

Retrospective evaluation of the inflammatory response in patients diagnosed with COVID-19 based on hematological and biochemical parameters

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ABSTRACT

Aims: This study aimed to compare the demographic characteristics, clinical symptoms, comorbidities, and hematological, biochemical, and inflammatory parameters of individuals with COVID-19 positivity with those of a healthy control group. Additionally, the relationship between the Systemic Inflammatory Index (SII) and the disease, the interaction between symptom presence and hematological variables, the association of thoracic computed tomography (CT) findings with clinical and laboratory parameters, and the effect of applied treatment protocols on length of hospital stay were evaluated.

Methods: This retrospective, observational study included a total of 286 individuals aged 18–80 years who presented to Yozgat City Hospital between January 1, 2020, and January 1, 2021. The study group consisted of 143 patients diagnosed with COVID-19 based on RT-PCR positivity, while the control group included 143 individuals had COVID-19–like symptoms with negative RT-PCR results and no known comorbid diseases. Demographic data and hematological, biochemical, and inflammatory parameters were recorded retrospectively, and SII values were calculated. Statistical analyses were performed using SPSS version 20.0. Appropriate parametric and non-parametric tests were applied, and a p-value <0.05 was considered statistically significant.

Results: In the COVID-19 group, the female/male ratio was 31.5%/68.5%, and the mean age was similar to that of the control group. The most common comorbidities were hypertension, diabetes mellitus, and chronic kidney disease. The most frequently reported symptoms were myalgia, cough, and fever. Thoracic CT findings compatible with COVID-19 were observed in 37.8% of the cases, and these patients had a longer duration of hospital stay. Compared with the control group, the COVID-19 group showed increased leukocyte and neutrophil counts as well as elevated C-reactive protein (CRP), erythrocyte sedimentation rate, and D-dimer levels, while lymphocyte counts were decreased. The SII value was significantly higher in the COVID-19 group than in the control group ($p < 0.001$). Patients with longer hospital stays were more likely to have received combination therapy.

Conclusion: COVID-19 is characterized by marked hematological and inflammatory alterations. In particular, elevated SII and lymphopenia are important indicators reflecting disease severity. Monitoring these parameters may provide valuable guidance in the clinical management of COVID-19.

Keywords: COVID-19, Systemic Inflammatory Index, length of hospital stay

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 and rapidly evolved into a global public health emergency. The clinical presentation of COVID-19 is highly heterogeneous, ranging from asymptomatic infection to severe respiratory failure, multiorgan dysfunction, and death. This variability has underscored the need for reliable, easily accessible biomarkers to support early risk stratification and clinical decision-making.¹⁻³

A dysregulated systemic inflammatory response plays a central role in the pathophysiology of COVID-19. Previous studies have consistently demonstrated that hematological and biochemical abnormalities -including neutrophilia, lymphopenia, and elevated levels of C-reactive protein (CRP), ferritin, and D-dimer- are closely associated with disease severity and adverse outcomes.^{1,2,4-6} Lamichhane et al.¹ and Bairwa et al.² reported marked deterioration in these parameters among severe and fatal cases, highlighting their prognostic relevance. Similarly, comprehensive reviews have

emphasized the clinical utility of inflammatory biomarkers in predicting disease progression.³

Despite their clinical value, individual biomarkers may be insufficient to fully reflect the complex and multidimensional inflammatory processes involved in COVID-19. This limitation has led to growing interest in composite inflammatory indices that integrate multiple immune components. The Systemic Inflammatory Index (SII), calculated using neutrophil, lymphocyte, and platelet counts, has emerged as a practical marker that reflects both immune activation and overall inflammatory burden. Prior studies have suggested that SII may serve as a prognostic indicator in various infectious and inflammatory conditions.^{1,3,4}

In severe COVID-19, excessive immune activation and cytokine-mediated inflammation may result in endothelial injury, coagulopathy, and multiorgan involvement.^{4,5} Elevated inflammatory markers during this process have been associated with poor clinical outcomes across different populations.⁶⁻⁸ Moreover, longitudinal analyses have shown that temporal changes in laboratory parameters parallel disease progression, while persistent inflammatory activity may have implications beyond the acute phase of infection.^{9,10}

In this context, the present study aimed to evaluate the relationship between the SII and clinical, laboratory, and radiological findings in patients hospitalized with COVID-19. In addition, the potential prognostic value of SII in relation to disease severity and length of hospital stay was investigated. By focusing on a readily available composite inflammatory marker, this study seeks to contribute to practical risk assessment strategies and support the integration of SII into routine clinical evaluation of COVID-19 patients.

METHODS

The study was approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 05.11.2025, Decision No: 2025-GOKAEK-2519_2025.11.05_653). Due to the retrospective nature of the study, written informed consent was not obtained from participants. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. All data were anonymized prior to analysis and protected in accordance with the Personal Data Protection Law. No additional diagnostic tests or interventions were performed as part of the study.

This study was designed as a retrospective and observational investigation. Individuals aged 18–80 years who presented to Yozgat City Hospital between January 1, 2020, and January 1, 2021, were included. The study group consisted of patients who tested positive for reverse transcription–polymerase chain reaction (RT-PCR) at presentation, were diagnosed with COVID-19, and were admitted to the inpatient ward. Diagnostic criteria were applied uniformly to all cases, based on the same laboratory infrastructure and national diagnostic algorithms.

The control group consisted of individuals who presented to the same emergency department during the same time period with COVID-19–like symptoms, underwent similar laboratory evaluations, had confirmed negative RT-PCR

test results, showed no evidence of acute pathology, and had no known chronic diseases. To minimize selection bias, particular attention was paid to ensuring that the control group was comparable to the study group in terms of age and sex distribution. The control group was selected such that the numbers of female and male participants were equal between the compared groups, with the difference in mean age by sex being less than 5 years and the difference in age distribution ranges not exceeding ± 5 years. Patients with missing hematological or biochemical data at the time of diagnosis, those admitted to the intensive care unit, and those managed on an outpatient basis were excluded from the study.

All data were obtained retrospectively from the hospital's electronic medical record system. Demographic characteristics, including age, sex, and medical history, were recorded. Laboratory parameters were evaluated using samples obtained at the time of presentation or within the first 24 hours of hospitalization, in order to reduce variability related to sampling time.

Hematological analyses included routine parameters such as erythrocyte count, hemoglobin, and haematocrit. In addition, white blood cell subtypes (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) and platelet counts were recorded. Biochemical assessments focused on parameters reflecting inflammatory response and organ function. These included inflammatory markers such as CRP, ferritin, and procalcitonin; liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin); renal function indicators (urea, creatinine); and coagulation parameters (D-dimer). All laboratory measurements were performed in the hospital's accredited laboratory using standard analytical methods.

The SII was calculated for each individual using neutrophil, lymphocyte, and platelet counts obtained within the same time frame ($SII = \text{neutrophil} \times \text{platelet} / \text{lymphocyte}$). Calculations were performed on a standardized dataset to minimize potential bias arising from differences in measurement timing or methodology.

Statistical Analysis

The data analyses were conducted using SPSS version 20.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. For normally distributed data, comparisons between two groups were performed using the independent samples t-test, and comparisons among more than two groups were conducted using one-way analysis of variance (ANOVA). For data that did not follow a normal distribution, the Mann–Whitney U test was used for two-group comparisons, and the Kruskal–Wallis test was applied for comparisons involving three or more groups.

Relationships between variables were evaluated using Pearson correlation analysis when parametric assumptions were met, and Spearman correlation analysis when they were not. To reduce the risk of type I error in multiple comparisons, results were interpreted within the framework of clinical relevance. In all analyses, p-values < 0.05 and < 0.01 were considered statistically significant.

RESULTS

During the study period, a total of 816 patients who presented to Yozgat City Hospital with suspected COVID-19 were assessed for eligibility. Of these, 96 patients who required intensive care unit admission at initial presentation and 21 patients who were referred to another medical center were excluded. Among the 149 hospitalized patients with RT-PCR-confirmed COVID-19, 6 patients were excluded due to missing hematological or biochemical laboratory data at admission. Consequently, 143 COVID-19-positive patients were included in the final analysis. The control group consisted of 143 RT-PCR-negative individuals without known comorbid diseases. There were no statistically significant differences between the COVID-19 and control groups with respect to age ($p=0.703$) or sex distribution ($p=1.000$), baseline demographic features are summarized in [Table 1](#).

Table 1. Demographic characteristics of the study population

Characteristic	COVID-19 patients (n=143)	Control group (n=143)	p value
Age, years (mean±SD)	42.1±19.8	41.5±17.4	0.703
Sex, n (%)			1.000
Female	45 (31.5)	45 (31.5)	
Male	98 (68.5)	98 (68.5)	

SD: Standard deviation

Briefly, hypertension, diabetes mellitus, and chronic kidney disease were the most frequently observed comorbidities among COVID-19-positive patients, while no comorbid conditions were present in the control group. The distribution of comorbid diseases is presented in [Figure 1](#).

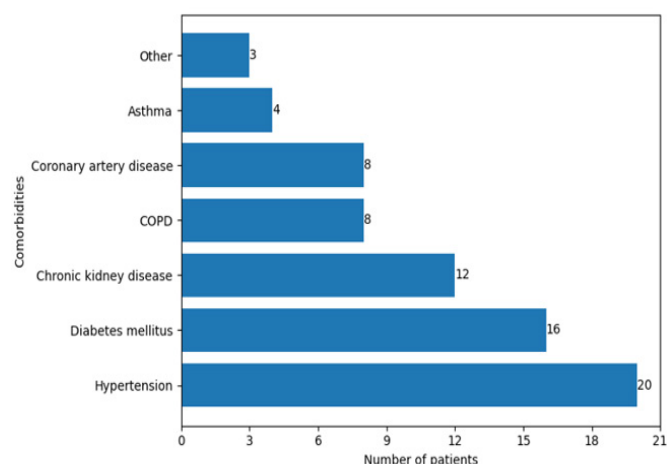


Figure 1. Distribution of comorbidities in COVID-19 positive patients

The most common presenting symptoms were myalgia, cough, and fever, and typical COVID-19-compatible findings on thoracic CT were observed in approximately one-third of patients ([Figure 2, 3](#)).

Hydroxychloroquine-based treatment regimens were the most frequently administered therapies ([Table 2](#)).

Comparison of hematological parameters between COVID-19 patients and controls demonstrated that platelet counts were significantly lower in the COVID-19 group ($p=0.008$),

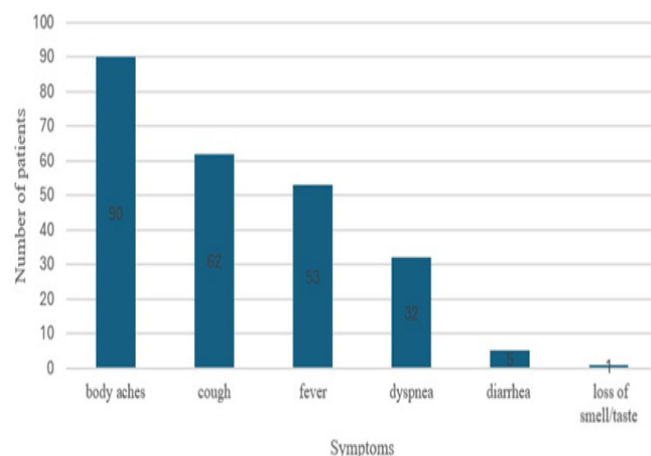
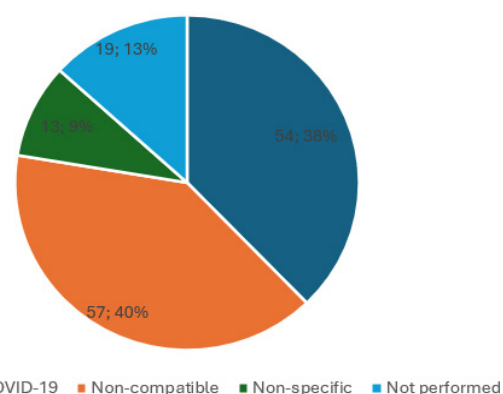


Figure 2. Distribution of symptoms in the COVID-19 positive patient group



■ Typical for COVID-19 ■ Non-compatible ■ Non-specific ■ Not performed

Figure 3. Distribution of thoracic CT findings by number and percentage of patients
CT: Computed tomography

Table 2. Treatment regimens and the number of COVID-19 positive patients received each therapy

Treatment protocols	Number of patients	% patients
Only HCQ	30	20.98
Only azithromycin	10	6.99
HCQ+azithromycin	48	33.57
HCQ+oseltamivir	14	9.79
HCQ+oseltamivir+azithromycin	28	19.58
HCQ+favipiravir+azithromycin	8	5.59
No treatment	5	3.50

HCQ: Hydroxychloroquine

while lymphocyte counts were markedly reduced ($p<0.001$) and neutrophil counts were significantly higher ($p=0.032$). Leukocyte and hemoglobin levels did not differ significantly between groups ([Table 3](#)). Symptom-based analyses showed that patients presenting with fever had significantly lower hemoglobin and lymphocyte levels (both $p<0.001$), whereas patients reporting myalgia exhibited higher leukocyte ($p=0.027$) and neutrophil counts ($p=0.030$).

Inflammatory marker analysis revealed that mean CRP and erythrocyte sedimentation rate (ESR) values were significantly higher in COVID-19 patients compared with controls (both $p<0.001$). Although CRP and ESR levels did not differ according to symptom presence, both markers demonstrated significant negative correlations with

Table 3. Hematological parameters in COVID-19 positive and control groups

Parameter	COVID-19 positive (mean±SD)	Control group (mean±SD)	p value
Leukocyte (10 ³ /μL)	7.21±3.95	6.49±1.76	p>0.05
Hemoglobin (g/dl)	13.6±2.81	13.84±2.6	p>0.05
Platelet (10 ³ /μL)	229.55±100.29	239.69±47.96	p=0.008
Lymphocyte (10 ³ /μL)	1.71±1.25	2.04±0.62	p<0.001
Neutrophil (10 ³ /μL)	4.78±3.37	3.91±1.59	p=0.032

SD: Standard deviation

lymphocyte count (CRP: $\rho=-0.17$, $p=0.039$; ESR: $\rho=-0.20$, $p=0.017$).

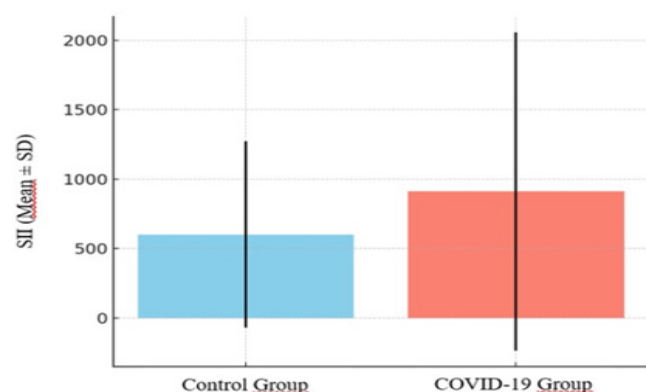
Evaluation of cardiac and coagulation biomarkers showed wide variability in troponin, pro-BNP, and D-dimer levels, indicating marked elevations in a subset of patients. D-dimer levels correlated positively with CRP ($p<0.001$) and neutrophil count ($p=0.019$), and inversely with hemoglobin ($p<0.001$) and lymphocyte count ($p=0.042$). Troponin levels were positively associated with CRP, neutrophil, and leukocyte counts and negatively correlated with hemoglobin. Pro-BNP levels increased in parallel with CRP ($p=0.003$) and ESR ($p<0.001$). Clinically, patients presenting with fever had significantly higher D-dimer levels ($p<0.001$), while those presenting with dyspnea had markedly elevated troponin ($p=0.004$) and pro-BNP ($p<0.001$) levels (Table 4).

Table 4. Marker relationships according to symptoms

Symptom	Marker	Result	p-value
Fever	D-dimer	Higher in patients with fever	<0.001
Dyspnea	Troponin	Higher in patients with dyspnea	0.004
Dyspnea	pro-BNP	Significantly higher in patients with dyspnea	<0.001
Body aches	pro-BNP	Difference observed, due to a few patients with high values	0.012

BNP: B-type natriuretic peptide

Mean SII values were significantly higher in COVID-19 patients (910.3 ± 1146.1) compared with controls (599.7 ± 670.9 ; $p<0.001$) (Figure 4). SII showed strong positive correlations with neutrophil ($\rho=0.73$) and platelet counts ($\rho=0.35$), and a negative correlation with lymphocyte count ($\rho=-0.37$). In addition, SII demonstrated weak but significant positive correlations with D-dimer ($\rho=0.20$; $p=0.021$), troponin ($\rho=0.18$; $p=0.029$), and CRP ($\rho=0.22$; $p=0.016$).

**Figure 4.** Comparison of the mean Systemic Inflammatory Index (SII) between COVID-19 and control groups

ROC curve analysis evaluating the discriminative performance of SII for COVID-19 positivity yielded an area under the curve of 0.623. The optimal SII cut-off value determined by the Youden index was 711.56, corresponding to a sensitivity of 41.4% and a specificity of 91.6%. In univariable logistic regression analysis, higher SII values were associated with increased odds of COVID-19 positivity (OR 1.73; 95% CI 1.22–2.47; $p=0.002$ per log-transformed SII). However, multivariable logistic regression analyses performed within the COVID-19 cohort and adjusted for age, sex, and major comorbidities demonstrated that SII was not an independent predictor of CT compatibility or prolonged hospitalization ($p>0.05$ for both outcomes).

Patients presenting with fever had significantly higher SII values than those without fever (median 871.6 vs. 526.3; $p=0.010$). No statistically significant correlation was observed between SII and length of hospital stay ($r=-0.155$; $p=0.067$). The mean length of hospital stay among COVID-19 patients was 12.8 ± 4.8 days. Hospitalization duration was significantly prolonged in patients with hypertension, diabetes mellitus, and chronic kidney disease (all $p<0.05$).

DISCUSSION

In this study, hospitalized patients with COVID-19 demonstrated distinct hematological and inflammatory alterations compared with the control group, supporting the central role of systemic inflammation in disease pathophysiology. The similarity in age and sex distribution between the patient and control groups represents an important methodological strength, allowing interpretation of laboratory findings with minimal demographic confounding. Although advanced age and male sex have been widely reported as risk factors for severe disease and mortality,¹⁻³ the balanced design of the present study enabled a clearer evaluation of biomarker-associated differences.

Hypertension, diabetes mellitus, and chronic kidney disease were the most prevalent comorbidities among COVID-19-positive patients and were associated with significantly prolonged hospital stay. These findings are consistent with previous reports indicating that chronic comorbid conditions adversely affect clinical course and recovery in COVID-19.^{14,20,22} Renal dysfunction and metabolic disorders have been shown to amplify inflammatory responses and reduce physiological reserve, thereby contributing to delayed clinical improvement and extended hospitalization.^{5,13,23}

The clinical presentation observed in this cohort reflects the heterogeneous nature of COVID-19. Myalgia, cough, and fever were the most frequently reported symptoms, consistent with earlier studies.³ Fever was associated with lymphopenia, while myalgia correlated with leukocytosis and neutrophilia, highlighting the close interaction between clinical manifestations and underlying inflammatory responses. Similar symptom-associated hematological patterns have been reported previously and are considered indicative of disease severity.^{4-6,8}

Thoracic computed tomography (CT) findings were heterogeneous, with typical COVID-19-compatible patterns identified in only a subset of patients. Patients with typical CT findings experienced longer hospital stays and received more intensive treatment regimens, suggesting a higher

inflammatory burden. Previous studies have reported discordance between RT-PCR results and CT findings, particularly in early disease stages, while also emphasizing the association between typical radiological patterns and adverse clinical outcomes.^{9,26} These observations support the role of thoracic CT not only in diagnosis but also in assessing disease severity and guiding clinical management.⁵

Hematological analysis revealed characteristic features of COVID-19, including lymphopenia and neutrophilia, which have consistently been associated with poor prognosis.⁶⁻⁸ Elevated CRP and ESR further confirmed the presence of a pronounced systemic inflammatory response. The observed negative correlations between inflammatory markers and lymphocyte counts suggest immune dysregulation proportional to inflammatory intensity, in line with previous studies identifying CRP and ESR as reliable indicators of disease severity and outcome.^{14,21,22}

Alterations in coagulation and cardiac biomarkers further underscore the multisystem involvement of COVID-19. Elevated D-dimer, troponin, and pro-BNP levels in a subset of patients indicate hypercoagulability and myocardial stress, both of which have been associated with unfavorable outcomes.^{9,16,19,21} The positive correlations between these biomarkers and inflammatory parameters support the concept that cardiovascular involvement in COVID-19 is largely mediated by systemic inflammation.

A key finding of the present study is the significantly elevated SII observed in COVID-19 patients compared with controls. As a composite marker integrating neutrophil, lymphocyte, and platelet counts, SII provides a comprehensive reflection of immune activation and inflammatory burden. The associations observed between SII and hematological as well as biochemical parameters -including D-dimer and cardiac biomarkers- suggest that SII captures both inflammatory and prothrombotic processes. Consistent with these findings, previous studies have highlighted the prognostic value of SII in COVID-19, particularly when interpreted alongside conventional inflammatory markers.²⁸⁻³²

Although no strong correlation was identified between SII and length of hospital stay, higher SII values in febrile patients suggest a relationship with clinical severity. The lack of association with hospitalization duration may reflect the influence of additional factors such as treatment strategies, comorbidities, and institutional discharge practices. Overall, our findings are also consistent with previous reports evaluating hematological, biochemical, and inflammatory biomarkers in COVID-19 across different populations.^{17-19,23-25,27,30,34-38}

Limitations

This study has several limitations. Its retrospective and single-center design limits generalizability, and laboratory parameters were assessed primarily at admission, precluding evaluation of dynamic changes over time. In addition, length of hospital stay is influenced by multiple clinical and organizational factors beyond inflammatory burden. Finally, given that SII is mathematically derived from hematological parameters, its correlations with these components should be interpreted cautiously. Despite these limitations, the study provides real-world evidence supporting the role of SII as a practical inflammatory marker in COVID-19.

CONCLUSION

COVID-19 infection is associated with significant alterations in hematological and inflammatory parameters, including lymphopenia, neutrophilia, and elevated inflammatory markers. In this study, SII values were significantly higher in COVID-19-positive patients compared with healthy controls, suggesting that SII may reflect the overall inflammatory burden of the disease. Given that SII can be easily derived from routine complete blood count parameters, it may serve as a practical adjunct marker in clinical assessment. In addition, the presence of comorbid conditions such as hypertension, diabetes mellitus, and chronic kidney disease was associated with prolonged hospital stay, indicating a more severe clinical course. Further prospective studies are warranted to clarify the prognostic value of SII and its role in clinical decision-making.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 05.11.2025, Decision No: 2025-GOKAEK-2519_2025.11.05_653).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: İA; Design: İA, İG; Supervision: İA, İG; Resources: İA; Materials: İA; Data Collection and/or Processing: İA; Analysis and/or Interpretation: İG; Literature Review: İG; Writing-Original Draft: İA, İG; Writing-Review & Editing: İA, İG.

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