymph node 19% most common sample followed by Pleural fluid & BAL 10% & CSF 2.5%.[13]

5. Conclusion

CBNAAT is a very useful tool for diagnosis as well as Rifampicin resistance detection for Mycobacterium tuberculosis. Rifampicin resistant Mycobacterium tuberculosis is low in our area as compare to other part of India give indirect indication of good implementation of RNTCP program in our area.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. World Health Organisation. Global Tuberculosis Report 2018. Document number: WHO/CDS/TB/2018.25 Website ;. Available from: http://www.who.int/tb/publications/global_report/en/.
2. Annex 2 Country profiles World Health Organisation. Global Tuberculosis Report 2018 ;. Available from: www.who.int/tb/data.
3. Weyer K, Mirzayev F, Migliori GB, Gemert WV, Ambrosio DL, et al. Rapid molecular TB diagnosis: evidence, policy making and global implementation of Xpert MTB/RIF. *ERJ*. 2013;42(1):252–271.
4. Xpert MTB/RIF for people living with HIV. World Health Organization October 2014 ; 2014,.
5. Walusimbi S, Bwanga F, A DC, Haile M, Joloba M, et al. Meta-analysis to compare the accuracy of GeneXpert, MODS and the WHO 2007 algorithm for diagnosis of smear-negative pulmonary tuberculosis. *BMC Infect Dis*. 2013;13:507.
6. Guidance document for use of Catridge Based-Nucleic Acid Amplification Test (CB-NAAT) under Revised National TB Control Programme (RNTCP) issued central TB division, directorate general of health services ; 2017,.
7. Policy update, World Health Organisation, Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Document No WHO/HTM/TB/2013.16 ;.
8. Sanjay MG, Radha PM, Babu NP, Sushant M, Jitesh A. Genotypic diagnosis of extra pulmonary tuberculosis- CBNAAT a novel tool. *Med Pulse Int J Med*. 2017;4(2):79–82. Print.
9. Rao DP, Sowjanya KL. Role of CBNAAT in rapid detection of Mycobacterium Tuberculosis in PLHIV in a highly prevalent state. *J Evid Based Med Healthc*. 2012;3(38):1896–1898.
10. Dewan R, Anuradha S, Khanna A, Garg S, Singla S, et al. Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. *J Indian Acad Clin Med*. 2015;16(2):114–117.
11. Tripathi R, Sinha P, Kumari R, Chaubey P, Pandey A, et al. Detection of rifampicin resistance in tuberculosis by molecular methods: A report from Eastern Uttar Pradesh, India. *Indian J Med Microbiol*. 2016;34(1):92–94.
12. Kasat S, Biradar M, Deshmukh A, Jadhav S, Deshmukh H. Effectiveness of CBNAAT in the diagnosis of extrapulmonary tuberculosis. *Int J Res Med Sci*. 2018;6(12):3925–3928.
13. Kandi S. Diagnosis of Pulmonary and ExtraPulmonary Tuberculosis: How Best is CBNAAT when Compared to Conventional Methods of TB Detection. *Pulm Res Respir Med Open J*. 2017;4(2):38–41.

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