e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2025; 17(1); 596-602

Original Research Article

Diagnostic Utility of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) and ZN Smear Microscopy in Mycobacterium Tuberculosis Detection

Krishna Agarwal[1], Arvind Debjibhai Nanera[2], Naresh Jain[3], Rambabu Sharma[4]

[1]Associate Professor, Department of Microbiology, PIMS, Udaipur

[2]Assistant Professor, Department of Microbiology, PIMS, Udaipur

[3]Assistant Professor, Department of Microbiology, PIMS, Udaipur

[4]Assistant Professor, Department of Microbiology, PIMS, Udaipur

Received: 20-11-2024 / Revised: 10-12-2024 / Accepted: 05-01-2025

Corresponding Author: Dr. Rambabu Sharma

Conflict of interest: Nil

Abstract:

Background: Tuberculosis (TB) remains a global health challenge, with multidrug-resistant tuberculosis (MDR-TB) emerging as a major concern. Early and accurate detection of Mycobacterium tuberculosis (MTB) and rifampicin resistance is crucial for effective treatment and control of TB. This study aimed to compare the diagnostic utility of Ziehl-Neelsen (ZN) smear microscopy and GeneXpert MTB/RIF, a rapid molecular test, in detecting MTB and rifampicin resistance.

Methods: A total of 1,959 clinical samples (including sputum, bronchial alveolar lavage, CSF, pleural fluid, pus, lymph node aspirates, and other extrapulmonary specimens) were processed from January 2024 to December 2024 at Pacific Institute of Medical Sciences, Udaipur. Samples were analyzed using both ZN smear microscopy and the GeneXpert MTB/RIF assay for the detection of MTB and rifampicin resistance.

Results: Among the 1,959 samples, 389 (19.85%) tested positive for acid-fast bacilli (AFB) using ZN staining, while 475 (24.25%) tested positive by GeneXpert. Rifampicin resistance was detected in 16 samples (0.81%). The highest rifampicin resistance was found in sputum samples (0.62%). GeneXpert identified MTB in 6.43% of smear-negative samples, with 5 of them being rifampicin-resistant. GeneXpert showed higher sensitivity and specificity compared to ZN smear microscopy, especially in smear-negative and extrapulmonary TB cases.

Conclusion: The GeneXpert MTB/RIF assay offers a reliable and rapid diagnostic solution for detecting MTB and rifampicin resistance, surpassing the limitations of ZN smear microscopy. Incorporating this molecular diagnostic method into routine laboratory practices will significantly improve the detection of drug-resistant TB, facilitating better treatment outcomes and the containment of MDR-TB.

Key words: Mycobacterium Tuberculosis, ZN Microscopy, GeneXpert MTB/RIF assay, WHO.

Introduction

Tuberculosis (TB) remains a significant global health issue, ranking among the top 10 causes of death worldwide and as a leading cause of mortality from a single infectious agent. TB is caused by *Mycobacterium tuberculosis* (MTB), an airborne pathogen transmitted through aerosolized droplets containing the bacilli. While pulmonary TB is the most common manifestation, MTB can infect other sites, resulting in extrapulmonary TB, which is often more challenging to diagnose. (World Health Organization, 2021). [1]

According to WHO reports, approximately 10 million TB cases were reported globally in 2019, with the highest burden observed among men aged 15 years and older, accounting for 56% of all cases. TB affects individuals across all age groups and genders but disproportionately impacts socioeconomically disadvantaged populations. Key factors driving the sustained transmission of TB include the co-infection with human immunodeficiency virus (HIV), delayed diagnosis, and inadequate control measures (WHO, 2021). [1]

The rising number of TB cases poses a significant challenge to current control efforts, especially with the emergence of drug-resistant strains. Resistance to anti-tuberculosis medications primarily arises from spontaneous genetic mutations in the Mycobacterium tuberculosis genome, occurring at predictable rates. Multidrug-resistant TB (MDR-TB), characterized by resistance to isoniazid (INH) and rifampicin (RIF), is a growing concern and has been reported across the globe. [2-3]

Africa and Asia carry the highest burden of tuberculosis (TB), accounting for 95% of new cases globally (WHO, 2020). [4-5] India leads the world in TB cases, contributing 27% of new global cases annually [6-7]. In 2018, an estimated 4,84,000 cases of multidrug-resistant TB (MDR-TB) or rifampicin-resistant TB were reported worldwide, with 6.2% classified as extensively drug-resistant TB (XDR-TB). MDR-TB involves resistance to isoniazid and rifampicin, with or without resistance to other first-line drugs. Globally, 3.4% of new cases and 18% of previously treated cases are MDR-TB or rifampicin-resistant. XDR-TB includes additional resistance to fluoroquinolones and second-line injectable drugs making it one of the most challenging forms of TB to treat. [6]

Treatment for drug-resistant TB, including MDR-TB and XDR-TB, is possible but costly, prolonged, and associated with higher failure and mortality rates. [5] In MDR-TB, genetic mutations are responsible for resistance, with the katG gene linked to isoniazid resistance and the rpoB gene to rifampicin resistance. [8]

Accurate and early detection of *MTB* is critical for reducing transmission and improving treatment outcomes. Smear microscopy, particularly using Ziehl-Neelsen (ZN) staining, has long been the cornerstone of TB diagnosis in resource-limited settings due to its simplicity and low cost. This method involves direct microscopic examination of sputum smears to detect acid-fast bacilli (AFB). However, it has significant limitations, including low sensitivity, particularly in paucibacillary cases and extrapulmonary TB. Detection by ZN smear microscopy requires a bacillary load of at least 10,000 organisms per milliliter of sputum, which often results in missed diagnoses, especially in HIV co-infected individuals or children (Chakravorty et al., 2017). [9]

To address these limitations, the WHO endorsed the Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) in 2011 as a rapid and automated diagnostic tool. CBNAAT, also known as GeneXpert. GeneXpert not only detects *MTB* but also confer mutational resistance with help of three specific primers and ensure a high specificity. This cartridge based testing platform with fully automated DNA detection used in *MTB* diagnosis with rifampicin resistance within two hours. Its sensitivity is markedly higher than smear microscopy, as it can detect as few as 131 colony-forming units per milliliter of sputum or five genome copies per reaction. CBNAAT is particularly beneficial for diagnosing smear-negative and extrapulmonary *TB*, although it cannot differentiate between active and cured *TB* due to its ability to detect both live and dead bacteria (Lawn et al., 2013; Steingart et al., 2014). [10-11]

This study aims to evaluate and compare the diagnostic utility of ZN smear microscopy and CBNAAT in detecting MTB. By highlighting their respective sensitivities, specificities, and limitations, this research seeks to provide insights into optimizing TB diagnostic strategies, particularly in resource-limited settings.

Materials and Methods

All clinical samples (2009) were processed from January 2024 to December 2024 at Pacific Institute of Medical Sciences, Udaipur. The sample sources were sputum, bronchial alveolar lavage, CSF followed by pleural fluid, endotracheal, PUS, Lymph-node aspirate, Liver abscess, Pericardial fluid, Ascitic fluid, Urine and all samples were further processed.

1. Sample Collection

Before collection of samples, all patients enrolled on NIKSHAY online portal. NIKSHAY is the official online portal launched by the Government of India for tracking and managing tuberculosis (TB) patients under the National TB Elimination Program (NTEP). For pulmonary tuberculosis, two sputum samples (one spot sample and the second one on the next day morning), measuring 50 mL, were collected in wide-mouthed sterile containers and all extrapulmonary samples were collected according to the National Tuberculosis Elimination Program (NTEP) guidelines. [12] Microscopy using Ziehl-Neelsen (ZN) staining was conducted, along with sample decontamination procedures. [13]

2. Preparation of Sample

All specimens were decontaminated using 5.0 mL of NaCl solution with N-acetyl-L-cysteine (NALC) and sodium hydroxide (NaOH). After a 15-minute incubation at room temperature, the specimens were neutralized with phosphate-buffered saline (PBS) at pH 6. The samples were then centrifuged at 4500 rpm for 20 minutes at 10°C. Finally, the pellets were suspended in 1.5 mL of sterile PBS and collected for further analysis. [14-16]

3. Microscopic Examination

3.1 Ziehl-Neelsen Staining

The purulent portion of the specimen was selected to prepare a direct smear on a clean 2 × 1 cm slide. After air-drying, the slides were heat-fixed and then subjected to Ziehl-Neelsen (ZN) staining. The smears were subsequently graded according to the National Tuberculosis Elimination Program (NTEP) guidelines. [13,17]

4. Xpert MTB/RIFAssay (Cartridge Based Nuclear Acid Amplification Test, CBNAAT)

A 1 mL sample was analyzed using the CBNAAT system on the Xpert MTB/RIF. The machine used for processing contained four cartridges. A sampling reagent was added to the sample in a 2:1 ratio and incubated at room temperature with intermittent shaking for 15 minutes, following the standard operating procedure. Afterward, 2 mL of the sample was transferred to the cartridge and placed into the CBNAAT machine module. The tests were performed according to the manufacturer's user manual, with results generated in approximately 1 hour and 50 minutes. This process allowed for the detection of Mycobacterium species and rifampicin resistance simultaneously. [18-19]

Results

A total of 2,009 pulmonary and extrapulmonary samples were collected from patients with clinical and radiological suspicion of tuberculosis. Out of these 2,009 MTB-suspected samples, 50 samples were excluded from the study. The reasons for exclusion included inadequate sample quantity, contamination, and machine test errors. The sources of the remaining samples are shown in Table 1. Samples were collected from both male and female patients. A total of 1,520 (77.60%) samples were obtained from male patients, while 439 (22.40%) samples were collected from female patients (Figure 1). Male patients were more predominant than females.

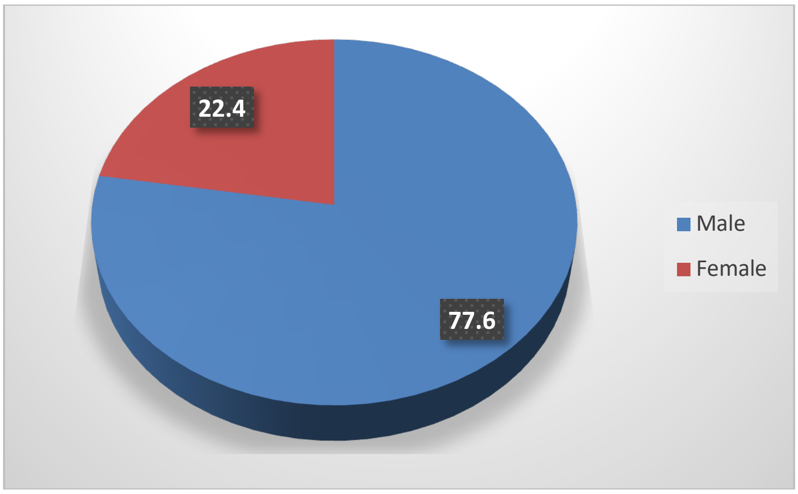

Figure 1: Gender distribution

Table 1: Sample distribution in patients of MTB.

Source of sample	No. of samples (n=1959)	%
Sputum	1293	66.00
BAL	299	15.26
ETA	37	1.89
PF	129	6.60
CSF	52	2.59
PUS	33	1.69
Pericardial Fluid	05	0.26
Liver Abscess	14	0.69
Lymph-node	03	0.14
AF	75	3.83
Tissue	03	0.154
Urine	03	0.14
GL	13	0.68
Total	1959	100%

[BAL-Bronchial Alveolar Lavage**,** ETA- Endotracheal aspirate, PF- Pleural Fluid, CSF- Cerebrospinal Fluid, AF- Ascitic Fluid, GL- Gastric Lavage]

Table 2: Sample distribution of patients in ZN smear positive, Gene Xpert (CBNAAT) positive with Rifampicin resistance.

Source of sample	No. of samples n=1959, (%)	ZN Smear positive, (%)	Gene Xpert (CBNAAT) Positive, (%)	Rifampicin Resistance, %
Sputum	1293, (66.00)	285, (22.04)	338, (26.14)	12, (0.92)
BAL	299, (15.26)	69, (23.07)	87, (29.09)	01, (0.33)
ET	37, (1.89)	8, (21.62)	9, (24.32)	0
PF	129, (6.60)	9, (6.97)	15, (11.62)	01, (0.77)
CSF	52, (2.59)	4, (7.69)	7, (13.46)	01, (1.92)
PUS	33, (1.69)	8, (24.24)	13, (39.39)	01, (03.03)
Pericardial Fluid	05, (0.26)	0	0	0
Liver Abscess	14, (0.69)	0	1, (7.14)	0
Lymph-node	03, (0.14)	2, (66.66)	2, (66.66)	0
AF	75, (3.83)	3, (4)	2, (2.66)	0
Tissue	03, (0.154)	0	0	0
Urine	03, (0.14)	0	0	0
GL	13, (0.68)	1, (7.69)	1, (7.69)	0
Total	1959, (100%)	389, (19.85)	475, (24.25)	16 (0.81)

Microscopic examination revealed that 389 samples (19.85%) tested positive for Acid-Fast Bacilli (AFB) using the ZN staining method. In contrast, 1,570 samples (80.15%) were smear-negative (Table 2). The AFB grading based on the samples is presented in **Figure 2**. Grading was done only for sputum samples.

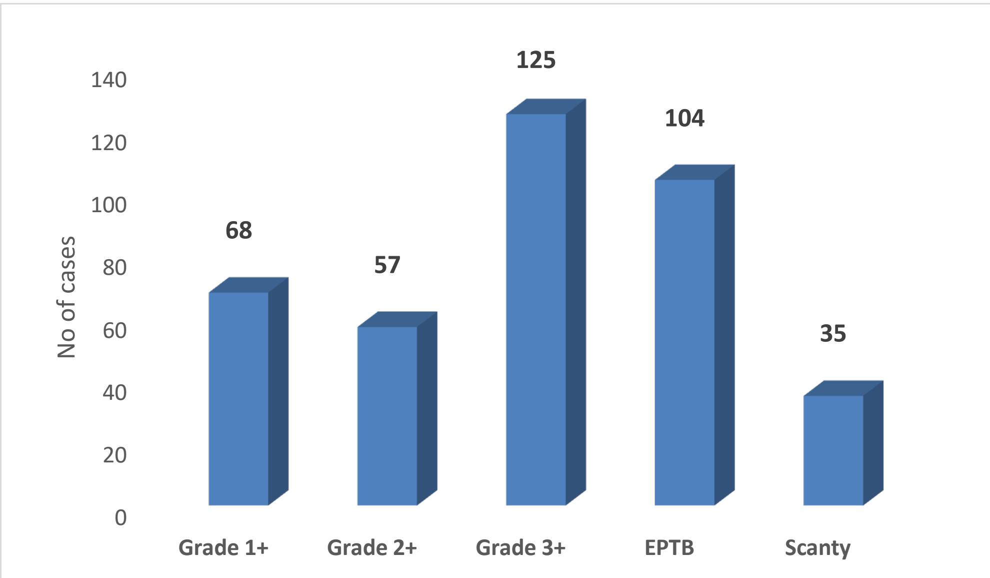

Figure 2: patients sample with AFB grading

In the study, out of 1,959 samples, 389 (19.85%) were smear-positive, as shown in Table 2. Additionally, 475 samples (24.25%) tested positive using CBNAAT. By CBNAAT positive samples, Rifampicin resistance was detected in 16 samples (16/1959, 0.81%). Highest rifampicin resistance was detected from sputum samples (08/1293). Among the 1,570 smear-negative samples processed directly for CBNAAT-Gene Xpert, 101 samples (6.43%) were found to be positive with 5 samples resistance to rifampicin and all other susceptible to Rifampicin.

Discussion

The rising incidence of MDR-TB in India and other developing nations poses a significant challenge to tuberculosis control efforts. One of the key issues in TB treatment is the delay in diagnosis and lack of drug sensitivity testing, which often results in the development of MDR-TB. The global prevalence of MDR-TB is increasing rapidly, highlighting the need for accurate and swift diagnostic methods. Such advancements are crucial to assist clinicians in the effective treatment, management, and control of TB. Consequently, this study was undertaken to assess the significance of the GeneXpert MTB/RIF, a new PCR-based technology, in detecting MTB and rifampicin resistance.

In this study, a total of 1959 samples were analyzed. The male population constituted 77.60%, making it more predominant compared to the female population, which accounted for 22.40%. The age range of participants was between 4 and 94 years. Our findings were consistent with the study conducted by Abyot Meaza et al. [20] . Among the 182 cases, 118 patients (65%) were male, while 64 patients (35%) were female.

The median age in our study was 49 years, with a range spanning from 4 to 94 years. This differs from the findings of Kandha Kumara et al. [21], who reported a median age of 26 years, with an age range from 1 to 68 years.

In our study, out of 1959 samples, 389 (19.85%) tested positive for AFB on smear examination, while 1570 (80.15%) tested negative. Among the 1959 pulmonary and extra-pulmonary samples analyzed, including sputum, pleural fluid, bronchial alveolar lavage, endotracheal aspirate, CSF, pus, lymph nodes, gastric lavage, pleural fluid, and ascitic fluid, CBNAAT Gene Xpert testing identified 1332 negative samples. The study also revealed a rifampicin resistance rate of 0.81%.

In our study, among the cohort of 1570 smear-negative samples, MTB was detected in 101 patients using CBNAAT. Of these, 5 were rifampicin-resistant, while 96 were rifampicin-sensitive. CBNAAT identified 101 cases (6.43%) from smear-negative samples, which was lower compared to the findings of Dash Manoranjan et al. [22]. The rifampicin sensitivity pattern observed in our study was consistent with the results reported by Vishal Chopra et al. [23].

In our study, sputum smear testing revealed AFB positivity in 389 patients (19.85%), while CBNAAT detected MTB in 353 patients (18.02%). This is may be due to mycobacteria other than tuberculosis (MOTT). Among these, 10 patients were found to have rifampicin resistance, aligning with the findings of Anushree Chakraborty et al. [24].

Various studies evaluating the performance of GeneXpert (MTB/RIF) have reported test sensitivities ranging from 57% to 76.9% in culture-positive but smear-negative cases. In culture-positive and smear-positive cases, sensitivities were observed to be between 98% and 100%. Overall, the specificity of GeneXpert has consistently been reported at 99% to 100%. [25-28]

Our study confirms that the Z-N smear is less sensitive than the GeneXpert MTB/RIF test. This difference can be attributed to the higher bacillary load required for a positive result with the Z-N smear method, which necessitates 5×10^3 to 1×10^4 bacilli/ml of specimen. In contrast, the GeneXpert assay can detect as few as 131 bacilli/ml. [29-30] Additionally, the GeneXpert MTB/RIF test identifies the DNA of Mycobacterium tuberculosis (MTB). In this study, isolates were detected by the Z-N stain but tested negative with the GeneXpert MTB/RIF assay. This discrepancy arises because GeneXpert is a nucleic acid amplification test designed to detect specific DNA of the MTB complex, excluding Mycobacteria other than tuberculosis (MOTT). [31]

Multidrug-resistant tuberculosis (MDR-TB) is defined as tuberculosis caused by strains of M. tuberculosis that are resistant to at least isoniazid and rifampicin. While mono-resistance to rifampicin is uncommon, 90% of rifampicin-resistant isolates are also resistant to isoniazid. As a result, the detection of rifampicin resistance can act as a reliable surrogate marker for MDR M. tuberculosis. The Xpert® MTB/RIF test provides accurate results for rifampicin resistance detection, enabling the rapid initiation of MDR-TB treatment. [32-34]

In our study, 16 (0.81%) of the samples were found to be rifampicin-resistant, while the remaining samples were rifampicin-sensitive. These results were lower compared to the studies by Olusoji et al., [35] Lawson et al., [36] and Ganguly et al., [37] which reported rifampicin resistance rates of 7.2%, 8.6%, and 19%, respectively. Similarly, Idigbe et al. [38] found a 2% rifampicin resistance rate in Lagos, Nigeria. However, Rasaki et al. [39] did not report any rifampicin-resistant strains in their findings.

Conclusion

The GeneXpert MTB/RIF assay offers a simple, rapid, and reliable method for detecting *M. tuberculosis* in sputum specimens. It is less reliant on the operator's expertise, meaning that even staff with minimal training can effectively use the system. While the GeneXpert MTB/RIF assay has significant advantages, it is important to note that, like other diagnostic tests for tuberculosis, a negative result does not completely rule out the disease. To confirm the diagnosis, patients with negative results should undergo further evaluation, including Z-N smear tests, culture, clinical symptoms, and radiographic findings. On the other hand, positive results from GeneXpert should be integrated into a comprehensive assessment. The assay's high sensitivity and specificity for detecting rifampicin resistance make it an excellent choice for initial testing of drug resistance. The incorporation of molecular diagnostic methods, such as GeneXpert, into routine laboratory practices would significantly enhance the adaptation of treatment regimens and help in limiting the spread of MDR-TB strains.

Furthermore, the development of a highly sensitive diagnostic screening test, which directly detects *M. tuberculosis* from decontaminated sputum without the need for time-consuming nucleic acid extraction, makes it especially suitable for point-of-care use, with results available within approximately two hours.

References

1. World Health Organization (WHO). (2021). Global Tuberculosis Report 2021.
2. Rai DK, Pandey S. A Hospital-Based Cross-sectional Study on Clinico demographic Characteristic of Extrapulmonary Tuberculosis Cases Coming to a Tertiary Hospital of Bihar. Indian J Community Med. 2018;2020.
3. Seung KJ, Keshavjee S, Rich ML. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis, Cold Spring Harb Perspect Med. 2015;5(9):a017863. Crossref.
4. Rutaihwa LK, Zwyer M, Borrell S, et al, Local adaptation in populations of Mycobacterium tuberculosis endemic to the Indian Ocean Rim. F1000 Research 2021; 10:60.
5. Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis; 2014, ISBN: 978924 154880 9, WHO/HTM/TB/2014.11.
6. Singh AV, Singh S, Yadav A, et al. Genetic variability in multidrug-resistant Mycobacterium tuberculosis isolates from patients with pulmonary tuberculosis in North India. BMC Microbiol. 2021;21(1):123. Crossref
7. Isakova J, Sovkhozova N, Vinnikov D, et al. Mutations of rpoB, katG, inhA and ahp genes in rifampicin and isoniazid-resistant Mycobacterium tuberculosis in Kyrgyz Republic. BMC Microbiol. 2018;18(1):22. Crossref
8. Isakova J, Sovkhozova N, Vinnikov D, et al. Mutations of rpoB, katG, inhA and ahp genes in rifampicin and isoniazid-resistant Mycobacterium tuberculosis in Kyrgyz Republic. BMC Microbiol. 2018;18(1):22. Crossref
9. Chakravorty, S., et al. (2017). "Detection of Mycobacterium tuberculosis in smear-negative sputum samples." *Journal of Clinical Microbiology*.
10. Lawn, S. D., et al. (2013). "GeneXpert MTB/RIF: A transformative diagnostic tool for tuberculosis." *The Lancet Infectious Diseases*.
11. Steingart, K. R., et al. (2014). "Performance of GeneXpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults." *Cochrane Database of Systematic Reviews*.
12. Yadav RN, Singh BK, Sharma SK, et al. Comparative Evaluation of GenoType MTBDRplus Line Probe Assay with Solid Culture Method in Early Diagnosis of Multidrug Resistant Tuberculosis (MDR-TB) at a Tertiary Care Centre in India. PLoS ONE. 2013;8(9):e72036. Crossref
13. Stinson KW, Eisenach K, Matsumoto M, et al. Mycobacteriology Laboratory Manual, First Edition. Global Laboratory Initiative. 2014.
14. Revised National Tuberculosis Control Programme Laboratory, Guidelines for Quality Assurance of smear microscopy for diagnosing tuberculosis. 2005.
15. Kazemian H, K-Y J, Bahador A, et al. Efficacy Of Line Probe Assay In Detection Of Drug-Resistant Pulmonary Tuberculosis In Comparison With GeneXpert And Phenotypic Methods In Iran And Genetic Analysis Of Isolates By MIRU-VNTR. Infect Drug Resist. 2019;12: 35 85-3593. Crossref
16. Schwartz D, Shafran I, Romero C, et al. Use of short-term culture for identification of Mycobacterium avium subsp. paratuberculosis in tissue from Crohn's disease patients. Clin Microbiol Infect. 2000;6(6)303-307. Crossref
17. Vijdea R, Stegger M, Sosnovskaja A, Andersen AB, Thomsen VO, Bang D. Multidrug resistant tuberculosis: rapid detection of resistance to rifampin and high or low levels of isoniazid in clinical specimens and isolates. Eur J Clin Microbiol Infect Dis. 2008; 27(11): 1079-1086. Crossref
18. Tripathi R, Sinha P, Kumari R, Chaubey P, Pandey A, Anupurba S. 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. Crossref
19. Dash M, Samal S, Swain TR, Behera B, Sahu S, Mahapatra S. Diagnostic yield of cartridge based nucleic acid amplification test in Mycobacterium tuberculosis in a tertiary care medical college and hospital of Southern Odisha, India. Int J Res Med Sci. 2019;7(12):4460-44 63. Crossref
20. Meaza A, Kebede A, Yaregal Z, et al. Evaluation of genotype MTBDRplus VER 2.0 line probe assay for the detection of MDR-TB in smear positive and negative sputum samples. BMC Infect Dis. 2017;17(1):280. doi: 10.1186/s12879-017-2389-6
21. Gandhi K, Selvaraj S, Kannaiyan K. Isolation of Diverse Mycobacterium Tuberculosis Strains Employing Automated and Conventional Culture from Lymphadenitis in a Tertiary Care Center, Pondicherry, India. Journal of Research in Medical and Dental Science. 2019;7(3):164-168.
22. Dash M, Samal S, Swain TR, Behera B, Sahu S, Mahapatra S. Diagnostic yield of cartridge based nucleic acid amplification test in Mycobacterium tuberculosis in a tertiary care medical college and hospital of Southern Odisha, India. Int J Res Med Sci. 2019;7(12):4460-

4463. doi: 10.18203/2320-6012. ijrms2019518 3
23. Barnard M, van Pittius NCG, van Helden PD, Bosman M, Coetzee G, Warren RM. The diagnostic performance of Genotype MTBDRplus Version 2 line probe assay is equivalent to the XpertMTB/RIF assay. J Clin Microbiol. 20 12;50(11):3712-3716. doi: 10.1128/JCM.019 58-12
24. Chakraborty A, Ramaswamy S, Shivananjiah AJ, Puttaswamy RB, Chikkavenkatappa N. The role of genexpert in the diagnosis of tubercular pleural effusion in India. Adv Respir Med. 2019;87(5):276-280. doi:10.5603/AR M. 2019.0049
25. Helb D, Jones M, Story E, Boehme C, Wallace E, Ho K, Kop J, Owens MR, Rodgers R, Banada P, Sa H. Rapid detection of Mycobacterium tuberculosis and rifampin resistance by use of on-demand, near-patient technology. Journal of clinical microbiology. 2010 Jan 1;48 (1):229-37.
26. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, Allen J, Tahirli R, Blakemore R, Rustomjee R, Milovic A. Rapid molecular detection of tuberculosis and rifampin resistance. New England Journal of Medicine. 2010 Sep 9;363(11):1005-15.
27. Armand S, Vanhuls P, Delcroix G, Courcol R Lemaître N. Comparison of the Xpert MTB/RIF test with an IS6110-TaqMan real-time PCR assay for direct detection of Mycobacterium tuberculosis in respiratory and non-respiratory specimens. J ClinMicrob. 2011; 49: 1772-6.
28. Boehme CC, Nicol MP, Nabeta P, Michael JS, Gotuzzo E, Tahirli R, Gler MT, Blakemore R, Worodria W, Gray C, Huang L. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. The lancet. 2011 Apr 30;377(9776):1495-505.
29. Marlowe EM, Novak-Weekley SM, Cumpio J, Sharp SE, Momeny MA, Babst A, Carlson JS, Kawamura M, Pandori M. Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of Mycobacterium tuberculosis complex in respiratory specimens. Journal of clinical microbiology. 2011 Apr 1;49(4):1621-3
30. Blakemore R, Story E, Helb D, Kop J, Banada P, Owens MR, Chakravorty S, Jones M, Alland D. Evaluation of the analytical performance of the Xpert MTB/RIF assay. Journal of clinical microbiology. 2010 Jul 1;48(7):2495-501.
31. WHO. Epidemiological fact sheets on HIV and AIDS, 2008 update: Core data on epidemiology and response Djibouti. WHO globalatlas.
32. American Thoracic Society. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. This is a Joint Statement of the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). This statement was endorsed by the Council of the Infectious Diseases Society of America (IDSA), September 1999, and the sections of this statement. Am J Respir Crit Care Med. 2000;161:S221-47.
33. David H, Lévy-Frébault V, Thorel MF. Méthodes de Laboratoirepour Mycobactériologie Clinique. Institute Pasteur, Paris. 1989:85.
34. Ioannidis P, Papaventsis D, Karabela S, Nikolaou S, Panagi M, Raftopoulou E., et al. Cepheid GeneXpert MTB/RIF Assay for Mycobacterium tuberculosis detection and rifampin resistance identification in patients with high clinical suspicion of TB and smear negative microscopy. Journal of clinical microbiology. 2011 Jun 15: JCM-00718.
35. Olusoji D, Eitayeb O, Olanrewaju O. Global Advance Research. J Microbiol. 2013; 2:022-025.
36. Lawson L, Habib AG, Okobi MI, Idiong D, Olajide I, Emenyonu N, Onuoha N, Cuevas LE, Ogiri SO. Pilot study on multidrug resistant tuberculosis in Nigeria. Annals of African medicine. 2010;9(3).
37. Ganguly J, Ray S, Nandi S, Halder S, Kundu S, Mandal A. Astudy to evaluate pattern of rifampicin resistance in cases of sputum positive pulmonary tuberculosis. Journal of Evolution of Medical and Dental Sciences. 2015 Apr 6;4(28):4762-8.
38. Idigbe O, Sofola T, Akinosho R, Onwujekwe D, Odiah F, Okoye R. Initial drug resistance tuberculosis amongst HIV seropositive and seronegative prison inmates in Lagos, Nigeria. InInt Conf AIDS 1998 (Vol. 12, p. 137).
39. Rasaki SO, AJibola AI, Musa SA, Moradeyo AK, Odeigah LO, Abdullateef SG, Adeoti W, Salamat IL. Rifampicin resistant tuberculosis in a secondary health institution in Nigeria, West Africa. Journal of Infectious Diseases and Therapy. 2014 Apr 26.