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NEUTROPHIL–LYMPHOCYTE RATIO AS A PREDICTOR OF DISEASE SEVERITY AND TREATMENT OUTCOME IN PULMONARY TUBERCULOSIS: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Pulmonary tuberculosis (PTB) remains a major global health challenge. Inflammatory biomarkers that are inexpensive and widely available may aid in predicting disease severity and outcomes. **Aims and Objectives:** To evaluate the association between baseline neutrophil–lymphocyte ratio (NLR) and disease severity, sputum smear grading, and treatment outcomes in newly diagnosed PTB patients. **Methods:** This eight-month hospital-based observational study was conducted at a tertiary care center. A total of 161 newly diagnosed, microbiologically confirmed PTB patients were enrolled. Baseline NLR was calculated from differential leukocyte counts. Disease severity was assessed radiologically and microbiologically. Treatment outcomes were classified according to national tuberculosis program guidelines. **Results:** The mean age was 41.6 ± 14.2 years with male predominance (62%). Mean baseline NLR was 4.6 ± 1.9. Patients with severe radiological disease had significantly higher NLR (5.8 ± 2.1) compared to those with mild-moderate disease (3.4 ± 1.2). Higher sputum smear grades were associated with elevated NLR (5.5 ± 2.0 vs 3.6 ± 1.4). An NLR cutoff of ≥4.5 was associated with delayed sputum conversion and higher unfavorable outcomes (17.6% vs 6.9%).**Conclusion:** NLR is a simple, cost-effective prognostic biomarker in PTB that correlates with disease severity and treatment outcomes.

KEYWORDS :

INTRODUCTION

Tuberculosis (TB) remains one of the leading causes of infectious morbidity and mortality worldwide. The WHO Global TB Report 2023 estimated 10.6 million incident cases and 1.3 million deaths globally in 2022.[1] India bears the highest burden, accounting for approximately 27% of all cases worldwide.[2]

Despite effective anti-tubercular therapy (ATT), significant variability exists in disease presentation, severity, and treatment response. Early identification of patients at higher risk for severe disease and poor outcomes is essential for optimizing therapeutic strategies.[3] Conventional methods of severity assessment including sputum microscopy, culture, chest radiography, and GeneXpert MTB/RIF may be limited by cost, availability, and turnaround time in resource-limited settings.[4]

The neutrophil–lymphocyte ratio (NLR), derived from routine complete blood counts, reflects the balance between innate immunity represented by neutrophils and adaptive immunity represented by lymphocytes.[5] Elevated NLR indicates heightened systemic inflammation and relative lymphocyte suppression, both of which are relevant in tuberculosis pathogenesis. NLR has demonstrated prognostic value in sepsis, malignancies, and various respiratory infections.[6–8]

In pulmonary tuberculosis, the host immune response plays a critical role in determining disease severity. Neutrophilia represents the acute inflammatory response, while relative lymphopenia suggests impaired cell-mediated immunity essential for mycobacterial control.[9] Several studies have reported associations between elevated NLR and extensive pulmonary disease, higher bacillary load, delayed sputum conversion, and poor treatment outcomes.[10–12]

However, evidence regarding the utility of NLR as a prognostic biomarker in PTB remains limited in the Indian population, and optimal cutoff values have not been well established. This study was therefore undertaken to evaluate the association between baseline NLR and disease severity, sputum smear grading, and treatment outcomes in newly diagnosed pulmonary tuberculosis patients at a tertiary care center.

REVIEW OF LITERATURE

Zahorec first described NLR as a marker of systemic inflammation in critically ill patients.[13] Subsequently, Imtiaz et al. reported elevated NLR in active tuberculosis compared to healthy controls, noting that higher NLR values were associated with extensive disease and delayed sputum conversion.[10] Lee et al. further established the prognostic significance of NLR in predicting mortality and treatment outcomes in PTB, identifying it as a reliable and cost-effective marker for disease assessment.[11]

Yoon et al. demonstrated that NLR was significantly higher in smear-positive compared to smear-negative TB patients and correlated with radiological severity.[12] Berhane et al. found that elevated NLR at the time of diagnosis predicted delayed sputum culture conversion and unfavorable treatment outcomes in an African cohort.[14] A meta-analysis by Liu et al. confirmed that NLR has moderate diagnostic and prognostic accuracy in tuberculosis, supporting its utility as an adjunctive biomarker in clinical practice.[15]

These findings collectively suggest that NLR may serve as a simple, accessible, and cost-effective prognostic tool, particularly valuable in resource-constrained settings where advanced laboratory biomarkers are unavailable or unaffordable.

MATERIALS AND METHODS

This was a hospital-based observational study conducted over eight months at a tertiary care center. A total of 161 adult patients aged 18 years and above with newly diagnosed, microbiologically confirmed pulmonary tuberculosis were enrolled in the study.

Patients with HIV co-infection, diabetes mellitus, malignancy, immunosuppressive therapy, extra-pulmonary tuberculosis,

and pregnancy were excluded from the study to minimize confounding variables that could independently affect NLR values and treatment outcomes.

Baseline demographic data including age and sex, sputum smear grading, chest radiographic findings, and complete blood counts with differential leukocyte counts were recorded at the time of diagnosis. NLR was calculated as the ratio of absolute neutrophil count to absolute lymphocyte count obtained from the differential leukocyte count.

Radiological severity was classified as mild-moderate or severe based on the extent of pulmonary involvement on chest radiography. Microbiological severity was assessed based on sputum smear grading, categorized as low smear grade or smear negative versus high smear grade (2+ or 3+). Treatment outcomes were classified according to the National Tuberculosis Elimination Programme (NTEP) guidelines as favorable (cured or treatment completed) or unfavorable (treatment failure, death, lost to follow-up, or not evaluated).

Statistical analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequencies and percentages. Independent sample t-test was used for comparison of continuous variables between groups, while chi-square test was used for categorical variables. A p-value of less than 0.05 was considered statistically significant. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants.

RESULTS

The study enrolled 161 newly diagnosed pulmonary tuberculosis patients. The mean age of the study population was 41.6 ± 14.2 years. There were 100 males (62%) and 61 females (38%). The mean baseline NLR of the study population was 4.6 ± 1.9.

Regarding radiological severity, patients with severe radiological disease had a significantly higher mean NLR of 5.8 ± 2.1 compared to patients with mild-moderate radiological disease who had a mean NLR of 3.4 ± 1.2. This difference was statistically significant ($p<0.001$).

When NLR was compared across sputum smear grades, patients with high smear grades (2+ and 3+) had a mean NLR of 5.5 ± 2.0, which was significantly higher than the mean NLR of 3.6 ± 1.4 observed in patients with low smear grades or smear-negative results ($p<0.01$).

With respect to treatment outcomes, among 129 patients with baseline NLR less than 4.5, 120 patients (93.1%) had favorable outcomes and 9 patients (6.9%) had unfavorable outcomes. In contrast, among 32 patients with baseline NLR of 4.5 or greater, 26 patients (82.4%) had favorable outcomes while 6 patients (17.6%) had unfavorable outcomes. This difference was statistically significant ($p<0.05$), indicating that patients with elevated baseline NLR had approximately 2.5-fold higher risk of unfavorable treatment outcomes.

DISCUSSION

This study confirms a significant association between elevated baseline NLR and increased disease severity in pulmonary tuberculosis. The finding that patients with severe radiological involvement had markedly higher NLR compared to those with mild-moderate disease is consistent with observations by Imtiaz et al.[10] and Lee et al.,[11] who reported similar associations in different populations.

The association between higher sputum smear grades and elevated NLR values aligns with the findings of Yoon et al.,[12] suggesting that a higher bacillary load triggers a more intense neutrophilic inflammatory response with concurrent lymphocyte suppression. This immune imbalance, reflected by elevated NLR, likely represents the body's attempt to contain a high mycobacterial burden through innate immune mechanisms while adaptive immunity becomes relatively suppressed.

The identification of an NLR cutoff of 4.5 or greater as a predictor of unfavorable treatment outcomes is a clinically significant finding. Patients with NLR above this threshold had an unfavorable outcome rate of 17.6% compared to only 6.9% in those below this cutoff. This is consistent with findings by Berhane et al.,[14] who reported similar associations in an African cohort, suggesting that the prognostic utility of NLR may be generalizable across different populations.

Elevated NLR in tuberculosis likely reflects neutrophil-driven systemic inflammation and relative lymphocyte suppression, indicating impaired cell-mediated immunity essential for mycobacterial control.[9] This immune dysregulation may contribute to disease progression, delayed sputum conversion, and poorer clinical outcomes.

The strengths of this study include its prospective design, standardized NLR measurement at baseline, and classification of treatment outcomes according to established national guidelines. However, several limitations should be acknowledged. The single-center design and relatively modest sample size may limit the generalizability of findings. The exclusion of HIV-positive and diabetic patients, while minimizing confounding, limits the applicability of results to these important subgroups. Serial NLR measurements during treatment were not performed, which could have provided additional insight into the dynamic relationship between NLR and treatment response.

In resource-limited settings where advanced biomarkers such as procalcitonin, C-reactive protein, and cytokine assays may be unavailable or expensive, NLR derived from a routine complete blood count offers a practical, cost-effective alternative for early risk stratification and individualized patient monitoring.

CONCLUSION

NLR is a simple, inexpensive, and readily available biomarker that correlates significantly with disease severity and treatment outcomes in pulmonary tuberculosis. Elevated baseline NLR of 4.5 or greater is associated with severe radiological disease, higher sputum smear grades, and unfavorable treatment outcomes. Its incorporation into routine clinical practice may improve early identification of high-risk patients and facilitate individualized management, particularly in resource-limited settings. Future multicenter studies with larger sample sizes and serial NLR monitoring are recommended to further validate these findings and establish standardized cutoff values.

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