# Comparison of Inflammatory Markers and Pressure Injuries in Intensive Care Unit Patients with and without Covid-19 Infection

# Covid-19 Enfeksiyonu Olan ve Covid- 19 Enfeksiyonu Olmayan Yoğun Bakım Hastalarının Enflamasyon Markerları ile Basınç Yaralanmalarının Karşılaştırılması

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Geliş Tarihi/Received: 14.01.2025 • Kabul Tarihi/Accepted: 15.04.2025 • Yayın Tarihi/Publication Date: 30.04.2025

Cite this article as: Ata A, Koca R, Saraçoğlu KT. Comparison of Inflammatory Markers and Pressure Injuries in Intensive Care Unit Patients with and without Covid-19 Infection. J Intensive Care Nurs. 2025;29(1):45-54.



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## Abstract

**Objective:** This study aimed to investigate the relationship between inflammatory markers and pressure injuries in intensive care unit (ICU) patients with and without COVID-19 infection.

**Methods:** Conducted as a single-centre retrospective case-control study. The study was conducted between April 2020 and February 2021 at Kartal Dr. Lutfi Kirdar City Hospital in Istanbul, affiliated to the Turkish Ministry of Health. After obtaining ethical approval, the researchers reviewed the patients' ICU records and laboratory results.

**Results:** This study found that the mean age of COVID-19 (+) patients was significantly higher than that of COVID-19 (-) patients. In that study, hypertension and diabetes mellitus were the most common comorbidities in both groups. In the current study, the Braden Scale of COVID-19 (+) patients were found to be lower than those of COVID-19 (-) patients. This study found that COVID-19 (+) patients had higher procalcitonin levels, lower lymphocyte and monocyte percentages. COVID-19 (+) patients had a shorter ICU stay compared to COVID-19 (-) patients. The incidence of stage 1 pressure injuries was higher in COVID-19 (+) patients, while stage 3 pressure injuries and suspected tissue damage were more common in COVID-19 (-) patients. COVID-19 (+) patients with stage 4 pressure injuries had lower monocyte levels than those with stage 1-2 injuries.

**Conclusion:** This study found that COVID-19 (+) patients had higher levels of procalcitonin, lower percentages of lymphocytes and monocytes, and lower percentages of monocytes as the stage of the pressure injury increased.

Keywords: Biomarkers, braden scale, COVID-19, infection, pressure injury

#### Öz

Amaç: Bu çalışma COVID - 19 enfeksiyonu olan ve olmayan yoğun bakım ünitesinde yatan hastaların enflamasyon markerları ile basınç yaralanmaları arasındaki ilişkiye bakmak amacıyla yapıldı.

Yöntemler: Tek merkezli retrospektif olgu-kontrol çalışması olarak yürütülmüştür. Çalışma, Nisan 2020 ile Şubat 2021 tarihleri arasında, Türk Sağlık Bakanlığı'na bağlı İstanbul'da Dr. Lütfi Kırdar Şehir Hastanesi'nde gerçekleştirilmiştir. Etik onay alındıktan sonra, araştırmacılar hastaların yoğun bakım ünitesi kayıtlarını ve laboratuvar sonuçlarını incelemiştir.

Bulgular: Bu çalışmada, COVID-19 (+) hastalarının ortalama yaşının, COVID-19 (–) hastalarına kıyasla anlamlı derecede yüksek olduğu bulunmuştur. Önceki çalışmada, hipertansiyon ve diyabetes mellitus her iki grupta da en yaygın eşlik eden hastalıklar olarak belirlenmiştir. Mevcut çalışmada, COVID-19 (+) hastalarının Braden risk skorlarının, COVID-19 (–) hastalarına göre daha düşük olduğu bulunmuştur. Bu çalışmada ayrıca COVID-19 (+) hastalarının prokalsitonin düzeylerinin daha yüksek, lenfosit ve monosit yüzdelerinin ise daha düşük olduğu tespit edilmiştir. COVID-19 (+) hastalarının yoğun bakımda kalış süresi, COVID-19 (–) hastalarına göre daha kışası insidansı COVID-19 (+) hastalarında daha yüksekken, evre 3 bası yaraları ve şüpheli doku hasarları COVID-19 (–) hastalarında daha yaygındır. Evre 4 bası yarası olan COVID-19 (+) hastalarında, evre 1-2 yaraları olanlara göre monosit düzeyleri daha düşüktür.

**Sonuç:** Bu çalışmada, COVID-19 (+) hastalarının prokalsitonin düzeylerinin yüksek, lenfosit ve monosit yüzdelerinin ise düşük olduğu, bası yarasının evresi ilerledikçe monosit yüzdesinin de azaldığı bulundu.

Anahtar Kelimeler: Basınç yarası, biyobelirteçler, braden risk skalası, COVID-19, enfeksiyon

#### INTRODUCTION

COVID-19, defined as a global pandemic that originated in Wuhan in December 2019 and subsequently spread globally<sup>1</sup>, is transmitted through direct or indirect contact, primarily via respiratory secretions from infected individuals.<sup>1,2</sup> Symptoms vary based on age, comorbidities, and immune system status, generally including high fever, cough, shortness of breath, muscle pain, sore throat, loss of appetite, and loss of taste and smell. Severe complications can include pneumonia, acute respiratory distress syndrome (ARDS), acute cardiac problems, gastrointestinal issues, renal failure, and severe neurological symptoms.<sup>1-4</sup> Patients with severe COVID-19 complications requiring close monitoring are admitted to intensive care units (ICUs), where they receive frequent ventilation and oxygenation support. ICU patients often experience significant respiratory distress and hemodynamic instability, which increases their risk of pressure injuries due to restricted movement. In these patients, hypoxemia disrupts vascular integrity, facilitating pressure injuries in pressure areas. In addition, vasopressor agents used to manage hemodynamic instability reduce blood flow and oxygenation, hence increasing the risk of pressure injuries. In such cases, hypoxemia, vasoconstriction, and decreased tissue perfusion can lead to ischemia and tissue necrosis, rendering pressure injuries inevitable.<sup>5</sup>

COVID-19 exacerbates patients' prognosis by targeting lung alveoli, cardiac myocytes, vascular endothelium, and angiotensin-converting enzyme 2 receptors, leading to severe symptoms such as systemic inflammatory response syndrome, ARDS, and disseminated intravascular coagulation. The ensuing inflammation increases thrombocyte activation, endothelial dysfunction, and immune response, enhancing thrombosis risk and impacting the coagulation system.<sup>6</sup>

The COVID-19 virus affects the body's circulatory system and vascular endothelium, resulting in tissue inflammation. This condition particularly disrupts the coagulation mechanism, thereby increasing the risk of pressure injuries. In ICUs, pressure injuries represent a complex issue requiring the monitoring of multiple disciplines, such as nutrition, circulation, and care, pose challenges in nursing care, increase workload, and affect costs. It is crucial to investigate the effects of COVID-19 infection within this context. This study, grounded in the existing literature, was conducted to evaluate the potential relationship between inflammation markers and pressure injuries.

This study aimed to evaluate the relationship between specific inflammatory markers(such as procalcitonin, lymphocyte count, and monocyte percentage) and the severity of pressure injuries in COVID-19 positive and negative ICU patients. Unlike previous studies, this research integrates laboratory findings with clinical wound assessments to provide a more comprehensive understanding of how systemic inflammation contributes to skin integrity deterioration in critically ill patients. A key strength of this study lies in its comparative design, which evaluates both COVID-19 positive and negative patients under similar ICU conditions. By exploring the association between inflammatory responses and pressure injury severity, this study addresses a gap in the literature and may contribute to the development of early identification and prevention strategies for high-risk patients, ultimately improving care quality and optimizing resource utilization in intensive care settings.

#### METHODS

**Research Design and Hypothesis:** This single-center retrospective case-control study was based on the hypothesis (H1) that there is a relationship between inflammatory markers and the presence of pressure injuries in ICU patients with and without COVID-19 infection.

*Inclusion criteria:* Adult patients (≥18 years) who were admitted to the ICU for more than 24 hours and had a documented diagnosis of pressure injuries in their medical or nursing records.

*Exclusion criteria:* Patients with other types of skin ulcers (vascular, surgical, traumatic, or neoplastic in origin), pediatric patients, and those admitted before April 1, 2020.

**Data Collection Tools:** Data were collected using a structured data extraction form developed by the researchers, aligned with the study objectives. This form included demographic characteristics such as age, gender, and date of admission to the ICU. It also gathered information on pressure injury characteristics,

including stage, location, area, temperature, size, and wound nature. Systemic infection markers recorded included CRP, procalcitonin, leukocytes, hemoglobin, lymphocytes, and monocytes, as well as body temperature records. Additionally, information on pressure injury characteristics was obtained from the records of the stoma and wound care nurse responsible for monitoring ICU pressure ulcers. The Braden Pressure Ulcer Risk Assessment Scale was utilized to assess the risk of pressure injuries in all patients. Pressure injuries were staged according to the National Pressure Injury Advisory Panel (NPIAP) classification system. All laboratory values were retrieved from the hospital information system and cross-checked with patient medical and nursing records to ensure data accuracy.

**Sample Size Determination:** The sample consisted of all eligible ICU patients who met the inclusion criteria between April 2020 and February 2021. Since this was a retrospective study, a priori power analysis was not performed. Instead, total sampling was conducted, and the sample size was determined based on the number of patients with complete records for both pressure injury diagnosis and relevant laboratory parameters on the first day of ICU admission. After applying the inclusion and exclusion criteria, a total of 355 patients were included in the final analysis, comprising 216 patients with COVID-19 and 139 patients without COVID-19.

**Data collection process:** The study was conducted in the ICU of a city hospital affiliated with the Turkish Ministry of Health, with 63 beds dedicated to patients with COVID-19 and 57 beds to those without COVID-19, from April 2020 to February 2021. Ethical approval was obtained prior to data collection. The researchers evaluated the ICU records and laboratory findings of patients, specifically the laboratory data obtained on the first day of hospital admission for those included in the study. During the specified period, local infection parameters (wound location, area, temperature, nature, size, and patient's body temperature) and systemic infection parameters (C-reactive protein [CRP], procalcitonin, leukocytes, hemoglobin, lymphocytes, and monocytes) of hospitalized patients were examined, and their relationships were assessed. In addition, the risk scores of COVID-19 (+) and (-) patients were compared using the Braden Scale. Pressure injury stages were classified using the pressure injury classification system of the National Pressure Injury Advisory Panel. A comparative analysis of local and systemic infection parameters was undertaken.

**Data analysis and statistical methods**: The data were analyzed using the SPSS software package. Statistical analyses were performed using R version 2.15.3 (R Core Team, 2013). Data were reported using minimum, maximum, mean, standard deviation, median, first quartile, third quartile, frequency, and percentage values. The Shapiro-Wilk test and graphical analysis were used to assess the normal distribution of quantitative data. The independent t-test was used for normally distributed variables between two groups. The Kruskal-Wallis test and the Dunn-Bonferroni test were used for the comparison of non-normally distributed variables among more than two groups. The Pearson chi-square and Fisher-Freeman-Halton exact tests were used for qualitative data comparisons. Statistical significance was set at P < .05.

**Ethical approval:** Institutional permission was obtained for this retrospective case-control study. Ethical approval was obtained from the Clinical Research Ethics Committee of Kartal Dr. Lutfi Kirdar City Hospital where the study was conducted as part of the quality and assurance activities. Written informed consent was not required from participants or their legal guardians in accordance with national regulations and institutional requirements.

## RESULTS

The mean age of COVID-19 (+) patients was  $75.12 \pm 13.07$  years, with 54.6% being male. In this group, the mean Braden Scale was  $9.77\pm.98$ , the mean length of ICU stay was  $22.19 \pm 50.79$  days, the mean body temperature was  $37.04 \pm .55$  °C, the mean procalcitonin score was  $4.1 \pm 8.43$  g/L, the mean lymphocyte percentage was  $7.68 \pm 6.51$ , and the mean monocyte percentage was  $4.32 \pm 5.44$ . Pressure injuries varied in location, with the sacrum being the most common site (74.5%). Pressure injuries due to prone positioning associated with treatment were observed in areas such as the knees, anterior legs, abdominal region, and ears. Stage 2 pressure injuries were found in 44.4% of patients, while stage 1 injuries were found in 31.5%. The mortality rate was 66.2%.

For COVID-19 (-), the mean age was  $71.65 \pm 14.97$  years, with 51.1% being male. This group had a mean Braden Scale of  $10.22 \pm 1.07$ , a mean length of ICU stay of  $41.43 \pm 44.15$  days, a mean body temperature of  $36.81 \pm .43$  °C, a mean procalcitonin score of  $3.96 \pm 8.86$  g/L, a mean lymphocyte percentage of  $9.74 \pm 7.18$ , and a mean monocyte percentage of  $4.88 \pm 3.58$ . The sacrum was the most common site for pressure injuries (83.5%). Stage 2 pressure injuries were found in 40.3% of patients, stage 3 in 23.7%, and suspected deep tissue injury in 23%. The mortality rate was 65.5% (Table 1).

|                          | COVID-19 (+) (n= 216) |                | COVID-19 (-) (n= 139) |                |  |
|--------------------------|-----------------------|----------------|-----------------------|----------------|--|
|                          | Min-Max               | Mean ± SD      | Min-Max               | Mean ± SD      |  |
|                          | (Median)              |                | (Median)              |                |  |
| Age                      | 20-95 (77)            | 75.12 ± 13.07  | 27-98 (75)            | 71.65 ± 14.97  |  |
| Braden Scale             | 8-12 (10)             | 9.77 ± 0.98    | 8-14 (10)             | 10.22 ± 1.07   |  |
| Length of ICU stay (day) | 0-385 (12)            | 22.19 ± 50.79  | 1-377 (28)            | 41.43 ± 44.15  |  |
| Body temperature (°C)    | 36-39 (36.8)          | 37.04 ± 0.55   | 36-38.4 (36.7)        | 36.81 ± 0.43   |  |
| Hemoglobin (g/dl)        | 5.6-16 (10)           | 10.3 ± 2.04    | 6.2-14.7 (9.5)        | 9.6 ± 1.74     |  |
| Procalcitonin (µg/L)     | .01-62 (1.18)         | 4.1 ± 8.43     | .03-62 (0.92)         | 3.96 ± 8.86    |  |
| Leukocytes (%)           | .5-46.9 (11.15)       | 13.05 ± 7.64   | 2.4-120 (11.4)        | 14.01 ± 12.16  |  |
| Lymphocytes (%)          | .5-40.9 (6.1)         | 7.68 ± 6.51    | 1.6-39.7 (7.9)        | 9.74 ± 7.18    |  |
| Monocytes (%)            | .1-67.9 (3.3)         | 4.32 ± 5.44    | .3-30.6 (4.2)         | 4.88 ± 3.58    |  |
| CRP (mg/L)               | 3.16-445 (132.5)      | 143.31 ± 88.81 | 7.99-395 (140)        | 143.51 ± 82.42 |  |
|                          | n                     | %              | n                     | %              |  |
| Gender                   |                       |                |                       |                |  |
| Female                   | 98                    | 45.4           | 68                    | 48.9           |  |
| Male                     | 118                   | 54.6           | 71                    | 51.1           |  |
| Stage                    |                       |                |                       |                |  |
| Stage 1                  | 68                    | 31.5           | 9                     | 6.5            |  |
| Stage 2                  | 96                    | 44.4           | 56                    | 40.3           |  |
| Stage 3                  | 21                    | 9.7            | 33                    | 23.7           |  |
| Stage 4                  | 5                     | 2.3            | 9                     | 6.5            |  |
| UPI/SDTI                 | 26                    | 12.1           | 32                    | 23.0           |  |
| Anemia                   | 186                   | 86.1           | 128                   | 92.1           |  |
| Outcome                  |                       |                |                       |                |  |
| Mortality                | 143                   | 66.2           | 91                    | 65.5           |  |
| Discharge                | 73                    | 33.8           | 48                    | 34.5           |  |

SD: Standard Deviation, ICU: Intensive Care Unit, CRP: C-reactive protein, UPI: Unstageable Pressure Injury, SDTI: Suspected Deep Tissue Injury

Statistically significant differences were observed in the ages of patients based on their COVID-19 status (P = .027), with COVID-19 (+) patients being older. There was also a significant difference in Braden Scale (P < .001), with lower scores observed in COVID-19 (+) patients. Stage percentages also showed significant differences (P < .001). Stage 1 was more common in COVID-19 (+) patients, while stage 3 and unstageable pressure injury (UPI) or suspected deep tissue injury (SDTI) were more prevalent in COVID-19 (-) patients (P < .001, P = .001, and P = .030, respectively).

Body temperature was significantly higher in COVID-19 (+) patients (P < .001). Hemoglobin values were also significantly different (P = .001), with higher values in COVID-19 (+) patients. Lymphocyte values were lower in COVID-19 (+) patients (P = .005). Although no significant difference was found in mortality rates, the length of ICU stay was different, with COVID-19 (+) patients having shorter ICU stays (22.19 ± 50.79 days vs. 41.43 ± 44.15 days) (P < .001) (Table 2).

|                          | COVID-19 (+) (n=216) | COVID-19 (-) (n=139) |                         |        |
|--------------------------|----------------------|----------------------|-------------------------|--------|
|                          | Mean ± SD            | Mean ± SD            | Test value <sup>a</sup> | Р      |
| Age                      | 75.12 ± 13.07        | 71.65 ± 14.97        | 2.229                   | .027*  |
| Braden Scale             | 9.77 ± .98           | 10.22 ± 1.07         | -4.113                  | <.001* |
| Length of ICU stay (day) | 22.19 ± 50.79        | 41.43 ± 44.15        | -3.776                  | <.001* |
| Wound length             | 3.98 ± 2.62          | 3.68 ± 1.83          | 1.290                   | .198   |
| Body temperature (°C)    | 37.04 ± .55          | 36.81 ± .43          | 4.351                   | <.001* |
| Hemoglobin (g/dl)        | 10.30 ± 2.04         | 9.60 ± 1.74          | 3.455                   | .001*  |
| Procalcitonin (µg/L)     | 4.10 ± 8.43          | 3.96 ± 8.86          | .149                    | .881   |
| Leukocytes (%)           | 13.05 ± 7.64         | 14.01 ± 12.16        | 912                     | .363   |
| Lymphocytes (%)          | 7.68 ± 6.51          | 9.74 ± 7.18          | -2.794                  | .005*  |
| Monocytes (%)            | 4.32 ± 5.44          | 4.88 ± 3.58          | -1.082                  | .280   |
| CRP (mg/L)               | 143.31 ± 88.81       | 143.51 ± 82.42       | 020                     | .984   |
|                          | n (%)                | n (%)                | Test value <sup>b</sup> | Р      |
| Gender                   |                      |                      | .428                    | .513   |
| Female                   | 98 (45.4)            | 68 (48.9)            |                         |        |
| Male                     | 118 (54.6)           | 71 (51.1)            |                         |        |
| Comorbidity              | 167 (77.3)           | 111 (79.9)           | 0.322                   | .571   |
| Hypertension             | 105 (48.6)           | 61 (43.9)            | 0.759                   | .384   |
| Diabetes mellitus        | 61 (28.2)            | 37 (26.6)            | 0.111                   | .739   |
| Chronic renal failure    | 17 (7.9)             | 18 (12.9)            | 2.465                   | .117   |
| Coronary artery disease  | 21 (9.7)             | 9 (6.5)              | 1.153                   | .283   |
| COPD                     | 17 (7.9)             | 12 (8.6)             | .066                    | .798   |
| Other                    | 92 (42.6)            | 60 (43.2)            | .011                    | .915   |
| Stage                    |                      |                      | 45.609                  | <.001* |
| Stage 1                  | 68 (31.5)            | 9 (6.5)              |                         |        |
| Stage 2                  | 96 (44.4)            | 56 (40.3)            |                         |        |
| Stage 3                  | 21 (9.7)             | 33 (23.7)            |                         |        |
| Stage 4                  | 5 (2.3)              | 9 (6.5)              |                         |        |
| UPI/SDTI                 | 26 (12.0)            | 32 (23)              |                         |        |
| Anemia                   |                      |                      | 2.956                   | .086   |
| Absent                   | 30 (13.9)            | 11 (7.9)             |                         |        |
| Present                  | 186 (86.1)           | 128 (92.1)           |                         |        |
| Outcome                  |                      |                      | .020                    | .886   |
| Mortality                | 143 (66.2)           | 91 (65.5)            |                         |        |
| Discharge                | 73 (33.8)            | 48 (34.5)            |                         |        |

Table 2: Comparison of demographic and clinical characteristics of patients with and without Covid-19

<sup>a</sup>Independent-samples t-test, <sup>b</sup>Pearson chi-square test, \**P* < .05 SD: standard deviation, COPD: chronic obstructive pulmonary disease, CRP: C-reactive protein, UPI: unstageable pressure injury, SDTI: suspected deep tissue injury, ICU: Intensive Care Unit

For COVID-19 (+) patients, no significant differences were found in procalcitonin, leukocyte, lymphocyte, and CRP values based on stage (P > .05). However, significant differences were found in monocyte values (P = .003). Post hoc evaluations using the Dunn-Bonferroni test revealed that stage 4 patients had lower monocyte values compared to stage 1 and 2 patients (P = .012 for both). No significant differences were observed between the remaining stages (P > .05) (Table 3).

|                         | Stage                 |                      |                     |                     |                        | Test<br>value | Р     |
|-------------------------|-----------------------|----------------------|---------------------|---------------------|------------------------|---------------|-------|
|                         | Stage 1               | Stage 2              | Stage 3             | Stage 4             | UPI/SDTI               |               |       |
| COVID-19 (+)<br>(n=216) |                       |                      |                     |                     |                        |               |       |
| Procalcitonin<br>(μg/L) | 1.2<br>(.3-2.4)       | 0.8<br>(.27-3.8)     | .7<br>(.3-3.04)     | 1.3<br>(1.18-3.8)   | 2.45<br>(.94-4.6)      | 9.130         | .058  |
| Leukocytes (%)          | 11.35<br>(8.04-15.35) | 11.55<br>(8.44-16.5) | 10<br>(8.4-15)      | 19.2<br>(11.1-19.9) | 10.2<br>(6.14- 20)     | 2.409         | .661  |
| Lymphocytes (%)         | 6.05<br>(3.25-8.65)   | 6.3<br>(3.65-9.85)   | 5<br>(3.2-10.7)     | 3<br>(2-7.3)        | 4.95<br>(3.2- 7.4)     | 3.986         | .408  |
| Monocytes (%)           | 3.65<br>(1.9-6.35)    | 3.7<br>(1.95-5.8)    | 2.1<br>(1.3-3.8)    | .7<br>(0.7-1.4)     | 3.15<br>(1.8-4.3)      | 16.139        | .003* |
| CRP (mg/L)              | 125.5<br>(56.15-190)  | 135.5<br>(67.3-191)  | 125<br>(96.6-162)   | 135<br>(128.44-206) | 154.4<br>(104- 217.4)  | 3.791         | .435  |
| COVID-19 (-)<br>(n=139) |                       |                      |                     |                     |                        |               |       |
| Procalcitonin<br>(μg/L) | .4<br>(.2-1.43)       | .88<br>(.39- 4)      | 1.03<br>(.26-2.23)  | .86<br>(.33- 6.5)   | .86<br>(.37-3.4)       | 2.128         | .712  |
| Leukocytes (%)          | 8.7<br>(7.4-13)       | 10.7<br>(7-17.1)     | 10.8<br>(8.12-16.7) | 16.4<br>(9.6-21.5)  | 13.2<br>(9.1- 21.01)   | 6.551         | .162  |
| Lymphocytes (%)         | 5.8<br>(5-11.2)       | 8<br>(3.4-13.5)      | 8.9<br>(5.1-12.7)   | 8.4<br>(5.9-12.3)   | 6.35<br>(4.5-13.1)     | 0.703         | .951  |
| Monocytes (%)           | 5.3<br>(3.1- 7.4)     | 4.2<br>(3-6.5)       | 4.8<br>(3.6-6.1)    | 2.6<br>(1.4-3.6)    | 3.85<br>(2.2-5.9)      | 6.213         | .184  |
| CRP (mg/L)              | 99<br>(73.6-191)      | 122<br>(70.9-172)    | 138<br>(78-169)     | 136<br>(63.4-161)   | 163.5<br>(94.75-244.5) | 3.972         | .410  |

Kruskal-Wallis test, results are presented as median (first quartile-third quartile). \*P < .05.

UPI: unstageable pressure injury, SDTI: suspected deep tissue injury, CRP: C-reactive protein

#### DISCUSSION

The COVID-19 pandemic has globally manifested in a wide spectrum of clinical presentations, ranging from asymptomatic cases to death, causing various systemic effects that can lead to mortality.<sup>7</sup> The structural and functional changes in the skin due to aging contribute to increased vulnerability and the development of pressure injuries, particularly in older adults with chronic conditions.<sup>8</sup> This study found that the mean age of COVID-19 (+) patients (75.12 ± 13.07) was significantly higher compared to COVID-19 (-) patients (71.65 ± 14.97). This finding is consistent with the existing literature indicating that hospital admission rates for COVID-19 patients are positively correlated with age.<sup>9-11</sup> It is crucial to identify high-risk age groups and take preventive measures against systemic diseases and skin damage.

In this study, hypertension and diabetes mellitus were the most prevalent comorbidities in both groups. These conditions are known to increase the risk of pressure injuries.<sup>12,13</sup> The advanced average age in our study likely contributed to the presence of chronic diseases, predisposing patients to pressure injuries.

The sacral region was the most common site for pressure injuries in both patient groups. COVID-19 (+) patients had a higher incidence of stage 1 pressure injuries, whereas COVID-19 (-) patients had more stage 3 and UPI/SDTI injuries. The prolonged ICU stay of COVID-19 (-) patients may have contributed to the progression of pressure injuries to more advanced stages. In addition, in contrast to the COVID-19 (-) group, COVID-19 (+) patients exhibited more pressure injuries in the ears, knees, and abdominal regions, possibly due to their prone position and frequent repositioning required to manage respiratory parameters and acute deterioration.<sup>14,15</sup> Furthermore, the shorter length of ICU stay for COVID-19 (+) patients (22.19  $\pm$  50.79 days) was associated with the higher mortality rate in this group, although the difference in mortality was not significant.

Individual and clinical characteristics are critical in assessing the risk of pressure injuries. In the Braden Scale assessment, the patient's emotional perception, skin moisture status, mobility, nutritional habits, and areas of the body under pressure should be evaluated.<sup>16</sup> In the current study, the Braden Scale of COVID-19 (+) patients were found to be lower compared to those of COVID-19 (-) patients. In the literature, lower Braden Scale have been associated with an increased incidence of pressure injuries.<sup>17</sup> In this study, the Braden Pressure Ulcer Risk Assessment Scale was used as the risk evaluation tool, as it is the standard instrument employed in healthcare institutions affiliated with the Ministry of Health in Türkiye for the assessment of pressure injury risks. This difference is also considered to stem from differences in the clinical courses of patient groups and their critical illness status.

The mortality rate for the COVID-19 (+) group was 66%, and this group had a shorter stay compared to the COVID-19 (-) group. In contrast, a study by Sen and Demirdal found no significant difference in the length of stay between COVID-19 (+) and (-) patients.<sup>18</sup> This discrepancy may be due to the different clinical courses and critical conditions of the patient groups.

Body temperature is a critical parameter for monitoring sepsis in COVID-19 patients admitted to the ICU.<sup>19,20</sup> An increase in body temperature is considered an alert for healthcare professionals, prompting early intervention. In terms of body temperature, COVID-19 (+) patients exhibited subfebrile temperatures, with no significant difference from COVID-19 (-) patients. Body temperature is a critical parameter for monitoring sepsis in COVID-19 patients admitted to the ICU.<sup>19,20</sup> An increase in body temperature is considered an alert for healthcare professionals, prompting early intervention. In a study of 7,614 patients diagnosed with COVID-19, Tharakan et al. found that temperatures exceeded 37°C.<sup>21</sup> This elevation is attributed to the binding of proinflammatory cytokines produced during COVID-19 infection to receptors on brain endothelial cells, leading to prostaglandin synthesis in these cells and, subsequently, fever.<sup>22</sup>

No significant relationship was found between leukocyte, procalcitonin, and CRP levels in COVID-19 (+) and (-) patients, likely due to the prolonged ICU stay and increased infection risk in the COVID-19 (-) group. A review of the literature indicates that CRP, procalcitonin, and leukocyte levels are important indicators for assessing the severity and prognosis of COVID-19. The lack of a significant difference in these parameters in the present study may be explained by factors such as the longer ICU stay and increased risk of secondary infections in the COVID-19 negative group.<sup>23,24</sup>

Concerning hemoglobin, both groups had low levels, although the levels were further reduced in the COVID-19 (-) group. In a study conducted by Unver-Ulusoy et al.<sup>25</sup>, it was found that the COVID-19 group exhibited lower hemogram values compared to the control group. Ozmen Süner et al.<sup>26</sup> similarly determined that COVID-19 patients had lower hemoglobin levels. Our findings align with the literature, indicating that COVID-19-induced sepsis leads to disturbances in blood parameters. The lower values observed in patients without COVID-19 are considered to be associated with their older age, multiple comorbidities, and prolonged ICU stay. In addition, lymphopenia was observed in the COVID-19 (+) group, with over half of these cases resulting in mortality. Similarly, in the literature, high mortality rates have been documented in patients with severe lymphopenia.<sup>27,28</sup>

When infection parameters were evaluated according to pressure injury stages, it was observed that COVID-19 patients with stage 4 injuries had lower monocyte levels compared to those with stage 1 or 2 injuries.<sup>29</sup> This finding is consistent with the literature, which reports reduced monocyte levels in critically ill COVID-19 patients, indicating a possible link between COVID-19 pathophysiology and the development of pressure injuries. One of

the most severe complications of COVID-19, the cytokine storm, plays a central role in systemic inflammation, hyperferritinemia, and hemodynamic instability. It is characterized by an excessive immune response, involving persistent activation and infiltration of cytokine-producing cells such as lymphocytes and macrophages. This inflammatory process is also reflected in clinical symptoms like myalgia.

#### CONCLUSION

COVID-19 infection is recognized as a global pandemic ranging from asymptomatic courses to fatal outcomes. Complications caused by the infection within the body disrupt physiological mechanisms. Cases that progress severely necessitate closer follow-up in ICUs. As revealed by this study, inflammatory markers tend to be elevated in patients infected with the COVID-19 virus, necessitating more frequent monitoring for the development of pressure injuries. Specifically, monitoring monocyte levels is crucial in patients with stage 4 pressure injuries. The systemic impact of COVID-19, including disrupted ventilation, impaired oxygenation, and cytokine storms, contributes to movement restrictions and the risk of developing pressure injuries. Standard measures for pressure injury prevention require frequent adjustments in this patient group. During intensive care, healthcare professionals should regularly evaluate systemic infection parameters, protect pressure areas with support surface systems, perform risk assessments, and closely monitor hemodynamic parameters.

**Ethics Committee Approval:** Ethical approval for this retrospective case-control study was obtained from the Clinical Research Ethics Committee of the Kartal Dr. Lutfi Kirdar City Hospital (decision number: 514/194/45, January 27, 2021), as part of quality and assurance activities.

**Informed Consent:** Written informed consent was not required from participants or their legal guardians in accordance with national regulations and institutional requirements.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – AA, RK, KTS; Design – AA, RK, KTS; Data Collection – AA, RK, KTS; Data Analysis – AA, RK, KTS; Data Interpretation – AA, RK, KTS; Writing the article – AA, RK, KTS; Critical revision of the article: AA, RK, KTS

Declaration of Interests: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declare that they received no financial support for this study.

**Etik Komite Onayı:** Bu retrospektif vaka-kontrol çalışması için etik onay, kalite ve güvence faaliyetlerinin bir parçası olarak Dr. Lütfi Kırdar Şehir Hastanesi Klinik Araştırma Etik Komitesi'nden (karar numarası: 514/194/45, 27 Ocak 2021) alınmıştır.

Hasta Onamı: Ulusal düzenlemeler ve kurumsal gereklilikler uyarınca katılımcılardan veya yasal vasilerinden yazılı onam alınması gerekmemektedir.

#### Hakem Değerlendirmesi: Dış bağımsız.

**Yazar Katkıları:** Fikir – AA, RK, KTS; Tasarım – AA, RK, KTS; Verilerin toplanması – AA, RK, KTS; Verilerin analizi – AA, RK, KTS; Verilerin yorumlanması – AA, RK, KTS; Makalenin yazılması – AA, RK, KTS; Makalenin eleştirel revizyonu: AA, RK, KTS

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışmanın herhangi bir finansal destek almadığını beyan etmişlerdir.

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