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ORIGINAL ARTICLE

Comparison of Cytokine Hemadsorption as an Immunomodulator Therapy in COVID-19 Patients with and without Bacterial Sepsis

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SUMMARY

Background: **In this retrospective study, we aimed to compare the laboratory and clinical results of cytokine hemadsorption as an immunomodulation therapy in COVID-19 ICU patients with or without sepsis.**
Methods: **The levels of PCT, CRP, and ferritin were determined as indicators of infection/sepsis; the levels of interleukins (IL-6, IL-8 and IL-10, and TNF-α) were determined as indicators of cytokine storm were compared. APACHE score, SOFA score, and mortality rates were compared for the progression of the disease in 23 COVID-19 patients.**
Results: **The therapy was generally successful in reducing the levels of IL-6, IL-8, IL-10, and TNF-α but the levels measured after the procedure did not differ among the patients with or without sepsis, suggesting that the presence of sepsis did not affect the efficacy and function of the cytokine hemadsorption procedure in COVID-19 patients. All parameters were reduced after the procedure except the levels of PCT and ferritin and mortality rates of patients diagnosed with sepsis. The level of PCT was significantly higher in these patients compared with the patients without sepsis while the ferritin and mortality did not show any significant difference between the two groups, suggesting that the cytokine hemadsorption may be safe in the treatment of critical COVID-19 patients.**
Conclusions: **As a result, the progression of sepsis in COVID-19 may be avoided with cytokine hemadsorption applied as an immunomodulator therapy. However, this therapy should be further explored and validated prior to its introduction to everyday clinical practice when the epidemic conditions end.**
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KEYWORDS

COVID-19, cytokine storm, cytokine hemadsorption, sepsis

INTRODUCTION

Since December 2019, coronavirus disease 2019 (COVID-19), caused by the coronavirus 2 that causes severe acute respiratory syndrome, has been circulating (SARS-CoV-2) and has produced a pandemic of respi-

ratory diseases [1]. By February 10, 2020, WHO confirmed COVID-19 in 106,321,987 people worldwide with 2,325,282 deaths [2]. In Turkey, 2,539,559 cases of COVID-19 with 26,900 deaths have been confirmed up to the present [2]. Nearly 20% of COVID-19 patients experience a severe or a serious illness requiring admission to an intensive care unit (ICU). In general, the mortality for COVID-19 patients is about 4% [3], increasing to 26% for severe patients and up to 60% for critically ill patients in the ICU [4,5].
Cytokine storm, an extreme and uncontrolled release of pro-inflammatory cytokines, is common among the severe and critical COVID-19 patients and is associated with the progression and development of COVID-19 [6]. Hyper-inflammatory activation during cytokine storm is characterized by immune cell infiltration and elevated levels of cytokines including interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) were reported as the underlying mechanisms resulting in sepsis or severe acute respiratory distress syndrome (ARDS) [7]. The levels of these cytokines in serum were also reported to be positively correlated with high mortality rates [8]. Therefore, an immunomodulation therapy targeting the cytokine storm may represent a potential favorable therapeutic strategy against COVID-19. One of these therapies, the extracorporeal cytokine hemadsorption, for patients with significant pulmonary involvement and cytokine release syndrome (CRS), proinflammatory compounds are useful [9]. A treatment using adsorption of cytokines has been extensively reported in the sepsis but there are limited number of studies showing the beneficial effects of cytokine hemadsorption in COVID-19 patients [10].
Proinflammatory drugs are effective for individuals with substantial lung involvement and cytokine release syndrome.

MATERIALS AND METHODS

Study design

In this retrospective, one-centered study, we analyzed the outcomes and laboratory findings of 23 patients diagnosed with COVID-19 from December 30, 2020 to May 01, 2021 hospitalized in ICU. Patients with COVID-19 induced sepsis were identified using available laboratory data (a positive throat swab nucleic acid test or a positive serum COVID-19 specific antibody test), and the criteria for patients with COVID-19 induced sepsis were bacterial agent detection in blood or tracheal culture. According to the New Coronavirus Pneumonia Prevention and Control Plan (seventh edition) of the National Health Commission of China, a patient with COVID-19 is considered critical when respiratory failure necessitates mechanical ventilation, or the patient experiences shock or multiple organ failure and is transferred to the hospital ICU [11]. All of the patients in this study were classified as serious cases after meticulous evaluation, and were separated into two groups: COVID-19 and COVID-19 + sepsis. Clinical indications for extracorporeal cytokine hemadsorption include the cytokine storm, CRS, multiple organ dysfunction, hyperkalemia, acidosis or severe sepsis.
The institutional ethics committee at Biruni University gave the approval to this investigation. (No. 2020/41-10 Date: June 19, 2021). ClinicalTrials.gov Identifier: NCT 04920851.

Data collection

All data were taken from the patients' medical records, including demographics, clinical history, and laboratory findings. The study included critically ill patients in ICU who were divided into two groups: COVID-19 and COVID-19 + sepsis, depending on whether or not they had sepsis.
Inflammatory cytokines such as interleukin-6 (IL-6), IL-8, IL-10, and tumor necrosis factor (TNF) were dosed in a single serum sample using flow cytometry (HA-330 disposable perfusion cartridge, Jafron, JAPAN). Hemadsorption was started on the day when the need for intubation developed and mechanical ventilation was started in patients without sepsis, and when the agent was detected in patients with sepsis. Hemadsorption was done for 3 hours for 7 days. The procedure was initiated by placing a double-lumen catheter through the femoral vein or the subclavian vein. All data of hemadsorption therapy were obtained before the procedure (pre-HAD), during the procedure (intra-HAD), and after the procedure (post-HAD).
Ferritin was measured by the chemiluminescent microparticle immunoassay (CMIA) method on the Abbot-I1000 SR device and procalcitonin (PCT) by a fast test kit using Immunofluorescence Assay (IA) method on Getein 1600 device). The expert physicians performed all of the patient's laboratory examinations.
The study's main purpose was to look at the laboratory and clinical results of cytokine hemadsorption as an immunomodulation therapy in COVID-19 ICU patients with and without sepsis.

Statistical analysis

The mean, standard deviation, minimum, maximum, and median values for continuous variables, as well as the frequencies and percentages for categorical variables, were calculated. Kolmogorov-Smirnov and Shapiro-Wilk Lambda were used to test the normal distribution. To see if there was a significant difference between the dependent variables, the Friedman test and Wilcox's sign-rank test were utilized. The Bonferroni Corrected Dunn Multiple Comparisons test was used to determine the variable contributing to the significant difference in the results of Friedman test. Mann-Whitney U test was used to compare the variables of COVID-19 and COVID-19 + Sepsis groups. Receiver Operating Characteristic (ROC) analysis was used to determine the variables that were significant in the prediction of mortality and the progression of sepsis. $p < 0.05$ was considered significant. Statistical analyzes were performed with SPSS 23 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, NY, USA) and MedCalc 18.5 (MedCalc Software Ltd., Ostend, Belgium).

RESULTS

Table 1 shows the distribution of age and gender among 23 patients with COVID-19. According to the table, the mean age was 67.35 ± 14.25 years. None of our patients had any co-morbidity. The mortality rate was 78.26% (Table 1).

The laboratory parameters measured before, during, and after the extracorporeal hemadsorption procedure were compared between six COVID-19 patients without sepsis and 17 COVID-19 patients with sepsis and the outcomes are presented in Appendix 1. The mean levels of IL-6 there was no statistically significant difference between two groups of patients but the intra-HAD and post-HAD levels decreased significantly compared with pre-HAD levels in each group ($p < 0.05$).

The mean level of intra-HAD IL-8 was significantly higher among the patients with COVID-19 + sepsis than those of the other group ($p = 0.030$). However, the differences between the levels pre-HAD, intra-HAD, and post-HAD IL-8 in each group did not show any significance.

The mean level of intra-HAD IL-10 was significantly higher among the COVID-19 patients without sepsis than those of COVID-19 patients with sepsis ($p = 0.025$). Moreover, IL-10 levels gradually decreased during the procedure in each group, showing a significant difference according the time of procedure ($p < 0.05$). The mean TNF levels did not differ statistically between the two groups of patients, but intra-HAD and post-HAD levels in each group fell significantly compared to pre-HAD levels ($p < 0.05$).

The mean levels of intra-HAD and post-HAD PCT were significantly higher among the COVID-19 patients with sepsis than those of COVID-19 patients without sepsis ($p = 0.049$ and 0.001, respectively). In addition, the levels post-HAD PCT in COVID-19 patients with sepsis were higher than pre-HAD and intra HAD ($p < 0.001$). The mean level of post-HAD CRP was higher in COVID-19 + sepsis group compared with COVID-19 group. Moreover, the intra-HAD and post-HAD levels decreased significantly compared with pre-HAD levels in each group ($p < 0.05$).

The death rates, ferritin levels, and APACHE (Acute Physiology and Chronic Health Evaluation) scores were not different between the two groups. However, the COVID-19 patients with sepsis had a significantly higher post-HAD SOFA (Sequential Organ Failure Assessment) score than COVID-19 patients without sepsis ($p = 0.009$) (Appendix 1).

The changes in laboratory parameters measured before, during, and after the procedure were compared and the outcomes are presented in Table 2. The changes in levels of IL-6, IL-8, TNF-α, PCT, and CRP did not differ significantly between two groups ($p > 0.05$). However, $\Delta_{\text{Intra-Post}}$ values of IL-10 and ferritin was positive and significantly higher among COVID-19 patients without sepsis compared with those with sepsis ($p = 0.006$ and 0.035, respectively). In addition, $\Delta_{\text{Pre-Post}}$ value of ferritin was also positive and significantly higher among COVID-19 patients without sepsis compared with those with sepsis ($p = 0.012$). Lastly, $\Delta_{\text{Pre-Post}}$ value of SOFA score was significantly higher in COVID-19 group than the value of COVID-19 + sepsis group ($p = 0.009$).

ROC analysis of pre-hemadsorption laboratory parameters in predicting the mortality showed that IL-6, IL-10, PCT, and CRP levels measured before the procedure were significant parameters to predict the mortality among all COVID-19 patients ($p < 0.05$; Table 3). IL-6 levels > 176.2 ng/L, IL-10 levels ≤ 152.3 ng/L, PCT levels > 0.16 ng/mL, and CRP > 160 mg/mL were significantly associated with the mortality rate among all COVID-19 patients (Table 3).

ROC analysis of pre-hemadsorption laboratory parameters in predicting the diagnosis of COVID-19-associated sepsis showed that CRP and ferritin levels measured before the procedure were significant parameters to predict the diagnosis among all COVID-19 patients ($p < 0.05$; Table 4). CRP > 213 mg/mL and ferritin ≤ 610 ng/mL were significantly associated with the diagnosis of COVID-19-associated sepsis among all COVID-19 patients (Table 4).

DISCUSSION

In this retrospective investigation, the cytokine hemadsorption was compared between COVID 19 patients with and without bacterial sepsis. It was determined that the hemadsorption was effective both in terms of laboratory values and clinical results. In addition, it was demonstrated that the cytokine hemadsorption led to an improvement in IL-6, IL-10, TNF α, CRP levels of COVID-19 patients, independently of the presence of sepsis, and a decrease in APACHE II and SOFA scores of both groups. It has been observed that the procedure reduced the mortality rate by 50% in COVID 19 patients without sepsis but did not change the mortality rates of patients diagnosed with the sepsis.

The excessive inflammatory response of cytokines can lead to CRS, or "cytokine storm," which occurs by the activation of white blood cells and release of the inflammatory cytokines that activate further white blood cells. IL-6, IL-8, ferritin, and TNF-α are certain proinflammatory cytokines released in this step. This cytokine storm is also observed in the postoperative period after a major surgery, and in various medical conditions such as sepsis and septic shock [12]. This disproportional release over a controlled immune response is a crucial cause of mortality and morbidity of COVID-19 disease [12].

Current emerging data have indicated that COVID-19 is

Table 1. The demographics of all patients with COVID-19.

		n (%)
Group	COVID-19	6 (26.09)
	COVID-19 + sepsis	17 (73.91)
Gender	female	8 (34.78)
	male	15 (65.22)
Bacterial replication	present	17 (100.00)
Day of bacterial replication	5	2 (11.76)
	7	2 (11.76)
	8	5 (29.41)
	9	3 (17.65)
	10	3 (17.65)
	11	1 (5.88)
	14	1 (5.88)
Outcome	discharge	5 (21.74)
	mortality	18 (78.26)
Age	mean ± SD median (min - max)	67.35 ± 14.25 70 (32 - 90)

Table 2. Comparison of the changes in laboratory parameters of the COVID-19 patients with or without sepsis according to the outcomes of extracorporeal hemadsorption.

Parameter		COVID-19 (n = 6) mean ± SD median (min - max)	COVID-19 + sepsis (n = 17) mean ± SD median (min - max)	p-value
IL-10 (ng/L)	$\Delta_{Pre\text{-}Intra}$	-102.82 ± 277.35 1.02 (-665.73 - 59.83)	-52.55 ± 381.12 45.56 (-1,524.11 - 93.87)	0.141
	$\Delta_{Pre\text{-}Post}$	65.08 ± 27.26 68.15 (21.55 - 93.11)	-70.35 ± 413.45 27.58 (-1,656.5 - 92.99)	0.141
	$\Delta_{Intra\text{-}Post}$	72.08 ± 21.63 75.74 (38.3 - 93.24)	-74.58 ± 194.83 -8.36 (-694.28 - 83.33)	<u>0.006</u>
	<u>p-value</u>	<u>0.011</u>	0.204	
Ferritin (ng/mL)	$\Delta_{Pre\text{-}Intra}$	-9.27 ± 22.98 1.92 (-41.36 - 13.27)	-43.33 ± 96.48 0 (-245.42 - 34.75)	0.916
	$\Delta_{Pre\text{-}Post}$	3.29 ± 108.97 46.09 (-216.96 - 60.38)	-227.09 ± 434.25 -32.12 (-1,639.13 - 39.83)	<u>0.012</u>
	$\Delta_{Intra\text{-}Post}$	18.22 ± 72.39 41.27 (-124.22 - 70.7)	-201.06 ± 424.65 0 (-1,512.9 - 61.75)	<u>0.035</u>
	<u>p-value</u>	0.119	0.807	
SOFA Score	$\Delta_{Pre\text{-}Post}$	38.02 ± 13.66 42.08 (16.67 - 50)	18.02 ± 13.43 20 (-16.67 - 45.45)	<u>0.009</u>

IL - Interleukin, SOFA - Sequential Organ Failure Assessment, $\Delta_{Pre\text{-}Intra}$ - Pre-HAD value - Intra-hemadsorption value, $\Delta_{Pre\text{-}Post}$ - Pre-HAD value - Post-hemadsorption value, $\Delta_{Intra\text{-}Post}$ - Intra-hemadsorption value - Post-hemadsorption value.

characterized by an impaired immune activation manifesting as hyperinflammation. Ruan et al. pointed out that higher systemic IL-2, IL-7, IL-10, and TNF-α levels were observed in critically ill patients admitted to the ICU [13].

Pro- and anti-inflammatory interleukins regulate the im-

Table 3. Receiver Operating Characteristic (ROC) analysis of pre-hemadsorption laboratory parameters in predicting the mortality among COVID-19 patients.

Pre-HAD parameters	Cutoff	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	AUC [95% CI]	p-value
IL-6	> 176.2	61.11 [35.7 - 82.7]	100 [47.8 - 100]	100 [0 - 0]	41.7 [28.6 - 56.0]	0.722 [0.498 - 0.886]	<u>0.0416</u>
IL-8	> 98.54	44.44 [21.5 - 69.2]	100 [47.8 - 100]	100 [0 - 0]	33.3 [24.9 - 43.0]	0.644 [0.42 - 0.83]	0.2753
IL-10	≤ 152.3	72.22 [46.5 - 90.3]	80 [28.4 - 99.5]	92.9 [68.8 - 98.7]	44.4 [25.2 - 65.5]	0.744 [0.522 - 0.901]	<u>0.0432</u>
TNF-α	> 145.9	27.78 [9.7 - 53.5]	100 [47.8 - 100.0]	100 [0 - 0]	27.8 [22.4 - 33.9]	0.553 [0.316 - 0.742]	0.8318
PCT	> 0.16	100 [81.5 - 100.0]	80 [28.4 - 99.5]	94.7 [75.7 - 99.0]	100 [0 - 0]	0.833 [0.621 - 0.954]	<u>0.0468</u>
CRP	> 160	72.22 [46.5 - 90.3]	80 [28.4 - 99.5]	92.9 [68.8 - 98.7]	44.4 [25.2 - 65.5]	0.772 [0.552 - 0.919]	<u>0.0146</u>
Ferritin	≤ 610	55.56 [30.8 - 78.5]	80 [28.4 - 99.5]	90.9 [62.3 - 98.4]	33.3 [20.3 - 49.6]	0.567 [0.346 - 0.769]	0.6854
APACHE Score	> 35	38.89 [26.0 - 74.0]	80 [28.4 - 99.5]	90 [59.5 - 98.2]	30.8 [19.0 - 45.7]	0.65 [0.425 - 0.835]	0.2401
SOFA Score	> 58.6	88.89 [65.3 - 98.6]	40 [5.3 - 85.3]	84.2 [71.9 - 91.7]	50 [15.6 - 84.4]	0.583 [0.362 - 0.783]	0.5944

Pre-HAD - Before hemadsorption, PPV - Positive Predictive Value, NPV - Negative Predictive Value, AUC - Area under ROC curve, CI - Confidence Interval, IL - Interleukin, TNF-α - Tumor necrosis factor alpha, CRP - C-reactive protein, PCT - Procalcitonin, APACHE - Acute Physiologic Assessment and Chronic Health Evaluation, SOFA - Sequential Organ Failure Assessment.

Table 4. Receiver Operating Characteristic (ROC) analysis of laboratory parameters in predicting the diagnosis of COVID-19-associated sepsis among COVID-19 patients.

Pre-HAD parameters	Cutoff	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	AUC [95% CI]	p-value
IL-6	> 176.2	58.82 [32.9 - 81.6]	83.33 [35.9 - 99.6]	90.9 [61.5 - 98.4]	41.7 [26.7 - 58.3]	0.716 [0.491 - 0.882]	0.0963
IL-8	> 98.54	41.18 [18.4 - 67.1]	83.33 [35.9 - 99.6]	87.5 [51.7 - 97.9]	33.3 [22.7 - 46.1]	0.559 [0.339 - 0.763]	0.6833
IL-10	≤ 102.3	35.29 [14.2 - 61.7]	83.33 [35.9 - 99.6]	85.7 [47.3 - 97.6]	31.3 [21.6 - 42.9]	0.52 [0.304 - 0.730]	0.8941
TNF-α	> 145.9	29.41 [10.3 - 56.0]	100 [54.1 - 100.0]	85.7 [47.3 - 97.6]	31.3 [21.6 - 42.9]	0.549 [0.330 - 0.755]	0.7254
PCT	> 0.8	70.59 [44.0 - 89.7]	83.33 [35.9 - 99.6]	92.3 [66.1 - 98.7]	50 [30.6 - 69.4]	0.745 [0.522 - 0.902]	0.0731
CRP	> 213	47.06 [23.0 - 72.2]	100 [54.1 - 100.0]	100 [0 - 0]	40 [29.9 - 51.1]	0.74 [0.517 - 0.898]	<u>0.0295</u>
Ferritin	≤ 610	64.71 [38.3 - 85.8]	100 [54.1 - 100.0]	100 [0 - 0]	50 [34.4 - 65.6]	0.73 [0.507 - 0.892]	<u>0.0278</u>
APACHE score	> 37	29.41 [38.3 - 85.8]	100 [54.1 - 100.0]	100 [0 - 0]	50 [34.4 - 65.6]	0.598 [0.375 - 0.795]	0.4665
Mortality	> 58.6	82.35 [56.6 - 96.2]	50 [11.8 - 88.2]	82.4 [67.1 - 91.5]	50 [21.4 - 78.6]	0.637 [0.413 - 0.825]	0.3408
SOFA score	≤ 16	76.47 [50.1 - 93.2]	0 [0.0 - 45.9]	68.4 [62.5 - 73.8]	0 [0 - 0]	0.505 [0.291 - 0.717]	0.9714

Pre-HAD - Before hemadsorption, PPV - Positive Predictive Value, NPV - Negative Predictive Value, AUC - Area under ROC curve, CI - Confidence Interval, IL - Interleukin, TNF-α - Tumor necrosis factor-alpha, CRP - C-reactive protein, PCT - Procalcitonin, APACHE - Acute Physiologic Assessment and Chronic Health Evaluation, SOFA - Sequential Organ Failure Assessment.

mune cell differentiation and activation. In particular, IL-6 has been located in the center of the COVID-19 pandemic [14]. Pedersen et al. argued that increased level of IL-6 (along with TNF-α and IL10) was associated with a significantly reduced possibility of recovery and with requiring ICU admission [15]. In addition, TNF-α plays a central role in the cytokine storm and has been an important marker for the progression COVID-19 disease, which are exacerbated in ICU patients compared to non-ICU patients [15,16].
In the light of these data, the extracorporeal treatments that are able to clear most of the cytokines that cause this cytokine storm from the body at the same time, instead of attacking eacg cytokines one by one, have been considered by the researchers. CytoSorb (CytoSorbents Corporation, Monmouth Junction, NJ, USA) is a newly designed, commercially available hemoadsorption device that reduces serum levels of both pro-inflammatory and anti-inflammatory cytokines through extracorporeal blood purification. Cytosorb has been used successfully in a variety of conditions including hyperinflammation, hemophagocytic lymphohistiocytosis (HLH) [17,18], virus-related HLH [19,20] intoxication, sepsis, and septic shock [21] and has been shown to reduce the excessive inflammatory mediator levels associated with lower vasopressor requirement [22,23]. In the present study, it was observed that the cytokine responses of IL-6, IL-10, TNF-α decreased significantly compared to pre-hemadsorption, whether accompanied with sepsis or not. IL-8 and ferritin levels were also decreased, without any significance.
PCT and CRP are biomarkers that are frequently examined in daily routine as the acute phase proteins. Although it has been shown in the literature that the hemadsorption is effective in reducing the level of PCT in septic shock [24,25], in our study, it was observed that it was effective in COVID-19 without a diagnosis of sepsis, but its level increased significantly in cases of COVID-19 accompanied by sepsis. The same study stated that PCT decreased in the first 12 hours, and that there may be an increase after the cessation of hemadsorption therapy [25]. PCT increase in the present study can be attributed to the fact that the pathophysiological role of PCT has not been fully elucidated yet in sepsis. Since CRP has a long half-life and follows the inflammatory process with a delay of around 48 hours, its application in monitoring disease progression or therapy efficacy in a short period of time may be limited (12 - 24 hours). The fact that there is conflicting information in the literature on this subject strengthens this hypothesis. According to the reports by Mitzner et al. [26] and Friesecke et al. [27], no change was observed in CRP levels following the hemadsorption procedure whereas a decrease in CRP level was found in the case report by David et al. [28]. In our study, although there was a decrease in CRP levels in both groups, it was more effective in COVID-19 without sepsis. It is beyond argument that advanced studies are needed on this subject.
Since the importance of using the organ failure scoring systems indicating the morbidity together with the prognostic scoring systems is appreciated in ICUs, we evaluated one of the prognostic scoring systems, i.e., APACHE II, and one of organ failure scores, i.e., SOFA score. In both groups, APACHE II and SOFA scores decreased following the cytokine hemadsorption. In a multicenter prospective study, Paul et al. also observed that these two scores regressed following the hemadsorption in the sepsis and septic shock [29,30]. In parallel with the findings, it was discovered in the current study that the death rate reduced significantly only in the COVID-19 group, but had no effect on the mortality rate in the other sepsis-affected group. In this case, however, the small number of patients in the single COVID-19 group should be taken into account.
A high level of IL-6 has been reported by Ruan et al. [13] and Zhou et al. [31] as a potential predictor of a fatal result of COVID-19 disease. Increased levels of IL-6 (together with TNF and IL10], according to Pedersen et al., greatly reduced the probability of healing [15]. In the instance of COVID-19, the powerful immune modulator IL-10 appears to be a key indicator of immunological failure. The rise in IL-10 levels in the second week after the onset of symptoms is thought to indicate a latent immunological response to suppress the cytokine storm [15]. In our research, we discovered that high IL-6 levels and low IL-10 levels in the start were linked to death.
High CRP and PCT levels, which are among the risk factors for the mortality, were also found to be associated with high mortality in our study. In a meta-analysis by Huang et al., it was stated that high CRP and PCT levels were associated with the poor outcomes of COVID-19 [32], while there are studies reported that high CRP and PCT levels were independent risk factors for the mortality [33-35]. Our findings are in line with the literature.
Limitations of the present study which should be considered are the retrospective nature of the single-center study and the small number of patients in the COVID-19 group without sepsis.

CONCLUSION

In this retrospective study, it was determined that the cytokine hemadsorption was effective both in terms of laboratory values and clinical results. In addition, it was also revealed that the cytokine hemadsorption, in COVID-19 patients, whether or not sepsis was present, IL-6, IL-10, TNF-, and CRP levels improved, while APACHE II and SOFA scores were reduced in both groups. The procedure was found to reduce the mortality rates by 50% in COVID-19 patients without sepsis but did not change the mortality rates in the presence of sepsis.

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Declaration of Interest:
None.

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