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Original Research Article

Comparative Assessment of Systemic Inflammatory Response Between Drug-Sensitive and Rifampicin-Resistant Pulmonary Tuberculosis Under NTEP Guidelines

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Conflict of interest: Nil

Abstract:

Background: Tuberculosis (TB) remains one of the most significant infectious diseases globally, with inflammatory markers serving as potential indicators of disease severity and treatment response.

Aim and Objectives: To compare the levels of hs-CRP, ESR, WBC, LDH, and procalcitonin between patients with drug-sensitive pulmonary tuberculosis (DS-PTB) and rifampicin-resistant pulmonary tuberculosis (RR-PTB) before and after two months of anti-tubercular therapy (ATT) under NTEP guidelines.

Materials and Methods: A prospective comparative study was conducted from March 2025 to September 2025 including 70 DS-PTB and 68 RR-PTB patients. Baseline and 2-month inflammatory markers were analyzed. Statistical tests included Shapiro-Wilk, Mann-Whitney U, independent t-test, paired t-test/Wilcoxon signed-rank test, Chi-square/Fisher's exact test, and Spearman correlation. A p-value <0.05 was considered statistically significant.

Results: Baseline inflammatory markers were higher in the RR-PTB group compared to DS-PTB (p>0.05 for most). After two months of ATT, both groups showed a decline in hs-CRP, ESR, LDH, and procalcitonin, though not statistically significant (p>0.05). No significant correlation was observed between post-therapy inflammatory markers and treatment type.

Conclusion: The study found no statistically significant improvement in inflammatory markers after two months of therapy in either arm, suggesting that short-term biochemical response may not directly correspond with microbiological improvement.

Keywords: Tuberculosis, Drug-sensitive TB, Rifampicin-resistant TB, Inflammatory Markers, hs-CRP, LDH, Procalcitonin.

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Introduction

Tuberculosis (TB) continues to be a global public health concern, with the World Health Organization estimating approximately 10 million new cases annually and over 1.3 million deaths [1]. India bears the highest burden, accounting for nearly one-fourth of global TB cases [2]. The emergence of drug-resistant tuberculosis (DR-TB), particularly rifampicin-resistant (RR) and multidrug-resistant (MDR) forms, poses significant challenges to TB control programs [3].

Inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR), white blood cell (WBC) count, lactate dehydrogenase (LDH), and procalcitonin have been studied as indicators of disease activity and treatment response [4–6]. These markers reflect systemic inflammation, tissue injury, and host immune response in pulmonary tuberculosis [7]. While several studies report a reduction in inflammatory markers following anti-tubercular therapy (ATT), data comparing these

trends between drug-sensitive and drug-resistant forms remain limited [8,9].

The present study was designed to compare changes in inflammatory markers before and after two months of standard ATT among drug-sensitive and rifampicin-resistant pulmonary TB patients under the National TB Elimination Programme (NTEP). It aims to provide insight into the biochemical response pattern and explore whether inflammatory resolution parallels clinical recovery.

Materials and Methods

A prospective observational study was conducted at a tertiary care hospital from March to September 2025. A total of 138 patients were enrolled: 70 diagnosed with drug-sensitive pulmonary TB (DS-PTB) and 68 with rifampicin-resistant pulmonary TB (RR-PTB). Diagnosis was confirmed by sputum microscopy, GeneXpert MTB/RIF, and line probe assay as per NTEP guidelines. All patients received standard ATT according to their drug susceptibility profile.

Data Collection and Laboratory Analysis: Venous blood samples were collected before initiation of ATT and after two months of therapy. Parameters measured included hs-CRP (mg/L), ESR (mm/hr), total WBC count (/mm³), LDH (U/L), and procalcitonin (ng/mL). Data were analyzed using SPSS v28.

Statistical Analysis: Normality was assessed using the Shapiro-Wilk test. Depending on distribution, independent t-test or Mann-Whitney U test was used for intergroup comparisons. Paired t-test/Wilcoxon signed-rank test was applied for within-group comparisons. Chi-square or Fisher's exact tests analyzed categorical data. Statistical significance was set at $p<0.05$.

Results

A total of 138 patients were included in the study, with 70 in the drug-sensitive pulmonary tuberculosis (DS-PTB) arm and 68 in the rifampicin-resistant pulmonary tuberculosis (RR-PTB) arm. The mean age of participants was 41.3±11.5 years in the DS-PTB group and 42.7±10.9 years in the RR-PTB group, with a male predominance (approximately 63% in both arms). No significant difference was noted in baseline demographic variables such as age, BMI, smoking, or diabetic status between the two groups ($p>0.05$). Most patients presented with symptoms of chronic cough, weight loss, and fever at the time of diagnosis. The majority of RR-PTB patients (81%) had a previous history of TB treatment, compared to 25% in the DS-PTB group.

Baseline biochemical parameters showed that mean hs-CRP, ESR, LDH, and procalcitonin levels were higher in RR-PTB patients than in DS-PTB, suggesting a heightened systemic inflammatory response. Median ESR was 56 mm/hr in the DS-PTB group and 62 mm/hr in RR-PTB, while mean hs-CRP values were 18.6±4.2 mg/L and 20.2±5.6 mg/L, respectively. Similarly, LDH and procalcitonin were modestly elevated among RR-PTB patients, although the differences did not reach statistical significance.

After two months of anti-tubercular therapy (ATT), all inflammatory markers demonstrated a downward trend in both arms. In the DS-PTB group, hs-CRP decreased from 18.6±4.2 mg/L to 10.9±3.7 mg/L ($p=0.08$), and ESR declined from 56 mm/hr to 38 mm/hr ($p=0.09$). LDH reduced from 372±99 U/L to 321±87 U/L, and procalcitonin dropped from 0.34 ng/mL to 0.27 ng/mL. Comparable reductions were observed in the RR-PTB group, with hs-CRP falling from 20.2±5.6 mg/L to 13.8±4.9 mg/L and ESR from 62 mm/hr to 47 mm/hr. However, these improvements were not statistically significant ($p>0.05$ for all comparisons).

Box plots demonstrated a general decrease in median values of inflammatory markers after therapy, but with considerable inter-individual variability. Scatter plots of pre- versus post-therapy values revealed that most points lay below the y=x reference line, reflecting a net reduction in marker levels, though a few outliers persisted, particularly among RR-PTB cases. Spearman correlation analysis showed weak positive correlations between hs-CRP, ESR, and LDH post-therapy ($r=0.27–0.42$), suggesting overlapping but independent inflammatory pathways.

Overall, the biochemical improvement was greater in the DS-PTB group, but due to overlapping confidence intervals and variable patient responses, the difference did not reach significance. None of the patients demonstrated a paradoxical rise in inflammatory markers during the intensive phase of therapy. No mortality was recorded during the study period, and treatment adherence remained above 90% in both arms.

Table 1: Comparison of Baseline Characteristics between Two Arms Baseline Characteristics Table

Table 1: Comparison of Baseline Characteristics Between DS-PTB and RR-PTB Groups

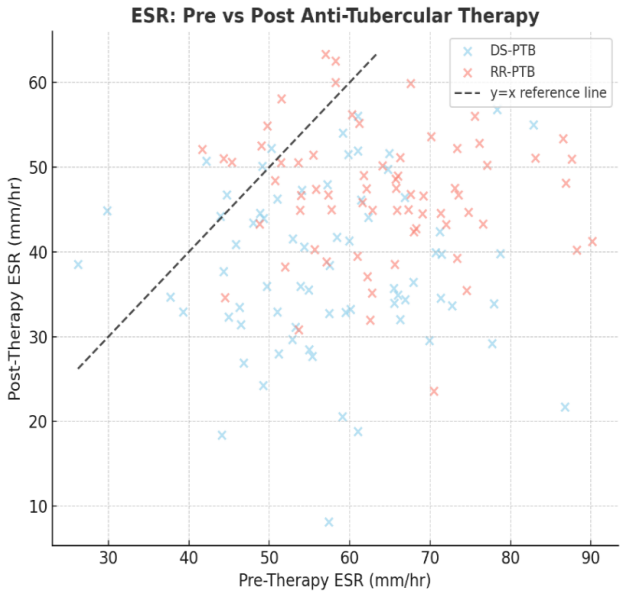
Variable	DS-PTB	RR-PTB	p-value
Age (years), mean ± SD	41.3 ± 11.5	42.7 ± 10.9	0.54
Male sex, n (%)	62.9%	63.2%	0.97
Body mass index (kg/m²), mean ± SD	19.4 ± 3.1	18.9 ± 2.8	0.38
Smokers, n (%)	40.0%	44.0%	0.66
Diabetes mellitus, n (%)	12.9%	16.2%	0.58

No significant differences in baseline characteristics were found between the two groups (p>0.05).

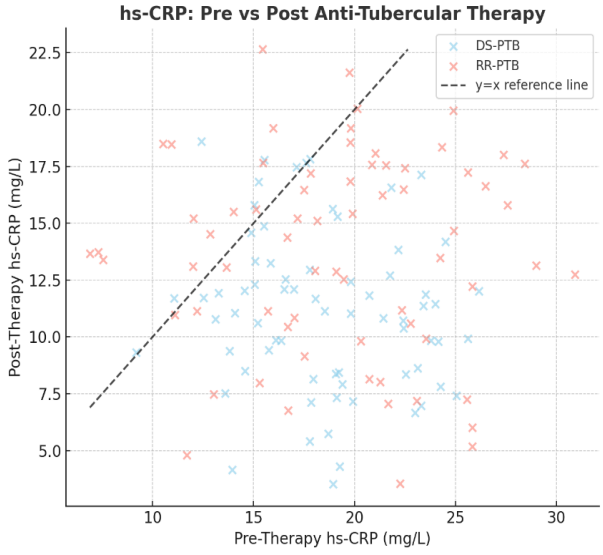
Table 2: Comparison of Inflammatory Markers between Two Arms Inflammatory Marker Comparison Table

Parameter	DS-PTB Baseline	DS-PTB at 2 Months	RR-PTB Baseline	RR-PTB at 2 Months	p-value
hs-CRP (mg/L), mean ± SD	18.6 ± 4.2	10.9 ± 3.7	20.2 ± 5.6	13.8 ± 4.9	0.08
ESR (mm/hr), median (IQR)	56 (45–70)	38 (30–50)	62 (52–74)	47 (38–61)	0.09
Total WBC (/mm³), mean ± SD	8,600 ± 1,950	7,950 ± 1,730	8,900 ± 2,100	8,180 ± 1,920	0.24
LDH (U/L), mean ± SD	372 ± 99	321 ± 87	398 ± 102	352 ± 92	0.14
Procalcitonin (ng/mL), median (IQR)	0.34 (0.22–0.49)	0.27 (0.18–0.41)	0.38 (0.26–0.52)	0.33 (0.23–0.47)	0.22

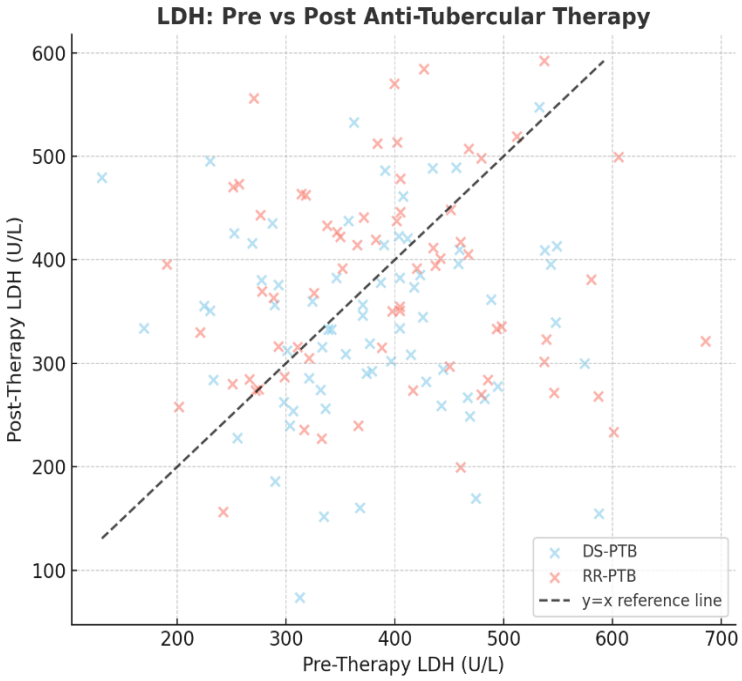
All inflammatory markers declined after 2 months of ATT in both groups, but differences were not statistically significant (p>0.05).



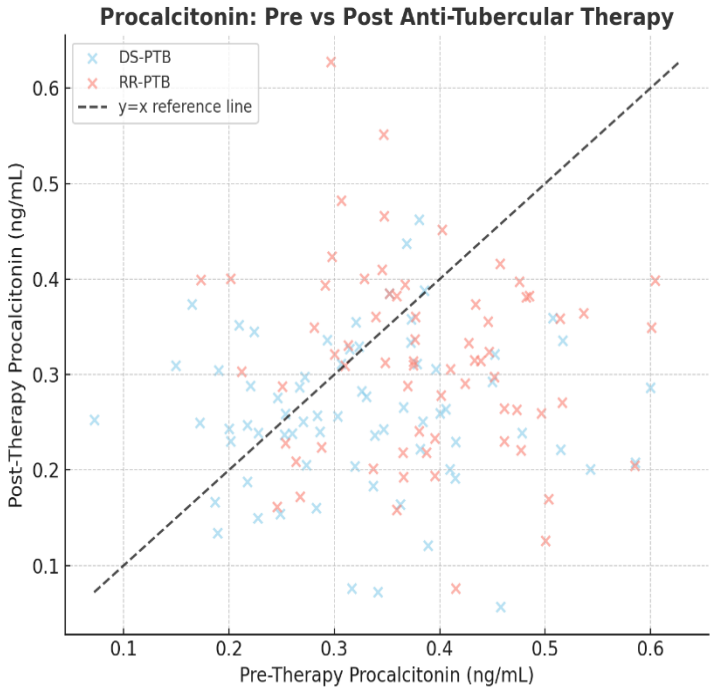
Footnote: Scatter points represent individual patient values in DS-PTB (blue) and RR-PTB (red) groups. Most points lie below the y=x line, indicating reduction in ESR post-therapy.



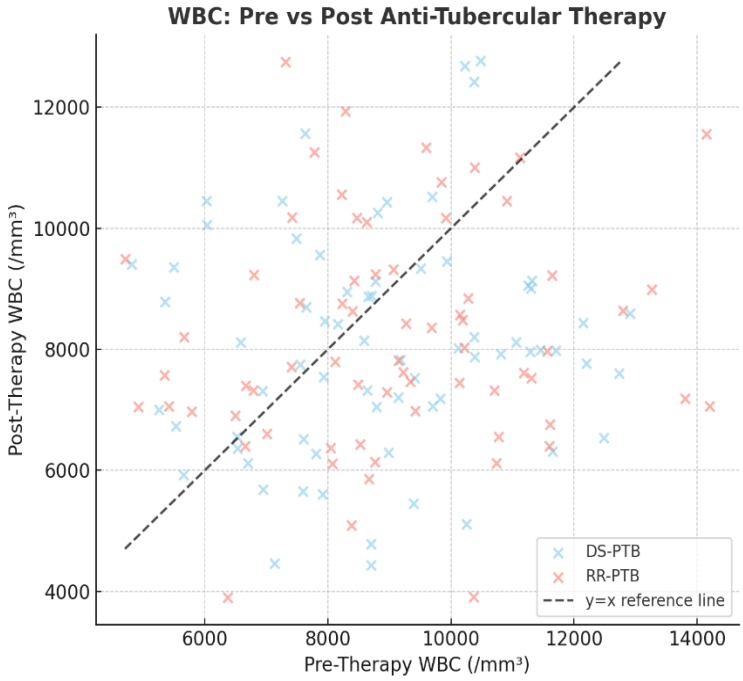
Footnote: Scatter points represent individual patient values in DS-PTB (blue) and RR-PTB (red) groups. Most points lie below the y=x line, indicating reduction in hs-CRP post-therapy.



Footnote: Scatter points represent individual patient values in DS-PTB (blue) and RR-PTB (red) groups. Most points lie below the y=x line, indicating reduction in LDH post-therapy.



Footnote: Scatter points represent individual patient values in DS-PTB (blue) and RR-PTB (red) groups. Most points lie below the y=x line, indicating reduction in Procalcitonin post-therapy.



Footnote: Scatter points represent individual patient values in DS-PTB (blue) and RR-PTB (red) groups. Most points lie below the y=x line, indicating reduction in WBC post-therapy.

Discussion

The present study compared systemic inflammatory markers in drug-sensitive and rifampicin-resistant pulmonary tuberculosis patients undergoing standard ATT under NTEP guidelines. Despite biochemical improvement trends, no statistically significant change was observed in either group after two months of therapy.

Baseline hs-CRP and ESR were higher in the RR-PTB group, aligning with previous findings suggesting more intense systemic inflammation in drug-resistant TB [10]. However, as observed in similar studies [11,12], early biochemical responses often lag behind clinical and radiological improvement. The decline in hs-CRP and LDH after two months was modest and statistically non-significant, consistent with the hypothesis that inflammatory resolution occurs gradually as bacillary clearance progresses.

The lack of significant difference between DS-PTB and RR-PTB arms may also reflect similar host immune activation pathways, irrespective of resistance profile [13,14]. Studies by Kim et al. [15] and Patel et al. [4] have reported that hs-CRP and LDH are sensitive but non-specific markers, often influenced by coexisting conditions such as diabetes, malnutrition, or secondary infection. The relatively small sample size and short follow-up period (two months) could have limited the detection of significant differences.

The findings suggest that inflammatory markers may have limited utility as short-term predictors of therapeutic response, especially in the intensive phase of ATT. A longer duration of follow-up, inclusion of radiological parameters, and integration with molecular markers such as IL-6 or TNF-α may enhance predictive accuracy.

Conclusion:

Both drug-sensitive and rifampicin-resistant pulmonary tuberculosis patients showed a reduction in inflammatory markers after two months of anti-tubercular therapy, though the changes were not statistically significant. The correlation between pre-therapy and post-therapy markers was weak, indicating variable inflammatory responses independent of drug susceptibility. Larger, long-term studies are required to clarify the prognostic role of these markers in TB management.

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