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Research Article

To Study the Diagnostic Yield of CBNAAT In Diagnosis of Tubercular Pleural Effusion in a Tertiary Care Centre

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ABSTRACT

Background: Tubercular pleural effusion (TPE) is one of the most common forms of extrapulmonary tuberculosis in high-burden countries like India. Its diagnosis is challenging due to the paucibacillary nature of pleural fluid, limiting the utility of conventional methods such as smear microscopy and culture. The Cartridge-Based Nucleic Acid Amplification Test (CBNAAT/Xpert MTB/RIF) offers rapid detection of Mycobacterium tuberculosis (MTB) and rifampicin resistance, but its diagnostic yield in pleural fluid remains variable.

Objectives: To evaluate the diagnostic yield of CBNAAT in pleural fluid samples of patients with suspected TPE and to study its association with ADA levels and cytological findings.

Materials and Methods: This hospital-based cross-sectional observational study was conducted at PGIMER and Capital Hospital, Bhubaneswar, over 12 months (May 2024 – April 2025). A total of 150 patients with clinically and radiologically diagnosed pleural effusions were included. Detailed clinical assessment, chest radiography, blood tests, and pleural fluid analysis (biochemical, cytology, ADA, AFB smear, and CBNAAT) were performed. Data were analyzed using SPSS v21, with diagnostic yield expressed in terms of positivity rates.

Results: Among 150 patients, the mean age was 42.8 ± 15.6 years, with male predominance (65.3%). The most common symptoms were dyspnea (93.3%) and fever (80%). Pleural fluid analysis revealed lymphocytic predominance in 94.7% and ADA ≥ 40 U/L in 92%. CBNAAT was positive in 30% of patients, while AFB smear showed positivity in only 3.3%. Rifampicin resistance was detected in 2% of cases. Most CBNAAT-positive cases also had high ADA and lymphocyte predominance.

Conclusion: CBNAAT demonstrated a moderate diagnostic yield (30%) in pleural fluid but provided high specificity and rapid detection of rifampicin resistance, making it a valuable adjunct in diagnosing TPE. When used alongside ADA and cytology, CBNAAT enhances diagnostic accuracy and facilitates the timely initiation of appropriate therapy in high-burden settings.

Keywords*: Tubercular pleural effusion, CBNAAT, ADA, cytology, rifampicin resistance, diagnostic yield.*

INTRODUCTION

Tuberculosis (TB) continues to remain a significant global health problem, particularly in developing countries such as India, which carries the highest burden worldwide [1]. While pulmonary tuberculosis (PTB) is the most common presentation, extrapulmonary tuberculosis (EPTB) accounts for a substantial proportion of cases, ranging from 15% to

53% depending on geographic region and population studied [2]. Among EPTB manifestations, tubercular pleural effusion (TPE) is one of the most frequent, second only to peripheral lymph node TB [3].

The pathogenesis of TPE is attributed to a delayed hypersensitivity reaction to Mycobacterium tuberculosis (MTB) antigens in the pleural space, leading to accumulation of protein-rich fluid with lymphocytic predominance [4]. However, the diagnosis of TPE remains a challenge due to its paucibacillary nature, where conventional diagnostic methods such as pleural fluid Ziehl–Neelsen (ZN) smear for acid-fast bacilli (AFB) and mycobacterial culture have limited sensitivity. While culture is considered the gold standard, its positivity in pleural fluid is only around 20–30% and requires 4–6 weeks for results, making it less useful in routine clinical practice [5,6].

Biochemical markers such as Adenosine Deaminase (ADA) and lymphocyte predominance in pleural fluid are widely used as surrogate indicators for TPE, with ADA ≥ 40 U/L being highly suggestive in endemic regions [7]. However, ADA can be elevated in other conditions such as empyema, rheumatoid pleuritis, and some malignancies, thereby limiting its specificity [8].

The introduction of nucleic acid amplification tests (NAATs) has revolutionized TB diagnostics by providing rapid, specific, and relatively sensitive detection. Among these, the Cartridge-Based Nucleic Acid Amplification Test (CBNAAT/GeneXpert MTB/RIF assay) has emerged as a promising tool. It simultaneously detects MTB DNA and rifampicin resistance within two hours and was endorsed by the World Health Organization (WHO) in 2010 as an initial diagnostic test for suspected multidrug-resistant TB and HIV-associated TB [9].

While CBNAAT shows excellent sensitivity and specificity in sputum samples, its role in pleural fluid is less clear. Studies from India and other high-burden countries have demonstrated variable diagnostic yields ranging from 15% to 50% in TPE, attributed to the paucibacillary nature of the disease [10,11]. Nonetheless, the specificity of CBNAAT in pleural fluid is consistently high, often exceeding 95% [12]. Hence, CBNAAT may serve as a useful adjunctive tool when interpreted in combination with ADA levels, cytology, and clinical findings.

Given the high burden of TPE in India and the limitations of existing diagnostic modalities, it is essential to evaluate the diagnostic yield of CBNAAT in pleural fluid samples. This study was therefore undertaken to determine the role of CBNAAT in diagnosing TPE and to study its association with ADA levels and pleural fluid cytology in patients presenting with pleural effusion at a tertiary care center in Eastern India.

MATERIAL AND METHODS

Study Design and Setting

This was a **hospital-based, cross-sectional observational study** conducted in the Department of Respiratory Medicine at PGIMER and Capital Hospital, Bhubaneswar, over 12 months **(May 2024 – April 2025)**.

Study Population

The study included **150 patients** attending OPD and IPD of the Department of Respiratory Medicine, who were **clinically and radiologically diagnosed with pleural effusion**.

Sample Size Calculation

Sample size was calculated using the formula:

n=Z2×p×(1−p)/d2n = Z^2 \times p \times (1-p) / d^2n=Z2×p×(1−p)/d2

where:

- n = sample size
- Z = confidence level (95%)
- p = anticipated diagnostic yield of CBNAAT
- d = desired level of precision.

Based on previous studies, the minimum required sample size was estimated as **150 patients**.

Inclusion Criteria

1. Patients > 18 years of age, willing to provide written informed consent.
2. Patients with a clinical history suggestive of tuberculosis and **radiological evidence of pleural effusion**.
3. **Exudative pleural effusion with lymphocyte predominance (≥70%)** and ADA ≥ 40 U/L (according to Light's criteria).
4. Patients with sputum AFB positivity or sputum CBNAAT positivity along with pleural effusion.

Exclusion Criteria

1. Exudative pleural effusions with neutrophil predominance or lymphocyte predominance with ADA < 40 U/L.
2. Transudative pleural effusions.
3. Patients with unresolved pleural effusion after six months of ATT.
4. Patients unwilling to provide informed consent.

Study Tools and Techniques

Each enrolled patient underwent a detailed evaluation using the following tools:

- **Clinical assessment**: Detailed history, physical examination, and symptom recording (fever, night sweats, anorexia, weight loss, hemoptysis).
- **Radiological assessment**: Chest X-ray for confirmation of pleural effusion.
- **Laboratory investigations**:
    - Blood tests: CBC, FBS, HbA1c, LFT, RFT, BT, CT, PT-INR, HIV, HBsAg, HCV.
    - **Sputum examination**: Ziehl–Neelsen smear for AFB, CBNAAT.
    - **Pleural fluid analysis**:
        - Biochemical: Protein, glucose, LDH.
        - Cytology: Cell counts and differential count.
        - ADA (Adenosine Deaminase) estimation.
        - CBNAAT (GeneXpert MTB/RIF assay) for detection of *Mycobacterium tuberculosis* and rifampicin resistance.
        - AFB smear (Ziehl–Neelsen staining).
- **Ultrasonography** was used wherever needed for diagnostic thoracocentesis guidance.

Ethical Considerations

- Written informed consent was obtained from all participants.
- Confidentiality of patient data was maintained throughout the study.
- Vulnerable groups were not included.
- Ethical clearance was obtained from the Institutional Ethics Committee of PGIMER & Capital Hospital, Bhubaneswar.

Statistical Analysis

Data were recorded in a structured proforma and entered into Microsoft Excel. Statistical analysis was performed using **SPSS software (version 21)**. Descriptive statistics (mean, standard deviation, percentages) were used for demographic and baseline variables. Diagnostic yield of CBNAAT was calculated in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), using ADA and cytological findings as reference standards. Chi-square test and Student's t-test were applied where appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

Baseline Characteristics of Study Population

A total of **150 patients** with pleural effusion were included in the study. The demographic and clinical profile is shown below.

Table 1: Demographic profile of patients (n = 150)

Parameter	Number of patients (%)
Age (years)	
18–30	32 (21.3%)
31–45	48 (32.0%)
46–60	45 (30.0%)
> 60	25 (16.7%)
Mean ± SD	42.8 ± 15.6
Sex	
Male	98 (65.3%)
Female	52 (34.7%)

Clinical Presentation

Table 2: Clinical symptoms among the study population

Symptom	Number of patients (%)
Fever	120 (80.0%)
Night sweats	86 (57.3%)
Loss of appetite	102 (68.0%)
Weight loss	95 (63.3%)
Hemoptysis	15 (10.0%)
Dyspnea	140 (93.3%)
Chest pain	110 (73.3%)

Pleural Fluid Analysis

Table 3: Pleural fluid characteristics (n = 150)

Parameter	Mean ± SD / n (%)
Appearance	Straw colored – 130 (86.7%) Hemorrhagic – 20 (13.3%)
Cell count (cells/mm³)	1250 ± 340
Lymphocyte predominance	142 (94.7%)
Neutrophil predominance	8 (5.3%)
ADA level (U/L)	67.5 ± 15.2
ADA ≥ 40 U/L	138 (92.0%)

Diagnostic Yield of CBNAAT

Table 4: Diagnostic performance of pleural fluid CBNAAT

Test result	Number of patients (%)
CBNAAT Positive for MTB	45 (30.0%)
CBNAAT Negative	105 (70.0%)
Rifampicin resistance	3 (2.0%)

Association between CBNAAT, ADA, and Lymphocyte Count

Table 5: Correlation between CBNAAT positivity and pleural fluid ADA levels

ADA levels (U/L)	CBNAAT Positive (n=45)	CBNAAT Negative (n=105)	p-value
≥ 40	44 (97.8%)	94 (89.5%)	0.08
< 40	1 (2.2%)	11 (10.5%)	

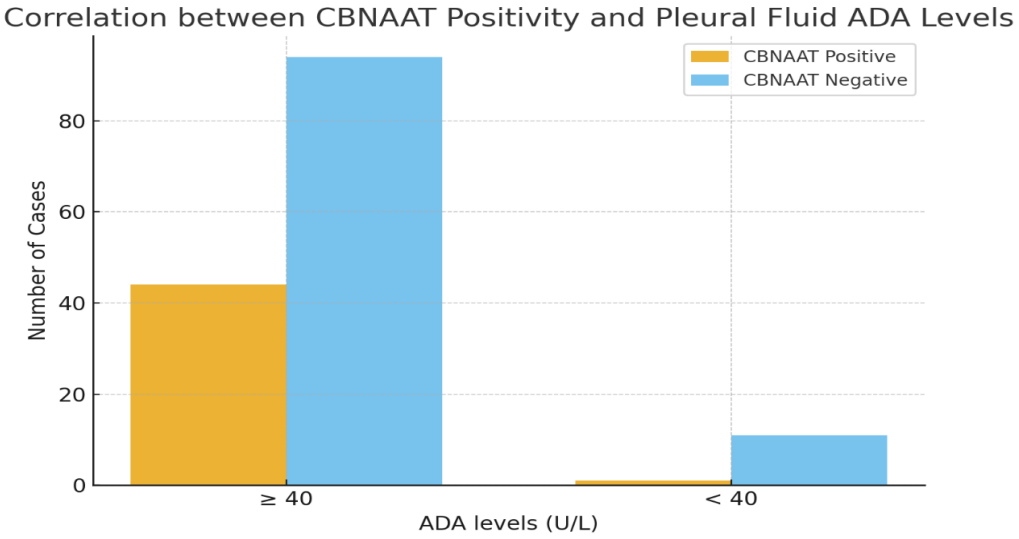


Figure 1: Correlation between CBNAAT positivity and pleural fluid ADA levels.

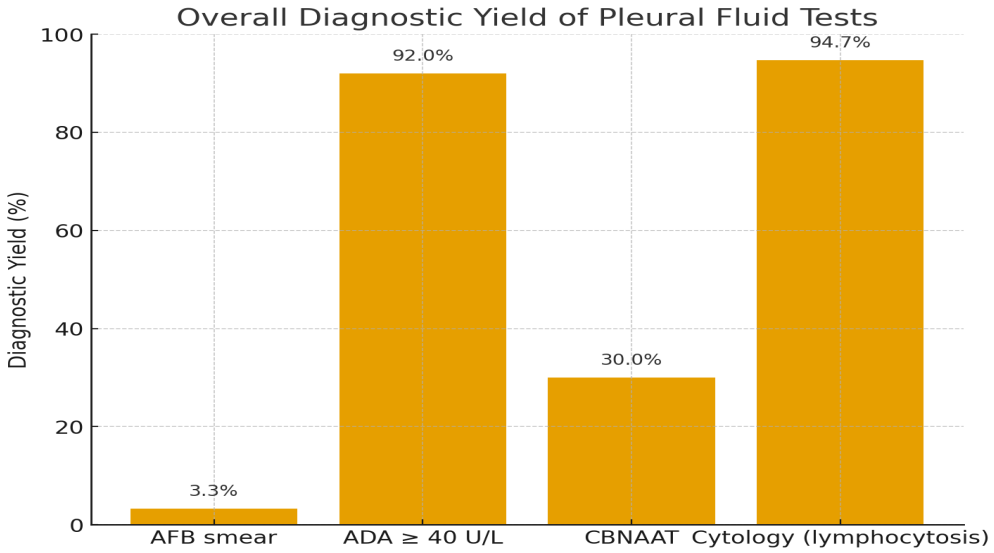
Table 6: Correlation between CBNAAT positivity and pleural fluid lymphocyte count (%)

Lymphocyte %	CBNAAT Positive (n=45)	CBNAAT Negative (n=105)	p-value
≥ 70%	42 (93.3%)	100 (95.2%)	0.65
< 70%	3 (6.7%)	5 (4.8%)	

Summary of Diagnostic Yield

Table 7: Overall diagnostic yield of pleural fluid tests

Investigation	Positive cases (n=150)	Diagnostic yield (%)
AFB smear	5	3.3%
ADA ≥ 40 U/L	138	92.0%
CBNAAT	45	30.0%
Cytology (lymphocytosis)	142	94.7%



Figure; 2 Overall diagnostic yield of pleural fluid tests

Laboratory Investigations

Table 8: Baseline Hematological and Biochemical Investigations of Study Population (n = 150)

Parameter	Mean ± SD / Range	Abnormal values n (%)
Hematological tests		
Hemoglobin (g/dL)	11.2 ± 2.1	65 (43.3%)
Total Leukocyte Count (/mm³)	8,200 ± 2,450	22 (14.7%)
Platelet Count (/mm³)	2.85 ± 0.75 × 10^5	15 (10.0%)
Biochemical tests		
FBS (mg/dL)	102 ± 28	25 (16.7%)
HbA1c (%)	5.8 ± 1.1	28 (18.7%)
LFT (ALT, AST, Bilirubin)	Within normal in majority	18 (12.0%)
RFT (Urea, Creatinine)	Normal in majority	12 (8.0%)
Coagulation profile		
BT (min)	2.4 ± 0.6	8 (5.3%)
CT (min)	5.1 ± 1.2	10 (6.7%)
PT-INR	1.05 ± 0.15	12 (8.0%)
Infectious disease markers		
HIV	Positive – 3 (2.0%)	Negative – 147 (98.0%)
HBsAg	Positive – 5 (3.3%)	Negative – 145 (96.7%)
HCV	Positive – 2 (1.3%)	Negative – 148 (98.7%)

Pleural Fluid Analysis

Table 9: Biochemical characteristics of pleural fluid (n = 150)

Parameter	Mean ± SD / Range	Abnormal values n (%)
Protein (g/dL)	4.9 ± 0.8 (Range: 3.2–6.5)	140 (93.3%) ≥ 3.0 g/dL (exudative)
Glucose (mg/dL)	65 ± 18 (Range: 30–110)	35 (23.3%) < 60 mg/dL
LDH (U/L)	520 ± 160 (Range: 300–950)	132 (88.0%) > 2/3 of serum upper limit

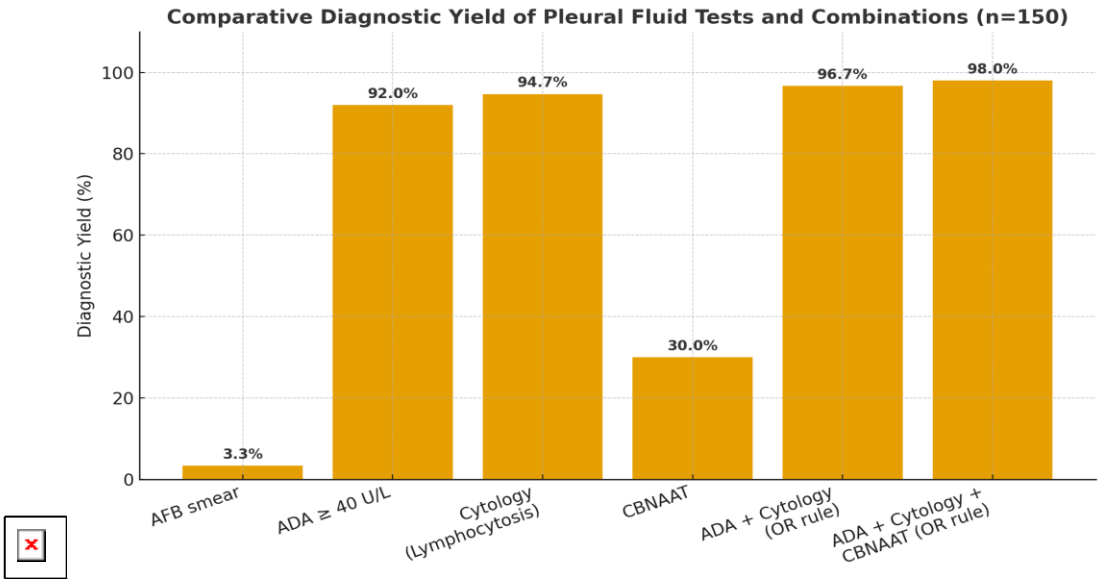
Radiological Assessment

Table 10: Chest X-ray findings in study population (n = 150)

Radiological feature	Number of patients (%)
Side of pleural effusion	
– Right sided	85 (56.7%)
– Left-sided	60 (40.0%)
– Bilateral	5 (3.3%)
Extent of effusion	
– Minimal	25 (16.7%)
– Moderate	95 (63.3%)
– Massive	30 (20.0%)
Associated radiological features	
– Mediastinal shift	22 (14.7%)
– Underlying parenchymal lesion	18 (12.0%)
– Consolidation/opacity	12 (8.0%)
– Fibrotic bands/pleural thickening	10 (6.7%)

Table;11 Comparative Diagnostic Yield of Pleural Fluid Tests and Their Combinations (n = 150)

Diagnostic Method	Positive Cases (n)	Diagnostic Yield (%)
AFB smear	5	3.3%
ADA ≥ 40 U/L	138	92.0%
Cytology (Lymphocytosis)	142	94.7%
CBNAAT	45	30.0%
ADA ≥ 40 U/L + Cytology (OR rule)	145	96.7%
ADA + Cytology + CBNAAT (OR rule)	147	98.0%



Figure; 3 Comparative Diagnostic Yield of Pleural Fluid Tests and Combinations (n = 150)

DISCUSSION

Tubercular pleural effusion (TPE) remains one of the most common forms of extrapulmonary tuberculosis in India and other high-burden countries [1–3]. The diagnostic challenge in TPE arises from its **paucibacillary nature**, which limits the utility of direct microbiological methods such as smear microscopy and culture [4–6]. In our study, pleural fluid AFB smear positivity was only 3.3%, which is consistent with earlier reports showing a sensitivity of <10% [5,6]. Mycobacterial culture, although considered the gold standard, has a low yield in pleural fluid (20–30%) and is time-consuming [6].

Biochemical tests such as **ADA estimation** remain valuable, particularly in endemic regions. In our cohort, ADA ≥ 40 U/L was seen in 92% of cases, aligning with previous meta-analyses showing high sensitivity for ADA in TPE diagnosis [7]. However, as highlighted in prior studies, elevated ADA is not disease-specific and can occur in empyema, rheumatoid pleuritis, and some malignancies [8]. Hence, ADA should be interpreted in conjunction with cytology and clinical findings.

The **Cartridge-Based Nucleic Acid Amplification Test (CBNAAT/Xpert MTB/RIF)** has emerged as a promising rapid diagnostic tool for tuberculosis, endorsed by WHO for pulmonary and certain extrapulmonary specimens [9]. In our study, CBNAAT detected *Mycobacterium tuberculosis* in 30% of pleural fluid samples, with rifampicin resistance detected in 2%. This diagnostic yield is comparable to previous Indian studies, which have reported positivity rates ranging from 15–50% [10,11]. The variability is likely due to differences in patient selection, bacillary load, and pre-analytical factors.

Despite its **moderate sensitivity**, CBNAAT demonstrates excellent **specificity (>95%)** in pleural fluid, making it a reliable rule-in test when positive [12]. Its ability to detect rifampicin resistance within hours is a major advantage over culture, which requires weeks. In our study, the detection of rifampicin resistance in 2% of cases highlights its utility in guiding early initiation of appropriate therapy.

When CBNAAT was correlated with pleural fluid ADA and cytology, we found that most CBNAAT-positive patients had ADA ≥ 40 U/L and lymphocyte-predominant effusion, consistent with the pathogenesis of TPE [4,7]. However, a subset of ADA-high patients were CBNAAT negative, reaffirming that CBNAAT should not be used in isolation but rather as part of a **diagnostic algorithm**.

Overall, our findings emphasize that while **ADA and cytology provide high sensitivity**, CBNAAT adds significant value by offering **rapid and specific confirmation of tuberculosis** and by detecting drug resistance. This is particularly crucial in high-burden regions like India, where early diagnosis and initiation of appropriate treatment are essential to reducing morbidity, mortality, and transmission [1,9].

CONCLUSION

Pleural effusion is a common clinical problem with varied causes. This study emphasizes the significance of pleural fluid analysis, combined with laboratory tests and radiological imaging, in distinguishing between transudative and exudative effusions. A combined diagnostic approach ensures accurate diagnosis, timely treatment, and improved patient outcomes.

REFERENCES

1. World Health Organization. *Global Tuberculosis Report 2023*. Geneva: WHO; 2023.
2. Sharma SK, Mohan A. Extrapulmonary tuberculosis. *Indian J Med Res*. 2004;120(4):316–353.
3. Chakrabarti B, Davies PD. Pleural tuberculosis. *Monaldi Arch Chest Dis*. 2006;65(1):26–33.
4. Light RW. Update on tuberculous pleural effusion. *Respirology*. 2010;15(3):451–458.
5. Conde MB, Loivos AC, Rezende VM, et al. Yield of sputum induction in the diagnosis of pleural tuberculosis. *Am J Respir Crit Care Med*. 2003;167(5):723–725.
6. Valdés L, Alvarez D, San José E, et al. Tuberculous pleurisy: a study of 254 patients. *Arch Intern Med*. 1998;158(18):2017–2021.
7. Aggarwal AN, Agarwal R, Sehgal IS, Dhooria S. Adenosine deaminase for diagnosis of tubercular pleural effusion: A systematic review and meta-analysis. *PLoS One*. 2019;14(3):e0213728.
8. Porcel JM. Biomarkers in the diagnosis of pleural diseases: a 2018 update. *Ther Adv Respir Dis*. 2018;12:1753466618808660.
9. World Health Organization. *WHO endorses new rapid tuberculosis test*. Geneva: WHO; 2010.
10. Chakraborty A, Ramaswamy S, Shivananjiah AJ, et al. The role of GeneXpert in the diagnosis of tubercular pleural effusion in India. *Adv Respir Med*. 2019;87(5):276–280.
11. Nishal N, Sharma A, Sharma N, et al. Diagnostic yield of CBNAAT in the diagnosis of extrapulmonary tuberculosis: A prospective observational study. *Lung India*. 2022;39(5):443–448.
12. Sehgal IS, Dhooria S, Aggarwal AN, Behera D, Agarwal R. Diagnostic performance of Xpert MTB/RIF in tuberculous pleural effusion: Systematic review and meta-analysis. *J Clin Microbiol*. 2016;54(4):1133–1136.