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Original Research Article

EVALUATING THE ROLE OF ADA AND GENEXPERT IN THE DIAGNOSIS OF EXUDATIVE PLEURAL EFFUSION: A RETROSPECTIVE STUDY FROM A TUBERCULOSIS-ENDEMIC REGION

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ABSTRACT

Background: Tuberculous pleural effusion remains a diagnostic challenge, especially in high-burden settings like India. While adenosine deaminase (ADA) is widely used, its specificity is limited. Cartridge-Based Nucleic Acid Amplification Test (CBNAAT/GeneXpert) offers high specificity for tuberculosis (TB) detection, but its sensitivity in pleural fluid is variable. This study aimed to evaluate the diagnostic utility of CBNAAT in pleural effusion and compare it with ADA levels.

Materials and Methods: A retrospective, observational study was conducted at a tertiary care center over two years, including 235 patients with pleural effusion. Clinical, radiological, and biochemical profiles were recorded. Pleural fluid was analyzed for ADA levels and subjected to CBNAAT. Final diagnoses were categorized into tuberculous, malignant, and other causes. Statistical analyses included sensitivity calculation, chi-square testing, and Cohen's kappa for concordance.

Results: Out of 235 patients, 164 were diagnosed with tuberculous pleural effusion and 11 with malignancy. CBNAAT detected TB in only 36 patients, yielding a sensitivity of 21.95%, though with high specificity. ADA >40 IU/L was observed in a majority of TB cases. CBNAAT positivity was significantly associated with elevated ADA levels ($p < 0.001$). All malignant effusions occurred in patients over 40 years of age, whereas 55% of TB cases occurred in those aged ≤40. Concordance between ADA and CBNAAT was low (kappa = 0.22), highlighting their complementary roles.

Conclusion: While CBNAAT offers high specificity, its limited sensitivity restricts its use as a standalone diagnostic tool for pleural TB. ADA remains useful for screening, especially in younger patients. Combining ADA with CBNAAT improves diagnostic yield and is recommended in cases with high clinical suspicion and ADA >40 IU/L.

Keywords: Tuberculous pleural effusion, CBNAAT, GeneXpert, ADA, pleural fluid, diagnostic accuracy, sensitivity, specificity.

INTRODUCTION

Pleural effusion, defined as the accumulation of fluid within the pleural space, is a frequent clinical finding across multiple specialties, including respiratory, cardiology, and oncology. The causes of pleural effusion range from systemic conditions such as congestive heart failure to localized processes like

infections, malignancies, and inflammatory disorders. Among exudative pleural effusions—those characterized by high protein content and inflammatory activity—tuberculosis and malignancy are recognized as the two most prevalent causes, particularly in high tuberculosis (TB) burden countries such as India.[1,2]

Tuberculous pleural effusion (TPE) represents one of the most common forms of extrapulmonary TB. It typically affects younger patients and demonstrates a male predominance. Clinically, TPE presents with symptoms such as fever, cough, chest pain, and weight loss, often mimicking other respiratory conditions. The pleural fluid is usually straw-colored, exudative, and lymphocyte-predominant. Despite its clinical relevance, diagnosing TPE remains a challenge due to its paucibacillary nature. Conventional diagnostic tools such as Ziehl–Neelsen (ZN) smear and culture for Mycobacterium tuberculosis have limited utility in pleural fluid, as smear positivity is rare and culture yields are often delayed and inconsistent.[3,4]

To overcome these limitations, surrogate biomarkers have been adopted. Among them, adenosine deaminase (ADA) has gained prominence as a sensitive and cost-effective tool for diagnosing TPE. ADA is an enzyme involved in purine metabolism and is secreted by activated T lymphocytes. Elevated ADA levels in pleural fluid, particularly values exceeding 40 IU/L, are considered highly suggestive of TB in the right clinical context. ADA's wide availability and affordability make it especially useful in resource-limited settings. However, its lack of specificity remains a concern, as increased levels can also be seen in empyema, certain lymphomas, and complicated parapneumonic effusions. Therefore, while ADA serves well as an initial screening test, it cannot be solely relied upon for definitive diagnosis.[5]

Recent advancements in molecular diagnostics have introduced the GeneXpert MTB/RIF assay (CBNAAT), a cartridge-based nucleic acid amplification test that enables rapid detection of Mycobacterium tuberculosis and rifampicin resistance. GeneXpert has shown excellent specificity and rapid turnaround time, especially in pulmonary specimens. However, its diagnostic yield in pleural fluid remains limited due to the inherently low bacillary burden in such samples. As a result, while a positive GeneXpert result in pleural fluid is considered confirmatory, a negative result does not exclude TPE, particularly in clinically suspected cases with elevated ADA.[6,7]

Malignant pleural effusion (MPE) is another significant cause of exudative effusion, especially among older individuals. It is commonly associated with primary malignancies of the lung, breast, ovary, and hematologic systems. Diagnosis of MPE primarily relies on pleural fluid cytology, which has high specificity but limited sensitivity. In cases where cytological analysis is inconclusive, additional diagnostic interventions such as image-guided pleural biopsy or thoracoscopy are often required to establish a definitive diagnosis.[8,9]

Given the overlapping clinical features and diagnostic limitations of various tests, a systematic and stepwise approach is essential. In TB-endemic settings, ADA serves as a useful initial screening tool, while GeneXpert can be utilized selectively to provide microbiological confirmation. Pleural fluid cytology continues to play a central role in the evaluation of suspected malignancy. Integrating clinical assessment with biochemical and molecular investigations enhances diagnostic precision, minimizes unnecessary invasive procedures, and enables early initiation of appropriate therapy.[10,11]

This study was designed to evaluate the diagnostic performance of ADA, GeneXpert, ZN staining, and cytology in patients with exudative pleural effusion. Specifically, it aimed to assess the concordance between ADA and GeneXpert, examine detection rates across different ADA strata, and categorize pleural effusion etiologies, with particular emphasis on tuberculosis and malignancy. Through this approach, the study seeks to support the formulation of a pragmatic diagnostic algorithm tailored for high TB burden and resource-constrained healthcare environments.

MATERIALS AND METHODS

Study Design and Setting

This was a retrospective, observational study conducted in the Department of Respiratory Medicine at Dr. N. D. Desai Faculty of Medical Science and Research, Dharmsinh Desai University, Nadiad. It received ethical approval from the Institutional Ethics Committee (Protocol No. Dr. NDDFMSR/IEC/2025/01/05) on 07 February 2025. The study involved the evaluation of two years patient data, pleural fluid analysis in patients with exudative effusions, with a specific focus on assessing the diagnostic role of GeneXpert/CBNAAT in identifying tuberculous pleural effusion.

Study Population

The study included all patients aged 16 years or older who presented with radiological evidence of pleural effusion—either on chest X-ray or computed tomography (CT)—and underwent thoracocentesis during the study period. Patient records were reviewed for relevant clinical details and pleural fluid analysis results.

Figure 1: Cohort flow diagram showing the selection and classification of study participants based on pleural fluid analysis and final diagnosis

Inclusion and Exclusion Criteria

Patients were eligible if they had undergone pleural fluid aspiration and had complete records of biochemical, cytological, and microbiological analysis. Excluded from the study were patients younger than 16 years, those with transudative pleural effusions as defined by Light's criteria, and cases with missing or incomplete data.

Data Collection and Diagnostic Workup

Data were retrieved from the hospital's Medical Records Department (MRD). For each case, demographic details, imaging findings, and pleural fluid test results were documented. The pleural fluid was routinely tested for cell count, differential cell count, protein, glucose, and ADA levels. Microbiological analysis included Ziehl–Neelsen (ZN) staining, bacterial culture, and GeneXpert/CBNAAT testing to detect Mycobacterium tuberculosis and rifampicin resistance. Cytological evaluation was performed to identify malignant cells. Effusions were first classified as transudative or exudative based on Light's criteria, and only exudative effusions were considered for further analysis.

Grouping and Analysis

Patients with exudative effusions were classified into three groups according to clinical and investigative findings: tuberculous, malignant, or other causes (such as parapneumonic effusion and empyema). Diagnostic test performance—including that of ADA, GeneXpert, ZN staining, and cytology—was assessed using the final clinical diagnosis as the reference standard. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each diagnostic method. Additionally, agreement between ADA and GeneXpert was measured using Cohen's Kappa coefficient.

Ethical Considerations

The study protocol received administrative approval for access to patient records. As the study was retrospective and based on anonymized data, informed consent from individual patients was not required.

RESULTS

Baseline Characteristics of the Study Population

Out of the total 235 patients, the majority presented with unilateral pleural effusion, observed in 212 cases (90.2%), while bilateral effusion was noted in 23 cases (9.8%). Among those with unilateral effusion, right-sided involvement was more common, accounting for 120 cases (56.6%), compared to 92 cases (43.4%) with left-sided effusion. This right-sided predominance, derived exclusively from the subset of unilateral cases, provides a more precise anatomical interpretation of effusion distribution. These findings are detailed in Table 1 and visually represented in Figure 2.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 235)

Variable	n (%)
Age Group (years)	Mean ± SD: 45.7 ± 15.7 (Range: 17–89)
	16–30: 37 (15.7%) 31–40: 56 (23.8%) 41–50: 49 (20.9%) 51–60: 40 (17.0%) 61–70: 32 (13.6%) 71+: 21 (8.9%)
Gender	
Male	179 (76.2%)
Female	56 (23.8%)
Laterality of Effusion	
Unilateral	212 (90.2%)
Bilateral	23 (9.8%)
Side of Effusion (among unilateral, n=212)	
Right	120 (56.6%)
Left	92 (43.4%)
Type of Effusion	
Exudative	223 (94.9%)
Transudative	12 (5.1%)

Percentages are calculated from the total study population (n = 235).

The study population was predominantly male and middle-aged, with a high prevalence of unilateral, right-sided, and exudative pleural effusions. These findings are consistent with the clinical profile commonly observed in infective or inflammatory causes of pleural disease. Figure 2: Baseline Characteristics of Study Population: A comprehensive visual summary of baseline characteristics is presented in Figure 2, including age distribution, sex, laterality, effusion side, and effusion type. The figure highlights the dominance of males, exudative effusions, and unilateral presentations in the cohort.

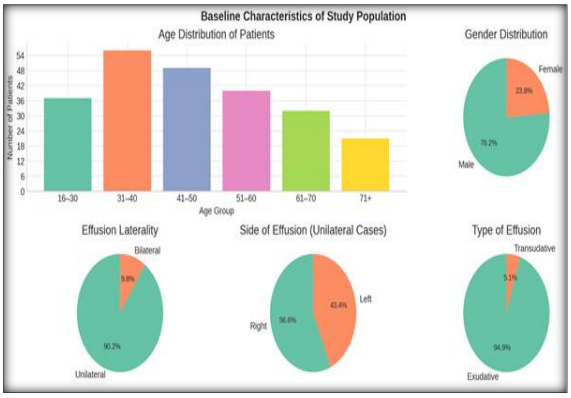

Figure 2: Baseline Characteristics

Pleural Fluid Characteristics Across Diagnostic Groups

To differentiate causes of exudative pleural effusion, pleural fluid parameters were compared across three diagnostic categories: tuberculous (n=164), malignant (n=11), and other causes (n=48). Key biochemical and cytological variables were analyzed to assess their diagnostic value.

Table 2: Pleural Fluid Characteristics Across Diagnostic Groups (Exudative Effusions Only)

Parameter	Tuberculous (Mean ± SD)	Malignant (Mean ± SD)	Others (Mean ± SD)	*p*-value
ADA (U/L)	61.92 ± 19.23	11.95 ± 5.45	52.15 ± 75.00	<0.0001
Pleural Sugar (mg/dL)	79.53 ± 50.52	93.55 ± 48.68	80.02 ± 55.03	0.5115
Pleural Protein (g/dL)	5.31 ± 0.64	4.74 ± 0.52	4.83 ± 0.73	<0.0001
Total Cell Count (/µL)	2537.83 ± 8603.16	2314.55 ± 2662.43	5123.31 ± 7250.78	0.5169
Lymphocyte %	78.36 ± 11.37	69.55 ± 16.80	29.48 ± 21.79	<0.0001

Statistical comparisons are based on one-way ANOVA or Kruskal–Wallis tests. Percentages and values reflect means ± SD for each diagnostic group.

Among the parameters assessed, ADA levels and lymphocyte percentage showed statistically significant differences across groups ($p < 0.0001$), with tuberculous effusions demonstrating markedly elevated ADA and lymphocytic predominance. Pleural protein was also significantly higher in TB compared to malignant effusions. In contrast, pleural sugar and total cell count did not differ significantly between the groups. These findings highlight the diagnostic value of ADA and lymphocyte percentage in distinguishing tuberculous pleural effusion from other causes.

Diagnostic Accuracy of Pleural Fluid Tests

To assess the effectiveness of different pleural fluid investigations in diagnosing tuberculosis and malignancy, we evaluated four commonly used tests: GeneXpert (CBNAAT), ADA (>40 IU/L), Ziehl-Neelsen (ZN) staining, and cytology. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using appropriate clinical or pathological standards.

Table 3: Diagnostic Accuracy of Pleural Fluid Tests in Exudative Effusions (N = 223)

Test	Test Purpose	Positive (n)	Negative (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
GeneXpert (CBNAAT)	TB diagnosis	36	187	21.95	100.00	100.00	31.55
ADA > 40 IU/L	TB diagnosis	176	47	100.00	79.66	93.18	100.00
ZN Stain (AFB)	TB diagnosis	3	220	1.83	100.00	100.00	26.82
Cytology	Malignancy detection	11	212	100.00	100.00	100.00	100.00

Values based on reference diagnosis: TB confirmed by clinical or microbiological methods; malignancy confirmed cytologically.

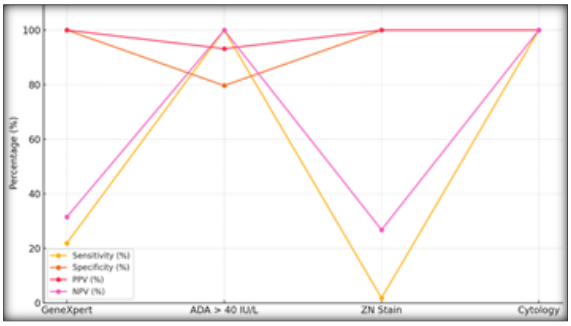

Figure 3: Diagnostic Accuracy of Pleural Fluid Tests

This figure 3 compares sensitivity, specificity, PPV, and NPV across the four diagnostic tests.

Among the evaluated tests, ADA (>40 IU/L) demonstrated the highest sensitivity (100%) and NPV (100%), making it an ideal screening tool for tuberculous pleural effusion. However, its specificity was lower (79.66%), indicating possible false positives. GeneXpert had perfect specificity and PPV (100%), confirming TB accurately when positive, but had low sensitivity (21.95%), missing many true cases. The ZN stain was nearly obsolete with very low sensitivity (1.83%), although its specificity was also perfect. In contrast, cytology provided 100% diagnostic accuracy for malignant pleural effusion in this cohort, underlining its diagnostic reliability.

Concordance Between ADA and GeneXpert for TB Diagnosis

To examine the agreement between ADA (>40 IU/L) and GeneXpert for diagnosing tuberculous pleural effusion, a concordance analysis was performed among 223 patients with exudative effusion. While ADA is known for high sensitivity, GeneXpert is highly specific; this table explores how often they detect the same cases.

Table 4: Concordance Between GeneXpert and ADA (>40 IU/L) in Diagnosing Tuberculous Pleural Effusion (N = 223)

	ADA ≤ 40 IU/L (n)	ADA > 40 IU/L (n)	Total (n)	Row % GeneXpert +
GeneXpert Negative	47	140	187	0.0%
GeneXpert Positive	0	36	36	100.0%
Total	47	176	223	—

Cohen's Kappa Coefficient = 0.098 → Slight agreement, Overlap: 36 patients were positive on both tests, Discordance: 140 patients were ADA-positive but GeneXpert-negative GeneXpert and ADA results are compared in patients with exudative effusions using ADA >40 IU/L as a screening threshold.

This analysis reveals that all GeneXpert-positive cases (n = 36) also had ADA levels > 40 IU/L, confirming that ADA reliably detects cases GeneXpert picks up. However, 140 additional patients were ADA-positive but GeneXpert-negative, suggesting that GeneXpert misses a significant proportion of TB cases. The Cohen's Kappa value of 0.098 reflects only slight agreement between the two tests, reinforcing that while GeneXpert is highly specific, it lacks sensitivity and should not replace ADA in screening protocols. These findings validate ADA as a reliable screening tool and GeneXpert as a confirmatory test in high TB burden settings.

Age and Gender Distribution by Diagnostic Group

To evaluate demographic patterns across diagnostic categories, the distribution of age and gender was analyzed for patients with tuberculous, malignant, and other causes of exudative pleural effusion (N = 223). Differences in age profiles and sex ratios may offer clinical cues to underlying diagnoses.

Table 5: Age and Gender Distribution by Diagnostic Group (Exudative Pleural Effusions Only, N = 223)

Diagnostic Group	n (Total)	Mean Age ± SD (years)	Male (n)	Female (n)
Tuberculous	164	41.84 ± 14.98	135	29
Malignancy	11	65.09 ± 9.35	4	7
Others	48	52.25 ± 13.69	30	18

The values represent mean age with standard deviation, and absolute counts for gender.

Patients with tuberculous pleural effusion were the youngest group (mean age 41.84 years), and the majority were male (82.3%), reflecting the demographic burden of TB. In contrast, malignant effusions occurred at a significantly higher mean age (65.09 years) and showed a female predominance (63.6%). The "others" group displayed intermediate values. These findings indicate a clear age and gender divergence between TB and malignancy, supporting demographic profiling as a supportive tool in initial clinical assessments.

Final Diagnosis Distribution of Exudative Effusions

Among the 223 patients with exudative pleural effusions, the most common diagnosis was tubercular effusion, accounting for 164 cases (73.5%). This was followed by parapneumonic effusions with 36 cases (16.1%), empyema in 12 cases (5.4%), and malignant effusions in 11 cases (4.9%). These findings underscore the overwhelming predominance of tuberculosis as the leading cause of exudative pleural effusions in this study cohort. Parapneumonic and malignant causes were less frequent, while empyema constituted a small yet significant fraction, often reflecting severe or late-stage infections.

The distribution is visually represented in Figure 4, which clearly illustrates the diagnostic breakdown

with both absolute case counts and proportional percentages.

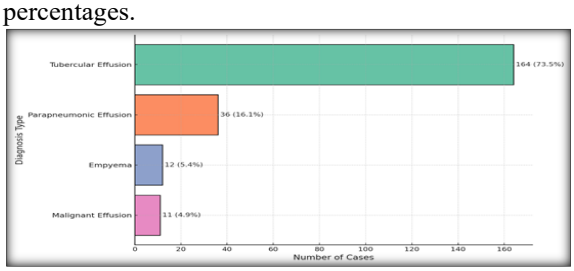

Figure 4: Final Diagnosis Distribution

GeneXpert Detection Rate Stratified by ADA Levels

To explore the relationship between ADA levels and the diagnostic yield of GeneXpert, patients with exudative pleural effusions were stratified based on an ADA threshold of 40 IU/L. The aim was to evaluate whether higher ADA levels correlate with increased molecular detection of tuberculosis.

Table 6: GeneXpert Detection Rate by ADA Level

ADA Range (U/L)	GeneXpert Negative (n)	GeneXpert Positive (n)	Total (n)	Detection Rate (%)
≤ 40 IU/L	47	0	47	0.00%
> 40 IU/L	140	36	176	20.45%

Detection rate calculated as (GeneXpert Positive ÷ Total in ADA range) × 100. ADA measured in U/L.

None of the patients with ADA ≤ 40 IU/L tested positive on GeneXpert, indicating zero detection yield in this group. In contrast, among patients with ADA > 40 IU/L, GeneXpert was positive in 36 of 176 cases (20.45%). This confirms that higher ADA levels significantly increase the likelihood of molecular detection of TB, though GeneXpert still fails to identify nearly 80% of ADA-positive TB cases. Therefore, ADA remains a more sensitive screening tool, while GeneXpert is most effective when used selectively among high-ADA patients to confirm diagnosis.

Age Stratification by Diagnostic Group (Tuberculous vs. Malignant)

To further understand the demographic differences between tuberculous and malignant pleural effusions, age-based stratification was performed. Recognizing age-related diagnostic patterns may assist clinicians in prioritizing investigations and ruling out specific conditions based on demographic predisposition shown in table 7.

Table 7: Age Stratification (≤ 40 vs > 40 years) by Diagnostic Group (Tuberculous vs Malignant, N = 175)

Diagnostic Group	Age ≤ 40 (n)	Age > 40 (n)	Total (n)
Tuberculous	90	74	164
Malignancy	0	11	11
Total	**90**	**85**	**175**
Chi-square test			**$\chi^2 = 10.424$, $p = 0.00131$**

This stratification reveals a marked age-dependent distribution between tuberculous and malignant effusions. All 11 patients diagnosed with malignant pleural effusion were aged above 40 years, while more than half (54.9%) of those with tuberculous effusion were 40 years or younger. The difference was statistically significant ($p = 0.00131$), highlighting a strong association between older age and malignant etiology. This emphasizes the importance of heightened clinical suspicion for malignancy in elderly patients presenting with exudative effusion, whereas younger patients are more likely to have a tuberculous cause.

DISCUSSION

This study provides a detailed analysis of the clinical, biochemical, and diagnostic features of exudative pleural effusion, with a particular focus on tuberculosis in a high-burden region. The results support the ongoing relevance of ADA as a sensitive screening tool while highlighting the limitations and confirmatory role of GeneXpert. The study population predominantly consisted of middle-aged males, with a high prevalence of unilateral and right-sided effusions. These demographic and clinical characteristics align with the established patterns seen in tuberculosis-endemic areas, where exudative effusions are most frequently associated with TB.[12,13] Among pleural fluid parameters, ADA and lymphocyte percentages showed statistically significant elevations in tuberculous effusions compared to malignant or other causes. These findings reaffirm ADA's utility in TB diagnosis, especially in resource-limited settings. Although pleural sugar and total cell count were measured, they showed no significant intergroup variation, indicating a limited role in differential diagnosis.[14]

Table 8 compares our findings with original studies conducted over the past 20 years. Our ADA sensitivity (100%) is at the higher end of published ranges, though specificity is slightly lower. GeneXpert's sensitivity remains poor but consistent with earlier reports, while its specificity remains excellent. This alignment with global findings strengthens the generalizability of our results.

Table 8: Comparison of Diagnostic Parameters – Current Study vs. Previous Original Studies.[15-17]

Parameter	Current Study (2025)	Baba et al. (2008),[1]	Sehgal et al. (2016),[2]	Chakraborty A (2019),-
Mean Age (TB cases)	41.8 ± 15.0	—	—	—
Male (%)	82.3%	—	—	—
ADA Cut-off (IU/L)	>40	≥30	40–70	—
ADA Sensitivity (%)	100%	94%	47–100%	—
ADA Specificity (%)	79.7%	95%	~90%	—
GeneXpert Sensitivity (%)	21.9%	—	46.4–51.4%	22.2%
GeneXpert Specificity (%)	100%	—	98.6–99.8%	75%
ZN Stain Sensitivity (%)	1.8%	—	~10%	—
Cytology Accuracy (MPE)	100%	—	—	—

Diagnostic evaluation showed that ADA (>40 IU/L) had excellent sensitivity (100%) and a high negative predictive value (100%), making it highly effective for ruling out TB when negative. However, its specificity was moderate (79.7%), indicating some false positives. In contrast, GeneXpert showed perfect specificity (100%) and positive predictive value (100%), confirming TB when positive but with low sensitivity (21.9%), highlighting its limitation in detecting all true cases. The ZN stain had negligible sensitivity (1.8%) but retained full specificity. Cytology showed perfect performance in detecting malignant pleural effusion, reaffirming its diagnostic utility. The agreement between ADA and GeneXpert was slight, as evidenced by a low Cohen's Kappa (0.098). Although all GeneXpert-positive patients had elevated ADA, the reverse was not true, with 140 ADA-positive cases not detected by GeneXpert. This underlines the importance of using ADA for screening and GeneXpert for confirmation in high-prevalence settings.[18]

Further, the GeneXpert detection rate was 0% in those with ADA ≤ 40 IU/L and only 20.45% in those with ADA > 40 IU/L, confirming that GeneXpert is more likely to detect TB in patients with high ADA levels but still misses most cases. This supports a two-tiered diagnostic approach. Tuberculosis accounted for over 70% of exudative effusions in this cohort, far exceeding the frequency of parapneumonic effusions, empyema, and malignancy. Stratified analysis also showed that tuberculous effusions were more common in younger males, while malignant effusions occurred in older females. These trends can inform early clinical suspicion.[19,20]

Limitations

This study was conducted at a single center, which may limit the generalizability of the findings to broader populations. The diagnostic gold standard for tuberculosis relied on clinical and biochemical parameters, as culture and biopsy were not universally available. Additionally, the relatively small number of malignant effusion cases restricted comparative analysis in that subgroup.

CONCLUSION

Tuberculosis remains the leading cause of exudative pleural effusion in high-burden settings. ADA continues to serve as a reliable and highly sensitive screening tool, while GeneXpert, despite its excellent specificity, has limited sensitivity and should be used selectively for confirmation. Combining ADA and GeneXpert improves diagnostic accuracy, particularly when ADA levels are elevated. Cytology retains excellent diagnostic yield in malignant effusions. An integrated approach using clinical, biochemical, and molecular tools remains essential for timely and accurate diagnosis.

Declarations

Ethical Approval and Consent to Participate

The study was conducted after obtaining approval from the Institutional Ethics Committee of Dr. N.D. Desai Faculty of Medical Science and Research, Dharmsinh Desai University, Nadiad (Protocol No. Dr. NDDFMSR/IEC/2025/01/05), dated 07 February 2025. As this was a retrospective, record-based study using anonymized data, individual informed consent was waived by the committee.

Consent for Publication

Not applicable. No identifiable personal data or images were used in this manuscript.

Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Author Contributions

- Dr. Jaimin Mansuriya: Conceptualization of the study, data analysis, manuscript drafting, and final approval. (Corresponding Author)
- Dr. Yagnang K. Vyas: Supervision of the study design, critical review of data interpretation, and manuscript editing.
- Dr. Krishnakumar Ashokbhai Patel: Data collection, tabulation, and statistical support.
- Dr. Akansha Singh: Literature review, manuscript formatting, and assistance in final proofing.

REFERENCES

1. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972;77(4):507-13.
2. Gao L, Wang W, Zhang Y, Hu X, An J, Li Y, Chen M, Shen Y. Adenosine deaminase-based measurement in the differential diagnosis of pleural effusion: a multicenter retrospective study. Ther Adv Respir Dis. 2023;17:1-11. doi:10.1177/17534666231155747.
3. Du J, Pan L, Wu H, Zhou Y, Song Y, Wang J. Diagnostic accuracy of Xpert MTB/RIF assay for tuberculous pleurisy: a meta-analysis. PLoS One. 2015;10(4):e0123715.
4. Meldau R, Peter J, Theron G, Calligaro G, Allwood B, Symons G, et al. Comparison of same day diagnostic tools including GeneXpert and unstimulated IFN-γ for the evaluation of pleural tuberculosis: a prospective cohort study. BMC Pulm Med. 2014;14:58.
5. Lusiba JK, Nakiyingi L, Kirenga BJ, Kiragga AN, Lukande R, Wolske J, et al. Evaluation of Cepheid's Xpert MTB/RIF test on pleural fluid in the diagnosis of pleural tuberculosis in Uganda: a prospective cohort study. BMC Res Notes. 2014;7:890.
6. Antonangelo L, Vargas FS, Teixeira LR, Sales RK, Genofre EH, Marchi E, et al. The role of pleural fluid analysis in the diagnosis of pleural effusion. J Bras Pneumol. 2019;45(2):e20180325.
7. Gopi A, Madhavan SM, Sharma SK, Sahn SA. Diagnosis and treatment of tuberculous pleural effusion in 2006. Chest. 2007;131(3):880-9.
8. Maskell NA, Butland RJ; Pleural Diseases Group, Standards of Care Committee, British Thoracic Society. BTS guidelines for the investigation of a unilateral pleural effusion in adults. Thorax. 2003;58(Suppl 2):ii8-17.
9. Hooper C, Lee YC, Maskell N; BTS Pleural Guideline Group. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65(Suppl 2):ii4-17.
10. Kruger D. Evaluating the adult with new-onset pleural effusion. JAAPA. 2013;26(7):20-7.
11. Ferreiro L, Toubes ME, San Jose ME, Suarez-Antelo J, Golpe A, Valdes L. Advances in pleural effusion diagnostics. Expert Rev Respir Med. 2020;14(1):51-66.
12. Papadakis MA, Rabow MW, McQuaid KR. Pleural Effusion. In: Quick Medical Diagnosis & Treatment 2025. New York: McGraw-Hill; 2025.
13. Jindal S. A study of pleural effusion with reference to different diagnostic modalities. Int J Adv Med. 2017;4(1):170-6.
14. Parikh P. Study of 100 cases of pleural effusion with reference to diagnostic approach. Int J Adv Med. 2017;4(1):163-9.
15. Baba K, Hoosen AA, Langeland N, Dyrhol-Riise AM. Adenosine deaminase activity is a sensitive marker for the diagnosis of tuberculous pleuritis in patients with very low CD4 counts. PLoS One. 2008;3(7):e2788. doi:10.1371/journal.pone.0002788.
16. 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):1133-6.
17. 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):276-80.
18. Yalcin NG, Choong CK, Eizenberg N. Anatomy and pathophysiology of the pleura and pleural space. Thorac Surg Clin. 2013;23(1):1-10.
19. Porcel JM. Chest imaging for the diagnosis of complicated parapneumonic effusions. Curr Opin Pulm Med. 2018;24(4):398-402.
20. Tsujimoto N, Saraya T, Light RW, et al. A simple method for differentiating complicated parapneumonic effusion/empyema from parapneumonic effusion using the split pleura sign and the amount of pleural effusion on thoracic CT. PLoS One. 2015;10(6):e0130141.