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# Retrospective Evaluation of COVID-19 Patients Receiving Low-Dose Dexamethasone Therapy in the Intensive Care Unit

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## Abstract

**Background:** COVID-19 is associated with high mortality in critically ill patients due to an exaggerated inflammatory response characterized by a cytokine storm. In this context, the anti-inflammatory properties of corticosteroids have emerged as a significant therapeutic option. This study retrospectively evaluated COVID-19 patients who received low-dose dexamethasone therapy in the intensive care unit, and the relationship between survival status and changes in laboratory parameters was investigated.

**Materials and Methods:** Between June and August 2020, 80 patients with a confirmed diagnosis of COVID-19 by RT-PCR who received low-dose dexamethasone therapy (6 mg/day, up to 10 days) in the intensive care unit were analyzed. Patients were divided into two groups according to their clinical outcomes: survivors (n=41) and non-survivors (n=39). Laboratory measurements were recorded at two time points: within the first 24 hours of ICU admission (T0) and on day 5 ±2 (T1). Percentage changes were calculated.

**Results:** The mean age of the survivor group was higher than that of the non-survivor group (77.1 vs. 62.3 years; $p<0.001$). At T0, WBC levels were lower in the non-survivor group ($p=0.027$). Regarding the change from T0 to T1 in IL-6 levels, a decrease of 76.6% was observed in the non-survivor group and 54.5% in the survivor group ($p=0.045$). Ferritin levels increased in the survivor group but decreased in the non-survivor group ($p=0.001$). D-dimer levels showed a marked increase in the survivor group, whereas a decrease was observed in the non-survivor group ($p<0.001$).

**Conclusion:** The literature has strongly demonstrated that corticosteroids can improve survival in patients with severe COVID-19. The unique contribution of this study lies in revealing the changes in laboratory parameters between survival groups under dexamethasone therapy. Although the findings do not establish a direct relationship with mortality, they may serve as hypothesis-generating data that contribute to understanding the heterogeneity of clinical responses.

**Keywords:** COVID-19, Intensive care, Dexamethasone, Inflammation

## Introduction

COVID-19 was first identified in Wuhan, China, in December 2019, with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) recognized as the causative agent [1]. Spreading rapidly across the globe, this infection evolved into a pandemic and has presented with a wide clinical spectrum ranging from fever, cough, dyspnea, and fatigue to hypoxemia, acute respiratory distress syndrome (ARDS), sepsis, and multiple organ failure [2,3]. Since the onset of the pandemic, numerous retrospective and prospective observational studies have been published worldwide in different patient populations, and data regarding the management of critically ill patients have played a pivotal role in the development of clinical guidelines [4].

In the pathogenesis of COVID-19, the exaggerated inflammatory response known as the cytokine storm has been shown to play a decisive role in disease progression and the development of complications. In this context, corticosteroids have emerged as a notable therapeutic option due to their suppressive effects on the inflammatory process [5,6]. Although there were initial concerns regarding the use of glucocorticoids, the results of studies, particularly the RECOVERY trial, demonstrated that systemic corticosteroid therapy reduced mortality in COVID-19 patients requiring respiratory support [7, 8]. Based on these findings, international health authorities such as the World Health Organization (WHO), the U.S. Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH) have strongly recommended the use of low-dose systemic corticosteroids in severe and critical COVID-19 cases managed in intensive care units [9, 10].

In intensive care units, elucidating the effects of corticosteroid therapy on laboratory parameters, inflammatory markers, and clinical prognosis in COVID-19 patients is essential for both the individualization of treatment approaches and the identification of factors influencing survival. Although not as robust as randomized controlled trials, retrospective analyses provide valuable insights by assessing treatment outcomes based on real-world data and generating hypotheses for future research.

The aim of this study was to retrospectively evaluate patients diagnosed with COVID-19 who were followed in the intensive care unit and received low-dose dexamethasone therapy, and to demonstrate the relationship between survival status and clinical as well as laboratory parameters. In this context, inflammatory markers and biochemical parameters during the course of COVID-19 treatment were compared, and possible changes observed under dexamethasone therapy were analyzed.

## Material and Methods

### *Study Design and Ethical Approval*

The study population of this retrospective research consisted of patients treated for COVID-19 in the intensive care unit of a university hospital between June and August 2020. Ethical approval for the study was obtained on October 14, 2020 (Protocol No: E1-20-1181). The study was conducted in accordance with the principles of the Declaration of Helsinki.

### *Inclusion and Exclusion Criteria*

Patients were included if they were older than 18 years, had a confirmed diagnosis of COVID-19 by RT-PCR, and received low-dose dexamethasone (Dekort®, Deva Holding, Turkiye) at a dose of 6 mg/day for up to 10 days or until discharge during their intensive care unit (ICU) stay. Patients were excluded if they had received corticosteroid protocols other than dexamethasone, if complete data could not be obtained, or if they were treated outside the intensive care unit.

### *Patient Grouping and Data Collection*

Patients were divided into two groups according to their clinical outcomes at the end of the ICU stay. Those who died during their ICU course were classified as non-survivors, while those discharged alive from the ICU were classified as survivors. These two groups were compared in terms of age, sex, duration of dexamethasone therapy, and laboratory parameters.

All data were retrospectively obtained from the hospital information management system and patient medical records. Demographic variables (age, sex), duration of dexamethasone therapy, and laboratory findings were evaluated. Two standard time points were defined for laboratory measurements:

- T0 (Baseline/ICU admission): The first laboratory value obtained within 24 hours after ICU admission.
- T1 (Early follow-up): The first laboratory value obtained within the window of day 5 ± 2 after ICU admission, following T0.

The laboratory parameters evaluated in the analysis were white blood cell (WBC) count, ferritin, interleukin-6 (IL-6) and D-dimer levels. Measurements at T0 and T1 were recorded separately, and percentage changes were calculated based on these values.

***Statistical Analysis***

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, 2012). The distribution of continuous variables was assessed with the Shapiro–Wilk test. Data with normal distribution were expressed as mean ± standard deviation, while non-normally distributed data were presented as median (minimum–maximum).

Measurements were recorded separately at T0 and T1, and the percentage change was calculated using the formula: % change = (T1 – T0) / T0 × 100. Comparisons between the two groups were conducted using the independent samples t-test or the Mann–Whitney U test for continuous variables, and Pearson's chi-square test or Fisher's exact test for categorical variables. A p-value of <0.05 was considered statistically significant.

**Results**

In this study, a total of 102 patients who were monitored in the ICU due to COVID-19 and received low-dose dexamethasone therapy were retrospectively evaluated. According to the exclusion criteria, 3 patients under the age of 18, 7 patients treated outside the ICU, 8 patients who received non-dexamethasone corticosteroid therapy, and 4 patients with incomplete medical records were excluded from the study. After these exclusions, 80 patients were included in the analysis. Based on clinical outcomes, these patients were divided into two groups: survivors (n=41) and non-survivors (n=39) at the end of the ICU stay (Figure 1).

These two groups were compared in terms of demographic characteristics and treatment courses. The mean age was 62.26 years in the non-survivor group and 77.10 years in the survivor group, with the survivor group showing a significantly higher mean age (p<0.001). No statistically significant difference was found between the groups regarding gender distribution (p=0.840). Similarly, no significant difference was observed between the two groups in terms of the duration of dexamethasone therapy (p=0.129) (Table 1).

**Table 1. Characteristics of the Study Population**

| Parameters | Non-survivors n=39 | Survivors n=41 | P* |
|---|---|---|---|
| **Gender** | | | |
| **Female n (%)** | 18 (46.15%) | 18 (43.90%) | 0,840[a] |
| **Male n (%)** | 21 (53.85%) | 23 (56.10%) | |
| **Age (years), mean ± SD** | 62.26 ± 12.44 | 77.10 ± 11.71 | <0,001[b] |
| **Treatment duration (days), med (min–max)** | 8 (3–10) | 6 (3–11) | 0,129[c] |

***n: Number; * P <0.05= Significance level; SD: Standard Deviation; med: Median; min: Minimum; max: Maximum. [a] Pearson's Chi-square test, [b] Independent samples t-test, [c] Mann–Whitney U test.***

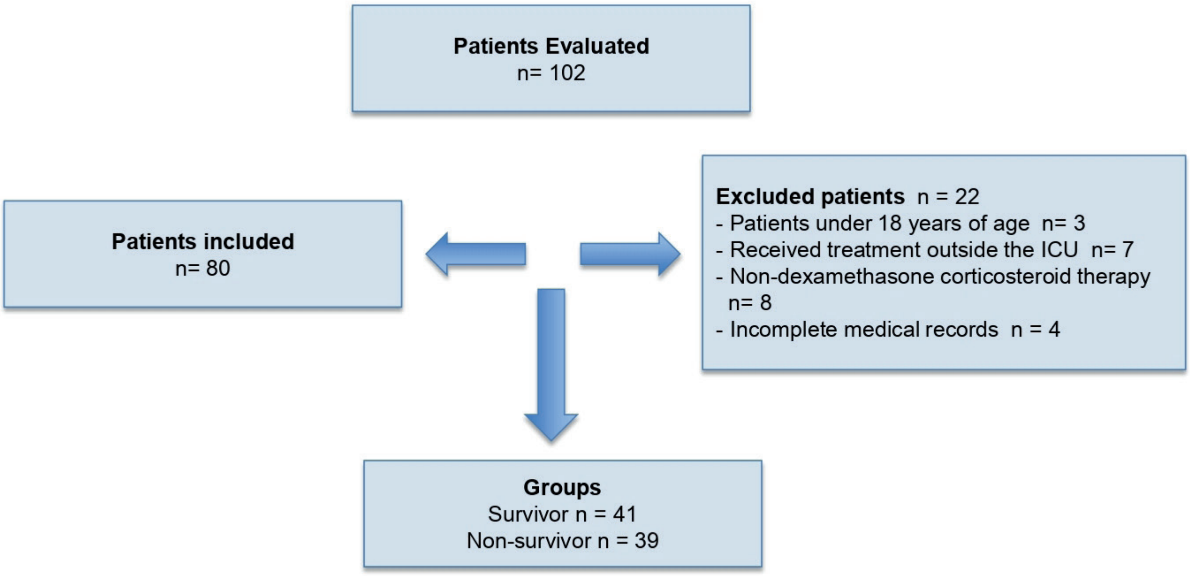


**Figure 1:** *Flow diagram of patient selection and grouping / ICU: Intensive care unit*

In Table 2, the findings of selected laboratory parameters (WBC, culture positivity, IL-6, ferritin, and D-dimer) in the survivor and non-survivor groups are presented at T0 (within the first 24 hours of ICU admission) and T1 (day 5 ±2 after admission), along with the percentage changes between these measurements.

Regarding WBC levels, the median WBC value at T0 was $6.80\times10^9$/L in the non-survivor group and $9.10\times10^9$/L in the survivor group. This difference between the groups was found to be statistically significant (p=0.027). When the change from T0 to T1 was examined, an increase of 39.51% was observed in the non-survivor group and 50.0% in the survivor group; however, this difference was not statistically significant (p=0.475).

Evaluation of IL-6 levels revealed no significant difference between the groups at T0 (p=0.933). However, analysis of changes from T0 to T1 showed a 76.61% decrease in the non-survivor group and a 54.50% decrease in the survivor group, with the difference reaching statistical significance (p=0.045). Similarly, evaluation of ferritin levels showed no significant difference between the groups at T0 (p=0.141). In contrast, from T0 to T1, ferritin levels decreased by 9.34% in the non-survivor group and increased by 20.57% in the survivor group, a difference that was statistically significant (p=0.001) (Table 2).

At T0, there was no significant difference in D-dimer levels between the groups (p=0.992). In contrast, from T0 to T1, D-dimer levels decreased by 47.33% in the non-survivor group, whereas they increased by 88.61% in the survivor group. This difference was statistically significant (p<0.001) (Table 2).

## Discussion

The COVID-19 pandemic has represented one of the greatest health crises faced by modern medicine, as it is an infectious disease with complex clinical management and multisystem involvement. The clinical spectrum of the disease ranges from asymptomatic infection to multiple organ failure and death [1]. Therefore, identifying prognostic markers that can predict the course of the disease and developing effective therapeutic strategies are of vital importance, particularly for critically ill patients managed in ICUS. In our study, retrospective data of COVID-19 patients who received low-dose dexamethasone therapy in the ICU were analyzed, and several key laboratory parameters were evaluated according to survival status.

In our study, the mean age of the survivor group was found to be higher than that of the non-survivor group (Table 1). This finding appears to be in contrast with the widely reported notion in the literature that

**Table 2. T0–T1 Laboratory Findings and Changes in Survivors and Non-survivors**

| Parametres | Non-survivors n=39 | Survivors n=41 | P* |
|---|---|---|---|
| **WBC (×10⁹/L)** | | | |
| **T0 - med (min–max)** | 6,80 (2,98–15,80) | 9,10 (2,27–39,0) | **0,027ᶜ** |
| **T1 - med (min–max)** | 9,20 (3,70–20,60) | 14,19 (4,90–128,40) | – |
| **T0→T1 : %** | ↑39.51% (–43.28–302.94) | ↑50.0% (–65.90–661.88) | 0,475ᶜ |
| **IL-6 (pg/mL)** | | | |
| **T0 - med (min–max)** | 51,80 (3,40–1360) | 82,0 (17,30–1000) | 0,933ᶜ |
| **T1 - med (min–max)** | 9,20 (2–836) | 59,80 (3,11–9000) | – |
| **T0→T1 : %** | ↓76.61% (–97.62–993.63) | ↓54.50% (–94.67–17547.06) | 0,045ᶜ |
| **Ferritin (µg/L)** | | | |
| **T0 - med (min–max)** | 537 (70–6928) | 454,50 (2,75–4351) | 0,141ᶜ |
| **T1 - med (min–max)** | 547 (84,40–16488) | 548 (12–5302) | – |
| **T0→T1 : %** | ↓9.34% (–72.77–154.29) | ↑20.57% (–99–5583.64) | **0,001ᶜ** |
| **D-dimer (mg/L)** | | | |
| **T0 - med (min–max)** | 1,33 (0,19–24,90) | 2,0 (0,19–17,10) | 0,992ᶜ |
| **T1 - med (min–max)** | 0,90 (0,19–18,99) | 6,22 (0,30–4560) | – |
| **T0→T1 : %** | ↓47.33% (–93.17–677.65) | ↑88.61% (–83.33–67959.70) | **<0,001ᶜ** |

***n: Number; *p < 0.05 = Level of statistical significance; med: Median; min: Minimum; max: Maksimum; T0: Within the first 24 hours of intensive care unit admission; T1: Day 5±2 after intensive care unit admission; WBC = White blood cell; IL-6 = Interleukin-6. [c] Mann–Whitney U test, [d] McNemar test.***

advancing age is associated with an increased risk of mortality. However, previous multicenter studies have demonstrated that advanced age increases COVID-19 related mortality due to immune senescence, higher comorbidity burden, and reduced physiological reserve [1,11]. The limited sample size of our study may have led to random differences in age distribution between the groups. In addition, factors such as treatment processes, the types of comorbidities, the severity of organ dysfunctions, and the timing of clinical interventions may have played a more prominent role in survival than age itself. Therefore, this finding suggests that advanced age may not be an absolute risk factor, and that multiple parameters influencing the clinical course should be carefully considered. Taken together with existing data in the literature, our results indicate that age alone may not be a definitive determinant in COVID-19 patients and highlight the importance of individualized patient assessment. This assessment, indicating that age alone may not be a decisive factor, is consistent with our treatment-related findings. Dexamethasone is among the glucocorticoids with the most pronounced anti-inflammatory effects. Following the RECOVERY trial, this treatment regimen has been recommended in many guidelines and has been shown to improve survival, particularly in patients requiring oxygen support [7]. In our study, no significant difference was observed between the groups regarding the duration of dexamethasone therapy (p=0.109) (Table 1) This finding suggests that factors such as the stage of the disease, the timing of treatment initiation, and individual variability in response may have a greater influence on survival than the duration of therapy itself.

In our study, total WBC levels at T0 were found to be significantly lower in the non-survivor group

(Table 2). This finding suggests that the patients' immune systems may have been suppressed in the pre-infectious period, rendering them more susceptible to infection. Although mild leukocytosis is generally expected in COVID-19 patients, some studies have reported a pattern characterized by marked neutrophilia accompanied by lymphopenia. This condition leads to a significant increase in the neutrophil-to-lymphocyte ratio (NLR) in parallel with disease severity, and this ratio is regarded as an indirect indicator of inflammation and disease progression [12,13]. However, in our study, the percentage change in WBC from T0 to T1 was not different between the two groups ($p=0.475$) (Table 2). This pattern may suggest that the leukocyte response was partially homogenized under the anti-inflammatory effect of dexamethasone, although no causal inference can be made.

IL-6 is a proinflammatory mediator that plays a central role in the pathogenesis of cytokine storm in COVID-19 patients. In our study, no significant difference was detected between the groups at T0 ($p=0.933$). However, when the percentage change from T0 to T1 was examined, a 76.61% decrease was observed in the non-survivor group and a 54.50% decrease in the survivor group, with the difference reaching statistical significance ($p=0.045$) (Table 2). Although this may appear paradoxical at first glance, it can be explained by immune exhaustion (immunoparalysis) in critically ill patients, a reduction in cytokine production during the advanced stages of disease, or the predominance of anti-inflammatory suppression mechanisms. Previous studies have reported that IL-6 levels may serve as a prognostic marker for disease severity and the need for mechanical ventilation [10,14]. Nevertheless, considering that IL-6 may play a heterogeneous role at different stages of the disease, this parameter should be interpreted with caution in the clinical context.

Ferritin is not only a protein that regulates iron metabolism but also an acute-phase reactant that serves as an important marker of systemic inflammation. In hyperinflammatory conditions such as COVID-19, elevated ferritin levels have been associated particularly with cytokine storm and macrophage activation syndrome [15]. Previous studies have reported that high ferritin levels are associated with disease severity and mortality [16]. In our study, no significant difference was observed between the groups at T0 ($p=0.141$). However, when the percentage change from T0 to T1 was analyzed, ferritin levels increased by 20.57% in the survivor group, whereas they decreased by 9.34% in the non-survivor group, and this difference was found to be statistically significant ($p=0.001$) (Table 2). The increase in the survivor group may reflect a physiological inflammatory response of the immune system aimed at infection control, whereas the decrease in the non-survivor group may be associated with mechanisms such as immune suppression or liver dysfunction in the advanced stages of disease. These results suggest that ferritin is a parameter that can reflect the course of the disease but may vary across different clinical stages.

COVID-19 is characterized by the dysfunction it induces in the coagulation system. Hypercoagulopathy and thromboembolic events are frequently observed, particularly in hospitalized and critically ill patients. D-dimer is a fibrin degradation product, and elevated levels are considered an indicator of both disease severity and an increased risk of thromboembolic complications [11,17]. In our study, no significant difference was observed between the groups at T0 in terms of D-dimer levels ($p=0.992$). However, when the T0→T1 period was examined, D-dimer levels decreased by 47.33% in the non-survivor group, whereas they increased by 88.61% in the survivor group, and this difference was statistically significant ($p<0.001$) (Table 2). One possible explanation for this finding is the occurrence of disseminated intravascular coagulation like conditions during the course of the disease or fibrinolytic processes emerging in later stages. In addition, the effect of corticosteroid therapy on coagulation parameters has not yet been fully elucidated [8]. Therefore, interpretation of D-dimer should take into account the timing of measurement and the stage of the disease.

### Strengths and Limitations of the Study

Our study is valuable in that it analyzes the effects of dexamethasone therapy on clinical and laboratory parameters in the management of critical illness due to COVID-19 using retrospective clinical data. However, its retrospective design and limited sample size may reduce the strength of interpretation. Furthermore, as the data were derived from past records, there is a possibility that certain measurements or assessment criteria might have been influenced by potential information bias in group assignments. Nevertheless, these limitations are consistent with the observational nature of the study, and the findings provide hypothesis-generating value for future research.

### Conclusion

Evidence accumulated during the pandemic has shaped our understanding of the clinical course and treatment of COVID-19. The high viral load in the early stages of infection and the potential for rapid clinical deterioration are of critical importance in treatment approaches. Although the beneficial effects of corticosteroid therapy on survival in severe and critical COVID-19 patients have been strongly demonstrated in the literature, the unique contribution of our study is the demonstration of changes in laboratory parameters according to survival status under treatment with dexamethasone, a corticosteroid. While these findings do not establish a direct causal relationship with mortality, the observed variations in laboratory parameters under dexamethasone treatment may contribute to understanding the heterogeneity of clinical responses and serve as hypothesis-generating evidence for future studies.

### Ethics / Informed Consent

Ethical approval for the study was obtained on October 14, 2020, with protocol number E1-20-1181. The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Data Availability Statement

Data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

### Disclosure

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

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