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Comparative Analysis of WBC-Derived Inflammatory Markers in Cavitary and Non-Cavitary Sputum-Positive Tuberculosis

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Abstract

Background: *Tuberculosis (TB), as an infectious disease, has consistently topped the list in any discussions owing to its spectrum of manifestations, morbidity, and mortality. The current diagnostic procedures are time consuming and cumbersome. Hence, there has been a constant search for highly sensitive and specific biomarkers with less turn-around-time as well as maintaining sensitivity and specificity. The current study aimed to examine the role of WBC and their derived inflammatory markers in sputum-positive active pulmonary tuberculosis (PTB) patients with and without cavity.*

Methods: *The study was conducted among sputum-positive PTB patients (n=27) who were further grouped into cavitatory (n=15) and non-cavitatory (n=12). The presence of cavities in the lungs were identified by chest X-ray. The study was conducted in the Department of General Medicine at a tertiary hospital in South India. Ethics approval was obtained from the institutional ethics committee (IEC), and written informed consent was obtained before the patients were inducted into the study. The various WBC-derived ratios were calculated from the data collected and compared between the two subgroup populations as indicative of their inflammation and prognosis. Statistics were performed using SPSS software version 16. P-value≤0.05 was considered statistically significant.*

Results: *The tuberculous patients with cavity were younger, and the absolute neutrophil counts (ANC), liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT), were significantly higher among the cavitatory group compared to noncavitatory group. Comparing inflammation between the groups showed statistically significant differences between the cavitatory and the non-cavitatory groups in most of the WBC-derived ratios.*

Conclusions: *Most of the inflammatory indices serve as easy and inexpensive biomarkers. Their prognostic value allows risk stratification among PTB patients. These markers can be used to predict the outcomes as well as assess the response to treatment.*

Keywords: Inflammation, Tuberculosis, Diagnosis, Cavitatory, Non-cavitatory.
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Introduction

Tuberculosis (TB) tops the list in mortality among single-agent infectious diseases. A consolidated report in 2021 by the WHO showed a halted decline in the incidence of TB and a new increase in TB-related deaths.[1] However, only 57% of the patients have a bacteriologically confirmed pulmonary disease. The infection occurs by inhaling the *Mycobacterium tuberculosis* bacilli (MTB) aerosols.[2] Disease progression occurs due to the alterations in the bacteriological virulence and/or the host immune system, affecting men three times more than women.[3] HIV co-infection is the most critical risk factor promoting disease progression from latency to active disease.[2]

Rapid and early diagnosis and treatment are crucial for the successful management of TB-infected individuals. Though few guidelines have been developed for improving TB diagnosis, prognosis, and therapeutic outcomes, there is no standardized scoring system to provide the outcome of TB patients after their treatment. The development of point-of-care testing for diagnosis will have potential benefits, such as decreasing morbidity and mortality and reducing transmission rates of TB from a public health point of view.[4] To achieve this, highly sensitive and at the same time precise biomarkers are needed for detecting active TB.

Chronic inflammation, which results in inflammatory exudation, hyperplasia, and necrosis, is a hallmark of TB infection. The white blood cell count (WBC) is frequently utilized to indicate inflammation. Numerous studies have assessed the possible involvement of different leukocyte ratios in chronic inflammatory disorders.[5] Table 1 shows the alterations in parameters derived from the complete blood count (CBC).

Table 1. The CBC-derived inflammatory markers include

Inflammatory marker	Pathogenesis indicated	Reference

Neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR)	Pulmonary tuberculosis (PTB) is known to be linked to chronic inflammation, as reflected by the changes in the white cell lineage's neutrophils, lymphocytes, and monocytes	6, 7
Platelet to lymphocyte ratio (PLR)	PLR is a marker of inflammation. Also altered in cardiovascular diseases and cancer.	8, 9
C-reactive protein (CRP)	The liver synthesizes CRP, which is the primary downstream mediator of the acute phase response, under interleukin (IL)-6 stimulus	10
Albumin	Albumin is a negative acute-phase reactant in inflammation and also it is an indicator of nutritional status.	11
Systemic immune inflammation index (SII) and systemic inflammatory response index (SIRI)	Combines three different WBC subsets and platelets; it reflects thrombocytosis, inflammation, and immunity	12
Inflammatory Prognostic Index (IPI)	Systemic inflammatory index in cerebrovascular accidents and certain cancers	13
Aggregate index of systemic inflammation (AISI)	Can forecast clinical outcomes in pulmonary fibrosis, diabetes mellitus, esophageal and prostate cancers, and cardiovascular diseases	14
CRP-to-albumin ratio (CAR)	Good predictor of progression to sepsis in patients presenting with clinical features of possible infection	15
CRP to lymphocyte ratio (CLR)	Reflect systemic inflammatory and immune status. Long-term chronic inflammation and oxidative stress impair lung structure and function. CRP may also play a role in regulating lung function. Lymphocytes, by producing cytotoxic perforins and granzyme B, induce cell death and apoptosis.	16
Prognostic nutritional index (PNI)	Immunonutritional marker that assesses a patient's combined nutritional and immune status to predict prognosis and outcomes in various diseases, especially cancers and infection	17

Studies are being done to assess the inflammatory status in TB patients, but a comprehensive evaluation of the inflammatory condition in TB-affected individuals is lacking in studies. The research question is whether the CBC-derived biomarkers are altered in patients with TB. Thus, the current study investigated the relationship between platelets, WBC, and derived inflammatory indices in sputum-positive pulmonary TB patients with and without cavity.

Materials and Methods

Study participants: The patients were enrolled from the Outpatient Department of General Medicine of a tertiary care teaching hospital in South India. Diagnosis of pulmonary tuberculosis (PTB) was based on sputum smear microscopy, chest radiography, and a strong clinical suspicion of TB. The baseline demographic, clinical, and laboratory parameters of all the patients were entered in a pre-structured proforma and used for analysis.

Ethics statement: The Institutional Ethics Committee (IEC) had approved the study vide IEC number IEC/21/JUN/163/43. The study was registered with the Indian Council of Medical Research (ICMR), India, CTRI/2023/08/056740 (https://ctri.nic.in/Clinicaltrials/login.php). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000, on Ethical Principles for Medical Research Involving Humans. All the participants provided written informed consent before enrolling in the study.

Inclusion and exclusion criteria: All sputum-positive PTB patients (male and female inclusive) (n=27) above the age of 18 years, tested in the DOTS centre (to assess the bacterial load in the sputum), along with the CBNAAT test (to evaluate the drug sensitivity and resistance of the organism), were enrolled in the study. The sample size is small because many patients are being effectively treated in the small district hospitals. So, the number of patients seeking medical attention at tertiary care hospitals has been reduced.

The study participants were further sub-grouped as the cavitatory (n=15) and the non-cavitatory (n=12) groups based on the presence or absence of cavity in the chest radiograph. All the patients with age less than 18 years, who were non-sputum-positive PTB diagnosed by chest imaging and symptoms, individuals on steroids in any form, past or current smoking history, previous history of lung disease – interstitial lung disease, chronic obstructive pulmonary disease etc, occupations at the risk of developing lung diseases and addictions in any form – tobacco, alcohol, drugs etc were excluded from the study. This is an ongoing study. Hence, control group participants have yet to be included. Figure 1 shows the methodology of participant inclusion in the study.

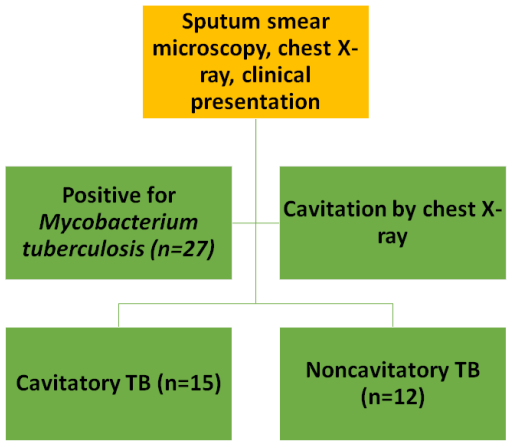

Figure 1. Shows the recruitment of study participants

Study indices: The study was conducted in the Department of General Medicine, SRIHER, Chennai, India. CRP was analyzed by immunoturbidity, and liver function tests by standard methods (Beckman Coulter AU 5800) Beckman Coulter, Inc., California, USA. Among the CBC, hemoglobin (Hb) was analyzed by spectrophotometry, WBC, red blood cell, and platelet counts were analyzed by impedance method, and differential count was performed by fluorescence flow cytometry (Sysmex XN-3100 six-part CBC analyser, Sysmex Corporation, Japan).

Derived indices were calculated as follows:

Neutrophil to lymphocyte ratio (NLR)=Neutrophil count/ Lymphocyte count[6,7]

Monocyte to lymphocyte ratio (MLR)=Monocyte count/ Lymphocyte count[6,7]

Platelet to lymphocyte ratio (PLR)=Platelet count/ Lymphocyte count[6,7]

Systemic immune-inflammation index (SII)=(Platelet in cells/L X Neutrophil)/ Lymphocyte[12]

Systemic inflammation response index (SIRI)=(Monocyte X Neutrophil)/ Lymphocyte[14]

Inflammatory prognostic index (IPI)=NLR X CAR[13]

Aggregate index of systemic inflammation (AISI)=NLR × absolute monocyte count × platelets[14]

CRP: albumin ratio (CAR)=CRP/albumin[15]

CRP: lymphocyte ratio (CLR)=CRP/ absolute lymphocyte count[16]

Prognostic nutritional index (PNI)=10 × serum albumin (g/dL) + 0.005 × Absolute lymphocyte count (per mm^3)[17]

Statistics: The data was analysed using SPSS software version 16.0. Mean and standard deviation were used to express the continuous variables, while the categorical variables were expressed as frequencies and percentages. The differences in variances between the two groups were analyzed using the F-test. Fisher Exact test analyzed the categorical variables. All the tests were two-tailed, and a statistical significance was considered with a P-value≤0.05.

Results

A total of 27 patients with PTB infection were confirmed positive by sputum analysis and included in the study. Among these patients, 26 (96.3%) were males, aged 19 to 86 years. The study patients were divided into 15 in the cavitatory group and 12 in the non-cavitatory group. The basic demographic characteristics and laboratory parameters were distributed among the two groups as shown in Table 2. Patients with non-cavitary PTB (58.5 years) appeared to be slightly older than those in the cavitatory group (46.86 years), though this difference was not statistically significant (P-value=0.07). The body mass index in the cavitatory and non-cavitary groups showed no statistical significance (P-value=0.26). (Table 2)

Table 2. Basic demographic and laboratory data of the study subgroups

Parameter	Cavitatory group (n=15)	Non-cavitatory group (n=12)	P-value
Age (in years)	46.86±17.37	58.5±10.02	0.07
Male n (%) #	14 (93%)	12 (100%)	0.99
Female n (%)	1 (7%)	0 (0%)	
BMI (kg/m2)	20.43±2.84	21.13±1.98	0.26
Hemoglobin (g/dL)	10.84±1.36	11.15±2.24	0.10
Total bilirubin (mg/dL)	1.027±0.60	0.84±0.37	0.11
AST (U/L)	29.46±15.41	24.41±7.26	0.01*

ALT (U/L)	22.60±28.50	18.83±6.61	<0.001**
ALP (U/L)	123.66±63.06	122.16±48.25	0.37
Albumin (g/dL)	2.88±0.50	3.01±0.59	0.58
Sputum positivity	2.33±0.72	2.75±0.45	0.12

BMI: body mass index; AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase

All the data are expressed in mean and SD; # expressed in frequency and percentage.

The F test compared all the data; #: compared by Fisher's Exact test

P-value≤0.05 was considered statistically significant; *: statistically significant; **: statistically highly significant

The mean Hb levels in the cavitatory and non-cavitatory groups showed no statistically significant difference (P-value=0.10). The liver enzymes, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), showed higher values among the cavitatory group compared to non-cavitatory TB with (P-value=0.01) and (P-value<0.001) respectively. The serum albumin levels were not statically significant between the groups (P-value=0.58). Sputum positivity showed higher values in the non-cavitatory group compared to the cavitatory group (P-value=0.12) (Table 2). Table 3 and Figures 2A and 2B show the comparison of biomarkers between the cavitatory and non-cavitatory TB patients.

The total WBC counts in the groups fell within the biological reference interval, and there was no statistically significant difference between the groups (P-value=0.43). The absolute neutrophil count (ANC) was higher in the non-cavitatory TB group compared to the cavitatory group, with a highly statistically significant (P-value<0.001). The absolute lymphocyte count (ALC) was greater in the cavitatory group than the non-cavitatory group, though this difference was not statistically significant (P-value=0.32). ESR levels were elevated in both groups, but there was no statistically significant difference (P-value=0.95). Platelet counts were normal in both groups (P-value=0.17). Serum CRP levels were elevated with no statistically significant difference (P-value=0.95). (Table 3)

NLR was higher in the cavitatory group than the non-cavitatory group with P-value=0.01. MLR was higher in the cavitatory group than the non-cavitatory group with P-value=0.01. PLR was lower in the cavitatory group than the non-cavitatory group with P-value=0.03. SII was higher in the cavitatory group compared to the non-cavitatory group with P-value=0.04. SIRI was higher in the cavitatory group than the non-cavitatory group with P-value=0.03 (Table 3).

IPI was lower in the cavitatory group than the non-cavitatory group with P-value=0.04. AISI was lower in the cavitatory group than the non-cavitatory group with P-value=0.04. CLR was lower in the cavitatory group compared to the non-cavitatory group with P-value<0.001. CAR was higher in the cavitatory group than the non-cavitatory group with P-value=0.01. PNI was lower in the cavitatory group than the non-cavitatory group with P-value=0.04 (Table 3).

Table 3. Comparative analysis of inflammatory markers between the study groups

Inflammatory markers	Cavitatory group	Non-cavitatory group	P-value
WBC – total (cells/µL)	8705.33±2707.96	9511.66±2101.54	0.43
ANC (cells/µL)	5976.58±2159.65	7479.28±1972.48	<0.001**
ALC (cells/µL)	1243.98±585.71	1170.29±434.28	0.32
ESR (mm/hour)	89.73±22.98	87.16±23.23	0.95
PLT (105 cells/ µL)	3.03±0.97	3.74 ±1.44	0.17
CRP (mg/L)	19.13±4.32	19.23±4.37	0.95
NLR	8.81±3.43	5.41±2.01	0.01*
MLR	0.13±0.09	0.27±0.18	0.01*
PLR	230.66±109.98	460.11±205.41	0.03*
SII	233.73 ±160.46	143.49±85.34	0.04*
SIRI	1.35±0.94	0.62±0.48	0.03*
IPI	41.11±24.33	68.86±43.63	0.04*
AISI	2156.08±1832.19	3295.09±3311.54	0.04*
CLR	18.11±8.67	19.35±10.11	<0.001**
CAR	8.26±4.20	4.59±1.77	0.01*
PNI	33.75±5.53	37.68±9.93	0.04*

WBC: white blood cell; ANC: absolute neutrophil count; ALC: absolute lymphocyte count; ESR: erythrocyte sedimentation rate; PLT: platelets; CRP: C-reactive protein; NLR: Neutrophil to lymphocyte ratio; MLR: Monocyte to lymphocyte ratio; PLR: Platelet to lymphocyte ratio: SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; IPI: Inflammatory prognostic index; AISI: Aggregate index of systemic inflammation; CLR: CRP-to-lymphocyte ratio; CAR: CRP-to-albumin ratio; PNI: Prognostic nutritional index

All the data are expressed in mean and SD; The F test compared all the data

P-value≤0.05 was considered statistically significant; *: statistically significant; **: statistically highly significant

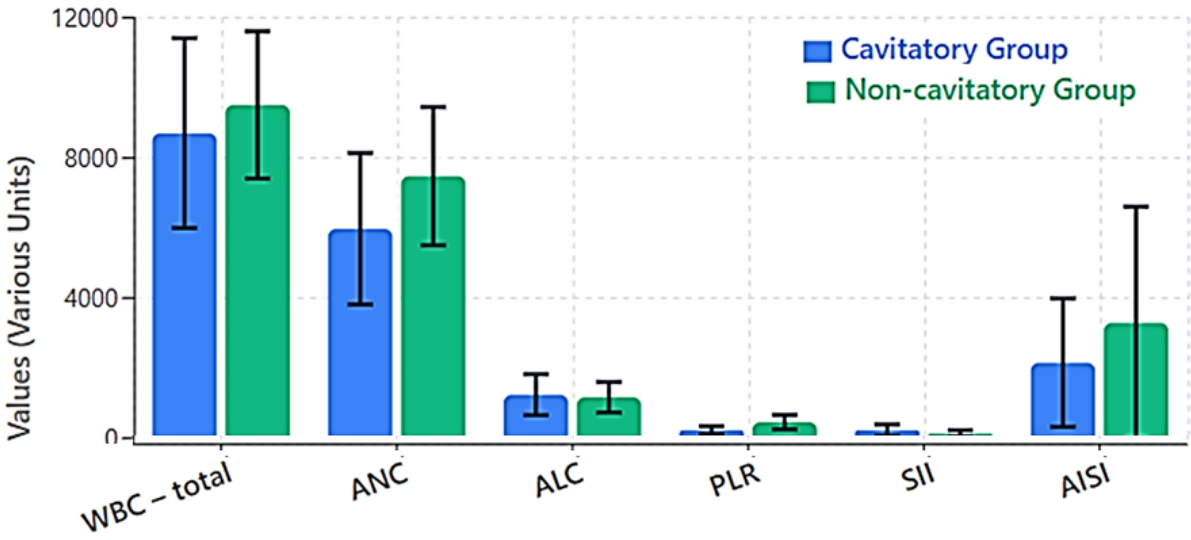

Figure 2A. Shows the comparison of total WBC, ANC, ALC, PLR, SII and AISI between the groups of TB patients

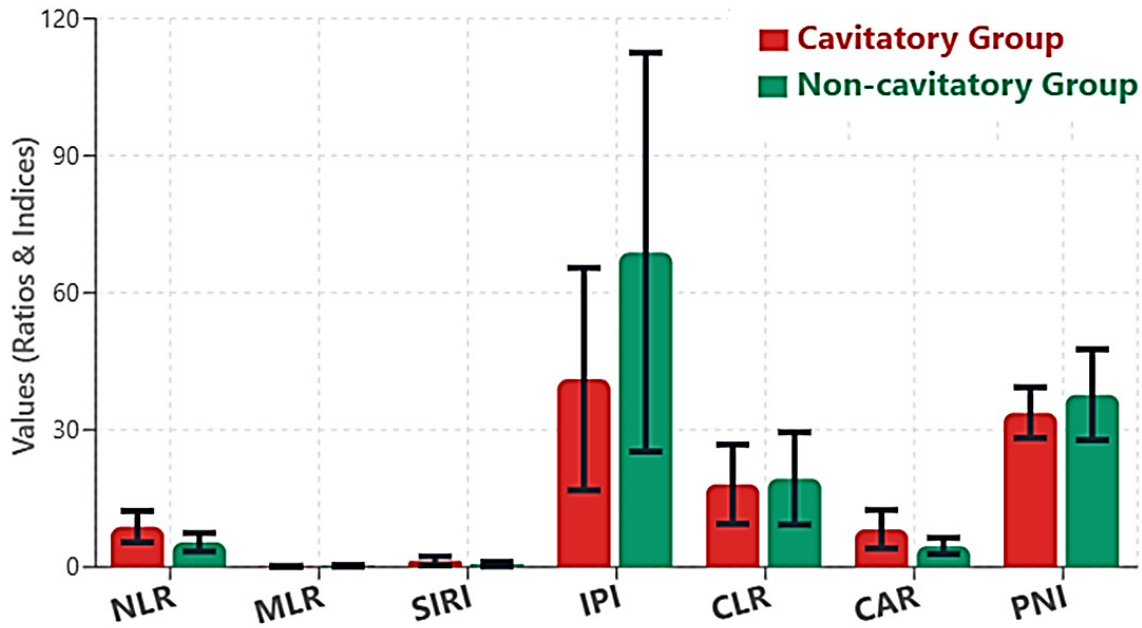

Figure 2B. Shows the comparison of NLR, MLR, SIRI, IPI, CLR, CAR, and PNI between the groups of TB patients

Discussion

TB is a chronic, wasting infectious disease mainly spread by the MTB complex through the air. A positive MTB culture is the gold standard for TB diagnosis, but it is not practically feasible due to the long time spent reporting the cultures.[18] MTB triggers innate and adaptive immunity in the host. The primary immunological response mediated by T cells in MTB-induced adaptive immunity is CD4+ T cells, which are crucial for anti-TB immunity.[19] The ALC in the peripheral blood are frequently utilized to diagnose TB and forecast the intensity and outlook of TB.[19]

A total of 27 sputum-positive PTB patients were included in the study. Among them, 26 (96.3%) were males, with ages ranging between 19 and 86 years. The difference in gender distribution is due to various factors, such as underreporting in females, the presence of social factors- smoking and alcoholism in males, access to treatment, biological differences, occupation-related issues in men, etc.[3] The patients with non-

cavitatory PTB were at a slightly higher age group than the cavitatory group, though not statistically significant (P-value=0.07). This finding was similar to that of the study by Lee KM et al., where the mean age of the tuberculous patients with cavity was 43.8 years.[20] According to the Zhang L et al. study, cavitatory and non-cavitatory TB are prevalent in those aged 45-64 years and above 64 years, respectively.[21] The body mass index in cavitatory and non-cavitatory TB had no statistical significance (P-value=0.26). Only pulmonary TB, not extra-pulmonary TB, have a high correlation with BMI. This is likely because low BMI may make the individual more susceptible to PTB,[22] probably due to variations in pulmonary mechanics, and altered body composition may increase a person's vulnerability to TB.[23]

Both the groups of patients had anemia, with the mean Hb levels in the cavitatory and non-cavitatory groups were 10.84 and 11.15g/dL, respectively (P-value=0.10). In a study by Selvan P et al., anemia is seen in 75.8% of TB patients irrespective of nutritional status. Presence of anemia in TB patients predisposes them to adverse outcomes and recurrences.[24] The liver enzymes, such as AST and ALT, were elevated among the cavitatory group compared to non-cavitatory TB with (P-value=0.01) and (P-value<0.001) respectively. As per the study by Gautam S et al., the transaminases can be elevated due to liver toxicity induced by anti-tuberculous medications, or in rare situations, this may be due to preexisting liver disease.[25] The patients had hypoalbuminemia as evidenced by the serum albumin levels of 2.88 and 3.01 g/dL in cavitatory and non-cavitatory TB respectively (P-value=0.58). (Table 2) Hypoalbuminemia and lymphocytopenia at the time of diagnosis of TB are crucial factors in-hospital death.[26] Compared to cavitary TB, TB pneumonia is associated with older age, lower serum albumin and Hb levels, and a random distribution of lesions in the lung.[20]

Like culture, direct microscopy remains essential for monitoring treatment response, assessing infectiousness, and predicting relapse risk in patients who test positive for smears at diagnosis.[4] A characteristic feature of TB is pulmonary cavitation, which causes infection propagation, poor clinical outcomes, and delayed sputum culture conversion. As age and lesion severity increase, the absolute counts of T, CD4+ T, CD8+ T, and B cells in peripheral blood decline. Consequently, most TB patients have compromised immunological defences, making it crucial to consider both the absolute counts of T lymphocytes and their proportions in TB cases. Absolute lymphocyte subset counts can serve as a basis for immunological intervention and monitoring therapeutic impact due to their strong correlation with lesion severity and aetiological outcomes.[19] In this study, the total WBC counts in the groups were within the biological reference interval, and there was no statistically significant difference between them (P-value=0.43). The ANC was higher in the non-cavitatory TB group than the cavitatory group, with a statistically significant difference (P-value<0.001). The ALC was greater in the cavitatory group than the non-cavitatory group, though this difference was not statistically significant (P-value=0.32). ESR levels were elevated in both groups, but there was no statistically significant difference (P-value=0.95). Platelet counts were normal in both groups (P-value=0.17). Compared to healthy controls, WBC counts, ANC, platelet counts, and ESR values are significantly elevated in TB patients.[27] Serum CRP was elevated, with no statistically significant difference (P-value=0.95) between the groups. (Table 3, Figure 2A) Elevated CRP in PTB is associated with severe disease, and a return to normal values of initially elevated CRP levels may indicate an adequate therapeutic response.[28] According to Chen G et al., the CRP level (84.41±0.76) in pulmonary TB is higher than that of controls (3.12±0.08).[29] Both acute and chronic inflammatory disorders are associated with elevated CRP levels and that CRP participates directly in the pathogenic processes. Improved treatment of inflammation-related disorders may be achievable by distinguishing between physiological and pathological CRP levels.[15,16]

Peripheral blood cell counts and their combinations, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), have recently been identified as indicators of systemic vascular and inflammatory diseases. The NLR accurately predicts patient survival rather than just the neutrophil or lymphocyte counts.[5] In bacteremia, the NLR effectively predicts outcomes and reflects the severity of the disease and is a marker of disease progression. Thus, compared to survivors, non-survivors exhibit a substantially higher NLR. As a marker of sepsis, the NLR is more precise and cost-effective than CRP.[19] MLR and NLR levels have been shown to decrease in TB patients after treatment, and delayed sputum smear conversion in TB patients is associated with elevated MLR and NLR levels at baseline during treatment.[6] The NLR may distinguish patients with pulmonary TB from those with bacterial community-acquired pneumonia.[30]

In the present study, NLR and MLR were higher in the cavitatory group than the non-cavitatory group (P-value=0.01). PLR was lower in the cavitatory group than the non-cavitatory group (P-value=0.03). SII and SIRI were higher in the cavitatory group than the non-cavitatory group, P-value=0.04 and P-value=0.03, respectively. (Table 3, Figure 2B) Thrombocytosis and lymphocytopenia are associated with the degree of systemic inflammation. Thrombocytosis is due to changes in the microcirculation, increased blood vessel permeability, platelet activation, and the aggregation of platelets. As a result, the general inflammatory response becomes worse. A potentially valuable strategy for accurately evaluating inflammatory activity is the combination of PLR and NLR. PLR has a strong correlation with systemic inflammation and is a prospective biomarker for COVID-19, acute coronary syndrome, and other respiratory conditions.[30]

In patients with TB, a high NLR might correlate with disease severity and could predict outcomes or response to treatment. Since it is not specific for TB, it must be interpreted in conjunction with other clinical findings and diagnostic tests. The sensitivity of MLR for identifying proven TB is shown to be on par with other quick diagnostic techniques for microbiologic confirmation that gather samples from children other than sputum.[31] According to Chen G et al., the mean PLR and NLR are higher in PTB patients compared to controls.[29] Pathological changes in pulmonary TB mainly include inflammatory exudation, hyperplasia, and caseous necrosis. PNI and Systemic Inflammatory Response Index (SIRI) may help in the auxiliary diagnosis of bacteria-negative PTB. Both markers help to evaluate systemic inflammation, nutrition, and

immune status, and they have been used in diagnosis and prognosis of cancer and infectious diseases.[12,17] Systemic immune inflammation index (SII) and fibrinogen are positively correlated with the degree of TB inflammation and the bacterial load of *Mycobacterium tuberculosis*.[32] In the present study, IPI and AISI were lower in the cavitatory group compared to the non-cavitatory group (P-value=0.04). PNI was lower in the cavitatory group than the non-cavitatory group (P-value=0.04) (Table 3). The PNI may indicate nutritional and immunological status in cancer patients.[17]

The serum albumin levels are also observed to be lower in patients with malignancies, TB, malnutrition, kidney disease, and hypoalbuminemia. Low serum albumin levels act as independent prognostic markers across various conditions. Hypoalbuminemia can compromise immune function at the cellular level. Inflammatory cytokines such as IL-1, IL-6, and tumor necrosis factor-α inhibit albumin synthesis.[32] Albumin also functions in the scavenging of oxygen-free radicals; when there is hypoalbuminemia as in the present study, the function of albumin is compromised.[33] Lymphocytes play a role in immune recognition and are divided into three types: B cells, T cells, and natural killer cells. Lymphocytopenia would impair the body's anti-cancer or anti-inflammatory response. Lymphocytopenia along with hypoalbuminemia has numerous adverse effects, illustrating efficacy of the PNI in malignancies and TB.[33] Elevated SIRI measurements indicate a heightened inflammatory response and can be a sign of acute immune system stress or an ongoing systemic inflammatory response. Providing helpful information on the body's balance between pro-inflammatory and anti-inflammatory forces aids in assessing the severity of the ailment and the patient's prognosis.[34] The AISI is a recently adopted predictive tool incorporating neutrophils, lymphocytes, monocytes, and platelets. It may offer superior predictive ability compared to simpler indices, as it reflects the inflammatory status of the disease.[35] Prior studies have examined the relationship between AISI and hospital stays in conditions such as COVID-19, idiopathic pulmonary fibrosis (IPF), elective thoracic surgery, and age-related macular degeneration and also in TB.[36]

In the present study, CLR was lower while CAR was higher in the cavitatory group than the non-cavitatory group (Table 3). CRP to albumin ratio (CAR) is significantly lower in patients who turned a negative culture. Studies have demonstrated that combining these two biomarkers, as the CAR, is a better prognostic indicator than CRP or albumin alone.[37-39] Similarly, the present study demonstrated significantly higher values among the cavitatory group than the non-cavitatory group.

In the study by Cao L Y et al, it was observed that the levels of SII, SIRI, NLR, MLR, CAR, CLR, and CRP were higher among those with obstructive airway pattern than those without among the TB patients, favouring higher levels of inflammation. SIRI has a positive predictive efficacy, which helps to understand the inflammatory response. Compared to the NLR or MLR, SIRI provides a thorough understanding of the inflammatory and immunological balance by briefly reflecting the situation with neutrophils, lymphocytes, and monocytes. Possible explanations for the rise in SIRI in TB patients include increased inflammation-related neutrophils, tissue hypoxia caused by obstructive airway patterns that affect immune cell formation and maturation, and a progressive decrease in lymphocyte counts.[40] The comprehensive pathology clarifies that cavitation entails far more active inflammation and ultimately tissue damage. This most likely explains why we found that the cavitatory group of TB patients had higher indices and inflammatory ratios than the non-cavitatory group. A chronic respiratory abnormality, with or without symptoms, that can be at least partially attributed to prior TB is known as post-TB lung disease (PTLD). It encompasses various illnesses, such as pleural disease, fibrotic lung disease, cavitary disease, bronchiectasis, obstructive lung disease, and pulmonary vascular disease. The interactions between microorganisms and the host, as well as the various immunological processes occurring within the host's body, are responsible for this notable clinicopathological heterogeneity.[35]

The clinical course of the patients was uneventful. They showed marked improvement in clinical features. None of the patients faced any complications of TB and the antituberculous drugs. We could not substantiate the same with laboratory or radiological data.

Limitations: The study was a single-centre study. The small sample size, restricted by financial and time constraints, hampered a comprehensive analysis. The patients with latent TB and a healthy group could have substantiated the findings and improved generalizability. Larger sample size would avoid selection bias and recall bias. We could not follow up the patients regarding their laboratory reports which could give a complete information. Future research should aim to validate these findings by comparing ratios across different disease and treatment stages.

Conclusion: The study highlights those inflammatory indices such as ANC, NLR, MLR, PLR, SII, SIRI, IPI, AISI, CLR, CAR, and PNI, serve as straightforward and cost-effective biomarkers at the time of diagnosis. These biomarkers provide valuable prognostic information and can help identify patients with and without cavity in PTB. PNI and CAR also serve as nutritional indices, which add information on prognosis. Further prospective studies and studies on drug-resistant TB could improve the management of TB.

Ethical Considerations

The IEC had approved the study vide IEC number IEC/21/JUN/163/43. The study was registered with the ICMR, India, CTRI/2023/08/056740 (https://ctri.nic.in/Clinicaltrials/login.php). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000, on Ethical Principles for Medical Research Involving Humans. All the participants provided written informed consent before enrolling in the study.

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Conflict of Interest

The authors declare that there were no conflicts of interest during the study as well as in the publication of this manuscript.

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