Original Article

Utility of Hematological Indices in Predicting the Sputum Conversion at the End of the Intensive Phase of Treatment for Patients With Pulmonary TB

Hage Yaja[1,*], Bineeta Kashyap[2], Mrinalini Kotru[3]

[1]University College of Medical Sciences & Guru Teg Bahadur Hospital, New Delhi, India
[2]Department of Microbiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, New Delhi, India
[3]Department of Pathology, University College of Medical Sciences & Guru Teg Bahadur Hospital, New Delhi, India

***Correspondence:** hageyaja1@gmail.com

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Abstract

Background: Early sputum conversion is a crucial marker of treatment response and infectivity reduction in pulmonary tuberculosis (TB). However, conventional microbiological monitoring methods such as culture are time-consuming and resource-intensive. Hematological indices derived from routine complete blood counts are simple, inexpensive markers of systemic inflammation and immune response and may provide additional prognostic information during treatment.
Aim: To evaluate the predictive value of baseline hematological indices and their dynamic changes in identifying sputum conversion at the end of the intensive phase of anti-tubercular therapy (ATT) in patients with pulmonary TB.
Methods: This observational longitudinal study included 56 treatment-naïve, CBNAAT-positive pulmonary TB patients. Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), neutrophil-monocyte-to-lymphocyte ratio (NMLR), and systemic immune-inflammation index (SII) were assessed at baseline and after two months of ATT. Sputum conversion was determined using smear microscopy and culture. Predictive performance was evaluated using receiver operating characteristic (ROC) curve analysis and logistic regression.
Results: Sputum conversion was achieved in 47 (83.9%) patients. Baseline values of all hematological indices were significantly higher in non-converters ($p < 0.001$) and declined significantly among converters following treatment. NMLR demonstrated the strongest predictive performance (AUC 0.922; OR 180), followed by MLR and NLR.
Conclusion: Hematological indices, particularly NMLR, MLR, and NLR, are effective, low-cost predictors of early microbiological response in pulmonary TB and may serve as useful adjuncts to routine treatment monitoring, especially in resource-limited settings.

Keywords: sputum Conversion; predictor; Hematological; Pulmonary TB

Introduction

Tuberculosis remains a significant global health challenge, with an estimated 10.6 million people falling ill and 1.6 million deaths annually, according to the World Health Organization (WHO) Global TB Report 2023. [1, 2] India bears the highest burden, contributing to approximately 27% of the global TB incidence.[2] Despite advances in diagnostics and therapeutics, early identification of patients at risk of poor treatment outcomes remains a critical gap, particularly in resource-limited settings.

Sputum conversion, defined as the shift from sputum smear or culture positivity to negativity following antitubercular therapy, is a crucial marker of microbiological response and treatment efficacy. [3, 4] Achieving sputum conversion at the end of the intensive phase (typically after two months of ATT) is associated with reduced transmission, lower relapse rates, and improved prognosis. [5] In contrast, persistent sputum smear or culture positivity during treatment reflects inadequate microbiological response and is recognized as an indicator of treatment failure, suboptimal drug activity, poor adherence, or underlying drug resistance, necessitating critical reassessment of the therapeutic regimen.[6, 7, 8] Evidence from clinical guidelines and cohort studies further demonstrates that delayed or absent bacteriological conversion is associated with an increased risk of relapse, unfavorable treatment outcomes, culture reversion, and mortality, particularly in drug-resistant and HIV-coinfected populations.[6, 9, 10, 11] Accordingly, early identification of patients with delayed conversion is essential to enable timely treatment modification, intensified monitoring, and supportive interventions aimed at improving overall treatment outcomes.[6, 8, 10, 11]

Traditionally, sputum smear microscopy and mycobacterial culture have been the cornerstone for monitoring treatment response in tuberculosis (TB).[2] Despite their widespread use, these microbiological methods have important limitations. Smear microscopy, although inexpensive and widely available, has variable sensitivity, particularly in patients with low bacillary load, while culture, though more sensitive, is time-consuming, technically demanding, and operationally challenging.[12, 13] These limitations are especially pronounced in high-burden and resource-limited settings, where access to culture facilities and rapid molecular diagnostics remains inconsistent due to infrastructural, logistical, and cost constraints.[2, 13, 14, 15] Consequently, reliance on microbiological markers alone may delay identification of patients at risk of poor treatment response, underscoring the need for simple, accessible, and cost-effective surrogate markers to aid in early prediction of sputum conversion and treatment outcomes.[9]

In recent years, hematological parameters derived from routine complete blood counts (CBC), including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), neutrophil-monocyte-to-lymphocyte ratio (NMLR), and the systemic immune-inflammation index (SII), have gained attention as potential indicators of systemic inflammation and immune response in TB.[16, 17, 18] The concept of NLR as a surrogate marker of systemic inflammatory stress was first introduced by Zahorec, highlighting its derivation from routine CBC parameters and its ability to reflect the balance between innate inflammatory activity and adaptive immune function.[16] Subsequently, composite indices such as SII, integrating neutrophil, lymphocyte, and platelet counts, were proposed to more comprehensively capture the host immune–inflammatory milieu.[17]

These hematological indices are biologically plausible in TB, as neutrophilia and relative lymphopenia, hallmarks of active infection and systemic inflammation, are commonly observed and reflect the underlying host–pathogen interaction and inflammatory burden.[19] Elevated NLR and related ratios have been consistently reported in patients with active pulmonary TB compared with controls, and higher baseline values have been associated with greater disease severity.[20, 21] Moreover, several studies have demonstrated that elevated pretreatment NLR and MLR correlate with delayed sputum conversion, unfavorable treatment outcomes, and increased mortality, suggesting a prognostic role beyond simple diagnostic utility.[22, 23, 24, 25, 26, 27]

Evidence also suggests that these hematological ratios are dynamic markers. Reductions in NLR and MLR have been observed during effective anti-tubercular therapy, reflecting normalization of immune and inflammatory responses with disease resolution. [28, 29] In particular, Choudhary et al. demonstrated a significant decline in MLR during treatment, with values approaching those of non-TB controls by 12 weeks, supporting its potential role as a treatment response marker.[30] However, despite growing interest, most existing studies have focused on individual indices in isolation, and comparative evaluation of multiple hematological markers, especially composite indices such as NMLR and SII, remains limited.[18]

Furthermore, the prognostic utility of microbiological markers alone has been questioned. Studies in multidrug-resistant TB (MDR-TB) have shown that smear and culture conversion have limited predictive validity, particularly early in treatment, and that incorporation of additional clinical or laboratory indicators improves risk stratification. [9] Large cohort data from India have further demonstrated that delayed culture conversion is strongly associated with unfavorable outcomes, reinforcing the need for early identification of high-risk patients using adjunctive markers.[10]

Therefore, the present study aimed to evaluate the role of hematological parameters at baseline and their changes over the intensive phase of treatment in predicting sputum conversion among patients with pulmonary TB. This analysis represents a focused evaluation of routinely available CBC-derived indices within a broader prospective cohort, with the objective of identifying reliable, low-cost biomarkers that may enhance early risk stratification and treatment monitoring. Such markers could serve as practical adjuncts to microbiological assessment, particularly in resource-limited, high-burden settings where timely access to culture and molecular diagnostics remains constrained.[2, 9, 10]

Materials and Methods

Study design and setting

This was an observational, longitudinal study conducted from May 2023 to November 2024 at the Departments of Microbiology, Medicine, Pathology, and the DOTS Centre, University College of Medical Sciences (UCMS) and Guru Teg Bahadur Hospital, Delhi.

The present manuscript represents a focused analytical component of a broader prospective cohort study that evaluated clinical, microbiological, hematological, inflammatory, and patient-reported outcomes in patients with pulmonary tuberculosis. This analysis was specifically designed to assess the role of hematological indices in predicting sputum conversion at the end of the intensive phase of anti-tubercular therapy. Other components of the parent study are beyond the scope of this report.

Study population

Adult patients ($\geq$18 years) with newly diagnosed, treatment-naïve pulmonary tuberculosis confirmed by sputum CBNAAT were enrolled from the DOTS Centre. Both hospitalized patients and outpatients were included.

Definition of sputum conversion and follow-up

Sputum smear conversion was defined as the change from sputum smear or culture positivity to negativity after completion of two months of anti-tubercular therapy. Patients were followed up at the end of the intensive phase of ATT for assessment of sputum conversion and hematological parameters.

Sample size

The sample size was calculated based on a study by Putra et al., [31] which reported that monocyte-to-lymphocyte ratio (MLR) was below the selected cut-off value in 56 out of 61 sputum-converted patients, corresponding to a sensitivity of 91.8% for predicting sputum conversion. Using a sensitivity (S) of 0.918, proportion of subjects with the target condition (P) of 0.924, confidence interval width (W) of 0.075, and a type I error (α) of 5% ($Z_{1-\alpha/2}$ = 1.96), the calculated sample size was 55.6, which was rounded to 56.

The achieved sample size was therefore adequate for evaluating the diagnostic and predictive performance of hematological indices with respect to sputum conversion.

Inclusion and exclusion criteria

The inclusion criteria were sputum CBNAAT-positive pulmonary tuberculosis, age >18 years, and treatment-naïve status.

The exclusion criteria were known hematological diseases, HIV infection, and severe comorbidities.

Baseline complete blood counts were performed prior to enrollment, and patients with abnormal leukocyte differentials, thrombocytopenia, or previously diagnosed hematological disorders were excluded.

Ethical clearance and informed consent

Ethical clearance for the study was obtained from the Institutional Ethics Committee for Human Research (IEC-HR), UCMS (IECHR-2023-59-85-R1). Written informed consent was obtained from all participants before enrollment. A detailed history and relevant clinical information were recorded using a pre-designed case record form.

Specimen collection and processing

Sputum samples were collected at two time points: at baseline (prior to initiation of ATT) and at the end of the intensive phase. Samples were collected under aseptic conditions in sterile, leak-proof containers and processed following standard biosafety precautions. If processing was delayed beyond one hour, specimens were refrigerated until processing.

Specimens were homogenized and decontaminated using the N-acetyl-L-cysteine–sodium hydroxide (NALC-NaOH) method. Concentrated sediments were used for smear microscopy and culture.

Microbiological methods

Ziehl–Neelsen staining was performed for direct demonstration of acid-fast bacilli, and smears were graded according to NTEP guidelines after examination of at least 300 oil-immersion fields.

Culture was performed on Lowenstein–Jensen medium and incubated at 37 °C for up to eight weeks, with weekly examination for growth. Preliminary identification was based on colony morphology and growth characteristics.

CBNAAT was performed using the Xpert MTB/RIF assay (Cepheid Inc., Sunnyvale, California, USA) according to the manufacturer's instructions. Culture isolates were confirmed as *Mycobacterium tuberculosis* using the SD Bioline TB Ag MPT64 Rapid Test (Standard Diagnostics, Republic of Korea).

Hematological assessment

Peripheral venous blood samples were collected at baseline and after completion of the intensive phase of ATT in EDTA vials. Complete blood counts were performed using an automated hematology analyzer (Mindray BC-6800). The parameters recorded included total leukocyte count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, platelet count, and hemoglobin.

The derived hematological indices were calculated as follows: neutrophil-to-lymphocyte ratio (NLR = N/L), monocyte-to-lymphocyte ratio (MLR = M/L), platelet-to-lymphocyte ratio (PLR = P/L), neutrophil-monocyte-to-lymphocyte ratio (NMLR = [N + M]/L), and systemic immune-inflammation index (SII = [N × P]/L).

Statistical analysis

Data were coded and analyzed using SPSS version 20.0. Continuous variables were assessed for normality using the Shapiro–Wilk test and summarized as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables were expressed as frequencies and percentages. Between-group comparisons were performed using independent-sample t-tests or Mann–Whitney U tests, while paired comparisons used paired t-tests or Wilcoxon signed-rank tests.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of hematological indices, with optimal cut-off values determined using Youden's index. Sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, diagnostic accuracy, and odds ratios with 95% confidence intervals were calculated. A p-value <0.05 was considered statistically significant.

Results

Baseline demographic and microbiological characteristics

A total of 56 sputum CBNAAT-positive patients with pulmonary tuberculosis were included in the study. The mean age of the participants was 30.86 ± 11.84 years. The majority of patients (64.3%) were in the 18–30-year age group. There was a near-equal gender distribution, with 29 (51.8%) males and 27 (48.2%) females.

All patients were culture-positive at baseline. Sputum smear microscopy showed grade 1 positivity in 10 (17.9%) patients, while 23 (41.1%) patients each had grade 2 and grade 3 positivity. CBNAAT semi-quantitative results demonstrated a high bacillary load in 24 (42.9%) patients, medium load in 23 (41.1%), and low load in 9 (16.1%). Baseline demographic and microbiological characteristics are summarized in Table 1.

Baseline hematological indices and sputum conversion status

At the end of the intensive phase of anti-tubercular therapy, sputum conversion was achieved in 47 patients (83.9%), while 9 patients (16.1%) remained sputum-positive. Baseline hematological indices were significantly higher in non-converters compared with converters across all evaluated parameters.

Mean baseline NLR, MLR, PLR, NMLR, and SII values were markedly elevated in the non-converter group, with all differences reaching high statistical significance ($p < 0.001$). Among these indices, NMLR demonstrated the greatest absolute difference between converters and non-converters. A detailed comparison of baseline hematological indices according to sputum conversion status is presented in Table 2.

Table 1: Baseline demographic and microbiological characteristics of the study population (n = 56).

Variable	Value
Age (years), mean ± SD	30.86 ± 11.84
Age group (18–30 years), n (%)	36 (64.3)
Male sex, n (%)	29 (51.8)
Female sex, n (%)	27 (48.2)
Baseline sputum smear grade, n (%)	
– Grade 1	10 (17.9)
– Grade 2	23 (41.1)
– Grade 3	23 (41.1)
Culture positive at baseline, n (%)	56 (100.0)
CBNAAT semi-quantitative category, n (%)	
– Low	9 (16.1)
– Medium	23 (41.1)
– High	24 (42.9)

SD: standard deviation; CBNAAT: cartridge-based nucleic acid amplification test.

Table 2: Baseline hematological indices among sputum converters and non-converters.

Hematological index	Converters (n = 47) Mean ± SD	Non-converters (n = 9) Mean ± SD	p-value
Neutrophil-to-lymphocyte ratio (NLR)	4.48 ± 2.04	13.16 ± 5.15	<0.001
Monocyte-to-lymphocyte ratio (MLR)	0.47 ± 0.13	0.83 ± 0.61	<0.001
Platelet-to-lymphocyte ratio (PLR)	240.3 ± 59.9	390.1 ± 198.8	<0.001
Neutrophil-monocyte-to-lymphocyte ratio (NMLR)	3.20 ± 1.17	6.50 ± 7.99	<0.001
Systemic immune-inflammation index (SII)	1703.7 ± 1046.9	4899.9 ± 2256.4	<0.001

p-values derived using independent-sample t-test or Mann–Whitney U test as appropriate.

Changes in hematological indices after the intensive phase of therapy

Paired analysis of hematological parameters before and after completion of the intensive phase revealed a significant decline in systemic inflammatory indices following treatment. NLR, MLR, PLR, NMLR, and SII all showed statistically significant reductions compared with baseline values ($p < 0.01$).

In addition, neutrophil percentages decreased significantly, while lymphocyte percentages showed a corresponding significant increase, reflecting immunological recovery and reduction in inflammatory burden. These changes indicate a favorable hematological response to effective anti-tubercular therapy. Post-treatment changes in hematological parameters are detailed in Table 3.

Table 3: Changes in hematological indices after the intensive phase of anti-tubercular therapy (n = 56).

Parameter	Direction of change	Statistical test	p-value
Neutrophil-to-lymphocyte ratio (NLR)	Decreased	Paired t-test	<0.001
Monocyte-to-lymphocyte ratio (MLR)	Decreased	Wilcoxon signed-rank	0.004
Platelet-to-lymphocyte ratio (PLR)	Decreased	Wilcoxon signed-rank	0.001
Neutrophil-monocyte-to-lymphocyte ratio (NMLR)	Decreased	Wilcoxon signed-rank	<0.001
Systemic immune-inflammation index (SII)	Decreased	Wilcoxon signed-rank	<0.001
Neutrophil percentage	Decreased	Wilcoxon signed-rank	<0.001
Lymphocyte percentage	Increased	Wilcoxon signed-rank	<0.001

Predictive performance of baseline hematological indices for sputum conversion

Baseline hematological indices were evaluated for their ability to predict sputum conversion at the end of the intensive phase. All five indices demonstrated statistically significant predictive value.

NMLR emerged as the strongest predictor, showing the highest diagnostic accuracy and odds ratio, followed by MLR and NLR. PLR and SII also demonstrated significant predictive associations, though with comparatively lower discriminative performance.

Receiver operating characteristic analysis, combined with logistic regression results, including optimal cut-off values, area under the curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, odds ratios, and p-values, are summarized in Table 4.

Table 4: Predictive performance of baseline hematological indices for sputum conversion.

Index	Cut-off	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Odds ratio (95% CI)	p-value
NLR	$\geq$ 4.08	0.813 (0.610–1.000)	91.5	66.7	93.5	60.0	29.60 (3.30–265.30)	<0.001
MLR	$\geq$ 0.56	0.809 (0.612–1.000)	97.9	66.7	93.9	85.7	39.00 (4.26–356.82)	<0.001
PLR	$\geq$ 312.26	0.766 (0.590–0.942)	59.6	88.9	96.6	29.6	10.21 (1.86–56.03)	0.002
NMLR	$\geq$ 5.22	0.922 (0.832–1.000)	97.9	77.8	95.8	87.5	180.00 (14.55–2227.10)	<0.001
SII	$\geq$ 1978.15	0.794 (0.606–0.983)	61.7	88.9	96.7	30.8	9.15 (1.68–49.93)	0.004

AUC: area under the curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value.

ROC analysis of neutrophil-monocyte-to-lymphocyte ratio

Among all evaluated indices, NMLR demonstrated the highest overall diagnostic accuracy for predicting sputum conversion. The ROC curve for baseline NMLR showed an AUC of 0.922, indicating excellent discriminative ability. At the optimal cut-off value ($\geq$ 5.22), NMLR exhibited high sensitivity and specificity, along with robust positive and negative predictive values.

The ROC curve for baseline NMLR is illustrated in Figure 1.

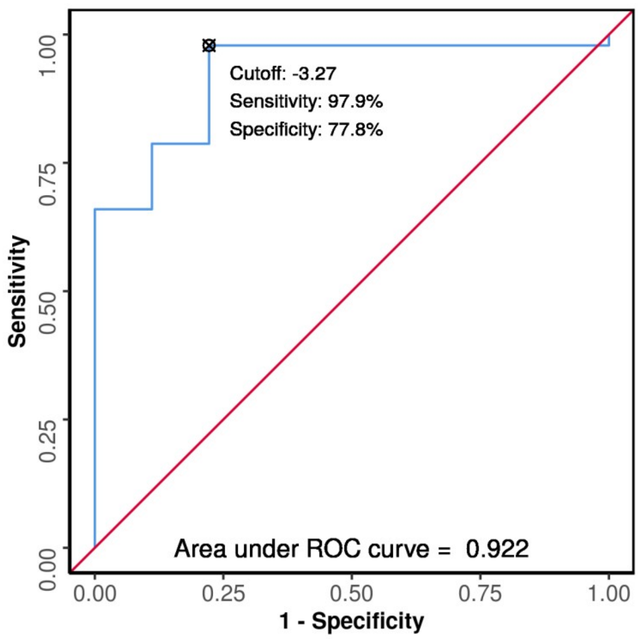

Figure 1: Receiver operating characteristic (ROC) curve of baseline neutrophil-monocyte-to-lymphocyte ratio (NMLR) for predicting sputum conversion at the end of the intensive phase of anti-tubercular therapy in patients with pulmonary tuberculosis (AUC = 0.922).

Association between baseline sputum smear grade and hematological indices

Baseline hematological indices were further analyzed according to sputum smear grading. Patients with higher smear grades exhibited significantly elevated inflammatory indices.

Grade 3 smear positivity was associated with significantly higher NLR, PLR, NMLR, and SII values compared with grades 1 and 2 ($p < 0.05$ for all). MLR showed an increasing trend with higher smear grades, although this did not reach statistical significance.

These findings demonstrate a clear association between bacillary burden and systemic inflammatory response. The relationship between baseline sputum smear grade and hematological indices is shown in Table 5.

Table 5: Association between baseline sputum smear grade and hematological indices (n = 56).

Index	Grade 1 (n = 10) Mean ± SD	Grade 2 (n = 23) Mean ± SD	Grade 3 (n = 23) Mean ± SD	p-value
Neutrophil-to-lymphocyte ratio (NLR)	4.92 ± 1.47	3.73 ± 1.88	8.44 ± 5.27	0.001
Monocyte-to-lymphocyte ratio (MLR)	0.43 ± 0.13	0.44 ± 0.13	0.83 ± 0.61	0.051
Platelet-to-lymphocyte ratio (PLR)	283.76 ± 59.92	206.01 ± 108.52	359.02 ± 198.76	0.017
Neutrophil-monocyte-to-lymphocyte ratio (NMLR)	2.90 ± 1.17	2.69 ± 1.51	8.05 ± 7.99	0.001
Systemic immune-inflammation index (SII)	1904.45 ± 635.43	1300.57 ± 869.77	3270.27 ± 2155.68	0.001

p-values derived using Kruskal–Wallis test.

Discussion

This study evaluated the prognostic role of hematological inflammatory indices, NLR, MLR, PLR, NMLR, and SII, in predicting sputum conversion at the end of the intensive phase of anti-tubercular therapy in patients with pulmonary tuberculosis. Our findings demonstrate that both elevated baseline values and inadequate decline of these indices during treatment are associated with failure to achieve early sputum conversion. Among all evaluated markers, NMLR emerged as the most robust predictor, followed by MLR and NLR.

Neutrophil-to-lymphocyte ratio

In the present study, a decline in NLR over the intensive phase was a stronger predictor of sputum conversion than baseline NLR alone, with an AUROC of 0.813 and high sensitivity. Shojaan et al. reported that NLR effectively distinguished pulmonary TB from bacterial pneumonia, with an AUROC of approximately 0.88. [32] Kissling et al. similarly demonstrated good diagnostic accuracy of NLR in pediatric TB.[33] Suryana et al. observed that a baseline NLR $\geq$5.1 was associated with delayed sputum conversion, although its significance diminished in multivariate models when MLR was included. [23] Yin et al. and Lee et al. reported associations between elevated NLR and retreatment risk or mortality.[34, 35] In contrast, Ştefănescu et al. reported that baseline NLR alone did not reliably predict two-month culture conversion, highlighting the importance of dynamic assessment. [29] Our findings support this observation and emphasize that serial monitoring of NLR provides greater prognostic value than a single baseline measurement.

Monocyte-to-lymphocyte ratio

MLR demonstrated strong predictive performance in our cohort, with an AUROC of 0.809 and a high odds ratio for non-conversion. Adane et al., in a meta-analysis, reported a pooled AUROC of approximately 0.88 for MLR in diagnosing active TB.[36] Suryana et al. identified MLR as a superior predictor of delayed sputum conversion compared to NLR, with a baseline cut-off $\geq$0.585 yielding high odds ratios in both univariate and multivariate models.[23] Our findings are consistent with these studies and further demonstrate that dynamic changes in MLR during therapy reflect immunological recovery and microbiological response.

Platelet-to-lymphocyte ratio

PLR showed moderate diagnostic accuracy in our study, characterized by lower sensitivity but high specificity. Chen et al. reported high diagnostic performance of PLR in TB among COPD patients, while He et al. demonstrated its association with cavitary disease.[37, 38] Ştefănescu et al. found no significant predictive value of PLR for sputum conversion. [29] In line with these findings, our results suggest that PLR may have limited utility as a standalone predictor but may serve as an adjunctive marker, particularly for ruling out non-conversion due to its high specificity.

Neutrophil-monocyte-to-lymphocyte ratio

NMLR was the strongest predictor of sputum conversion in our cohort, demonstrating the highest AUROC (0.922) and odds ratio among all evaluated indices. Jeon et al. showed that NMLR outperformed NLR in differentiating pulmonary TB from other infectious lung diseases. [39] Kissling et al. similarly reported superior performance of NMLR in pediatric TB. [33] While previous studies have focused primarily on the diagnostic role of NMLR, our study extends existing evidence by demonstrating its prognostic value for predicting sputum conversion, highlighting its potential role in treatment monitoring.

Systemic immune-inflammation index

SII demonstrated fair diagnostic accuracy with high specificity for predicting sputum conversion. Previous studies have reported variable performance of SII in TB, including its association with cavitary disease, disease classification, and treatment-related hepatotoxicity.[37, 40, 41] Ştefănescu et al. observed significant post-treatment declines in SII without strong baseline predictive value. [29] Our findings align with this pattern and suggest that SII may be more useful as a supportive marker reflecting systemic inflammatory resolution rather than a primary predictor of conversion.

Relationship with bacillary burden and treatment response

Higher baseline sputum smear grades were associated with significantly elevated NLR, PLR, NMLR, and SII values, indicating a clear relationship between mycobacterial burden and systemic inflammation. Although these indices declined after treatment across all smear grades, patients with higher baseline grades continued to show relatively elevated values at follow-up, suggesting persistent immune activation. Similar post-treatment declines have been reported by Ştefănescu et al. and Omair et al., particularly among sputum converters. [29, 22] These findings support the role of hematological indices as markers of both disease severity and treatment response.

Clinical implications

Hematological indices derived from routine complete blood counts offer a simple, low-cost adjunct to microbiological monitoring in pulmonary TB. In resource-limited settings where access to culture or molecular follow-up may be delayed, elevated baseline NMLR, MLR, or NLR may help identify patients requiring closer surveillance during the intensive phase, while dynamic declines may provide early reassurance of treatment response.

Limitations

The relatively small sample size and single-center design may limit the generalizability of these findings. Radiological severity scoring and long-term outcomes beyond the intensive phase were not evaluated in this focused analysis, and future multicenter studies with extended follow-up are required to validate cut-off values and clinical applicability.

In summary, this study demonstrates that hematological inflammatory indices, particularly NMLR, followed by MLR and NLR, are strong predictors of early sputum conversion in pulmonary tuberculosis. NMLR showed the highest diagnostic accuracy and biological plausibility, supporting its role as a promising adjunctive marker for treatment monitoring, especially in resource-limited settings.

Conclusion

This study demonstrates that hematological inflammatory markers derived from routine complete blood counts, specifically NLR, MLR, PLR, NMLR, and SII, are significantly associated with sputum conversion outcomes in patients with pulmonary tuberculosis. At baseline, all five markers were markedly elevated in non-converters compared with converters, indicating their potential role as predictors of persistent disease activity. Importantly, dynamic changes in these indices during the intensive phase of anti-tubercular therapy enhanced their prognostic utility beyond baseline values alone.

Among the evaluated indices, NMLR emerged as the most potent predictor of early sputum conversion, demonstrating the highest diagnostic accuracy and odds ratio, followed by MLR and NLR, which also showed robust and clinically meaningful predictive performance. In contrast, PLR and SII exhibited moderate but complementary predictive value, supporting their role as adjunctive markers rather than standalone predictors.

Given their low cost, wide availability, and ease of calculation, these hematological ratios offer a practical adjunct to conventional microbiological monitoring, particularly in resource-limited settings where access to rapid culture or molecular follow-up may be constrained. Incorporation of markers such as NMLR, NLR, and MLR into routine clinical assessment may facilitate early identification of patients at risk for delayed sputum conversion and enable closer monitoring during the intensive phase of therapy.

Further large-scale, multicenter studies with diverse populations and longer follow-up periods are warranted to validate these findings, refine optimal cut-off values, and establish the role of hematological indices within standardized tuberculosis treatment-monitoring algorithms.

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