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Effects of Uric Acid on Disease Severity and Mortality in Hospitalized Covid-19 Patients

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Abstract

Objective: High and low uric acid (UA) levels in the general population are associated with mortality. Information on the association of UA levels with clinical outcomes in COVID-19 patients is contradictory. We investigated the relationship between UA levels and clinical endpoints in COVID-19 patients.

Methods: Laboratory and clinical parameters, including UA at the admission of hospitalized COVID-19 patients, were recorded retrospectively. Binary logistic regression analysis determined risk factors for mortality and the intensive care unit (ICU) needs.

Results: This study included 708 patients (57.1% men), and the median age was 63 (18-98) years. Two hundred and three (28.7%) patients needed ICU, and 107 (15.7%) died. Uric acid levels were significantly higher in the deceased (6.5 vs. 4.9; p<0.001). Uric acid levels were similar in patients who needed ICU and those who did not (5 vs. 5.1; p=0.348). High UA (>median value 5.1 mg/dL) group have higher mortality rate (22.4% vs. 9.5%; p<0.001). In multivariate analyses, a high UA level was a risk factor for mortality [OR 1.93 (1.08 – 3.44); p=0.026]. In addition, age [OR 1.03 (1.01 – 1.05); p=0.004], albumin [OR 0.30 (0.17 - 0.52); P<0.001], neutrophil-to-lymphocyte ratio [OR 1.04 (1.01 – 1.06); p=0.003] and procalcitonin [OR 1.06 (1.0 – 1.11); p=0.048] was associated with mortality. A high UA level was not a risk factor for ICU need (p=0.780).

Conclusion: High serum UA level affects mortality in COVID-19 patients. Risk assessment for the prognosis of patients can be made according to the UA levels at admission.

Key words: COVID-19, intensive care, mortality, uric acid

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INTRODUCTION

Coronavirus disease (COVID-19) was reported firstly in December 2019 and announced as a pandemic later. The first case of COVID-19 in Turkey was reported on March 10, 2020, and as of May 12, 2022, the total number of cases has exceeded 14 million (1). Patients with COVID-19 may be asymptomatic or have a serious life-threatening illness. Initially, mild cases may become severely symptomatic afterward. The need for ICU and mortality rates increase in patients with a severe course (2,3). For this reason, it is essential to estimate the risk levels and prognosis during the initial evaluation of patients or at admission. Various laboratory parameters were used to predict the prognosis in patients with COVID-19 (4,5).

Although uric acid (UA) is the end product of purine metabolism, increased UA levels have various pathophysiological effects, such as oxidative stress and inflammation (6). There is a relationship between increased UA levels and mortality, especially cardiovascular, in the general population (7). In some studies, low UA levels cause an increase in cardiovascular mortality, suggesting the existence of a "U"-shaped relationship (8,9). Different results are noteworthy in studies on the association of UA levels with mortality in COVID-19 patients. Studies report an increase in mortality with only hyperuricemia (10) or only hypouricemia (11), or both (12).

This study aimed to determine whether serum UA levels at admission in hospitalized patients were associated with clinical endpoints such as ICU need and mortality.

METHODS

This study was approved by the local ethics committee and was conducted to the Declaration of Helsinki. Among the adult COVID-19 patients aged 18 years and older, hospitalized in Ondokuz Mayıs University Hospital between January 1, 2021, and March 1, 2022, and whose diagnosis was confirmed by PCR, whose UA level at admission were included in the study. Patients under 18 years of age or those whose UA level was not measured at admission were excluded from the study. All biochemical parameters, including UA, at admission [blood urea nitrogen (BUN), creatinine, sodium, potassium, alanine aminotransferase (ALT), glucose, albumin, D-dimer], inflammation markers [white blood cell (WBC) and lymphocyte cell count, C-reactive protein (CRP), procalcitonin, neutrophil-lymphocyte ratio (NLR)] and hematological parameters [Hemoglobin, platelet count, mean platelet volume (MPV), red cell distribution width (RDW)] were recorded to be used in the analysis. Comorbid diseases and demographic characteristics were obtained from the medical records. The primary endpoint was the need for ICU or in-hospital death after hospitalization.

Statistical Analysis

Data were analyzed with IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA). Analysis results were presented as mean ± standard deviation and median (minimum-maximum) for continuous variables and frequency and percentage for categorical variables. Conformity to normal distribution was evaluated with the Kolmogorov-Smirnov test. The Mann-Whitney U test compared the data not normally distributed according to the paired groups. The chi-square test was used to determine a relationship between two categorical variables. Spearmans' correlation analysis was performed in the correlation analysis between serum UA levels and the inflammation markers. Binary

logistic regression analysis examined the risk factors affecting mortality and admission to ICU. ROC analysis determined the cut-off value of UA according to mortality. The significance level was taken as $p<0.05$.

RESULTS

Seven hundred and eight people, 404 (57.1%) men, were included, and the median age was 63 (18-98) years. Of the patients, 41.2% had hypertension, 22.5% had diabetes mellitus, and 19.2% had chronic kidney disease. Pneumonia was detected in 85.7 of the patients at admission. Median UA level was 5.1 mg/dl. The clinical features and the laboratory parameters of the patients are shown in Table 1.

Table 1. Patients' demographic characteristics, comorbid diseases, and laboratory parameters at admission

		n (%)	
Gender (Female)		304 (42,9)	
Presence of pneumonia		607 (85,7)	
Chronic kidney disease		136 (19,2)	
Hypertension		292 (41,2)	
Diabetes mellitus		159 (22,5)	
Coronary artery disease		157 (22,2)	
Heart failure		37 (5,2)	
Pulmonary disease		50 (7,1)	
	n	**Mean ± SD**	**Median (min - max)**
Age (year)	708	60,88 ± 15,87	63 (18 - 98)
Uric acid (mg/dL)	708	5,57 ± 2,51	5,1 (0,1 - 20)
Albumin (g/dL)	637	3,53 ± 0,61	3,56 (1,5 - 5,1)
CRP (mg/dL)	704	58,88 ± 68,91	26,64 (0,02 - 342)
D-dimer (ng/mL)	684	1959,04 ± 6982,16	656,5 (50 - 100000)
Procalcitonin (ng/mL)	660	1,1 ± 6,05	0,1 (0,02 - 100)
BUN (mg/dL)	704	23,69 ± 21,13	17,45 (3,2 - 189,2)
Creatinine (mg/dL)	708	1,29 ± 1,24	0,97 (0,35 - 10,98)
Glucose (mg/dL)	707	151,7 ± 79,78	125 (40 - 608)
Sodium (mEq/L)	708	137,07 ± 4,54	138 (111 - 145)
Potassium (mEq/L)	708	4,33 ± 0,58	4,3 (2,69 - 6,65)
ALT (U/L)	704	33,5 ± 67,18	21 (2,7 - 1508)
WBC ($x10^3/\mu L$)	708	7,83 ± 7	6,58 (0,18 - 116,95)
Hemoglobin (gr/dL)	708	12,41 ± 2,16	12,6 (0 - 18,7)
Platelet ($x10^3/\mu L$)	708	218,08 ± 93,12	203,5 (2 - 659)
Lymphocyte count ($x10^3/\mu L$)	708	1,42 ± 3,86	1,13 (0,06 - 101,3)
NLR	701	7,79 ± 10,1	4,14 (0,07 - 110,25)
MPV (fL)	692	10,28 ± 0,97	10,2 (8 - 13,9)

SD: Standart Deviation, CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; ALT: Alanine aminotransferase; WBC: White blood cell; NLR: Neutrophil-Lymphocyte Ratio, MPV: Mean Platelet Volume

Comparison of patient groups in terms of intensive care unit need and mortality

The need for ICU developed in 203 (28.7%) patients, and UA levels were similar in patients who needed ICU and did not need it (5 vs. 5.1 mg/dL; p=0.348). Among the comorbid diseases, only heart failure was more common in patients hospitalized in the ICU (8.9% vs. 3.8%; p=0.006). The comparison of admission laboratory parameters and comorbid diseases according to the need for intensive care is shown in Table 2.

Table 2. Comparison of patients according to the need for intensive care unit and mortality

	Intensive care unit need			Mortality		
	Yes	No	p	Yes	No	p
Uric acid (mg/dL)	5,00 (0,1 - 16,60)	5,10 (0,90 - 20,00)	0,348	6,50 (1,00 - 20,00)	4,90 (0,1 - 17,70)	**<0,001**
Albumin (gr/dL)	3,66 (1,61 - 5,10)	3,20 (1,50 - 4,90)	**<0,001**	3,11 (1,50 - 4,32)	3,63 (1,61 - 5,10)	**<0,001**
NLR	**7,69 (0,07 - 66,64)**	**3,47 (0,10 - 110,25)**	**<0,001**	9,73 (0,30 - 66,64)	3,64 (0,07 - 110,25)	**<0,001**
CRP (mg/dL)	25,00 (0,02 - 342,00)	33,20 (0,10 - 318,00)	0,098	61,90 (0,91 - 318,00)	24,50 (0,02 - 342,00)	**<0,001**
D-dimer (ng/mL)	540 (50 - 100000)	1064 (100 - 100000)	**<0,001**	1070 (120 - 30145)	588 (50 - 100000)	**<0,001**
Procalcitonin (ng/mL)	0,09 (0,02 - 45,45)	0,23 (0,03 - 100,00)	**<0,001**	0,43 (0,04 - 100,00)	0,09 (0,02 - 45,45)	**<0,001**
BUN (mg/dL)	17,20 (3,20 - 189,20)	18,20 (3,50 - 152,90)	0,174	21,50 (6,70 - 152,90)	16,90 (3,20 - 189,20)	**<0,001**
Creatinine (mg/dL)	0,96 (0,36 - 10,36)	0,98 (0,35 - 10,98)	0,552	1,16 (0,35 - 7,64)	0,94 (0,36 - 10,98)	**<0,001**
Glucose (mg/dL)	124,50 (40 - 497)	131 (66 - 608)	0,354	121 (43 - 535)	125,50 (40 - 608)	0,455
Sodyum (mEq/L)	138 (111 - 145)	137 (123 - 145)	**0,001**	137 (116 - 145)	138 (111 - 145)	**0,010**
Potasyum (mEq/L)	4,30 (2,80 - 6,65)	4,30 (2,69 - 6,37)	0,926	4,38 (2,69 - 6,37)	4,30 (2,80 - 6,65)	0,094
ALT (U/L)	20,80 (2,70 - 282,20)	21 (3 - 1508)	0,779	18,60 (3 - 1508)	21,00 (2,70 - 594,00)	0,131
WBC (x10^3/µL)	6,26 (0,18 - 113,02)	7,33 (1,36 - 116,95)	**<0,001**	7,38 (1,36 - 29,79)	6,37 (0,18 - 116,95)	**0,017**
Hemoglobin (gr/dL)	13,00 (0,00 - 18,00)	11,80 (6,00 - 18,70)	**<0,001**	11,60 (6,00 - 15,90)	12,90 (0,00 - 18,70)	**<0,001**
Platelet (x10^3/µL)	207,00 (2,00 - 659,00)	185 (9 - 534)	**0,003**	184 (30 - 534)	206 (2 - 659)	0,054
MPV (fL)	10,10 (8,00 - 13,00)	10,30 (8,40 - 13,90)	**0,004**	10,30 (8,60 - 13,90)	10,20 (8,00 - 13,00)	**0,005**
Diabetes mellitus (%)	22,4	22,7	0,935	26,1	21,8	0,313
Chronic kidney disease (%)	19,4	18,7	0,834	16,2	19,8	0,383
Hypertension (%)	39,2	46,3	0,083	47,7	40	0,130
Coronary artery disease (%)	21,4	24,1	0,425	25,2	21,6	0,400
Heart failure (%)	3,8	8,9	**0,006**	7,2	4,9	0,307

NLR: Neutrophil-Lymphocyte Ratio, CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; ALT: Alanine aminotransferase; WBC: White blood cell; MPV: Mean Platelet Volume

One hundred and eleven (15.7%) patients died. The median UA levels of those who died were significantly higher than those who survived (6.5 vs. 4.9 mg/dL; p<0.001). There was no difference between the groups in terms of comorbid diseases. In Table 2, patients who died and those who survived were compared with admission laboratory parameters and comorbid conditions.

When all patients were divided into groups according to the median value (5.1 mg/dl below and above) and laboratory reference values (normal range 3-6.5 mg/dl), no significant difference was observed between the groups in terms of ICU need. However, significantly higher mortality rates were observed in the groups with higher UA levels than the median and reference values (p<0.001). Table 3 shows the need for ICU and mortality rates by UA groups.

Tablo 3. Distribution of endpoints by different serum uric acid level groups

	According to median						
	Low UA (≤5,1 mg/dL)	High UA (5,1>mg/dL)	p	Low UA (≤3 mg/dL)	Normal (3,1-6,5 mg/dL)	High UA (>6,5 mg/dL)	p
Intensive care need	27,7	29,7	0,559	25,7[a]	34,7[a]	33[a]	0,085
Death	9,5	22,4	**<0,001**	9,8[a]	18,1[a, b]	27,9[b]	**<0,001**

[a,b,c] The chi-square test was used and the groups with the same letter were statistically similar . UA: Uric acid

- **Univariate and multivariate binary logistic regression analyses for intensive care unit need and mortality**

The results of logistic regression analyses for ICU needs are shown in Table 4. In univariate and multivariate analyses, high UA levels compared to the median value were a risk factor for the need for ICU (p=0.780). When analyses were performed according to laboratory reference values, UA levels were not associated with the need for ICU (low; p=0.855 and high; p=0.917). Analyses showed that pneumonia was the most important factor for ICU needs [OR 27.92 (5.43 – 143.48); p<0.001]. Albumin [OR 0.42 (0.28 - 0.65); p<0.001], NLR [OR 1.04 (1.02 - 1.06); p=0.001], D-dimer [OR 1 (1 - 1); p=0.039], hemoglobin [OR 0.90 (0.81 – 1.0); p=0.041] and platelet count [OR 0.997 (0.995 – 1.0); p=0.027] were other factors associated with the ICU need.

Table 4. Binary logistic regression analysis results for intensive care need in COVID-19 patients

Factors	**Univariate**			**Multivariate**		
	OR (%95 CI)	p	AR	OR (%95 CI)	p	AR
Gender (Male)	1,063 (0,764 - 1,478)	0,716	71,3	1,022 (0,652 - 1,601)	0,924	75,4
Pneumonia (Yes)	24,506 (5,983 - 100,376)	**<0,001**	71,3	27,915 (5,431 – 143,476)	**<0,001**	
Age	1,018 (1,007 - 1,029)	**0,001**	71,3	0,999 (0,984 - 1,014)	0,861	
Albumin	0,27 (0,195 - 0,372)	**<0,001**	73,0	0,422 (0,276 - 0,645)	**<0,001**	
NLR	1,065 (1,044 - 1,086)	**<0,001**	72,8	1,037 (1,016 - 1,058)	**0,001**	
CRP	1,004 (1,002 - 1,006)	**0,001**	71,3	0,998 (0,995 - 1,001)	0,177	
D-dimer	1 (1 - 1)	0,051	71,5	1 (1 - 1)	**0,039**	
Procalcitonin	1,061 (1,015 - 1,109)	**0,008**	71,1	1,014 (0,979 - 1,051)	0,433	
BUN	1,003 (0,996 - 1,01)	0,435	71,3	0,993 (0,98 - 1,007)	0,344	
Creatinine	1,083 (0,958 - 1,224)	0,204	71,3	1,141 (0,924 - 1,409)	0,220	
Glucose	1,001 (0,999 - 1,003)	0,176	71,3	1,002 (0,999 - 1,004)	0,175	
Sodium	0,948 (0,916 - 0,982)	**0,003**	70,6	0,984 (0,94 - 1,03)	0,495	
Potassium	1,02 (0,771 - 1,349)	0,889	71,3	0,831 (0,582 - 1,186)	0,308	
ALT	1,002 (0,999 - 1,004)	0,208	71,4	1,001 (0,997 - 1,005)	0,568	
Hemoglobin	1,031 (1,001 - 1,063)	**0,043**	71,3	0,896 (0,806 - 0,995)	**0,041**	
Platelet	0,812 (0,751 - 0,878)	**<0,001**	71,6	0,997 (0,995 - 1)	**0,027**	
MPV	0,998 (0,996 - 1)	**0,018**	71,3	1,094 (0,88 - 1,362)	0,418	
Uric acid (High)	1,102 (0,796 – 1,527)	**0,559**	71,3	0,94 (0,608 - 1,452)	0,780	

NLR: Neutrophil-Lymphocyte Ratio, CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; ALT: Alanine Transaminase; MPV: Mean Platelet Volume, AR: Accuracy rate

Table 5 shows the results of univariate and multivariate logistic regression analysis for mortality. Univariate and multivariate analyses showed that UA level higher than the median value was the risk factor for mortality [OR 2.74 (1.78 – 4.22); p<0.001 and OR 1.93 (1.08 – 3.44); p=0.026]. In addition, older age [OR 1.03 (1.01 – 1.05); p=0.004], lower serum albumin levels [OR 0.30 (0.17 - 0.52); P<0.001], higher neutrophil-to-lymphocyte ratio [OR 1.04 (1.01 – 1.06); p=0.003] and higher procalcitonin levels [OR 1.06 (1.0 – 1.11); p=0.048] were associated with mortality.

Similarly, when multivariate analyses were performed according to laboratory reference values, high UA levels were found to be a risk factor for mortality [OR 1.90 (1.01 - 3.58)); p=0.046], while low UA levels are not to be a risk for mortality [OR 1.80 (0.76 – 4.24); p=0.182].

Table 5. Binary logistic regression analysis results for mortality in COVID-19 patients

Factors	Univariate		Multivariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Gender (Male)	1,344 (0,885 - 2,042)	0,165	1,244 (0,692 - 2,238)	0,465
Pneumonia (Yes)	5,189 (1,868 - 14,414)	**0,002**	0,213 (0,043 - 1,067)	0,060
Age	1,046 (1,03 - 1,063)	**<0,001**	1,031 (1,009 - 1,053)	**0,004**
Albumin	0,193 (0,129 - 0,288)	**<0,001**	0,297 (0,17 - 0,518)	**<0,001**
NLR	1,06 (1,04 - 1,08)	**<0,001**	1,035 (1,012 - 1,058)	**0,003**
CRP	1,006 (1,004 - 1,009)	**<0,001**	1,001 (0,997 - 1,005)	0,596
D-dimer	1 (1 - 1)	0,349	1 (1 - 1)	0,537
Procalcitonin	1,109 (1,044 - 1,178)	**0,001**	1,055 (1,001 - 1,113)	**0,048**
BUN	1,013 (1,005 - 1,021)	**0,001**	1,004 (0,988 - 1,021)	0,608
Creatinine	1,22 (1,072 - 1,388)	**0,003**	1,022 (0,791 - 1,322)	0,867
Glucose	1 (0,997 - 1,003)	0,990	0,999 (0,995 - 1,002)	0,524
Sodium	0,938 (0,901 - 0,977)	**0,002**	0,984 (0,928 - 1,042)	0,577
Potassium	1,409 (1,001 - 1,983)	0,050	1,015 (0,648 - 1,59)	0,949
ALT	1,001 (0,999 - 1,004)	0,291	1,001 (0,998 - 1,003)	0,629
Hemoglobin	0,8 (0,729 - 0,878)	**<0,001**	0,931 (0,821 - 1,057)	0,271
Platelet	0,999 (0,996 - 1,001)	0,253	1 (0,997 - 1,003)	0,980
MPV	1,463 (1,192 - 1,796)	**<0,001**	1,306 (0,987 - 1,728)	0,062
Uric acid (High)	2,739 (1,779 – 4,218)	**<0,001**	1,929 (1,082 - 3,439)	**0,026**

NLR: Neutrophil-Lymphocyte Ratio; CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; ALT: Alanine Aminotransferase; MPV: Mean Platelet Volume

ROC analysis for uric acid levels in predicting mortality and the association between uric acid levels and inflammation markers

When the serum UA cut-off value was 5.9 mg/dL in estimating the mortality, the area under the curve (AUC) was obtained as 0.654 (p<0.001). The sensitivity and specificity of the cut-off value were 59.46% and 67.34% (Figure). The correlation analyses, serum UA levels were correlated with procalcitonin (r:0.310; p<0.001), NLR (r:0.102; p=0.007) and MPV (r:0.104; p=0.006), while there was no correlation between CRP and UA levels (p=0.704) (Table 6).

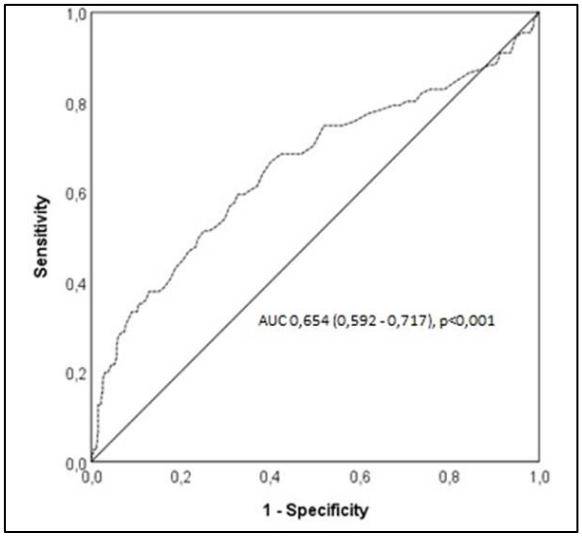

Figure. ROC curves showed the predictive value of uric acid level in predicting mortality.

Table 6. Correlation analysis of uric acid levels and inflammation parameters

	Uric acid levels	
	r	p
NLR	0,102	**0,007**
CRP	0,034	0,366
Procalcitonin	0,31	**<0,001**
MPV	0,104	**0,006**
Albumin	-0,059	0,136
D-dimer	0,023	0,549

NLR: Neutrophil-Lymphocyte Ratio, CRP: C-Reactive Protein; MPV: Mean Platelet Volume

DISCUSSION

We showed that UA levels at admission were higher in hospitalized COVID-19 patients, those who needed ICU, and those who died. In addition, high UA levels at admission were associated with in-hospital mortality.

Although high UA levels are often thought to indicate tissue damage and cell destruction or impaired excretion, it causes various pathologies by itself. For example, hyperuricemia causes cardiovascular diseases by different mechanisms (6). It is also associated with increased CV death (13,14). There are similar relationships between serum UA levels and infectious diseases. The study by Liu et al. in 954 ICU patients with sepsis showed that high UA level was associated with mortality (HR: 1.65) and AKI (HR:1.77) (15). In a study conducted on ICU patients with sepsis, UA levels were higher in patients with acute respiratory distress syndrome (ARDS) and who died. The same study showed that the last UA level>4.5 mg/dL increased mortality (2.638 times) (16). This study found high UA levels (according to the median value) at admission increased mortality by 1.93 times. Similarly, Ting Zeng et al. reported that the rate of hyperuricemia (>400 μmol/L) was 23.6% in patients who died due to COVID-19 and high UA levels increased mortality by 3.17 times (17). In a study conducted in China that included 1854 patients with COVID-19, high serum UA values (≥ 423 μmol/) increased the risk of mortality (OR: 3.94) (12). Another large study including 854 patients showed that high UA levels increase the risk of acute kidney injury (OR: 2.8), major adverse kidney events (OR: 2.5), and mortality (OR: 1.7). Notably, the UA level caused a gradual increase in all three endpoints from 4.5 mg/dl (10).

Depending on the severity of the disease, COVID-19 patients may require admission to the ICU. There was no correlation between UA levels and ICU needs in this study. However, some studies showed that high UA levels affected the disease severity in COVID-19 patients. In a study, high serum UA levels were associated with disease severity in COVID-19 patients, but different definitions were used for disease severity, except for the need for ICU (18). Bo Chen et al. showed that high serum UA values increased the risk of composite outcome (OR: 2.60) and mechanical ventilation (OR: 3.01). However, in the same study, similar to our results, the increase in UA levels did not cause an increase in the risk of ICU need (12).

It is still unclear how UA elevation affects clinical outcomes in COVID-19 patients. However, some speculative mechanisms can be suggested. The binding of the SARS-CoV-2 virus to the respiratory system is via the angiotensin-converting enzyme2 (ACE2) receptor. S protein on the virus binds to the ACE2 protein in type 2 alveolar cells, and the virus is replicated in the host cells. Infected host cells initiate inflammatory cascades and cause the release of chemokines and cytokines. (19). The entry of the S protein-ACE2 complex into the cell decreases ACE2 functions and, therefore, increases tissue angiotensin II (Ang-II) concentration (20). High levels of Ang-II can promote the inflammatory processes, the release of inflammatory cytokines, and eventually lead to ARDS. Ang-II increases can facilitate the virus's entry into the cell and increase tissue damage due to inflammation through pro-inflammatory cytokines. Liu et al. showed that the Ang-II levels were markedly increased, and high Ang-II levels were associated with viral load and lung damage in COVID-19 patients (21). High UA levels may cause an increase in mortality in these patients by activating the renin-angiotensin-aldosterone system (RAAS). Uric acid can increase RAAS activation. Min-A Yu et al. showed that UA stimulated mRNA expression of RAAS components and receptors in human

vascular endothelial cells (22). Increased inflammation is responsible for tissue damage in COVID-19 patients. Uric acid increases inflammation by activation of the NLRP3 inflammasome (23). Some studies have shown a correlation between UA levels and inflammation markers in COVID-19 patients. Even a decrease in inflammation markers has been noted in patients receiving UA-lowering therapy (17, 18). In this study, inflammation parameters were high both in patients who needed ICU and in patients who died, and a correlation was found between UA levels and inflammation parameters. Increased oxidative stress due to high UA may be responsible for the negative effect on disease prognosis in COVID-19 patients. Uric acid increases oxidative stress (24). A study showed that high UA levels were correlated with increased oxidative stress and inversely correlated with decreased antioxidant capacity in COVID-19 patients (18).

In some studies, it has been found that low UA levels were associated with mortality and disease severity in COVID-19 patients (11,25). Uric acid has antioxidant properties (26), and these antioxidant effects are evident at low UA levels (6). Decreased antioxidant capacity due to low UA levels could increase mortality in these patients. Bo Chen et al. also showed that high and low admission UA levels were associated with clinical endpoints (U-shaped) (12). We found no association between low UA levels at admission and mortality. However, previous studies have shown that hypouricemia developing during hospitalization affects mortality (11,27,28). However, in most of our patients, UA levels were not rechecked during hospitalization, so we could not comment on whether there was a relationship between low UA levels and clinical endpoints.

Our study has some limitations. First of all, the most important limitations of our study are that it is retrospective, and only the patients whose UA levels were measured were included in the study. In addition, we didn't know the course of UA was not in most of the patients during the hospitalization. Another significant limitation of our study is that drugs (such as diuretics and allopurinol) that may affect uric acid levels are not recorded. On the other hand, it has many patients and presents real-life data of patients with various comorbid diseases.

CONCLUSIONS

High serum UA levels at admission were associated with mortality in COVID-19 patients and could be considered in the risk assessment of patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of Ondokuz Mayıs University. (Ethical committee date 27.03.2022 and no: 2022/163)

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