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RESEARCH ARTICLE

Investigating how Interleukin 6 Serum Level, Blood Group Type, and Underlying Diseases are Associated in Patients Admitted to the COVID-19 Intensive Care Unit: A Retrospective Study

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Abstract:

Aims:

This study intended to examine correlations between interleukin 6 serum levels, blood group, and underlying disease in patients admitted to the COVID-19 intensive care unit.

Background:

Understanding the relationship between a patient's blood group, underlying disease(s), and the body's cytokine reactions is essential for care provision to COVID-19 patients.

Materials and Methods:

The clinical records of 31 patients admitted to an intensive care unit were analyzed using a census method. Data were collected using a researcher-developed checklist and analyzed with SPSS-22 statistical software using one-way analysis of variance and Tukey-Kramer post hoc, independent t, and multiple regression. The level of significance was set to $p < 0.05$.

Results:

The mean serum level of interleukin 6 was significantly higher in patients with blood type B and those with two or more underlying diseases ($p < 0.05$). The mean serum interleukin 6 levels in patients differed significantly based on the history of COVID-19 vaccine injection and the length of hospitalization ($p < 0.05$). The mean serum interleukin 6 levels were associated with the length of COVID-19 intensive care unit stay and survival ($p < 0.05$).

Conclusion:

Effective and timely care provision for COVID-19 patients is a top priority, which can be achieved by understanding the correlation between the body's cytokine reactions in the fight against COVID-19, blood type, and underlying diseases.

Keywords: : Interleukin 6, Blood group, COVID-19, Underlying disease, Patient, Intensive care unit.

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1. INTRODUCTION

In late 2019, the Chinese city of Wuhan experienced an outbreak of a new coronavirus called SARS-CoV-2, which causes a severe respiratory disease known as COVID-19. The COVID-19 virus quickly spread from China to other countries, posing a wide range of health-related, economic, social, and political issues for the global population [1, 2]. On January 30, 2020, in response to the rise in cases and global spread of this virus, the World Health Organization declared the spread of the new coronavirus a public health emergency, a threat to not only China but also to the whole world [3].

Since this virus has spread worldwide, new and efficient treatments are required to help patients and lower the infection rate. Inhibiting the RdRp-dependent RNA polymerase enzyme is the primary strategy for treating COVID-19 because it prevents the virus from entering the host cells and performing transcription. Spike protein (S), which consists of subunits S1 and S2, is the most important structural protein of the virus. The S1 subunit is in charge of attaching the virus to the ACE2 (angiotensin-converting enzyme 2) receptors found on host cells, and the S2 subunit is responsible for fusing the virus membrane to the host cell membrane [4]. In the second or pulmonary phase of COVID-19, monoclonal antibodies can be effective, particularly in the third or hyper-inflammation phase. The cytokine storm primarily occurs at this point.

Cytokine storm is an immune response of an uncontrolled host to a virus characterized by a sharp increase in pro-inflammatory cytokines. Following an increase in pro-inflammatory cytokines, cytotoxic T-lymphocytes undergo apoptosis, which can reduce viral component clearance. The airways' alveolar and epithelial cells undergo apoptosis due to the released interferons, which damage pulmonary microvessels and destroy the alveolar epithelial barrier. Upon this injury, the microvascular bed of the lung will leak, and alveolar edema will develop, resulting in a disruption of gas exchange and hypoxemia [5, 6].

In COVID-19, the increase in interleukin 6 (IL-6) levels correlates directly with the severity of the disease. Increased concentration of IL-6 enhances the production and activity of T helper 17 (Th 17) cells, which are present in the COVID-19 disease. Patients with elevated IL-6 activity present with increased permeability and vascular leakage [7]. The results of the studies indicate that examining the level of interleukin-6 at the time of admission of patients with severe type of COVID-19 in the hospital helps to manage the treatment better, reduce complications and also reduce the mortality of these patients. [8, 9].

Historically, blood group antigens have only been employed for transfusion compatibility testing. Today, we understand that ABO and Rh blood groups are among the factors that can cause susceptibility or resistance to viral attacks such as influenza, Ebola, enteric viruses, and SARS-COV infections and affect the prognosis of infectious diseases [10 - 12].

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The ABO blood group is known for its distinct carbohydrate epitopes found on the surface of blood cells and respiratory and gastrointestinal epithelium [13]. This blood group has been investigated for its potential role in influencing susceptibility to various infectious diseases. Studies suggest that there may be associations between ABO blood type and the risk or severity of infections such as HIV [14], hepatitis B [14, 15], West Nile virus (WNV) [16], and *Helicobacter pylori* [17, 18]. Blood group antigens can affect infections directly by acting as receptors or co-receptors for microorganisms and toxins or indirectly by producing anti-blood group antibodies prompted by bacteria and enveloped viruses bearing blood group-like antigens [10].

However, the implications and underlying mechanisms of these associations remain unclear. Some hypothesized mechanisms include a protective effect of ABO antibodies [19], a link between ABO blood type and cardiovascular risk [20], and a potential role for ABO(H) antigens in facilitating viral entry into target cells.

Recent research has examined the connection between blood group types and COVID-19 [21]. Nonetheless, there are uncertainties and ambiguities in the results of these studies, and additional investigation and research is required to clarify this relationship. In some of these studies, a higher infection rate was observed among AB and A blood groups [22], whereas the infection rate was lower among people with blood type O [12]. Examining the blood group with the clinical course of the disease has not revealed any association between the ABO blood group and COVID-19 severity or mortality. Another study has indicated that people with the AB blood group are probably at a higher risk of severe illness and death, whereas people with blood type B are likely to be at a lower risk of death from COVID-19 [21].

According to what has been stated, it appears that the cytokine responses of the body in the fight against COVID-19 are related to the patients' blood group and underlying diseases. However, accurate and reliable information regarding these connections is not yet available. This study sought to determine the links between the serum IL-6 level, blood group, and the underlying disease in patients admitted to the intensive care unit (ICU) of COVID-19 at 22nd-Bahman Hospital of Khaf.

2. METHODS AND MATERIALS

This retrospective study intended to explore the associations between the serum IL-6 level, blood group, and underlying disease in patients admitted to the ICU of the 22nd-Bahman Hospital of Khaf affiliated with Mashhad University of Medical Sciences. The study was conducted in 2021 using the census method and information from the clinical records of 31 patients who met the inclusion criteria. In this study, according to other related studies [8, 9], the level of interleukin-6 was measured at the time of admission of patients in the intensive care unit of COVID-19. Some of the admission criteria for COVID-19 patients in the Corona Special Care Department at 22 Bahman Khaf Hospital were patients with severe respiratory distress, reduced level of consciousness, old age, underlying diseases, expert physician's opinion, *etc*.

After the research protocol was approved by the research

ethics committee at Mashhad University of Medical Sciences, the researcher was given a formal letter of introduction to present to the appropriate individuals at Khaf's 22nd-Bahman Hospital. A research colleague consulted the hospital's medical records department to review all eligible patients admitted to the COVID-19 ICU during the specified timeframe. Patients were eligible if they met the following criteria: a positive PCR for COVID-19, age 18 or older, hospitalization in the COVID-19 ICU, a request for IL-6 testing, and documented blood type. The absence of required data in the patient's inpatient file was the exclusion criterion. In this study, according to the inclusion criteria, we did not have missing data and the cases that were examined, all had the desired variables.

The data collection instrument was a researcher-created checklist that included patient demographic characteristics (age, gender, level of education, marital status, occupation, length of hospitalization, type of underlying disease, number of underlying diseases, history of smoking, history of COVID-19 vaccine injection, treatment outcome) as well as tables to record IL-6 test result and blood group type. The IL-6 test result was recorded on the checklist based on the initial tests requested upon the patient's admission to the COVID-19 ICU.

The SPSS-22 statistical program was used to analyze the data. Because of the normal distribution of the data, one-way analysis of variance and Tukey-Kramer post hoc, independent t, and multiple regression tests were employed. The significance level was established at $p<0.05$.

3. RESULTS

This research examined 31 patients hospitalized in the COVID-19 ICU of 22nd-Bahman Hospital. The patients were primarily male (51.6%), illiterate (61.3%), married (80.6%), aged 40-60 years (48.4%), and homemakers (51.6%). The majority (n=23; 74.2%) were hospitalized for three days or longer, and the vast majority (80.6%) had a history of diabetes. Four patients (12.9%) did not have a history of underlying disease, whereas fourteen (45.2%) had a history of two underlying diseases. The majority of COVID-19 patients admitted to the ICU had blood group B (38.7%). Moreover, 16 patients (61.3%) had a smoking history, while 16 patients (51.6%) had no history of COVID-19 vaccine injection. Lastly, 8 patients (25.8%) passed away, while 23 patients (74.2%) recovered and were released from the hospital (Table **1**).

Table 1. Demographic characteristics and clinical specifications of the examined patients.

Variable		Frequency	Percent
Gender	Female	15	48.4
	Male	16	51.6
Education	Illiterate	19	61.3
	Non-tertiary	12	38.7
Marital status	Single	6	19.4
	Married	25	80.6
Age (year)	< 40	12	38.7
	40-60	15	48.4
	> 60	4	12.9
Occupation	Homemaker	16	51.6
	Self-employed	4	12.9
	Retired	4	12.9
	Unemployed	7	22.6
Length of hospital stay	< 3 days	8	25.8
	3 days and more	23	74.2
Presence of underlying diseases	Diabetes	25	80.6
	Blood pressure	17	54.8
	Renal	4	12.9
	Cancer	1	3.2
	Respiratory disease	2	6.5
Number of underlying diseases	None	4	12.9
	1	9	29
	2	14	45.2
	3	4	12.9
Blood group	AB	5	16.1
	A	7	22.6
	B	12	38.7
	O	7	22.6
Smoking history	No	12	38.7
	Yes	19	61.3
History of COVID-19 vaccine injection	No	16	51.6
	Yes	15	48.4
Patient's treatment outcome	Recovery and discharge	23	74.2
	Death	8	25.8

Table 2. Comparison of the mean IL-6 serum levels according to blood group, number of underlying diseases, history of smoking, history of COVID-19 vaccine injection, patient treatment result, and length of hospitalization in the examined patients.

Variable		IL-6	ANOVA Test Result	
		Mean ± SD	For t value	P-value
Blood group	AB	50.10±80.13	*13.04	<0.001
	A	279.200±71.69		
	B	548.277±58.09		
	O	26.9±57.96		
Number of underlying diseases	None	38.32±25.87	*14.38	<0.001
	1	47.20±67.56		
	2	398.238±29.04		
	3	705.306±75.25		
Smoking history	No	284.314±92.21	**0.07	0.95
	Yes	292.295±74.87		
History of COVID-19 vaccine injection	No	399.336±38.46	**2.26	0.03
	Yes	172.201± 73.15		
Patient's treatment outcome	Recovery and discharge	172.205±61.88	**4.96	<0.001
	Death	626.269±38.29		
Length of hospital stay	< 3 days	60.92±38.23	**2.80	0.009
	≥ 3 days	369.304±48.18		

Note: *: one-way ANOVA **: independent t

IL-6 levels were significantly higher ($p < 0.05$) in patients with blood type B. The mean serum levels of IL-6 in patients with blood types AB, A, and O were not significantly different ($p > 0.05$). In patients with two or three underlying diseases, the mean IL-6 serum level was significantly higher than in patients with no history of underlying diseases or with a single underlying disease. Similarly, it was elevated in patients with three underlying diseases compared to those with two underlying diseases ($p < 0.05$) (Table **2**).

According to the results, the mean serum level of IL-6 in patients did not differ significantly by smoking history ($p=0.95$). However, there were significant differences in terms of the history of COVID-19 vaccine injection, the patient's treatment outcome, and length of hospitalization ($p < 0.05$) (Table **2**).

In this study, multiple linear regression was used to investigate the effect of demographic variables on interleukin-6 serum levels in patients. Quantitative variables such as the number of comorbidities and qualitative variables such as gender, education level, marital status, age, occupation, length of hospital stay, underlying diseases, blood group, history of smoking, history of vaccination, and patient treatment outcome were included in the equation. Duming Coding was used to input qualitative variables into the model. The test results showed no significant relationship ($p > 0.05$) between gender, education level, marital status, age, occupation, diabetes, cancer, respiratory diseases, and history of smoking with interleukin-6 serum levels in the studied patients. However, a significant relationship ($p < 0.05$) was found between length of hospital stay, hypertension and kidney diseases, number of comorbidities, blood group B, history of vaccination, patient treatment outcome, and interleukin-6 serum levels. Specifically, interleukin-6 serum levels were significantly higher in patients who had been hospitalized for more than 3 days compared to those who had been hospitalized for less than 3 days and in patients with hypertension and kidney diseases. Also, with an increase in the number of comorbidities, interleukin-6 serum levels increased significantly. Interleukin-6 serum levels were significantly higher in patients with blood group B compared to patients with blood group AB. Moreover, interleukin-6 serum levels were significantly lower in patients with a history of vaccination compared to those without a history of vaccination, and significantly higher in deceased patients compared to those who recovered and were discharged from the hospital ($p < 0.05$) (Table **3**).

4. DISCUSSION

One of the crucial aspects of clinical care for COVID-19 patients is familiarity with laboratory results and their association with blood type and underlying diseases. Awareness of this relationship can facilitate the use of timely and appropriate treatment methods for these patients, allowing for the provision of effective care in the shortest time and in the most appropriate clinical circumstances for the patients. The present study aimed to determine the correlation between IL-6 serum levels, blood group, and underlying disease in COVID-19 ICU patients.

The majority of hospitalized COVID-19 ICU patients were men, according to the findings of the present study. Other studies have similarly found that males are disproportionately represented among COVID-19 cases [23 - 26]. Several hypotheses can be advanced to explain why men are more susceptible to contracting COVID-19 than women. According to Li *et al*., the higher incidence of COVID-19 in men may be due to sex hormones and the protective role of the X chromosome, which is essential for innate immunity [24]. However, the majority of the causes of this disease in men in Iran can be attributed to cultural factors. The presence of more women at home to take care of household matters and the presence of more men in the work environment outside the home as a result of the Iranian culture and, as a result, more person-to-person contact between men may be one of the reasons for the increase in the number of men diagnosed with COVID-19 compared to women [25].

Table 3. Regression coefficients related to the effect of demographic variables on interleukin-6 serum levels in the studied patients.

Variable		Non-standard Coefficient		Standard Coefficient	T-value	Significance Level	Correlation Coefficient	Coefficient of Determination
		B-value	Standard Error	β-value				
Constant		676.34	566.78		1.19	0.26	0.92	0.54
Gender	Female	8.09	108.88	0.01	0.07	0.94		
Education	Non-tertiary	-45.97	115.53	-0.08	0.40	0.69		
Marital status	Married	152.78	134.79	0.21	1.13	0.27		
Age (year)	40-60	103.46	306.53	0.17	0.34	0.74		
	> 60	275.74	301.11	0.46	0.92	0.37		
Occupation	Self-employed	-107.38	168.61	-0.12	0.64	0.53		
	Retired	183.38	168.61	0.21	1.09	0.29		
	Unemployed	-60.77	136.68	-0.09	0.45	0.66		
Length of hospital stay	3 days and more	309.10	110.33	0.46	2.80	0.009		
Presence of underlying diseases	Diabetes	18.43	110.75	0.03	0.17	0.87		
	Blood pressure	375.14	85.05	0.64	4.41	< 0.001		
	Renal	285.98	107.87	0.33	2.65	0.01		
	Cancer	38.80	207.56	0.02	0.19	0.85		
	Respiratory disease	74.02	142.97	0.06	0.52	0.61		
Number of underlying diseases		248.60	42.04	0.74	5.91	< 0.001		
Blood group	A	228.91	117.50	0.33	1.95	0.06		
	B	497.78	106.87	0.83	4.66	< 0.001		
	O	-24.23	117.50	-0.04	0.21	0.84		
Smoking history		7.82	111.71	0.01	0.07	0.95		
History of COVID-19 vaccine injection		-226.64	100.43	-0.39	2.26	0.03		
Patient's treatment outcome		453.77	91.47	0.68	4.96	< 0.001		

Regarding age, the present study revealed that the highest frequency was associated with patients between 40 and 60, with the average age of the patients being approximately 50 years. Many physiological changes in the body tissue can be attributed to aging and the onset of old age, which can help explain this research finding. Changes during this period include muscle wasting, diminished endurance capacity, muscle weakness [27], heightened susceptibility to infectious agents, reduced immune system function [28], hormonal alterations, and a lower anabolic to catabolic hormones ratio [29]. The increased risk of infection in older adults is due to impaired cellular and humoral immune function, nutritional deficiencies, bacterial colonization in some mucosal surfaces, a decrease in the body's physiological defense reflexes such as cough and wound healing, and an increase in the prevalence of chronic diseases associated with infections [30]. Defects in the body's immune response to pathogenic agents, dysfunction of the body's organs, and, as a result, the highest mortality rates, hospital visits, admissions in the ICU, and complications caused by this disease are observed in older adults who suffer from multiple diseases. This finding is consistent with the findings of Guan *et al*. [31], Li *et al*. [24], and Shahriarirad *et al*. [25] in that the mean age of hospitalized patients in the COVID-19 ward was also approximately 50 years.

The present study found that 87.1% of COVID-19 patients admitted to the ICU had at least one underlying disease, with diabetes, cardiovascular disease, kidney disease, respiratory disease, and cancer being the most common. This research finding can be explained by noting that individuals with underlying diseases have a less effective immune response. Consequently, the risk of contracting COVID-19 is increased in these individuals. Moreover, in the event of infection, it can result in a fatal illness that requires hospitalization [32]. The presence of at least one underlying condition, such as diabetes, cardiovascular or respiratory disease, or hypertension, increases the likelihood of developing a severe form of this disease. Therefore, among the underlying diseases, diabetes is recognized as the greatest risk factor for contracting COVID-19, as it affects and weakens all organs, thereby increasing the risk of contracting the severe form of COVID-19 [33].

Consistent with this finding, research findings elsewhere indicate that the majority of COVID-19 cases are associated with underlying diseases. For instance, in the studies by Shahriarirad *et al*. [25] and Nikpouraghdam *et al*. [34], diabetes, hypertension, lung disease, and heart disease were the most prevalent underlying diseases in patients with COVID-19. In line with these findings, a 2020 cohort study conducted in the United States demonstrated that type 2 diabetes is associated with the risk of contracting COVID-19 [35]. Likewise, in England, a cohort study found that diabetes and high body mass indices are associated with an increased likelihood of COVID-19-related admission to the hospital [36]. Additionally, the Chinese Center for Disease Control and Prevention published in 2020 that individuals with cardiovascular disease and diabetes were the most susceptible

to this virus, followed by those with chronic respiratory disease, hypertension, and cancer [36, 37].

This study revealed that 61.3% of patients had a smoking history. This finding can be explained by pointing out that COVID-19 is an acute respiratory disease and that people who start smoking or continue smoking during the COVID-19 epidemic may become infected more easily and have worse clinical outcomes, necessitating treatment in specialized COVID-19 units. In fact, among people who have contracted the severe form of COVID-19 and required mechanical ventilation in ICUs, a greater proportion involves current smokers or those with a smoking history [38]. This finding is consistent with a number of studies that have identified smoking as a risk factor for the hospitalization of COVID-19 patients [39, 40].

The majority of patients hospitalized in the COVID-19 ICU had blood type B (38.7%), and the average IL-6 serum level was significantly higher in patients with blood type B than in the other examined patients ($p < 0.05$). The mean serum levels of IL-6 in patients with blood groups AB, A, and O did not differ significantly ($p > 0.05$).

Zietz *et al*., in their study titled "Associations between blood type and COVID-19 infection, intubation, and death", found that the prevalence of COVID-19 infection was higher among individuals with blood groups other than O. Compared to type O, the risk of intubation was lower for type A and higher for types AB and B. In contrast, the risk of death was higher for type AB and lower for types A and B. We estimate that Rh-negative blood type protects against all three outcomes. Our findings contribute to the growing body of evidence indicating that blood type may play a role in COVID-19 [41].

The findings of Cheng *et al*. also support this finding of the present study. They investigated the relationship between ABO blood groups and susceptibility to SARS. They examined 45 hospital employees with no protective gear who had direct contact with infected patients. Their study revealed that individuals with blood type O were less likely to contract SARS [42].

Contrary to the current study's findings, Göker *et al*.'s study revealed that blood group A (57%) was the most frequently detected blood group among COVID-19 patients, followed by blood group O (24.8%). Blood group types did not influence clinical outcomes. Those infected with COVID-19 were significantly more likely to have blood group A than controls (57% *vs*. 38%). In contrast, the frequency of blood group O was significantly lower among COVID-19 patients compared to the control group (24.8% *vs*. 37.2%). Based on the findings of their study, blood group A may play a role in increased susceptibility to COVID-19 infection, whereas blood group O may be somewhat protective [22].

Still, a review of a different study whose results are at odds with those of the current study found that those with blood type AB are more likely to suffer from severe disease and death from COVID-19, while those with blood type B are likely to have a lower risk of death from the virus [21]. This discrepancy between studies can be explained by the different clinical conditions of COVID-19 patients in the present study from those in the other studies that found contradictory results.

Serum IL-6 levels were found to be significantly higher in patients with two or more underlying diseases compared to those with no history of underlying diseases or with a single underlying disease. Patients with three underlying diseases had a higher prevalence than those with two. This research finding can be explained by noting that the immune system response is less effective in people with underlying diseases and that contracting COVID-19 in people with underlying diseases causes severe changes in blood tests, such as IL-6 and lung tissue damage.

Consistent with this finding of the present study, the results of other studies indicate that underlying diseases are one of the most remarkable risk factors for COVID-19 infection. Indeed, the results of studies on people with underlying diseases indicate that not only is the risk of contracting the disease higher in these individuals but so is the likelihood of dying from the disease. It is because the presence of underlying diseases can lead to severe disease symptoms, extensive changes in serum levels of liver enzymes, LDH, CRP, and IL-6, a lengthy treatment course, and a poor prognosis in COVID-19 patients [38, 43 - 45].

The present study found that the mean serum level of IL-6 in patients varied significantly based on the patient's history of COVID-19 vaccine injection, treatment outcome, and hospital stays. Patients with a history of COVID-19 vaccine injection had a markedly lower IL-6 serum level than those without such a history. Patients hospitalized for less than three days had significantly lower IL-6 serum levels than patients hospitalized for more than three days. In addition, the IL-6 level in patients who recovered and were discharged was significantly lower than that of patients who perished. This research finding can be explained by noting that in the acute phase of COVID-19, an increase in the serum level of IL-6 leads to extensive and widespread lung alveolar damage and the formation of a hyaline membrane in the lung alveoli [46]. According to what was stated in the explanation of this research finding, it can be concluded that the increase in the serum level of IL-6 is associated with the deterioration of the patients' condition and can ultimately result in lengthened hospitalization and a high mortality rate.

In addition, the injection of the COVID-19 vaccine induces the production of active immunity and fortifies the immune system, which can be mentioned when explaining this research finding. Therefore, if a patient who has been immunized develops COVID-19 disease, the patient will experience fewer complications. Indeed, the present study revealed that the serum level of IL-6 in vaccinated patients is significantly lower than in patients without a vaccination history. Vaccinated patients had a shorter hospital stay, and the rate of discharge and recovery was significantly higher among them than those without a vaccination history.

In line with this finding, Haghigi *et al*. found that 90.58 percent of ICU patients with elevated levels of IL-6, lactate dehydrogenase, creatinine, liver enzymes, hypoalbuminemia, hypercalcemia, hyperphosphatemia, hypermagnesemia, ESR, and CRP died from COVID-19 infection [47]. Likewise, Qual

et al.'s systematic review revealed that the majority of ICU-admitted COVID-19 patients with elevated levels of IL-6, liver enzymes, ESR, C-reactive protein, and lactate dehydrogenase required invasive and non-invasive mechanical ventilation, were hospitalized for a longer period, and ultimately died in ICUs [48].

CONCLUSION AND RECOMMENDATIONS

This study found a significant correlation between the IL-6 serum level, hospitalization period, underlying disease, number of underlying diseases, blood type B, history of vaccine injection, and patient's treatment result. Awareness of this important relationship is one of the crucial aspects of the clinical care of these patients. Familiarity with this clinical connection can aid in predicting and utilizing medical and nursing care for these patients in a timely and appropriate manner. IL-6 is one of the most vital markers of inflammation and immune system response and can play a significant role in assisting physicians in diagnosing patients with severe COVID-19 virus in the early stages of the disease. In addition, researchers should develop a scoring system incorporating IL-6, blood group type, and underlying diseases to aid clinicians in the early diagnosis of patients at risk of developing a severe form of COVID-19, thereby shortening the length of hospitalization, decreasing the mortality rate, and increasing the rate of discharge and recovery.

LIMITATIONS OF THE STUDY

This study had certain limitations, the most significant of which was a shortage of related studies that would have allowed for comparisons to be made between the current study and other parallel and non-parallel studies. The inability to calculate the body mass index was another drawback resulting from the absence of height and weight information in the patient records. A number of patients were excluded from the study due to incomplete documentation of specific data in their records. Additionally, this study was conducted solely on patients admitted to the ICU of 22nd Bahman Hospital of Khaf; thus, caution should be exercised when extrapolating the results. Besides, due to limited medical resources and the inability to provide new beds for all critically ill patients in the ICU, many critically ill patients were not admitted to this unit, and this group of patients could not be studied. In order to obtain more accurate results and a clearer description of the COVID-19 disease, it is recommended that more extensive studies be conducted over extended periods of time and on all critically ill patients requiring intensive care.

LIST OF ABBREVIATIONS

ACE2	=	Angiotensin-converting enzyme 2
Th 17	=	T helper 17
WNV	=	West Nile Virus

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article reports the results of a research project approved by Mashhad University of Medical Sciences with the code of ethics (IR.MUMS.REC.1401.179).

HUMAN AND ANIMAL RIGHTS

No animals were used for studies that are the basis of this research. All human procedures followed were per the guidelines of the Helsinki Declaration of 1975.

CONSENT FOR PUBLICATION

Informed consent was obtained from the participants.

STANDARDS OF REPORTING

STROBE guideline has been followed.

AVAILABILITY OF DATA AND MATERIALS

The data of current study are available from author, [R.R], on a reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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