ORIGINAL ARTICLE

CLINICAL EVALUATION OF SYSTEMIC INFLAMMATION MARKERS IN PATIENTS DIAGNOSED WITH PULMONARY TUBERCULOSIS

Akciğer Tüberkülozu Tanılı Hastalarda Sistemik İnflamasyon Göstergelerinin Klinik Değerlendirilmesi

Ummuhan Tugba TUMUKLU[1], Seyma TASTEMUR[2], Mert USTUNDAG[3], Duygu FELEK[4], Omer Tamer DOGAN[3], Zehra SEYFIKLI[1]

[1]Yozgat Bozok Üniversitesi, Tıp Fakültesi, Göğüs Hatsalıkları Anabilim Dalı, Yozgat, Türkiye.
[2]Sivas Cumhuriyet Üniversitesi, Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Genel Dahiliye Bilim Dalı, Sivas, Türkiye.
[3]Sivas Cumhuriyet Üniversitesi, Tıp Fakültesi, Göğüs Hastalıkları ve Tüberküloz Anabilim Dalı, Sivas, Türkiye.
[4]Yozgat Bozok Üniversitesi, Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Yozgat, Türkiye.

Ümmühan Tuğba TÜMÜKLÜ, Dr. Öğr. Ü.
(https://orcid.org/0009-0002-2998-9740)
✉ tugba.tumuklu@bozok.edu.tr

Şeyma TAŞTEMUR, Dr. Öğr. Ü.
(https://orcid.org/0000-0002-9013-6395)
✉ seymatastemur@cumhuriyet.edu.tr

Mert ÜSTÜNDAĞ, Arş. Gör.
(https://orcid.org/0009-0005-3800-3762)
✉ merstappen277@gmail.com

Duygu FELEK, Dr. Öğr. Ü.
(https://orcid.org/0000-0002-7689-4552)
✉ d.kocamemik@gmail.com

Ömer Tamer DOĞAN, Prof. Dr.
(https://orcid.org/0000-0002-4527-7754)
✉ tdogan@cumhuriyet.edu.tr

Zehra SEYFİKLİ, Prof. Dr.
(https://orcid.org/0000-0002-6204-8224)
✉ zehraseyfikli@gmail.com

İletişim:
Dr. Öğr. Ü. Ümmühan Tuğba TÜMÜKLÜ
Yozgat Bozok Üniversitesi, Tıp Fakültesi, Göğüs Hatsalıkları Anabilim Dalı, Yozgat, Türkiye.

Geliş tarihi/Received: 04.12.2025
Kabul tarihi/Accepted: 05.02.2026
DOI: 10.16919/bozoktip.1834930

ABSTRACT

Objective: This study aimed to investigate the levels of systemic inflammation markers including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hematological ratios, and complete blood count parameters in individuals diagnosed with pulmonary tuberculosis (TB). The clinical significance of these biomarkers in the diagnosis, disease activity, and treatment response was evaluated, and their associations with age, sex, and comorbidities were also analyzed.

Material and Methods: Following ethics approval (2025-GOKAEK-2517), hospital records of patients aged 18-80 years diagnosed with pulmonary tuberculosis between 2023 and 2025 at Yozgat Bozok University and Sivas Cumhuriyet University were retrospectively reviewed. The control group consisted of healthy individuals who presented during the same period. Hemogram parameters, CRP, ESR, and the Systemic Immune-Inflammation Index (SII) were assessed, and statistical analyses were performed using SPSS v22.0.

Results: A total of 134 individuals (67 TB and 67 controls) were included. In the TB group, 70.1% were male, and the mean age was 48.76±18.01 years. Comorbidities were present in 70.1% of patients, most commonly COPD, hypertension, and coronary artery disease. The TB group demonstrated significantly higher leukocyte, neutrophil, monocyte, platelet, CRP, ESR, and SII levels, while hemoglobin and lymphocyte levels were significantly lower (all $p<0.0001$). Although the mean SII value was elevated (2772.51±4004.20), it did not show a significant association with diagnostic test results or clinical outcomes.

Conclusion: The markedly elevated SII levels in patients with pulmonary tuberculosis suggest that this index may serve as a potential biomarker reflecting increased systemic inflammation. However, its limited correlation with diagnostic and clinical endpoints indicates that it should be considered a supportive-not standalone-parameter in clinical evaluation.

Keywords: *Pulmonary Tuberculosis; Systemic Immune-Inflammation Index (SII); C-Reactive Protein (CRP)*

ÖZET

Amaç: Bu çalışma, akciğer tüberkülozu (ATB) tanısı alan bireylerde sistemik inflamasyon göstergelerinin (C-reaktif protein (CRP), Eritrosit Sedimentasyon Hızı (ESR), hematolojik oranlar ve hemogram parametreleri) düzeylerini inceleyerek, bu belirteçlerin hastalığın tanı, aktivite ve tedaviye yanıt süreçlerindeki klinik değerini değerlendirmeyi amaçlamaktadır. Ayrıca, bu biyobelirteçlerin yaş, cinsiyet ve komorbiditelerle ilişkisi analiz edilmiştir.

Gereç ve Yöntemler: 2025-GOKAEK-2517 etik kurul onayıyla, 2023-2025 yılları arasında Yozgat Bozok ve Sivas Cumhuriyet Üniversiteleri'nde akciğer tüberkülozu tanılı 18-80 yaş arası bireylerin hastane kayıtları retrospektif olarak incelenmiştir. Kontrol grubunu benzer dönemde başvuran sağlıklı bireyler oluşturmuştur. Verilerden hemogram parametreleri, CRP, ESR ve sistemik immün-inflamasyon indeksi (SII) değerlendirilmiş; analizler SPSS v22.0 ile yapılmıştır.

Bulgular: Toplam 134 bireyin (67 ATB, 67 kontrol) dahil edildiği çalışmada, ATB grubunda erkek oranı %70,1, yaş ortalaması 48,76±18,01 yıl idi. Komorbidite oranı %70,1 olup en sık KOAH, hipertansiyon ve koroner arter hastalığı görüldü. ATB grubunda lökosit, nötrofil, monosit, trombosit, CRP, ESR ve SII düzeyleri anlamlı derecede yüksek; hemoglobin ve lenfosit düzeyleri düşük bulundu (tümü $p<0,0001$). SII değeri 2772,51±4004,20 idi ancak tanısal testler ve klinik sonlanımlarla anlamlı ilişki göstermedi.

Sonuç: ATB hastalarında SII değerlerinin yüksek bulunması, bu indeksin artmış sistemik inflamasyonu yansıtan potansiyel bir biyobelirteç olabileceğini düşündürmektedir.

Anahtar Kelimeler: *Akciğer Tüberkülozu; Sistemik İmmün-İnflamasyon İndeksi (SII); C-Reaktif Protein (CRP)*

INTRODUCTION

Tuberculosis (TB) remains one of the most common and deadly chronic infectious diseases throughout human history and continues to pose a significant global public health threat. Caused by members of the Mycobacterium tuberculosis complex, the disease primarily affects the lungs but can involve multiple organs and systems. Pulmonary TB cases constitute the main source of transmission, thereby sustaining the infectious cycle (1). The World Health Organization (WHO) describes tuberculosis as "a preventable and treatable infectious disease that nevertheless remains inadequately controlled worldwide" (1). Despite notable advances in diagnostic and therapeutic strategies, the persistent challenges in TB eradication underscore the need for a comprehensive approach that encompasses its biological, socioeconomic, epidemiological, and clinical dimensions.

Globally, although the annual incidence of TB has shown only a slow decline over the past decade, the 2024 WHO report highlights that approximately 10.6 million new cases and 1.3 million TB-related deaths still occur each year. Furthermore, underreporting of cases increased in the aftermath of the COVID-19 pandemic, during which TB control programs were disrupted (2). These trends reinforce the necessity for more innovative, rapid, and accessible diagnostic tools in TB management.

Türkiye has long maintained nationwide TB control programs; however, national data indicate that the disease has not yet been fully controlled and that the decline in incidence is slowing (3-5). As of 2023, the incidence of TB in Turkey was reported as 13.1 per 100,000 population (3). Regional disparities, socioeconomic inequalities, migration dynamics, and delayed diagnosis in elderly populations further complicate the epidemiological landscape (4,5).

Sputum microscopy, culture, and molecular assays constitute the primary diagnostic methods for TB. Nevertheless, these tests have notable limitations, including variable sensitivity, long turnaround times, laboratory infrastructure requirements, and reduced applicability in extrapulmonary cases (6-9). Consequently, the need for inexpensive, rapid, easily obtainable biomarkers that can reflect systemic inflammation has gained increasing importance in recent years.

TB infection triggers a pronounced inflammatory response by affecting the host immune system, leading to significant alterations in acute phase reactants and hematological parameters (10,11). Although elevations in biomarkers such as CRP, ESR, and fibrinogen have long been recognized, their limited specificity prevents them from serving as standalone diagnostic tools (10-12).

Consequently, in recent years, new biomarker models that may aid both diagnosis and prognostic assessment have garnered increasing attention. Indices derived from complete blood count parameters such as the neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), and the Systemic Immune Inflammation Index (SII) have been reported to be significantly elevated in TB and may correlate with disease activity (12-14). Additionally, other inflammation associated metrics, such as the fibrinogen to albumin ratio and red cell distribution width (RDW), have been proposed as potential indicators of TB severity and treatment response (13,14).

However, most studies evaluating these biomarkers have been conducted in different countries and patient populations, and research assessing their diagnostic accuracy, optimal cut-off values, and prognostic relevance in the Turkish population remains limited (3-5,12-15). Recent evidence also suggests that the performance of inflammatory biomarkers may vary in patients with comorbidities such as diabetes mellitus-highlighting the need for population-specific investigations (15). This underscores the importance of conducting independent, region specific studies to better define the clinical utility of these parameters.

The present study aims to evaluate the diagnostic and prognostic value of inflammation-based hematological markers in patients diagnosed with pulmonary tuberculosis, assess their suitability for clinical use, and contribute to the existing literature with population specific data. Designed in accordance with ethical standards, this study seeks to provide a scientific evaluation of easily accessible biomarkers that may support TB diagnosis and monitoring.

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

MATERIAL AND METHOD

This study was initiated following approval from the Non-Interventional Clinical Research Ethics Committee of Yozgat Bozok University (2025-GOKAEK-25172025.10.01 649). Hospital records of adult patients aged 18-80 years who were diagnosed with pulmonary tuberculosis and presented to the Departments of Chest Diseases and Internal Medicine at Yozgat Bozok University and Sivas Cumhuriyet University between January 1, 2023 and January 1, 2025 were retrospectively reviewed.

The control group consisted of healthy individuals who presented to the same clinics during the same period, had no active infections or chronic diseases, possessed complete laboratory data, and were accepted as "healthy." Individuals with similar age and sex characteristics to the patient group were identified using simple random sampling through the hospital information system.

Data were obtained retrospectively from the digital medical record systems of the affiliated hospitals of Yozgat Bozok University and Sivas Cumhuriyet University. In addition to basic demographic parameters such as age, sex, and medical history, laboratory variables including red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), total leukocyte count (WBC), neutrophil, lymphocyte, monocyte, eosinophil and basophil percentages, platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) were recorded.

Inflammatory markers, including ESR and CRP, were also documented. Additionally, to provide a more integrative assessment of systemic inflammation, the Systemic Immune-Inflammation Index (SII) was calculated for each participant using the formula: (neutrophil × platelet) / lymphocyte.

No additional medical intervention or biological sampling was performed as the study relied entirely on archived clinical data.

The data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA)The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test, and appropriate statistical tests were selected based on distribution characteristics. For normally distributed variables, group comparisons were performed using the Independent Samples t-test, whereas the Mann-Whitney U test was used for non-normally distributed data.

Associations between variables were evaluated using Pearson or Spearman correlation coefficients, depending on data distribution. A p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 134 individuals were included in this retrospective study. Of these, 67 constituted the patient group diagnosed with pulmonary tuberculosis, while the remaining 67 individuals formed the healthy control group. As per the study design, the groups were matched for age and sex. Among the TB patients, 70.1% were male and 29.9% were female; a similar sex distribution was observed in the control group. The mean age of the TB group was 48.76±18.01 years (range: 15-80 years), and the mean age of the control group was comparable. No statistically significant differences were found between the groups in terms of age (p=0.91) or sex (p=0.83).

Evaluation of smoking history revealed that 25 of the 67 TB patients (37.3%) were smokers, compared to 35 individuals (52.2%) in the control group. Smoking status in both groups was categorized as "present" or "absent" based on patient records. Detailed information regarding pack-years was unavailable; therefore, the assessment was limited to presence or absence of smoking. The comparison of smoking prevalence between the groups showed no statistically significant difference (p=0.118).

A substantial proportion of individuals in the TB group had accompanying chronic comorbidities. Analysis showed that 47 patients (70.1%) had at least one comorbid condition, while only 20 patients (29.9%) had no reported comorbidities. Comorbidity data were obtained directly from patient medical records. Among the comorbid conditions, chronic obstructive pulmonary disease (COPD) was the most prevalent, identified in 27 patients (40.3%). This was followed by hypertension (HT) in 22 patients (32.8%), coronary artery disease (CAD) in 21 patients (31.3%), malignancy

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

in 11 patients (16.4%), and diabetes mellitus (DM) in 8 patients (11.9%).

When comorbidity combinations were examined, the most common pairing was HT and CAD, concurrently present in 14 patients. This was followed by CAD + COPD (n=12), HT + COPD (n=7), COPD + malignancy (n=7), and DM + HT (n=5). In contrast, individuals in the control group were selected specifically to be healthy, with no chronic medical conditions, in accordance with the study's inclusion criteria. This approach minimized the confounding effects of comorbidities when comparing inflammatory parameters and ensured a more clinically balanced comparison between patient and control groups.

Evaluation of presenting symptoms among TB patients revealed that the disease typically manifested with prominent clinical findings. The most frequently reported symptom was cough, present in 63 patients (94.0%). This was followed by sputum production in 53 patients (79.1%), weight loss in 40 patients (59.7%), and hemoptysis in 28 patients (41.8%), indicating the frequent coexistence of respiratory and systemic manifestations. Additional systemic symptoms included fever in 25 patients (37.3%), night sweats in 12 patients (17.9%), loss of appetite in 11 patients (16.4%), and fatigue in 10 patients (14.9%). In contrast, dyspnea was observed in only 3 patients (4.5%), and no cases of chest pain were recorded (Figure 1).

Among the 67 individuals diagnosed with TB, acid-fast bacilli (AFB) smear positivity was detected in 47 patients (70.1%), while 19 patients (28.4%) were smear-negative. One patient (1.5%) could not provide a sputum sample and was therefore excluded from smear analysis. Polymerase chain reaction (PCR)-based TB DNA testing-one of the sensitive molecular diagnostic tools used in TB diagnosis-was also evaluated in this study. Of the 67 TB patients, 37 (55.2%) tested positive for TB DNA, whereas 24 (35.8%) tested negative; results were unavailable for 6 patients (9.0%) in the medical record system.

Examination of mycobacterial culture results revealed that 43 patients (64.2%) demonstrated growth of Mycobacterium tuberculosis complex, confirming the diagnosis microbiologically. No growth was observed in 19 patients (28.4%), while atypical mycobacteria (e.g., M. kansasii, M. abscessus) were isolated in 3 patients. Culture results for 2 patients were not recorded.

In cases where diagnostic test results were negative but clinical and radiological suspicion remained high, advanced diagnostic procedures were required. Accordingly, a definitive diagnosis was established by lung biopsy in four patients whose AFB smear, TB DNA test, and culture results were all negative. Overall, AFB smear positivity was the most frequently observed diagnostic outcome (70.1%), followed by culture positivity (64.2%) and TB DNA test positivity (55.2%). However, in the subgroup of four patients with negative results across these three methods, histopathological confirmation by biopsy was necessary.

Analysis of diagnostic concordance revealed a statistically significant association between AFB smear positivity and culture positivity ($p<0.001$). Similarly, a significant correlation was observed between TB DNA test results and culture findings ($p<0.01$).

Comparative analysis between TB patients and healthy controls demonstrated significant differences in hematological parameters. The mean leukocyte (WBC) count was significantly higher in the TB group (9.02±2.99 $\times10^3/\mu L$) compared to controls (6.53±1.82 $\times10^3/\mu L$) ($p<0.0001$). Platelet (PLT) count was also significantly elevated in the TB group (356.13±134.32 $\times10^3/\mu L$) compared with the control group (240.24±48.35 $\times10^3/\mu L$) ($p<0.0001$). In contrast, hemoglobin (HGB) levels were significantly lower in TB patients (12.45±2.12 g/dL) than in controls (13.76±2.67 g/dL) ($p<0.0001$).

Evaluation of white blood cell subparameters revealed that the neutrophil count was significantly higher in the TB group (6.56±2.63 $\times10^3/\mu L$) compared with the control group (3.95±1.62 $\times10^3/\mu L$) ($p<0.0001$). Lymphocyte levels were significantly lower in TB patients (1.51±0.95 $\times10^3/\mu L$) than in controls (2.04±0.62 $\times10^3/\mu L$) ($p<0.0001$). Additionally, the monocyte count was markedly elevated in the TB group (0.74±0.29 $\times10^3/\mu L$) compared with healthy individuals (0.37±0.10 $\times10^3/\mu L$), and this difference was statistically significant ($p<0.0001$) (Table 1).

Significant differences were also found between TB patients and healthy controls regarding acute-phase reactants. The mean CRP level in the TB group was 58.64±49.55 mg/L, whereas it was 1.89±2.44 mg/L in the control group ($p<0.0001$). Similarly, erythrocyte

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

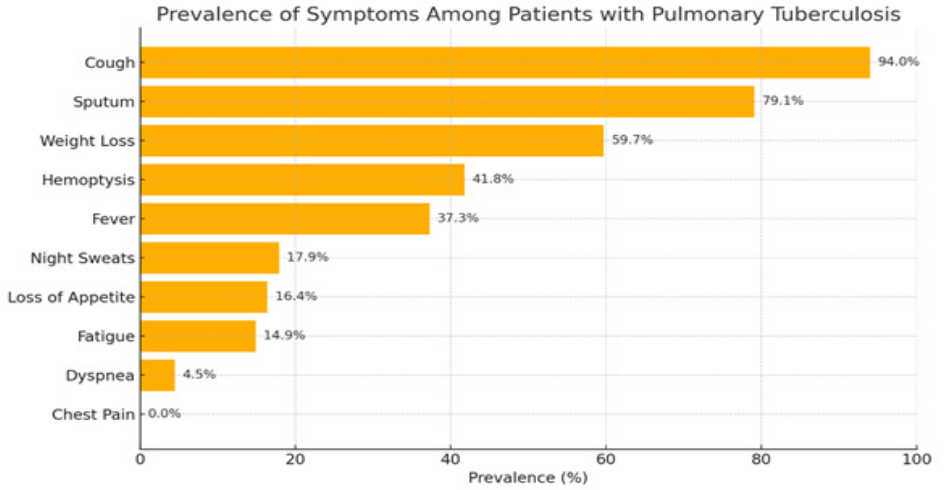

Figure 1. Prevalence of reported symptoms among patients diagnosed with pulmonary tuberculosis.

Table 1. Comparison of hematological parameters between TB and control groups

Parameter (unit)	TB mean ± SD	Control mean ± SD	p-value
WBC (x10³/µL)	9.02±2.99	6.53±1.82	< 0.0001
Hemoglobin (g/dL)	12.45±2.12	13.76±2.67	< 0.0001
Platelet (x10³/µL)	356.13±134.32	240.24±48.35	< 0.0001
Neutrophil (x10³/µL)	6.56±2.63	3.95±1.62	< 0.0001
Lymphocyte (x10³/µL)	1.51±0.95	2.04±0.62	< 0.0001
Monocyte (x10³/µL)	0.74±0.29	0.37±0.10	< 0.0001

TB: Pulmonary tuberculosis, SD: Standard deviation, g/dL: Gram/desiliter, WBC: White blood cells

sedimentation rate (ESR) values were markedly elevated in TB patients (52.21±33.04 mm/hour) compared with controls (7.00±4.39 mm/hour) (p<0.0001) (Table 2).

The mean SII value was substantially higher in the TB group (2772.51±4004.20) compared with the control group (545.74±488.44), and this difference was statistically significant (p<0.0001) (Figure 2).

The relationship between SII values-representing systemic inflammation-and the three main diagnostic modalities (AFB smear, TB DNA PCR, and mycobacterial culture) was also examined. Although SII levels were higher in AFB-positive patients (3223.45±4745.51) compared with AFB-negative patients (1829.30±1385.23), this difference did not reach statistical significance (p=0.486). Similarly, TB DNA-positive patients had higher mean SII values (3451.47±5017.66) compared with TB DNA negative individuals (1942.50±2117.05), but the difference was not statistically significant (p=0.163). Mycobacterial culture-positive patients had a mean SII of 3171.24±4713.90, whereas culture-negative patients had a mean value of 2108.94±2363.99 (p=0.372).

To explore the association between systemic inflammatory burden and clinical presentation, the number of reported symptoms per patient was quantified, and a correlation analysis was performed. Spearman correlation testing revealed no statistically significant association between symptom count and SII values (ρ=0.002, p=0.986).

In our study, all individuals diagnosed with TB received the standard four-drug anti-tuberculosis regimen isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) recommended by the Ministry of Health. At the end of the treatment course, clinical outcomes were categorized into six distinct groups. Complete clinical recovery was achieved in 35 patients (52.2%), while 12 patients (17.9%) were followed with documented culture conversion. Sequelae developed in 8 patients (11.9%), complications occurred in 5 patients (7.5%),

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

Table 2. Comparison of CRP and sedimentation levels between TB and control groups

Parameter (unit)	TB mean ± SD	Control mean ± SD	p-value
CRP (mg/L)	58.64±49.55	1.89±2.44	<0.0001
ESR (mm/h)	52.21±33.04	7.00±4.39	<0.0001

CRP: C-reaktif protein, TB: Pulmonary tuberculosis, SD: Standard deviation, mg/L: Milligram/liter, mm/h: Millimeter/hour, ESR: Erythrocyte sedimentation rate

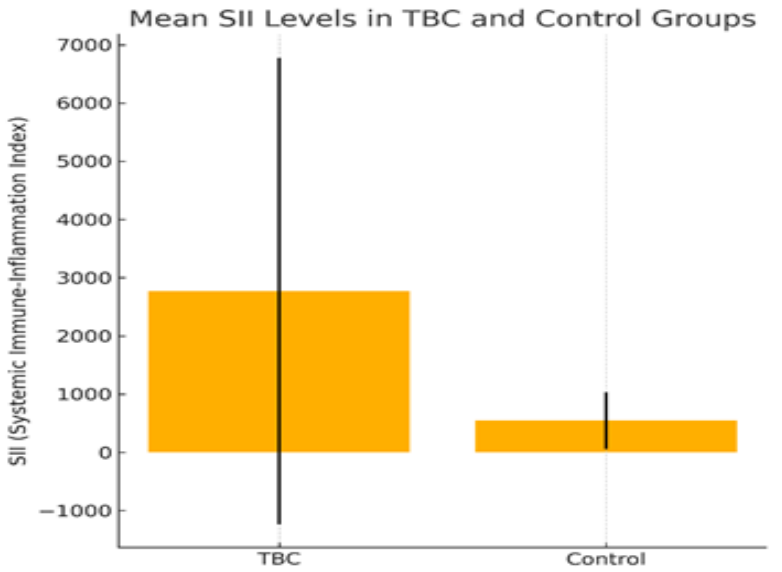

Figure 2. Mean Systemic Immune-Inflammation Index (SII) Levels in TB and Control Groups

disease relapse was observed in 4 patients (6.0%), and death occurred in 3 patients (4.5%).

SII (Systemic Immune-Inflammation Index) values, reflecting systemic inflammatory burden, were also evaluated across these outcome categories. The mean SII value was 2573.76±3882.33 in patients who achieved full recovery, and 3064.20±5510.14 among those monitored through culture conversion. Patients who developed sequelae had a mean SII of 1489.52±882.94; those who experienced complications had a mean value of 2302.46±1403.31. In cases with disease relapse, the mean SII was 3213.23±4593.64, while the highest values were observed in patients who died, with a mean SII of 5564.89±7513.27.

Statistical analysis indicated that SII values did not significantly differ across clinical outcome categories (p=0.132).

DISCUSSION

In this study, the retrospective design with age- and sex-matched patient and control groups allowed the findings to be interpreted independently of demographic confounders. The majority of individuals diagnosed with TB were male (70.1%), and the mean age of the patient group (48.76±18.01 years) represented the middle-aged adult population. This demographic pattern is consistent with previous global epidemiological reports on tuberculosis. For instance, World Health Organization (WHO) data indicate that TB incidence is significantly higher in men than in women (1). Similarly, a national epidemiological study conducted in Türkiye reported that approximately two-thirds of all TB cases occur in males (2). This sex-related disparity may be linked to higher exposure risk among men, behavioral differences in healthcare-seeking practices, or physiological variations in immune responses across sexes. Moreover, the wide age range of TB patients in our study (15-80 years) highlights that tuberculosis affects not only elderly or immunocompromised individuals but also young adults. The demographic balance obtained in this study strengthens the objectivity of biomarker analysis by

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

minimizing age- and sex-related confounding effects. In our cohort, 37.3% of TB patients and 52.2% of controls reported a history of smoking, with no statistically significant difference between the two groups. This finding reflects the ongoing debate regarding whether smoking is an independent determinant of TB development. Numerous studies have explored the association between smoking and TB, yet results vary widely depending on study design, population characteristics, and measurement approaches. For example, a meta-analysis by Lin et al. reported that active smoking significantly increases the risk of developing TB (16). WHO data likewise identify tobacco use as a key environmental risk factor that increases both susceptibility to TB infection and the likelihood of poor treatment outcomes (1). However, the absence of quantitative smoking metrics such as pack years in our study limits the ability to examine the association at a granular level. Additionally, the high prevalence of smoking in the general population and the influence of sociodemographic variables unrelated to TB further complicate the interpretation of this relationship. Consequently, our study could evaluate smoking status only in binary terms (present/absent), which did not yield a significant difference between groups. These findings underscore the need for more detailed, population-specific research to clarify the smoking-TB relationship.

Pulmonary tuberculosis is not merely a respiratory infectious disease; rather, it is closely intertwined with the overall health status of the individual and frequently coexists with chronic systemic comorbidities. In our study, the presence of at least one comorbid condition in approximately 70% of TB patients underscores the clinical relevance of this association. Notably, cardiopulmonary disorders such as COPD, hypertension, and coronary artery disease were the most prevalent. A large-scale cohort study from Taiwan demonstrated that individuals with COPD have a significantly increased risk of developing TB, suggesting that COPD may serve as an independent risk factor for tuberculosis (17).

Similarly, emerging evidence indicates that latent TB infection may negatively influence the cardiovascular system even in the absence of active disease. In a long-term cohort study conducted among immigrant populations in Canada, Hossain et al. reported a significantly higher incidence of cardiovascular disease in individuals with latent TB infection (18). The systemic inflammatory burden of TB is not limited to infection-related complications; it may also exert effects on vascular structures, predisposing individuals to acute cardiovascular events. This was corroborated by findings from Chung et al., who demonstrated that individuals with a history of TB had a markedly increased risk of acute coronary syndrome (19).

Furthermore, the coexistence of COPD and TB appears to be critical not only in terms of inflammatory status but also in susceptibility to infection. A population-based prospective cohort study from Sweden identified COPD as a significant risk factor for TB development, particularly among older adults (20). Collectively, these findings indicate that the evaluation of comorbid conditions is essential in the management of TB and that a comprehensive, multidisciplinary clinical approach is warranted. The use of a healthy, comorbidity-free control group in our study minimized the confounding effects of chronic diseases and allowed for a more objective assessment of inflammatory markers.

The clinical symptoms observed in individuals with pulmonary tuberculosis are closely linked to the infectious burden and the intensity of the host immune response. In the present study, cough was the most frequently reported symptom (94%), consistent with the classical clinical presentation of TB. This was followed by sputum production, weight loss, and hemoptysis-findings that align with those reported in retrospective analyses from high-prevalence regions. For example, a five-year cohort analysis by Autentico and Lim (2025) showed that cough and sputum production were the most common presenting symptoms, observed in more than 85% of TB cases (21). The clinical symptomatology of pulmonary tuberculosis extends beyond the respiratory system and often presents alongside systemic inflammatory responses. According to the 2024 position statement of the Indian Society of Critical Care Medicine (ISCCM), systemic symptoms such as fever, night sweats, weight loss, and anorexia become more prominent during periods of heightened immune activity and offer important diagnostic clues (22). In our study, these systemic manifestations were observed at comparable

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

frequencies, supporting the concept that TB is not merely a localized pulmonary infection but a systemic disease with wide-ranging clinical implications.

In addition, the symptom profile of TB may be closely associated with an individual's immunological status, the duration of infection, and the pattern of pathogen dissemination. Carabalí-Isajar et al. (2023) demonstrated that the severity of symptoms in TB correlates with the host's immunological response profile and that clinical presentation is influenced not only by mycobacterial burden but also by host-related factors (23). This highlights the need for clinicians to interpret symptom diversity in conjunction with immunological status rather than solely as a marker of disease extent. In our cohort, the notably low frequencies of dyspnea and chest pain (4.5% and 0%, respectively) may be explained by the absence of pleural involvement or severe respiratory compromise in most cases.

The complementary roles of conventional and molecular diagnostic tools in TB are becoming increasingly evident. Acid-fast bacilli (AFB) microscopy using Ziehl-Neelsen staining remains one of the most widely used diagnostic methods in clinical practice and is particularly advantageous for rapidly identifying highly infectious individuals. However, its sensitivity is limited, especially in cases with low bacterial load (24). In recent years, nucleic acid amplification tests (NAATs) particularly PCR based TB DNA assays have gained prominence due to their rapid turnaround time and high specificity (25). Nonetheless, a negative PCR result does not reliably exclude TB, as false negatives can occur due to technical limitations, suboptimal specimen quality, or low bacillary burden. Such circumstances may necessitate histopathological confirmation through biopsy, as observed in several patients in our study.

Similarly, although culture remains the gold standard for TB diagnosis, the lengthy processing time limits its utility in scenarios requiring rapid clinical decision-making (26). Previous studies have reported strong associations between culture positivity and both AFB smear results and NAAT findings an observation that aligns with our own results. The robust correlation between AFB microscopy and culture outcomes in our study underscores the complementary value of these methods in microbiological diagnosis. Conversely, the presence of patients who were negative across smear, PCR, and culture but ultimately diagnosed via biopsy highlights the critical importance of a multidisciplinary diagnostic approach in managing TB.

Hematological alterations in patients with tuberculosis are widely recognized as important biomarkers reflecting the systemic impact of the infection. In the study by Yaranal et al., leukocytosis, neutrophilia, lymphopenia, anemia, and thrombocytosis were reported to occur at significantly higher frequencies in individuals with TB, underscoring the intense inflammatory response elicited by the disease (27). Consistent with these findings, our study also demonstrated markedly elevated leukocyte, neutrophil, and platelet counts in the TB group compared with healthy controls, while hemoglobin levels were significantly reduced.

The influence of tuberculosis on the immune response is particularly evident at the level of cellular immunity. Kim et al. emphasized the critical role of the adaptive immune system especially lymphocyte mediated responses in TB pathogenesis and suggested that disruption of this process may lead to lymphopenia (28). The significant lymphopenia observed in our cohort likely reflects this underlying immunopathological mechanism. Moreover, platelet abnormalities in TB extend beyond quantitative elevations; functional platelet parameters may also be affected. As demonstrated by Şahin et al., TB patients exhibit significant alterations not only in platelet counts but also in platelet volume and distribution indices, highlighting the need to consider platelet functionality in the hematological assessment of TB (29). Additionally, Lee et al. reported that anemia associated with TB is typically normochromic and normocytic, often developing as a consequence of chronic inflammatory processes (30). The significant anemia identified in our study is consistent with these observations. Collectively, these findings support the role of hematological parameters as complementary biomarkers in the diagnosis, monitoring, and prognostic evaluation of tuberculosis.

In our study, both classical acute-phase reactants and systemic inflammation markers were significantly elevated in TB patients compared with healthy controls. Notably, CRP levels averaged 58.64±49.55 mg/L in

Bozok Tıp Derg 2026;16(1):37-47
Bozok Med J 2026;16(1):37-47

the TB group, whereas they remained much lower in the control group (1.89±2.44 mg/L) ($p<0.0001$). This marked difference reflects the strong systemic inflammatory response associated with TB. Consistent with our findings, Kang et al. (2009) highlighted CRP as an important biomarker in differentiating TB from bacterial community-acquired pneumonia, noting that although CRP levels are elevated in TB, they tend to be lower than those observed in acute bacterial infections (31). In contrast, CRP levels in our cohort were considerably high, which may be attributed to factors such as extensive disease burden, the presence of comorbidities, or heightened inflammation at the time of diagnosis.

Significant elevations were also noted in other inflammatory parameters, including ESR and SII. When considered alongside the findings of Kang et al., our results underscore that TB is not merely a localized pulmonary infection but a systemic inflammatory disease. These biomarkers may therefore serve as valuable tools in clinical decision-making during the diagnostic process (31).

In the context of our discussion, the markedly elevated levels of CRP, ESR, and SII observed in individuals diagnosed with TB clearly reinforce the notion that tuberculosis carries a strong systemic inflammatory component. In particular, the significantly higher SII values in the TB group compared with healthy controls suggest that this parameter may provide insight into the immunopathogenesis of TB. This finding aligns with the results of Pang et al. (2025), who reported a positive relationship between latent TB infection and elevated SII levels (32). Similarly, Tiu et al. (2025) demonstrated that increased inflammatory indices in TB patients may have potential utility not only in diagnosis but also in predicting disease severity (12).

However, in our study, no statistically significant associations were found between SII and the three principal diagnostic modalities AFB smear, TB DNA PCR, and mycobacterial culture. This suggests that while SII may not possess strong diagnostic sensitivity, it likely reflects underlying immunological activity. Indeed, a systematic review by Espinosa Pereiro et al. (2024) highlighted that certain biomarkers may not directly correlate with mycobacterial burden but can nonetheless provide valuable information regarding treatment response and inflammatory dynamics (33).

In this context, the absence of a clear relationship between systemic inflammatory burden and clinical outcome categories further indicates that SII should not be considered a standalone determinant. However, when interpreted alongside clinical and microbiological findings, it may serve as a supportive marker. Consistent with the literature, the higher SII values observed among patients who developed complications or died suggest that this index may have prognostic relevance.

Taken together, our findings support the consideration of SII as a complementary biomarker in TB, although it is unlikely to function as an independent diagnostic tool.

While the present study contributes to a better understanding of hematological and inflammatory changes in individuals with TB, several limitations should be acknowledged. First, the retrospective design necessitated reliance on medical records and hospital databases, which may have resulted in missing or incomplete data for certain variables. Second, symptom assessment depended on subjective patient reports at the time of admission; thus, important clinical details such as symptom severity or duration could not be evaluated. Another limitation relates to the modest sample size, which restricts the generalizability of subgroup comparisons and may reduce statistical power.

CONCLUSION

This study demonstrates that tuberculosis is not merely a localized respiratory infection but a systemic inflammatory condition. The marked alterations observed in hematological and immuno-inflammatory parameters clearly reflect the substantial impact of TB on the host immune system. The significantly elevated SII values among individuals with TB suggest that this index may serve as a potential biomarker reflecting the immunopathogenesis of the disease. However, the limited association between SII and conventional diagnostic tools or clinical outcomes indicates that SII is unlikely to function as a standalone diagnostic or prognostic marker; rather, it may serve as an adjunctive parameter within the broader clinical assessment.

Hematological abnormalities observed in TB patients,

together with elevated CRP and ESR levels, underscore the importance of recognizing the systemic effects of the infection. This is particularly relevant in patients with comorbid conditions, in whom clinical monitoring should be conducted with greater caution. The findings of this study indicate that novel inflammatory indices such as SII may play a supportive role in the diagnosis, monitoring, and potentially the evaluation of treatment response in TB. Nevertheless, larger, prospective, and controlled studies are required to further clarify the clinical utility, diagnostic performance, and prognostic potential of these biomarkers.

Acknowledgment

The authors declared that this study has received no financial support and no conflict of interest between the authors.

REFERENCES

1. World Health Organization. WHO consolidated guidelines on tuberculosis: Module 6 - tuberculosis and comorbidities. Geneva: World Health Organization; 2024.

2. Goletti D, Meintjes G, Andrade BB, Zumla A, Lee SS. Insights from the 2024 WHO global tuberculosis report: more action, innovation, and investment required to achieve End-TB goals. Int J Infect Dis. 2025;150:1-5.

3. Yigci D, Kayı İ, Demiroğlu YZ, Kutlu M, Kılıçaslan Z, Ergönül Ö. Tuberculosis in Türkiye: epidemiological insights and recommendations for progress. Eur J Clin Microbiol Infect Dis. 2025;44:1-10.

4. Avcı E, Muharremoğlu ZD, Bozkurt ENN, Kaygusuz S. Changing epidemiology of tuberculosis and actions taken in the world and Türkiye. J Clin Pract Res. 2024;46(5):421-30.

5. Kıran P, Emecen AN, Çağlayan D. Temporal trend analysis of tuberculosis in Turkey between 2005 and 2019. Mediterr J Infect Microbes Antimicrob. 2023;12:1-8.

6. Leo S, Narasimhan M, Rathinam S, Banerjee A. Biomarkers in diagnosing and therapeutic monitoring of tuberculosis: a review. Ann Med. 2024;56(1):2386030.

7. Gaeddert M, Glaser K, Chendi BH, Sultanli A, Koeppel L, MacLean EL, et al. Host blood protein biomarkers to screen for tuberculosis disease: a systematic review and meta-analysis. J Clin Microbiol. 2024;62(11):e0078624.

8. Zimmer AJ, Lainati F, Aguilera Vasquez N, Chedid C, McGrath S, Benedetti A, et al. Biomarkers that correlate with active pulmonary tuberculosis treatment response: a systematic review and meta-analysis. J Clin Microbiol. 2022;60(2):e0185921.

9. Nogueira BM, Krishnan S, Barreto-Duarte B, Araújo-Pereira M, Queiroz AT, Ellner JJ, et al. Diagnostic biomarkers for active tuberculosis: progress and challenges. EMBO Mol Med. 2022;14(12):e14088.

10. Şahin F, Yıldız P. Distinctive biochemical changes in pulmonary tuberculosis and pneumonia. Arch Med Sci. 2013;9(4):656-61.

11. Martins C, Gama ACDC, Valcarenghi D, Batschauer APDB. Markers of acute-phase response in the treatment of pulmonary tuberculosis. J Bras Patol Med Lab. 2014;50:428-33.

12. Tiu DN, Sirajuddin Ahmed Siddiqi SMFM, Ranjan R. Hematological Changes in Pulmonary Tuberculosis: Focus on Anemia, Disease Severity, and Therapeutic Implications. Cureus. 2025;17(6):e86550.

13. Fu H, Liu H, Sun W, Zhang H, Zhu H. Diagnostic value of neutrophil-to-lymphocyte ratio, fibrinogen-to-albumin ratio and red blood cell distribution width in tuberculosis with bacterial co-infection. BMC Pulm Med. 2025;25(1):134.

14. Stanciu IV, Fildan AP, Thakur BR, Ilie AC, Stanga L, Oancea C, et al. Full-blood inflammatory ratios predict length of hospital stay in pulmonary tuberculosis. Medicina (Kaunas). 2025;61(7):1238.

15. Zhang X, Fu H, Li J, Yan J, Huang J, Xu Z, et al. Development and validation of a predictive model using inflammatory biomarkers for active tuberculosis risk in diabetic patients. J Inflamm Res. 2025;18:4725-39.

16. Lin HH, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. PLoS Med. 2007;4(1):e20.

17. Lee CH, Lee MC, Shu CC, Lim CS, Wang JY, Lee LN, et al. Risk factors for pulmonary tuberculosis in patients with chronic obstructive airway disease in Taiwan: a nationwide cohort study. BMC Infect Dis. 2013;13:194.

18. Hossain MB, Johnston JC, Cook VJ, Sadatsafavi M, Wong H, Romanowski K, et al. Role of latent tuberculosis infection on elevated risk of cardiovascular disease: a population-based cohort study. Epidemiol Infect. 2023;151:e68.

19. Chung WS, Lin CL, Hung CT, Chu YH, Sung FC, Kao CH, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome. Int J Tuberc Lung Dis. 2014;18(1):79-83.

20. Inghammar M, Ekbom A, Engström G, Ljungberg B, Romanus V, Löfdahl CG, et al. COPD and the risk of tuberculosis. PLoS One. 2010;5(4):e10138.

21. Autentico ART, Lim BA. Characteristics and in-hospital outcomes of clinically diagnosed tuberculosis patients in a high-burden setting: A five-year retrospective analysis. Respir Med. 2025;247:108309.

22. Chacko B, Chaudhry D, Peter JV, Khilnani GC, Saxena P, Sehgal IS, et al. ISCCM position statement on the approach to and management

of critically ill patients with tuberculosis. Indian J Crit Care Med. 2024;28(Suppl 2):S67-S82.

23. Carabalí-Isajar ML, Rodríguez-Bejarano OH, Amado T, Patarroyo MA, Izquierdo MA, Lutz JR, et al. Clinical manifestations and immune response to tuberculosis. World J Microbiol Biotechnol. 2023;39(8):206.

24. Steingart KR, Henry M, Ng V, Hopewell PC, Ramsay A, Cunningham J, et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis. Lancet Infect Dis. 2006;6(9):570-81.

25. Zifodya JS, Kreniske JS, Schiller I, Kohli M, Dendukuri N, Schumacher SG, et al. Xpert Ultra versus Xpert MTB/RIF for pulmonary tuberculosis. Cochrane Database Syst Rev. 2021;2(2):CD009593.

26. Sharma SK, Mohan A. Tuberculosis: from an incurable scourge to a curable disease. Indian J Med Res. 2013;137(3):455-93.

27. Yaranal PJ, Umashankar T, Harish SG. Hematological profile in pulmonary tuberculosis. Int J Health Rehabil Sci. 2013;2(1):50-5.

28. Kim H, Choi HG, Shin SJ. Bridging the gaps to overcome hurdles in next-generation tuberculosis vaccines. Front Immunol. 2023;14:1193058.

29. Şahin F, Yazar E, Yıldız P. Prominent features of platelet indices in pulmonary tuberculosis. Multidiscip Respir Med. 2012;7(1):38.

30. Lee SW, Kang YA, Yoon YS, Um SW, Lee SM, Yoo CG, et al. The prevalence and evolution of anemia associated with tuberculosis. J Korean Med Sci. 2006;21(6):1028-32.

31. Kang YA, Kwon SY, Yoon HI, Lee JH, Lee CT. Role of C-reactive protein and procalcitonin in differentiation of tuberculosis from bacterial pneumonia. Korean J Intern Med. 2009;24(4):337-42.

32. Pang T, Wang L, Zhang J, Duan S. Association between systemic immune-inflammation index and latent tuberculosis infection. Front Med. 2025;12:1615302.

33. Espinosa-Pereiro J, Alagna R, Saluzzo F, González-Moreno J, Heinrich N, Sánchez-Montalvá A, et al. Potential biomarkers for bacterial burden and treatment efficacy in tuberculosis trials. J Infect Dis. 2024;229(5):1584-95.