European Review for Medical and Pharmacological Sciences 2022; 26: 8612-8619

# The significance of a novel inflammatory biomarker, presepsin, in predicting disease prognosis in patients with COVID-19

C. KARACAER[1], H. SERT[2], T. DEMIRCI[1], C. VARIM[1], G. KAYA[3], A.B. GENC[1], D. CEKIC[1], H. ERGENC[4], Z. ERGENC[4], S. YAYLACI[1], A. NALBANT[1], T. KAYA[1], A. DEMIRCI[1], K.E. OZTOP[1]

[1]Department of Internal Medicine, Faculty of Medicine, [2]Department of Internal Medicine Nursing, Faculty of Health Science, Sakarya University, Sakarya, Turkey
[3]Medical Microbiology Department of Health Sciences University, Sakarya University, Training And Research Hospital, Sakarya, Turkey
[4]Department of Internal Medicine, Ayancik State Hospital, Sinop, Turkey

**Abstract. – OBJECTIVE: This study aims at determining the significance of a novel inflammatory biomarker, presepsin, in predicting disease prognosis in patients with COVID-19.**

**PATIENTS AND METHODS: This retrospective study was concluded at the University Hospital between April and August 2020. The study involved 88 COVID-19 patients (48 men and 40 women). The patients were categorized into two groups: the patients admitted to the COVID-19 clinic, described as the moderate COVID-19 patients (Group-1; n=44), and those admitted to the internal medicine outpatient clinic, who were the mild COVID-19 patients (Group-2; n=44). The groups were compared using inflammatory markers: presepsin, C-Reactive Protein to Albumin Ratio, Neutrophil to Lymphocyte Ratio, and procalcitonin.**

**RESULTS: Serum presepsin levels (195.29 *vs.* 52.12 pg/ml) were significantly higher in the Group-1 compared to the Group-2 ($p$=0.001). The gender distribution and average age were similar in both groups ($p > 0.05$). While ferritin, lactate dehydrogenase, D-Dimer, platelet lymphocyte ratio, C-Reactive Protein to Albumin Ratio ($p$=0.001), erythrocyte sedimentation ratio, C-Reactive Protein and presepsin were significantly higher in the Group-1 compared to Group-2 ($p<0.05$), while hemoglobin and lymphocyte were significantly lower in the Group-1 than in Group-2 ($p<0.05$).**

**CONCLUSIONS: Serum presepsin levels were found to be significantly higher in moderate clinical group COVID-19 patients compared to mild group. Presepsin, a new inflammatory biomarker, may be useful in predicting the prognosis and early treatment of COVID-19 infection.**

*Key Words:*
COVID-19 disease, C-Reactive Protein to Albumin Ratio, Presepsin, Prognosis.

## Introduction

The diagnosis and treatment of this pneumonia, whose medical classification is unknown, was very challenging. With the clinical course ranging from asymptomatic to death, it requires continuous guideline updates. The importance of early diagnosis, risk stratification, therapy monitoring, and prognosis cannot be overstated[1]. COVID-19 is a severe form of pneumonia that results in acute respiratory distress syndrome (ARDS).

It is considered to be the primary symptom of the SARS-CoV-2 respiratory virus. In recent years, it has been demonstrated that early diagnosis is highly beneficial for preventing infectious disease fatalities[2,3].

C-Reactive Protein (CRP) and procalcitonin (PCT) levels in the serum are inflammatory indicators of the host-pathogen response[4]. CRP is primarily created by the liver in reaction to IL-6 in the cytokine storm, whereas PCT is produced by monocytes and the liver[5].

Presepsin biomarker (sCD14-ST) is a soluble CD14 subtype that has been proposed as a new early signal for the detection of different infections[6]. When combined with other indicators, such as PCT, high presepsin levels appear to si-


*Corresponding Author:* Cengiz Karacaer, MD; e-mail: karacaerc@yahoo.com

gnal the development of septic shock and severe community-acquired pneumonia[7]. Presepsin has been demonstrated to be useful for identifying sepsis as well as predicting sickness severity and fatality[8,9]. In comparison to the commonly used CRP and PCT, the advantages of presepsin include an earlier blood rise, enhanced sensitivity, specificity, and prognostic value[10,11].

The aim of this study is to determine the significance of a novel inflammatory biomarker, presepsin, in predicting disease prognosis in patients with COVID-19.

## Patients and Methods

### Study Population

This retrospective, cross-sectional, single-center study was conducted at the Sakarya University Training and Research Hospital (Sakarya, Turkey) between April and August of 2020. The information such as age, gender, chronic diseases, disease symptoms, length of stay in the clinic, and length of stay in the hospital was obtained from the hospital automation system within the scope of this study. The patients were categorized into two groups: the patients admitted to the internal medicine clinic were moderate COVID-19 patients (Group-1); the patients admitted to the outpatient internal medicine clinic were non-COVID-19 patients (Group-2). The positivity of nasal and pharyngeal swab samples was confirmed by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) tests, and patients with COVID-19 disease involvement in thorax tomography were included in the study. Patients with negative rRT-PCR tests, malignancy, renal failure, and immunosuppressive therapy were excluded from the study. Hospital records (demographic and clinical) of patients above 18 years of age were retrospectively reviewed.

The immunoturbidimetric approach was employed to measure biochemical parameters and CRP levels using an Olympus AU5800 auto analyzer (Beckman Coulter, Inc., Brea, CA, USA). The ferritin level was determined by the chemiluminescence method using Abbott Architect I 2000 SR (Abbott Laboratories, Lake Bluff, IL, USA). The CELL-DYN 3700 CD-3700SL (Abbott Laboratories, Lake Bluff, IL, USA) was used to identify CBC parameters using laser measurements and the LED flow cell technique. The prothrombin time, activated partial thromboplastin time, and fibrinogen were measured using an immunoturbidimetric approach utilizing an optical method, and the latex agglutination method was also used to detect D-dimer using the instrument Diagon Coag XL (Baross, Budapest, Hungary). The immunoassay method was applied to measure procalcitonin, and Roche Cobas e 411 (Hitachi, Tokyo, Japan). The serum was stored at -80°C until the day of the neopterin test. All samples were brought to room temperature (15-18°C) before being combined and homogenized.

### Presepsin Analysis

Presepsin levels were measured in blood serum samples taken from patients in both groups. It was studied with the consent of the patients, with the blood stored at -80°C. The name of the kit studied is Sinogeneclon Biotech. This kit worked with microplate reader RT 2100 C and microplate washer RT 2600 devices. The Sandwich ELISA method (Elabscience, Bioassay Technology Laboratory, Shanghai, China) was used to measure the serum presepsin (8-300 pg/ml) levels. In the precision study conducted by the manufacturer, the interstudy and intrastudy CV% values of the kits were <10%, and the measurement range was 200-60.000 ng/L.

The Ethics Committee of Sakarya University's Faculty of Medicine approved the study protocol, which was carried out in accordance with the principles of the Helsinki Declaration (27.04.2021/E71522473-050.01.04-26361-264).

### Statistical Analysis

Data analysis was performed by using SPSS 22 for Windows (Statistical Package for Social Science, SPSS® Corp., Armonk, NY, USA). The variables were analyzed in terms of normality distribution using the Kolmogorov-Simirnov test. Depending on the normality of the distribution, continuous variables were reported as mean and standard deviation or median and interquartile range. Categorical variables were expressed using frequency tables. The Mann-Whitney U test was used to compare non-normally distributed variables, while the Student's *t*-test was used to compare normally distributed variables. A suitable Chi-square test was used to analyze categorical traits and relationships between groups. The role of presepsin level in predicting the clinical prognosis of the disease was analyzed with the "Receiver operating characteristic (ROC)" curve analysis. When evaluating the area under the curve, a 5% type 1 error level was used to accept a statistically significant predictive value of the test variables. While investi-

gating the associations between non-normally distributed variables, the correlation coefficients and their significance were calculated using the Spearman test. The statistically significant two-tailed *p*-value was considered as 0.05.

## Results

This study enrolled 88 patients, comprising 48 (54.5%) males and 40 (45.4%) females. The distribution rate of male/female patients was 22 (50.00%)/22 (50.00%) in the Group-1, and 26 (59.09%)/18 (40.90%) in the Group-2. Mean age of the Group-1 was 47.88±18.15 and the Group-2 was 47.29±15.53 years. Gender and age distribution were similar in both groups (respectively, *p*=0.646; *p*=0.870) (Table I).

In the Group-1, patients mainly complained of coughing (59.1%), weakness (50.0%), fever (36.4%), dyspnea (31.8%), and muscle and joint pain (25.0%). The most common comorbidities for the patients in the Group-1 were respectively diabetes mellitus type (15.9%), hypertension (9.1%) and coronary artery disease (4.5%); and in the Group-2 were hypertension (4.5%), coronary artery disease (4.5%) and diabetes mellitus type 2 (2.3%) (Table I).

When the laboratory parameters of the patients were evaluated; ferritin, lactate dehydrogenase (LDH), D-dimer, PLR, mean platelet volume (MPV), prothrombin time (PT), CAR, erythrocyte sedimentation rate (ESR), CRP, lactate and presepsin ratio in the Group-1 to the Group-2 (*p*=0.007, *p*=0.001, *p*=0.036, *p*=0.001, *p*=0.002, *p*=0.002, *p*=0.001, *p*=0.001, *p*=0.006, *p*=0.001, *p*=0.001, respectively). Hemoglobin (HGB), albumin and lymphocyte rate were significantly decrease in the Group-1 than in the Group-2 (respectively; *p*=0.010, *p*=0.001, *p*=0.001) (Table II). WBC, PLT, Platelet Distribution Width, neutrophil count, NLR, PCT, urea, creatine, creatine kinase (CK), and CK myocardial band, Aspartate Alanine aminotransferase, Aminotransferase test, Globulin and international normalized ratio were found to be similar in both groups (respectively; *p*=0.203, *p*=0.071, *p*=0.259, *p*=0.688, *p*=0.124, *p*=0.400, *p*=0.942, *p*=0.134, *p*=0.601, *p*=0.060, *p*=0.246, *p*=0.067, *p*=0.909, *p*=0.799 (Table II). Presepsin levels were significantly higher in the Group-1 when compared to the Group-2 (*p*=0.001). Figure 1 illustrates the plasma presepsin levels of both groups individually.

Receiver Operating Characteristics (ROC) Curve Analysis was performed for presepsin. The AUC value for presepsin 0.751 (95% CI 0.634-

**Table I.** Demographics, symptoms and comorbidities in COVID-19 patients.

| | | Group-1 (n=44) | Group-2 (n=44) | *p*-value |
|---|---|---|---|---|
| **Age** | | 47.88±18.15 | 47.29±15.53 | 0.870 |
| **Gender** | **Male** | 22 (50.00) | 26 (59.09) | 0.646 |
| | **Female** | 22 (50.00) | 18 (40.90) | |
| **Hypertension** | | 4 (9.1) | 2 (4.5) | 0.397 |
| **Chronic obstructive pulmonary disease** | | 2 (4.5) | 2 (4.5) | 1.000 |
| **Diabetes mellitus** | | 7 (15.9) | 1 (2.3) | **0.026** |
| **Fever** | | 16 (36.4) | 0 | **0.001** |
| **Throat ache** | | 6 (13.6) | 0 | **0.011** |
| **Cough** | | 26 (59.1) | 0 | 0.152 |
| **Dyspnea** | | 14 (31.8) | 0 | **0.001** |
| **Chest pain** | | 5 (11.4) | 0 | **0.021** |
| **Headache** | | 7 (15.9) | 0 | **0.005** |
| **Backache** | | 3 (6.8) | 0 | 0.078 |
| **Loss of smell** | | 6 (13.6) | 0 | **0.011** |
| **Loss of taste** | | 6 (13.9) | 0 | **0.011** |
| **Diarrhea** | | 0 | 0 | 1.000 |
| **Muscle joint pain** | | 11 (25.0) | 0 | **0.001** |
| **Weakness** | | 22 (50.0) | 0 | **0.001** |

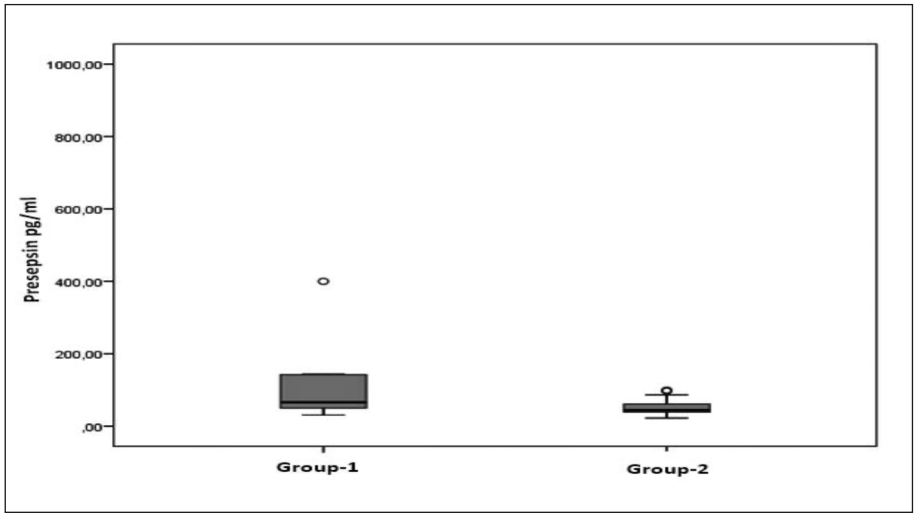



**Figure 1.** The plasma presepsin levels of patients in the Group-1 and Group-2.

0.869 $p<0.001$), which was found to be significant and associated with disease prognosis. The descriptive cut off value of presepsin was 41.75 (88% sensitivity and 63% specificity) for the disease prognosis (Figure 2).

In the correlation analysis, there was a statistically significant correlation between CAR and presepsin values, but no significant difference was found between NLR, PCT, CRP, and presepsin ($p=0.003$, r=0.363 for CAR-presepsin;

**Table II.** Laboratory parameters of patients in the Group-1 and Group-2.

| Laboratory parameters | Group-1 (n=44) | | Group-2 (n=44) | | *p*-value |
|---|---|---|---|---|---|
| | Mean±SD | Median | Mean±SD | Median | |
| **WBC** ($10^3/mm^3$) | 6.365±3.543 | 5.720 | 7.088±1.188 | 7.210 | 0.203 |
| **Hgb** (g/dL) | 13.19±2.01 | 13.20 | 14.15±1.29 | 14.10 | **0.010** |
| **Plt** ($10^3/mm^3$) | 193.64±59.07 | 189.00 | 218.20±66.06 | 218.00 | 0.071 |
| **MPV** (fL) | 8.93±1.56 | 8.75 | 7.96±1.20 | 7.82 | **0.002** |
| **Neutrophil** (K/uL) | 3.88±3.02 | 3.43 | 4.07±0.95 | 3.84 | 0.688 |
| **Lymphocyte** (K/uL) | 1.57±0.71 | 1.43 | 2.32±0.60 | 2.45 | **0.001** |
| **Eosinophil** (K/uL) | 0.09±0.19 | 0.02 | 0.16±0.13 | 0.10 | **0.001** |
| **ESR** (mm/h) | 23.48±22.74 | 18.00 | 10.31±7.60 | 8.50 | **0.001** |
| **CRP** (mg/L) | 17.76±23.74 | 5.93 | 5.13±6.75 | 3.11 | **0.006** |
| **CAR** | 4.55±6.68 | 1.33 | 0.13±0.19 | 0.07 | **0.001** |
| **NLR** | 2.53±2.39 | 1.78 | 1.93±0.90 | 1.58 | 0.124 |
| **PCT**(μg/L) | 0.86±2.67 | 0.03 | 0.21±0.33 | 0.05 | 0.400 |
| **PLR** | 145.75±75.74 | 126.23 | 100.16±37.88 | 95.40 | **0.001** |
| **Ferritin** (μg/L) | 117.8±135.44 | 66.19 | 48.56±59.54 | 30.50 | **0.007** |
| **LDH** (U/L) | 218.54±61.22 | 217.00 | 130.85±70.93 | 148.50 | **0.001** |
| **Presepsin** (ng/L) | 195.29±258.39 | 65.75 | 52.12±21.53 | 44.25 | **0.001** |

WBC: white blood cells, HGB: hemoglobin, PLT: Platelet, MPV: Mean Platelet Volume, ESR: erythrocyte sedimentation rate, CRP: C-Reactive Protein, CAR: C-Reactive Protein Albumin ratio, NLR: Neutrophil lymphocyte rate, PCT: procalcitonin, PLR: Platelet lymphocyte rate, LDH: lactate dehydrogenase.

**Table III.** Correlation analysis of presepsin level with other indicators.

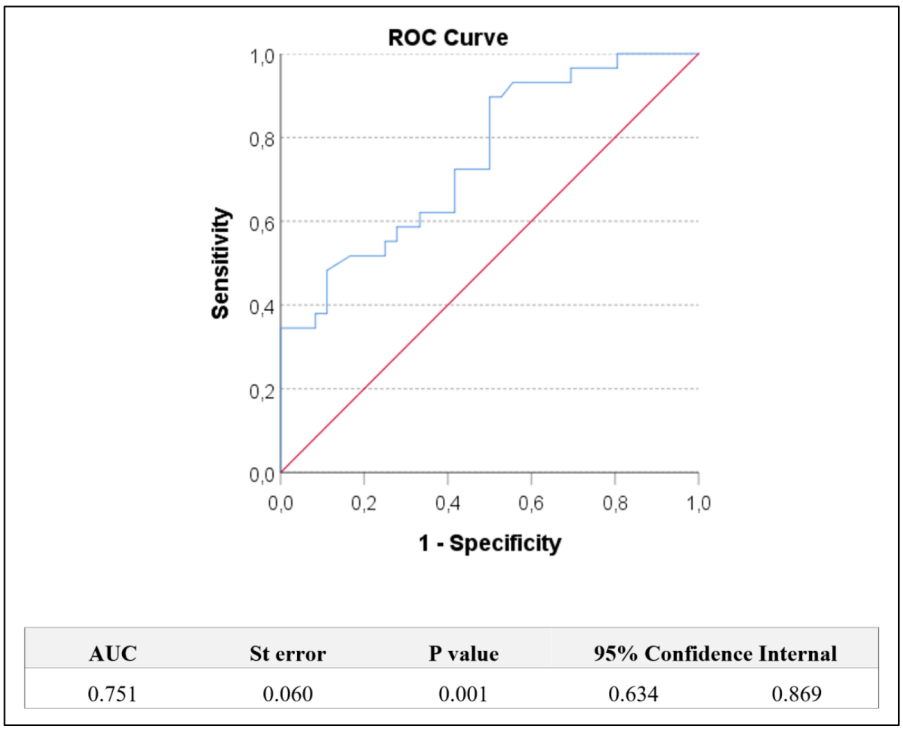
| | r value | *p*-value |
|---|---|---|
| C-Reactive Protein | -0.002 | 0.987 |
| Neutrophil to lymphocyte ratio | 0.074 | 0.556 |
| Procalcitonin | -0.039 | 0.761 |
| CRP to albumin ratio | 0.363 | 0.003 |

*p*=0.987, r=-0.002 for CRP-presepsin; *p*=0.556, r=0.074 for NLR-presepsin; *p*=0.761, r=-0.039 for PCT-presepsin) (Table III).

## Discussion

The current investigation shows that moderate COVID-19 patients (Group-1) had serum presepsin levels that were considerably greater than those of non-COVID-19 patients (control group, Group-2). The results demonstrate the usefulness of presepsin in separating bacterial infections from other infectious causes, but they also provide a novel function for presepsin in predicting organ dysfunction and morbidity in COVID-19 patients. In terms of prognosis and morbidity, clinical application of presepsis, a biomarker, may be easier than a multivariate disease severity score.

Early detection and treatment of COVID-19 pneumonia are associated with a decreased death rate. As a result of the dysregulated host-immune response in COVID-19 illness, it is a potentially fatal disorder. The immunological response of humans serves as the major defense against bacterial infections and serves as a biological marker for presepsin activity[12]. Presepsin is a very sensitive and specific inflammatory marker in comparison to other inflammatory indicators, making it an invaluable tool for early identification and evaluation




| AUC | St error | P value | 95% Confidence Internal | |
|---|---|---|---|---|
| 0.751 | 0.060 | 0.001 | 0.634 | 0.869 |

**Figure 2.** ROC curves of the presepsin levels in predicting patients' hospital mortality. AUC, area under the curve; ROC, receiver operating characteristic.

of illness severity and prognosis[13]. Presepsin was found to be considerably more prevalent in patients with sepsis than those with severe pneumonia in research evaluating its function in the diagnosis and assessment of sepsis and severe pneumonia. Thus, it has been shown[14] that a high presepsin level is indicative of an active infectious illness and correlates with the severity of pneumonia and sepsis development. As a marker of host response in patients with severe sepsis or septic shock, circulating presepsin can be used as an early indicator of host response and mortality in septic patients[15].

An advantage of the presepsin determination is its power to predict the severity of bacterial infections. In addition, measurement of presepsin can be performed in the ICU and emergency room with an easy procedure that takes less than seventeen minutes. Presepsin levels rise before PCT and CRP. Presepsin has been reported to be better than PCT in predicting 30-day mortality of sepsis and to be higher in non-survivors than in survivors[16,17].

In a few studies[18,19], presepsin and other inflammatory markers, especially PCT and CRP, were found to be higher in the moderate group than in the mild clinical group. As shown in Table II, ESR, CRP, CAR, PLR, and ferritin, which are other inflammatory markers besides presepsin, were considerably higher in Group-1. This is in line and consistent with the exiting literature. Further, the CAR, an inflammatory measure, was established as a novel and promising prognostic diagnostic in cancer patients, with the emphasis on its greater prognostic relevance and ability to distinguish it from other inflammatory diseases[20]. Likewise it was determined that the PLR, CAR, CRP, D-Dimer, and ferritin levels were substantially higher in the Group-1 ($p$=0.001, $p$=0.001, $p$=0.006, $p$=0.036, and $p$=0.007, respectively) (Table II). There is a strong evidence that patients with COVID-19 exhibit hyperinflammation-related characteristics such as increased blood CRP, PCT, D-dimer, and hyperferritinemia. These data strongly imply that cytokine storm plays a significant role in the pathogenesis of COVID-19[21].

We determined a presepsin cut off value of 41.75 with acceptable sensitivity and specificity. Notably, with appropriate sensitivity and specificity, researchers calculated a presepsin cutoff value of 41.75. There was no association or cutoff value established between presepsin and CRP, NLR, or PCT levels. CAR and presepsin were significantly correlated in moderately severe COVID-19 patients, as shown by Spearman's correlation analysis ($p$=0.003). However, there was no significant link between NLR, PCT, and CRP values and presepsin ($p$-value=0.556, 0.761, 0.02, respectively) (Table III).

### Limitations

The limitations of the present study include the fact that it was conducted retrospectively on a small group of respondents. The data came from a single clinical research center, as opposed to multiple clinical research centers. The findings of this study may vary from those of other domestic and international researchers, and they should be tested in clinical settings.

## Conclusions

Presepsin, which can be swiftly measured according to CRP and PCT in COVID-19 patients, can be employed as a new biomarker to assist clinicians in identifying high-risk patients and determining early treatment methods.

### Conflict of Interest

The authors declare that they have no conflict of interest.

### Acknowledgements

We thank all the medical and nursing equipment of Sakarya University Education and Training Hospital for their dedicated care of our patients during the COVID-19 pandemic.

### Informed Consent

Informed consent was obtained from all individual participants included in the study.

### Funding

This research did not receive any specific grants from any funding agency in the public, commercial, or not-profit sectors.

### Authors' Contributions

CK: Planning, designing, data collection, literature survey, interpretation of the results, active intellectual support. HS: Collecting data of the work and statistical analysis. TD: Collecting data of the work and statistical analysis. CV: Conception of the work. GK: Collecting data of the work. ABG: Collecting data of the work. DC: Collecting data of the work. HE: Collecting data of the work. ZE: Contributed to the collecting data of the work. SY: Collecting data of the work. AN: Conception of the work. TK: Conception of the work. AD: Planning, designing, data collection, literature survey, interpretation of the results, active intellectual support. KEO: English editing.

**ORCID ID**
Cengiz Karacaer: 0000-0002-7164-4810
Havva Sert: 0000-0002-1658-6515
Taner Demirci: 0000-0002-9579-4530
Ceyhun Varim: 0000-0002-8369-0857
Gulsum Kaya: 0000-0003-2810-0153
Ahmed Bilal Genc: 0000-0002-1607-6355
Deniz Cekic: 0000-0002-7114-9334
Hasan Ergenc: 0000-0003-0519-026
Zeynep Ergenc: 0000-0001-7598-4508
Selcuk Yaylacı: 0000-0002-6768-7973
Ahmet Nalbant: 0000-0003-4756-3575
Tezcan Kaya: 0000-0003-0483-2333
Ayse Demirci: 0000-0002-6291-7573
Kenan Evren Oztop: 0000-0002-7694-8354

**Ethics Approval**

The study protocol was approved by the Ethics Committee of the Faculty of Medicine of the Sakarya University and was conducted in accordance with the principles of the Declaration of Helsinki (27.04.2021/E71522473-050.01.04-26361-264).

## References

1) Yaegashi Y, Shirakawa K, Sato N, Suzuki Y, Kojika M, Imai S, Takahashi G, Miyata M, Furusako S, Endo S. Evaluation of a newly identified soluble CD14 subtype as a marker for sepsis. J Infect Chemother 2005; 11: 234-238.
2) Walls AC, Park YJ, Tortorici MA, Wall A, Mc Guire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell 2020; 181: 281-292.e6.
3) Caliendo AM, Gilbert DN, Ginocchio CC, Hanson KE, May L, Quinn TC, Tenover FC, Alland D, Blaschke AJ, Bonomo RA, Carroll KC, Ferraro MJ, Hirschhorn LR, Joseph WP, Karchmer T, MacIntyre AT, Reller LB, Jackson AF; Infectious Diseases Society of America (IDSA). Better tests, better care: improved diagnostics for infectious diseases. Clin Infect Dis 2013; 57:139-170.
4) Hung SK, Lan HM, Han ST, Wu CC, Chen KF. Current Evidence and Limitation of Biomarkers for Detecting Sepsis and Systemic Infection. Biomedicines 2020; 8: 494.
5) Tang BM, Eslick GD, Craig JC, McLean AS. Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis. Lancet Infect Dis 2007; 7: 210-217.
6) Memar MY, Baghi HB. Presepsin: A promising biomarker for the detection of bacterial infections. Biomed Pharmacother 2019; 111: 649-656.
7) Klouche K, Cristol JP, Devin J, Gilles V, Kuster N, Larcher R, Amigues L, Corne P, Jonquet O, Dupuy AM. Diagnostic and prognostic value of soluble CD14 subtype (Presepsin) for sepsis and community-acquired pneumonia in ICU patients. Ann Intensive Care 2016; 6: 59.
8) Zou Q, Wen W, Zhang XC. Presepsin as a novel sepsis biomarker. World J Emerg Med 2014; 5: 16-19.
9) Endo S, Suzuki Y, Takahashi G, Shozushima T, Ishikura H, Murai A, Nishida T, Irie Y, Miura M, Iguchi H, Fukui Y, Tanaka K, Nojima T, Okamura Y. Usefulness of presepsin in the diagnosis of sepsis in a multicenter prospective study. J Infect Chemother 2012; 18: 891-897.
10) El Shabrawy R, Gawish A, Elgabry R, Nasr F, Diab M, Gamal D. Presepsin, procalcitonin and C reactive protein as diagnostic biomarkers of sepsis in intensive care unit patients. Microbes Infect Dis 2021; 2: 119-129.
11) Ying HQ, Deng QW, He BS, Pan YQ, Wang F, Sun HL, Chen J, Liu X, Wang SK. The prognostic value of preoperative NLR, d-NLR, PLR and LMR for predicting clinical outcome in surgical colorectal cancer patients. Med Oncol 2014; 31: 305.
12) Chenevier-Gobeaux C, Borderie D, Weiss N, Mallet-Coste T, Claessens YE. Presepsin (sCD14-ST), an innate immune response marker in sepsis. Clin Chim Acta 2015; 450: 97-103.
13) Tanimura S, Fujieda Y, Kono M, Shibata Y, Hisada R, Sugawara E, Nakamura H, Ohmura K, Shimamura S, Mitani A, Shida H, Watanabe T, Kato M, Oku K, Bohgaki T, Amengual O, Yasuda S, Shimizu C, Atsumi T. Clinical significance of plasma presepsin levels in patients with systemic lupus erythematosus. Mod Rheumatol 2018; 28: 865-871.
14) TItova EA, Eyrikh AR, Titova ZA. The role of presepsin in the diagnosis and assessment of severity of sepsis and severe pneumonia. Ter Arkh 2018; 90: 44-47.
15) Masson S, Caironi P, Fanizza C, Thome R, Bernasconi R, Noto A, Oggioni R, Pasetti S G, Romero M, Tognoni G, Latini R, Gattinoni L. Circulating presepsin (soluble CD14 subtype) as a marker of host response in patients with severe sepsis or septic shock: data from the multicenter, randomized ALBIOS trial. Intensive Care Med 2015; 41: 1736.
16) Zaninotto M, Mion MM, Cosma C, Rinaldi D, Plebani M. Presepsin in risk stratification of SARS-CoV-2 patients. Clin Chim Acta 2020; 507: 161-163.
17) Behnes M, Bertsch T, Lepiorz D, Lang S, Trinkmann F, Brueckmann M, Borggrefe M, Hoffmann U. Diagnostic and prognostic utility of soluble CD 14 subtype (presepsin) for severe sepsis and septic shock during the first week of intensive care treatment. Crit Care 2014; 18: 507.
18) Fukada A, Kitagawa Y, Matsuoka M, Sakai J, Imai K, Tarumoto N, Orihara Y, Kawamura R, Takeuchi S, Maesaki S, Maeda T. Presepsin as a predictive biomarker of severity in COVID-19: A case series. J Med Virol 2020; 93: 99-101.
19) Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol. 2020; 84: 106504.

20) Liu Z, Jin K, Guo M, Long J, Liu L, Liu C, Xu J, Ni Q, Luo G, Yu X. Prognostic Value of the CRP/Alb Ratio, a Novel Inflammation-Based Score in Pancreatic Cancer. Ann Surg Oncol 2017; 24: 561-568.

21) Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. Ther Adv Respir Dis 2020; 14: 1753466620937175.