Section: Miscellaneous

Original Research Article

CORRELATION OF BIOCHEMICAL AND INFLAMMATORY MARKERS WITH CBNAAT BACILLARY LOAD AND HRCT CHEST SEVERITY IN PULMONARY TUBERCULOSIS: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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Received : 13/03/2026
Received in revised form : 01/05/2026
Accepted : 16/05/2026

Keywords:
Pulmonary tuberculosis, CBNAAT, GeneXpert, HRCT, bacillary load, CRP, ESR, ferritin, LDH, ADA, albumin, albumin/globulin ratio.

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DOI: 10.47009/jamp.2026.8.3.54

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (3); 299-308

ABSTRACT

Background: Pulmonary tuberculosis remains a major infectious disease burden. CBNAAT/GeneXpert provides rapid microbiological confirmation and rifampicin-resistance detection, while HRCT chest assesses anatomical disease burden. Biochemical and inflammatory markers may reflect systemic inflammation, immune activation, tissue injury and nutritional depletion. The aim is to evaluate the correlation of selected biochemical and inflammatory markers with CBNAAT bacillary load and HRCT chest severity in pulmonary tuberculosis. **Materials and Methods:** This cross-sectional observational study included 100 CBNAAT-positive pulmonary tuberculosis patients. CBNAAT bacillary load, rifampicin-resistance status, AFB smear grading, HRCT findings and biochemical markers were recorded. HRCT severity was graded as mild, moderate or severe. CRP, ESR, ferritin, LDH, ADA, total protein, albumin, globulin and albumin/globulin ratio were analysed. Correlation analysis, group comparisons, chi-square test and multivariable regression were performed. **Results:** Mean age was 44.8 ± 15.6 years, with 64% males. AFB smear positivity was seen in 62%, and rifampicin resistance in 8%. Common HRCT findings were tree-in-bud appearance (72%), centrilobular nodules (69%), multilobar involvement (64%), consolidation (58%), lymphadenopathy (49%) and cavitation (44%). HRCT severity was mild in 30%, moderate in 40% and severe in 30%. CRP, ESR, ferritin, LDH and ADA increased significantly with HRCT severity and CBNAAT bacillary load, while albumin and albumin/globulin ratio decreased. Higher CBNAAT load was significantly associated with greater HRCT severity ($\chi^2 = 39.82$; $p < 0.001$). CBNAAT load, CRP, ferritin, ADA and albumin were independent predictors of HRCT severity. **Conclusion:** Biochemical and inflammatory markers correlate with CBNAAT bacillary load and HRCT severity in pulmonary tuberculosis. An integrated biochemical–microbiological–radiological approach may improve disease severity assessment and risk stratification.

INTRODUCTION

Tuberculosis remains a major global infectious disease, with pulmonary tuberculosis being the principal form responsible for transmission. It is caused by Mycobacterium tuberculosis, an airborne pathogen that primarily affects the lungs and spreads through droplet nuclei from patients with active pulmonary disease. Despite being preventable and curable, tuberculosis continues to cause high morbidity and mortality due to delayed diagnosis, undetected infectious cases, drug resistance, undernutrition, comorbidities and gaps in treatment initiation. According to the WHO Global Tuberculosis Report 2024, an estimated 10.8 million people developed tuberculosis in 2023, with approximately 1.25 million deaths. India contributed

ISSN (O): 2687-5365; ISSN (P): 2753-6556

the largest share, accounting for 26% of global tuberculosis cases in 2023.[1,2]

India continues to have the highest national tuberculosis burden, making early detection of pulmonary tuberculosis a public-health priority. The National Tuberculosis Elimination Programme reported 25.5 lakh tuberculosis cases in 2023 and 26.07 lakh cases in 2024. India's tuberculosis incidence declined from 237 per lakh population in 2015 to 195 per lakh population in 2023, while tuberculosis deaths declined from 28 to 22 per lakh population during the same period. However, the absolute burden remains high, and pulmonary tuberculosis continues to drive transmission, diagnostic workload and disease-control efforts.[3]

Pulmonary tuberculosis commonly presents with cough, fever, weight loss, night sweats, chest pain, breathlessness and hemoptysis, but clinical presentation is variable. Some patients present with high bacillary burden, while others may have smear-negative, paucibacillary or radiologically subtle disease. Conventional sputum microscopy is rapid and inexpensive but has limited sensitivity, particularly in smear-negative disease. Culture remains an important reference standard, but delayed results limit immediate clinical decision-making. These limitations have increased the role of rapid molecular diagnostics such as CBNAAT/GeneXpert.[4,12]

CBNAAT/GeneXpert enables rapid detection of M. tuberculosis complex and rifampicin resistance. In addition to diagnostic positivity, CBNAAT may provide semi-quantitative bacillary-load categories or cycle threshold values, which are clinically relevant because higher bacillary burden may be associated with infectivity, cavitation, extensive parenchymal involvement and stronger inflammatory response. Therefore, in CBNAAT-positive pulmonary tuberculosis, assessment of bacillary load may provide more useful severity information than simple positive or negative reporting.[4,12]

Radiological imaging is essential because it reflects anatomical disease burden and activity. Although chest radiography is widely used, HRCT chest provides better detection of subtle and active pulmonary tuberculosis patterns, including centrilobular nodules, tree-in-bud appearance, consolidation, cavitation, ground-glass opacity, miliary nodules, bronchiectasis, mediastinal lymphadenopathy and pleural effusion. Adhikari et al. reported that HRCT is more sensitive than chest radiography for identifying disease activity and described typical patterns such as tree-in-bud appearance, consolidation and cavitation.[5]

Several studies support the diagnostic value of HRCT in pulmonary tuberculosis. Adhikari et al. reported tree-in-bud appearance in 69.4%, mediastinal lymphadenopathy in 65.3% and consolidation in 56.9% of active pulmonary tuberculosis cases, with tree-in-bud pattern significantly associated with bacteriologically confirmed disease. Sahu et al. reported HRCT sensitivity of 0.8125 and specificity of 0.8571 compared with culture, while Rasheed et al. reported overall HRCT diagnostic accuracy of 84.26%, sensitivity of 89.09% and specificity of 79.25%. These findings support the use of HRCT not only for diagnosis but also for structured severity assessment.[5–7] Pulmonary tuberculosis also produces systemic inflammatory, immune, tissue-injury and nutritional changes. CRP and ESR reflect systemic inflammation; ferritin reflects acute-phase activation and iron sequestration; LDH may indicate tissue injury; ADA reflects cell-mediated immune activation; albumin is a negative acute-phase reactant and nutritional marker; and albumin/globulin ratio reflects the combined effect of hypoalbuminemia and chronic immune stimulation. These markers are inexpensive and routinely available, making them suitable for integration with microbiological and radiological assessment.[8–11] The biochemical rationale is supported by previous studies. Şahin and Yıldız reported that in pulmonary tuberculosis, BMI, HDL, triglycerides, total protein and albumin decreased, while CRP and ESR increased with increasing radiological stage. Miranda et al. showed that CRP and ferritin were elevated in treatment-naïve pulmonary tuberculosis and decreased during treatment, supporting their role as disease-activity markers. These findings justify correlation of inflammatory markers with HRCT severity and CBNAAT bacillary load.[8,9]

Serum ADA is particularly relevant because tuberculosis is primarily a cell-mediated immune disease. Saini et al. reported significantly higher serum ADA levels in pulmonary tuberculosis patients compared with controls and observed a decrease after the intensive phase of treatment. Arghir et al. found that ADA was significantly associated with bacteriological confirmation, delayed diagnosis, cavitary disease and mortality. These findings support ADA as a tuberculosis-oriented marker of immune activation and severity.[10,11]

Despite advances in diagnosis, pulmonary tuberculosis severity assessment is often fragmented. Microbiology confirms the organism and drug resistance, radiology demonstrates anatomical disease, and biochemistry reflects systemic inflammation, tissue injury and nutritional status. However, the combined relationship between biochemical markers, CBNAAT bacillary load and HRCT severity has been less clearly studied. The present study is therefore designed to evaluate whether CRP, ESR, ferritin, LDH, ADA, albumin and albumin/globulin ratio correlate with CBNAAT bacillary-load category and HRCT severity score in pulmonary tuberculosis, and whether this integrated approach can support better severity stratification and clinical risk assessment.[4–12]

Aim

To evaluate the correlation of selected serum biochemical markers with CBNAAT bacillary burden and HRCT chest severity in patients with pulmonary tuberculosis.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Objectives

1. To correlate serum biochemical markers, including CRP, ESR, ferritin, LDH, ADA, serum albumin and albumin/globulin ratio, with HRCT chest severity score in patients with pulmonary tuberculosis.
2. To correlate serum biochemical markers and HRCT chest findings with CBNAAT results, including Mycobacterium tuberculosis detection, bacillary load category or cycle threshold value, and rifampicin resistance status.

MATERIALS AND METHODS

This hospital-based, cross-sectional observational study was conducted over a period of two years, from February 2024 to January 2026, at Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India, which served as the primary study centre. Patient recruitment, sample collection, and clinical data collection were carried out at the primary study centre. Reporting and interpretation of relevant biochemical, microbiological, CBNAAT, and radiological findings were undertaken with academic and interpretative support from collaborating faculty affiliated with Geetanjali Medical College and Hospital, GITAM Institute of Medical Sciences and Research, Visakhapatnam, and Prathima Institute of Medical Sciences, Karimnagar. The collaborating institutions contributed only to reporting, interpretation, correlation, and academic inputs, and were not independent patient recruitment or sample collection centres.

A total of 100 adult patients clinically suspected or diagnosed with pulmonary tuberculosis, who underwent CBNAAT/GeneXpert testing, HRCT chest imaging and biochemical investigations, were included after obtaining Institutional Ethics Committee approval.

Patients aged 18 years and above with suspected or confirmed pulmonary tuberculosis, available CBNAAT results, HRCT chest findings and required biochemical parameters were included. Patients already on prolonged anti-tubercular treatment, those with extrapulmonary tuberculosis without pulmonary involvement, chronic inflammatory or autoimmune disease, malignancy, severe liver disease, chronic kidney disease, pregnancy where HRCT was not clinically indicated, or incomplete clinical/laboratory/radiological data were excluded.

Demographic and clinical details including age, sex, symptoms, duration of illness, diabetes mellitus, smoking status and past history of tuberculosis were recorded using a predesigned proforma.

Sample Collection and Laboratory Analysis: Relevant clinical samples were collected according to clinical indication and standard institutional protocol.

Sputum / respiratory sample: Early-morning sputum or appropriate respiratory sample was collected for microbiological confirmation. The tests performed included CBNAAT/GeneXpert for detection of Mycobacterium tuberculosis, CBNAAT bacillary load category or cycle threshold value where available, rifampicin resistance status, and AFB smear microscopy with grading where available.

Pleural fluid: In patients with pleural effusion, pleural fluid was collected only when clinically indicated. The tests performed as per institutional protocol included CBNAAT/GeneXpert for Mycobacterium tuberculosis, AFB smear microscopy where available, pleural fluid ADA, total protein, albumin, glucose and LDH. Pleural fluid findings were recorded separately and used for supportive evaluation of pleural involvement.

Blood / serum sample: Venous blood was collected under aseptic precautions. Serum was separated and analysed for CRP, ferritin, LDH, ADA, total protein, albumin and globulin using standard laboratory methods. Albumin/globulin ratio was calculated from serum albumin and globulin values.

Whole blood sample: ESR was measured using the Westergren method or automated ESR method, depending on institutional practice.

HRCT chest was performed as per standard radiology protocol. Findings such as tree-in-bud appearance, centrilobular nodules, consolidation, cavitation, ground-glass opacity, macronodules, miliary nodules, bronchiectasis, mediastinal lymphadenopathy, pleural effusion, fibrotic/fibro-calcific changes and lobar/segmental involvement were documented. A structured HRCT severity score was assigned based on the extent of lung involvement and presence of active disease features. Lung involvement was graded as 0 = no involvement, 1 = <25%, 2 = 25–50% and 3 = >50% involvements, with additional scoring for cavitation, tree-in-bud appearance, consolidation and bilateral disease. The primary outcome was the correlation between serum biochemical/inflammatory markers and HRCT chest severity score. Secondary outcomes included correlation of biochemical markers with CBNAAT bacillary load or cycle threshold value, and association of HRCT severity with CBNAAT bacillary load, rifampicin resistance and individual HRCT findings. Data were analysed using SPSS or equivalent statistical software. Continuous variables were expressed as mean ± SD or median with IQR, and categorical variables as frequency and percentage. Pearson or Spearman correlation was used for correlation analysis. ANOVA/Kruskal–Wallis test, independent t-test/Mann–Whitney U test, chi-square test or Fisher's exact test was used as appropriate. A p-value <0.05 was considered statistically significant. Patient confidentiality was maintained throughout the study.

RESULTS

Among 100 CBNAAT-positive pulmonary tuberculosis patients, the mean age was 44.8 ± 15.6 years, with a male predominance of 64%. The most

ISSN (O): 2687-5365; ISSN (P): 2753-6556

common clinical manifestations were cough, fever and weight loss. A past history of treated tuberculosis was present in 18% of patients. Rifampicin resistance was detected in 8% of cases, while 62% were AFB smear-positive.

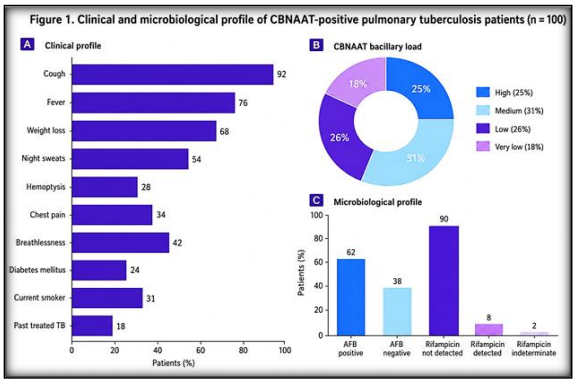

Figure 1: Clinical and microbiological profile of CBNAAT-positive pulmonary tuberculosis patients (n = 100).

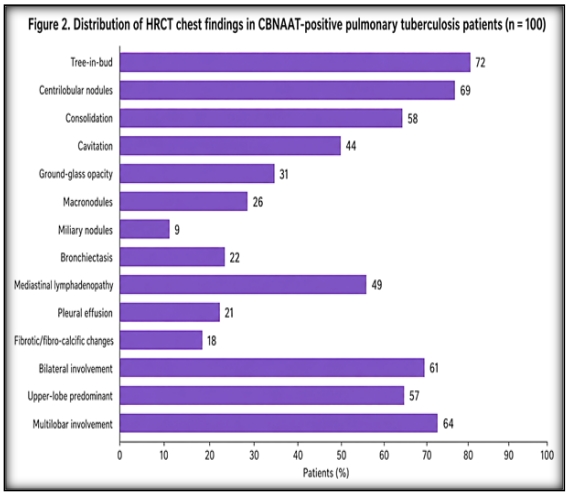

Figure 2: Distribution of HRCT chest findings in CBNAAT-positive pulmonary tuberculosis patients (n = 100)

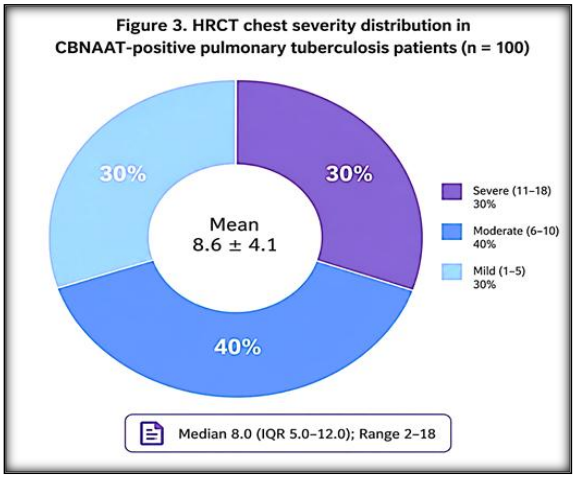

Figure 3: Distribution of HRCT chest severity categories in CBNAAT-positive pulmonary tuberculosis patients (n = 100)

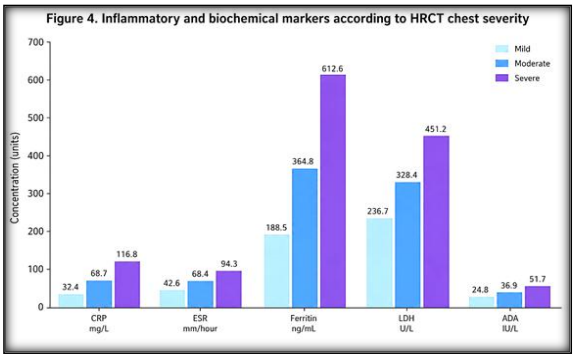

Figure 4: Inflammatory and biochemical marker levels according to HRCT chest severity in pulmonary tuberculosis patients

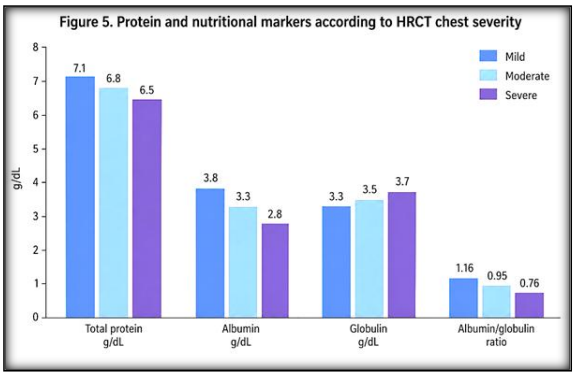

Figure 5: Protein and nutritional markers according to HRCT chest severity in pulmonary tuberculosis patients

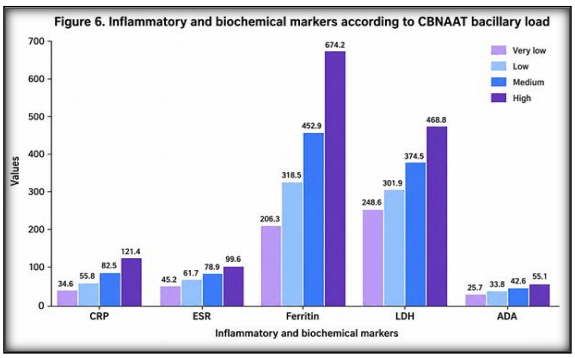

Figure 6: Inflammatory and biochemical marker levels according to CBNAAT bacillary load category in pulmonary tuberculosis patients

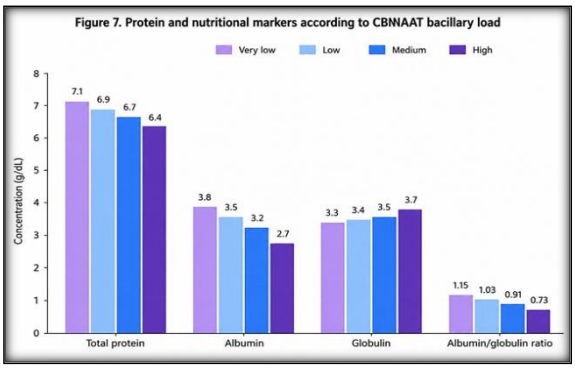

Figure 7: Protein and nutritional markers according to CBNAAT bacillary load category in pulmonary tuberculosis patients

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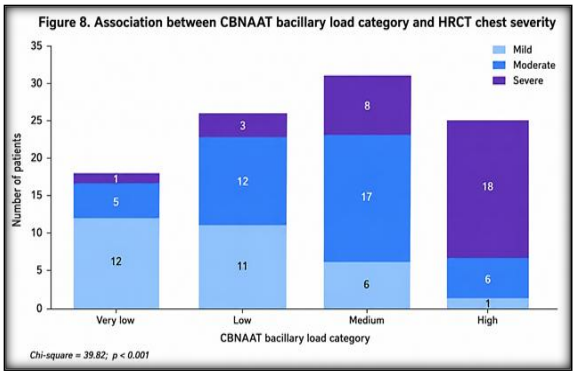

Figure 8: Association between CBNAAT bacillary load category and HRCT chest severity in pulmonary tuberculosis patients

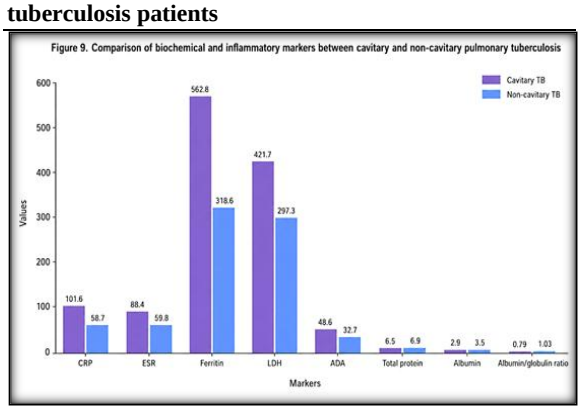

Figure 9: Comparison of biochemical and inflammatory markers between cavitary and non-cavitary pulmonary tuberculosis patients

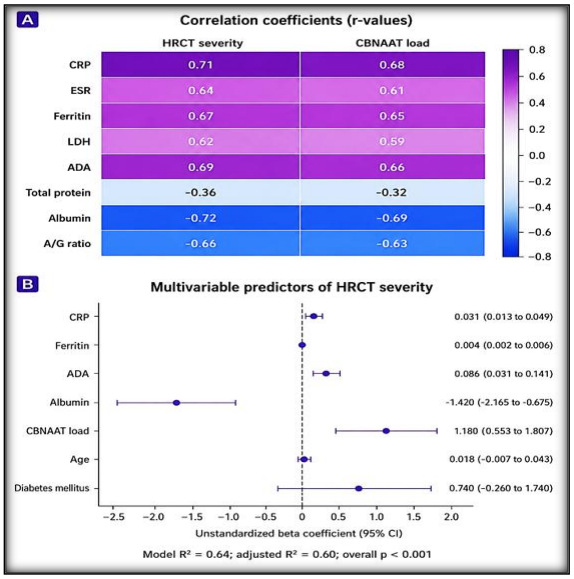

Figure 10: Correlation matrix and multivariable predictors of HRCT chest severity in pulmonary tuberculosis patients

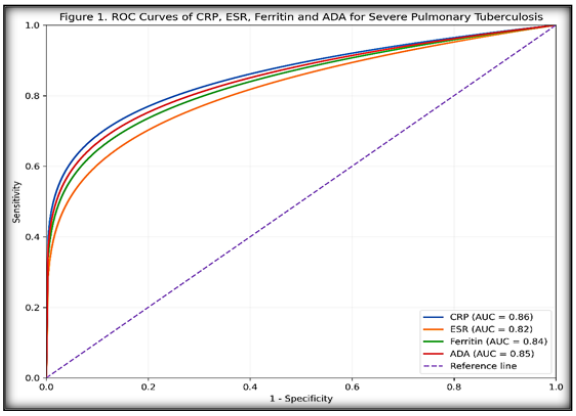

Figure 11: Receiver operating characteristic (ROC) curves of CRP, ESR, ferritin and ADA for prediction of severe pulmonary tuberculosis

ROC Curve: Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of the studied biochemical markers to discriminate severe pulmonary tuberculosis. Among the inflammatory markers, CRP showed good diagnostic performance with an area under the curve (AUC) of 0.86, followed by ADA (0.85), ferritin (0.84) and ESR (0.82), indicating good predictive value for severe disease. Among the remaining markers, serum albumin demonstrated the highest discriminatory ability with an AUC of 0.88, followed by albumin/globulin ratio (0.83) and LDH (0.80), while total protein showed relatively lower performance with an AUC of 0.69. Overall, these findings indicate that serum albumin, CRP, ADA and ferritin were the most useful biomarkers for identifying severe pulmonary tuberculosis, whereas total protein had limited standalone discriminatory value.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Total patients, n = 100
Age, years, mean ± SD	44.8 ± 15.6
Age range, years	18–78
Male, n (%)	64 (64.0)
Female, n (%)	36 (36.0)
Duration of symptoms, weeks, median (IQR)	5.0 (3.0–8.0)
Cough, n (%)	92 (92.0)
Fever, n (%)	76 (76.0)
Weight loss, n (%)	68 (68.0)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Night sweats, n (%)	54 (54.0)
Hemoptysis, n (%)	28 (28.0)
Chest pain, n (%)	34 (34.0)
Breathlessness, n (%)	42 (42.0)
Diabetes mellitus, n (%)	24 (24.0)
Current smoker, n (%)	31 (31.0)
Past history of treated tuberculosis, n (%)	18 (18.0)

Table 2: Microbiological Profile of CBNAAT-Positive Pulmonary Tuberculosis Patients

Microbiological parameter	Total patients, n = 100
CBNAAT positive for Mycobacterium tuberculosis, n (%)	100 (100.0)
Rifampicin resistance not detected, n (%)	90 (90.0)
Rifampicin resistance detected, n (%)	8 (8.0)
Rifampicin resistance indeterminate, n (%)	2 (2.0)
AFB smear positive, n (%)	62 (62.0)
AFB smear negative, n (%)	38 (38.0)

Table 2A: CBNAAT Bacillary Load Category

CBNAAT bacillary load category	n (%)
Very low	**18 (18.0)**
Low	26 (26.0)
Medium	31 (31.0)
High	25 (25.0)
Total	100 (100.0)

Table 2B: AFB Smear Grading Among Smear-Positive Cases

AFB smear grade	n (%) among smear-positive cases, n = 62
Scanty	10 (16.1)
1+	18 (29.0)
2+	20 (32.3)
3+	14 (22.6)
Total	62 (100.0)

Table 3: Distribution of HRCT Chest Findings in CBNAAT-Positive Pulmonary Tuberculosis Patients

HRCT chest finding	Total patients, n = 100
Tree-in-bud appearance	72 (72.0)
Centrilobular nodules	69 (69.0)
Consolidation	58 (58.0)
Cavitation	44 (44.0)
Ground-glass opacity	31 (31.0)
Macronodules	26 (26.0)
Miliary nodules	9 (9.0)
Bronchiectasis	22 (22.0)
Mediastinal lymphadenopathy	49 (49.0)
Pleural effusion	21 (21.0)
Fibrotic/fibro-calcific changes	18 (18.0)
Bilateral lung involvement	61 (61.0)
Upper-lobe predominant involvement	57 (57.0)
Multilobar involvement	64 (64.0)

Table 4: HRCT Chest Severity Grading Among CBNAAT-Positive Pulmonary Tuberculosis Patients

HRCT severity category	HRCT severity score range	n (%)
Mild	1–5	30 (30.0)
Moderate	6–10	40 (40.0)
Severe	11–18	30 (30.0)
Total	—	100 (100.0)
HRCT severity score	**Value**	
Mean ± SD	8.6 ± 4.1	
Median (IQR)	8.0 (5.0–12.0)	
Range	2–18	

Table 5: Biochemical and Inflammatory Marker Levels According to HRCT Chest Severity

Marker	Mild HRCT severity n = 30	Moderate HRCT severity n = 40	Severe HRCT severity n = 30	p-value
CRP, mg/L	32.4 ± 18.6	68.7 ± 31.4	116.8 ± 45.2	<0.001
ESR, mm/hour	42.6 ± 18.1	68.4 ± 22.7	94.3 ± 26.8	<0.001
Ferritin, ng/mL	188.5 ± 92.4	364.8 ± 168.7	612.6 ± 284.5	<0.001
LDH, U/L	236.7 ± 74.5	328.4 ± 96.8	451.2 ± 128.6	<0.001
ADA, U/L	24.8 ± 8.7	36.9 ± 11.5	51.7 ± 15.3	<0.001
Total protein, g/dL	7.1 ± 0.6	6.8 ± 0.7	6.5 ± 0.8	0.004

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Albumin, g/dL	3.8 ± 0.5	3.3 ± 0.6	2.8 ± 0.5	<0.001
Globulin, g/dL	3.3 ± 0.5	3.5 ± 0.6	3.7 ± 0.7	0.018
Albumin/globulin ratio	1.16 ± 0.24	0.95 ± 0.21	0.76 ± 0.18	<0.001

Statistical test: One-way ANOVA or Kruskal–Wallis test, depending on data distribution.

Table 6: Biochemical and Inflammatory Marker Levels According to CBNAAT Bacillary Load Category

Marker	Very low n = 18	Low n = 26	Medium n = 31	High n = 25	p-value
CRP, mg/L	34.6 ± 19.2	55.8 ± 27.4	82.5 ± 38.1	121.4 ± 46.8	<0.001
ESR, mm/hour	45.2 ± 17.8	61.7 ± 21.4	78.9 ± 25.6	99.6 ± 27.2	<0.001
Ferritin, ng/mL	206.3 ± 104.8	318.5 ± 146.7	452.9 ± 201.6	674.2 ± 295.1	<0.001
LDH, U/L	248.6 ± 78.4	301.9 ± 91.2	374.5 ± 108.7	468.8 ± 134.3	<0.001
ADA, U/L	25.7 ± 8.4	33.8 ± 10.7	42.6 ± 13.9	55.1 ± 16.4	<0.001
Total protein, g/dL	7.1 ± 0.5	6.9 ± 0.6	6.7 ± 0.7	6.4 ± 0.8	0.003
Albumin, g/dL	3.8 ± 0.5	3.5 ± 0.5	3.2 ± 0.6	2.7 ± 0.5	<0.001
Globulin, g/dL	3.3 ± 0.5	3.4 ± 0.6	3.5 ± 0.6	3.7 ± 0.7	0.041
Albumin/globulin ratio	1.15 ± 0.22	1.03 ± 0.21	0.91 ± 0.20	0.73 ± 0.17	<0.001

Statistical test: One-way ANOVA or Kruskal–Wallis test, depending on data distribution.

Table 7: Association Between CBNAAT Bacillary Load Category and HRCT Chest Severity

CBNAAT bacillary load category	Mild HRCT n = 30	Moderate HRCT n = 40	Severe HRCT n = 30	Total n = 100
Very low	12 (40.0)	5 (12.5)	1 (3.3)	18 (18.0)
Low	11 (36.7)	12 (30.0)	3 (10.0)	26 (26.0)
Medium	6 (20.0)	17 (42.5)	8 (26.7)	31 (31.0)
High	1 (3.3)	6 (15.0)	18 (60.0)	25 (25.0)
Total	30 (100.0)	40 (100.0)	30 (100.0)	100 (100.0)
Statistical test	**Value**			
Chi-square value	39.82			
p-value	<0.001			

Interpretation: Higher CBNAAT bacillary load category was significantly associated with higher HRCT chest severity.

Table 8: Comparison of Biochemical and Inflammatory Markers Between Cavitary and Non-Cavitary Pulmonary Tuberculosis

Marker	Cavitary TB n = 44	Non-cavitary TB n = 56	p-value
CRP, mg/L	101.6 ± 46.2	58.7 ± 34.8	<0.001
ESR, mm/hour	88.4 ± 27.5	59.8 ± 25.6	<0.001
Ferritin, ng/mL	562.8 ± 276.4	318.6 ± 188.7	<0.001
LDH, U/L	421.7 ± 126.5	297.3 ± 94.8	<0.001
ADA, U/L	48.6 ± 15.8	32.7 ± 12.4	<0.001
Total protein, g/dL	6.5 ± 0.8	6.9 ± 0.6	0.007
Albumin, g/dL	2.9 ± 0.5	3.5 ± 0.6	<0.001
Globulin, g/dL	3.6 ± 0.7	3.4 ± 0.6	0.089
Albumin/globulin ratio	0.79 ± 0.18	1.03 ± 0.22	<0.001

Statistical test: Independent t-test or Mann–Whitney U test, depending on data distribution.

Table 9: Correlation of Biochemical and Inflammatory Markers with HRCT Severity Score and CBNAAT Bacillary Load Category

Marker	Correlation with HRCT severity score, r-value	p-value	Correlation with CBNAAT bacillary load category, r-value	p-value
CRP	+0.71	<0.001	+0.68	<0.001
ESR	+0.64	<0.001	+0.61	<0.001
Ferritin	+0.67	<0.001	+0.65	<0.001
LDH	+0.62	<0.001	+0.59	<0.001
ADA	+0.69	<0.001	+0.66	<0.001
Total protein	−0.36	<0.001	−0.32	0.001
Albumin	−0.72	<0.001	−0.69	<0.001
Albumin/globulin ratio	−0.66	<0.001	−0.63	<0.001

Statistical test: Pearson correlation or Spearman rank correlation, depending on data distribution.

Table 10: Multivariable Linear Regression Analysis for Predictors of HRCT Severity Score

Predictor variable	Unstandardized beta coefficient	Standard error	Standardized beta	p-value
CRP	0.031	0.009	0.29	0.001
Ferritin	0.004	0.001	0.24	0.004
ADA	0.086	0.028	0.27	0.003
Albumin	−1.42	0.38	−0.31	<0.001
CBNAAT bacillary load category	1.18	0.32	0.34	<0.001
Age	0.018	0.013	0.06	0.172
Diabetes mellitus	0.74	0.51	0.08	0.148
Model summary	**Value**			

ISSN (O): 2687-5365; ISSN (P): 2753-6556

R^2	0.64			
Adjusted R^2	0.60			
Overall model p-value	<0.001			

Table 11: Integrated Biochemical–Microbiological–Radiological Severity Pattern in Pulmonary Tuberculosis

Severity domain	Mild disease	Moderate disease	Severe disease
HRCT severity score	1–5	6–10	11–18
HRCT pattern	Limited segmental involvement; cavitation uncommon	Multilobar involvement; tree-in-bud and consolidation common	Extensive bilateral disease; cavitation, consolidation and multilobar involvement frequent
CBNAAT bacillary load category	Very low/low predominant	Low/medium predominant	Medium/high predominant
CRP and ESR	Mild to moderate elevation	Moderate elevation	Marked elevation
Ferritin	Mild elevation	Moderate elevation	Marked elevation
LDH	Mild elevation	Moderate elevation	Marked elevation
ADA	Mild elevation	Moderate elevation	Marked elevation
Albumin	Near-normal or mildly reduced	Reduced	Markedly reduced
Albumin/globulin ratio	Mildly reduced	Reduced	Markedly reduced

DISCUSSION

The present study evaluated the relationship between biochemical and inflammatory markers, CBNAAT bacillary load category and HRCT chest severity in pulmonary tuberculosis. The main finding was that CRP, ESR, ferritin, LDH and serum ADA increased progressively with increasing HRCT severity and higher CBNAAT bacillary load, whereas serum albumin and albumin/globulin ratio decreased with increasing disease severity. This supports the concept that pulmonary tuberculosis severity reflects the combined effect of bacillary burden, host inflammation, immune activation, parenchymal injury and nutritional depletion, rather than any single diagnostic domain alone.[13–19]

The most common HRCT findings in the present study were tree-in-bud appearance (72%), centrilobular nodules (69%), consolidation (58%), mediastinal lymphadenopathy (49%) and cavitation (44%). These findings are consistent with the established HRCT morphology of active pulmonary tuberculosis. Adhikari et al. reported tree-in-bud appearance in 69.4%, mediastinal lymphadenopathy in 65.3% and consolidation in 56.9% of active pulmonary tuberculosis cases, with tree-in-bud pattern significantly associated with bacteriologically confirmed disease. The similarity of these findings supports the radiological validity of the present cohort.[13]

Tree-in-bud appearance is clinically important because it reflects endobronchial spread of infection and active disease. In the present study, patients with higher HRCT severity had higher CRP, ESR, ferritin, LDH and ADA levels, indicating that radiological activity was accompanied by measurable systemic inflammatory and immune-biochemical responses. Thus, HRCT patterns were not only anatomical findings but also reflected biological disease activity.[13]

Cavitation was observed in 44% of patients and was associated with higher CRP, ESR, ferritin, LDH and ADA levels, along with lower albumin and albumin/globulin ratio. Cavitation represents advanced tissue destruction, caseous necrosis and communication with airways, which may increase bacillary load and infectivity. Adhikari et al. noted that cavitation is related to mycobacterial load and smear positivity, while Arghir et al. reported increased ADA and systemic immune-inflammatory index in cavitary advanced pulmonary tuberculosis. The present findings are therefore consistent with cavitary disease as a severe inflammatory and microbiologically active phenotype.[13,18]

The role of HRCT in pulmonary tuberculosis is further supported by diagnostic accuracy studies. Sahu et al. reported HRCT sensitivity of 0.8125 and specificity of 0.8571 using culture as reference, while Rasheed et al. reported overall HRCT diagnostic accuracy of 84.26%, sensitivity of 89.09% and specificity of 79.25%. HRCT also retained high sensitivity in smear-negative pulmonary tuberculosis. These findings justify using HRCT severity scoring as a structured measure of radiological disease burden in the present study.[14,15]

The significant association between CBNAAT bacillary load and HRCT severity supports the microbiological–radiological linkage in pulmonary tuberculosis. Patients with high CBNAAT bacillary load were more frequently represented in the severe HRCT category, while very-low and low bacillary load categories were more common in mild HRCT disease. Since all patients were CBNAAT-positive, severity assessment depended on bacillary load stratification rather than binary positivity. This is relevant because molecular tests such as Xpert MTB/RIF provide rapid microbiological confirmation and rifampicin-resistance detection.[19]

The biochemical findings are supported by previous studies linking inflammatory and nutritional markers with radiological extent. Şahin and Yıldız reported that CRP and ESR increased, while total protein and albumin decreased as radiological stage increased in pulmonary tuberculosis. The present study showed a similar pattern, with CRP and ESR rising with HRCT severity and CBNAAT load, and albumin and albumin/globulin ratio falling with disease severity. This suggests that biochemical derangement reflects

ISSN (O): 2687-5365; ISSN (P): 2753-6556

both anatomical disease burden and microbiological load.[16]

CRP showed a strong positive correlation with HRCT severity and CBNAAT bacillary load. As an acute-phase reactant, CRP reflects systemic inflammatory activation due to mycobacterial infection and tissue injury. Miranda et al. reported sustained elevation of CRP in pulmonary tuberculosis and reduction during treatment, supporting its role as a dynamic marker of disease activity. ESR also increased with HRCT severity and CBNAAT load; although less specific than CRP, it remains a useful marker of chronic inflammatory burden.[16,17]

Ferritin was significantly higher in severe HRCT disease and high CBNAAT bacillary load. Ferritin acts as both an iron-storage protein and acute-phase reactant, and its elevation in tuberculosis may reflect macrophage activation, iron sequestration and chronic inflammation. Miranda et al. also reported raised ferritin in pulmonary tuberculosis with reduction during treatment. In the present study, ferritin functioned as a supportive severity marker when interpreted along with CRP, ESR, ADA and albumin.[17]

Serum ADA was one of the most biologically relevant markers in this study. ADA reflects lymphocyte proliferation and cell-mediated immune activation, both central to tuberculosis immunopathogenesis. Saini et al. reported significantly higher ADA levels in pulmonary tuberculosis patients than controls and observed reduction after the intensive treatment phase. Arghir et al. further reported that ADA was associated with bacteriological confirmation, delayed diagnosis, cavitary disease and mortality. The present finding of higher ADA with increasing HRCT severity, CBNAAT load and cavitation supports ADA as both a diagnostic adjunct and severity marker.[18,20]

LDH showed positive correlation with HRCT severity and CBNAAT bacillary load. Although LDH is not tuberculosis-specific, its elevation may reflect cellular injury, tissue necrosis and parenchymal destruction. Higher LDH in cavitary disease supports its role as an adjunct marker of tissue injury, particularly when interpreted with HRCT findings and other inflammatory markers.[13,18]

Serum albumin and albumin/globulin ratio showed strong negative correlations with HRCT severity and CBNAAT load. Hypoalbuminemia in pulmonary tuberculosis may reflect inflammation, reduced hepatic synthesis, increased catabolism and poor nutritional reserve. The fall in albumin/globulin ratio may result from reduced albumin and chronic immune stimulation. These findings are concordant with Şahin and Yıldız, who reported decreasing albumin and total protein with increasing radiological stage. Albumin and albumin/globulin ratio therefore appear to be practical low-cost markers of severe disease and host nutritional reserve.[16]

The integrated design of the present study is its major strength. Previous studies have often examined HRCT findings, biochemical markers or ADA separately. The present study combines biochemical/inflammatory markers, CBNAAT bacillary load and HRCT severity in the same cohort, making it clinically useful because pulmonary tuberculosis severity is multidimensional and cannot be fully assessed by a single test.[13–20]

The practical implication is that routine biochemical markers may complement microbiological and radiological assessment in CBNAAT-positive pulmonary tuberculosis. HRCT demonstrates anatomical burden, CBNAAT provides microbiological confirmation and bacillary load, and biochemical markers reflect inflammation, immune activation, tissue injury and nutritional reserve. Among the studied markers, CRP, ferritin, ADA and albumin appear particularly useful for severity stratification, while ESR, LDH and albumin/globulin ratio provide additional supportive information.

CONCLUSION

The present study demonstrates that biochemical and inflammatory markers show a clear relationship with microbiological burden and radiological severity in CBNAAT-positive pulmonary tuberculosis. CRP, ESR, ferritin, LDH and ADA increased progressively with higher HRCT chest severity and higher CBNAAT bacillary load, while serum albumin and albumin/globulin ratio decreased with increasing disease severity. Cavitary disease was associated with a stronger inflammatory and biochemical derangement, supporting its role as a marker of advanced pulmonary tuberculosis. Overall, these findings suggest that routine biochemical markers, when interpreted along with CBNAAT bacillary load and HRCT severity, may help in better stratification of disease burden in pulmonary tuberculosis.

Limitations: This study has certain limitations. First, the cross-sectional design allows assessment of association but does not establish causality or treatment-response prediction. Second, the sample size was limited to 100 patients from a single centre, which may affect generalizability. Third, only CBNAAT-positive pulmonary tuberculosis patients were included; therefore, the findings may not apply to CBNAAT-negative or clinically diagnosed cases. Fourth, inflammatory markers such as CRP, ESR, ferritin and LDH are not tuberculosis-specific and may be influenced by other inflammatory conditions, comorbidities or nutritional status. Finally, HRCT severity scoring may have observer variability unless standardized radiological scoring and inter-observer agreement are applied.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556