Original Article / Özgün Makale

MEDICINE PALLIATIVE CARE

DOI: 10.47582/jompac.1166061

J Med Palliat Care 2022; 3(3): 234-240

The role of hyperuricemia in acute renal failure

Akut böbrek yetmezliğinde hiperüriseminin rolü

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Cite this article as/Bu makaleye atıf için: Uysal E, Seğmen F, Erdem D. The role of hyperuricemia in acute renal failure. J Med Palliat Care 2022; 3(3): 234-240.

ABSTRACT

Objective: Acute renal failure is one of the most important factors affecting mortality in intensive care patients. The aim of this study was to elucidate whether there was a relationship between uric acid levels and/or acute kidney imjury/failıre (AKI).

Material and Method: A total of 1000 individuals who were admitted to intensive care unit (ICU) of our institution without any prior renal disease and glomerular filtration rate (GFR) of 80-120 ml/minutes, have been enrolled in this retrospective analysis. The development of AKI in the ICU were evaluated via RIFLE criteria. In patients who developed AKI, it was checked whether there was an indication for renal replacement therapy (RRT). All patients in the ICU including the unconscious indivuduals and COVID-19 patients have been included in the analysis.

Results: Acute renal failure (ARF) was observed in 27.1% (n=271) of the individuals. Hemodialysis had been administered in 44.3% (n=120) of patients with ARF. The reasons for hemodialysis were ischemia in 36%, sepsis and multifactorial reasons in 32% of the subjects. A statistically significant difference was found compared to the initial measurements in urea, creatinine, uric acid and sodium (Na) increased compared to baseline ($p<0.001$) as all parameters except potassium (K). All values from baseline increased at the time of diagnosis, while a decrease was observed in the GFR value ($p<0.001$). There was a statistically significant difference between the uric acid measurements of the patients undergoing hemodialysis ($p<0.05$) and uric acid measurements were increased compared to baseline.

Conclusion: Regarding the results of this study one can conclude that serum uric acid level has been shown to be an independent risk factor for decreased renal function. Additionally, elevated uric acid levels lead to increased hemodialysis, morbidity and mortality in the ICU.

Keywords: Acute renal failure, hemodialysis, hyperuricemia, uric acid, intensive care unit

ÖZ

Amaç: Akut böbrek yetmezliği (ABY) yoğun bakım hastalarında mortaliteyi etkileyen en önemli faktörlerden biridir. Bu çalışmanın amacı, ürik asit düzeyleri ile akut böbrek hasarı (AKI) / ABY arasında bir ilişki olup olmadığını aydınlatmaktır.

Gereç ve Yöntem: Bu retrospektif çalışmamıza, önceden böbrek hastalığı olmayan ve glomerüler filtrasyon hızı (GFR) 80-120 ml/dakika olan hastanemiz yoğun bakım ünitesine kabul edilen toplam 1000 hasta dahil edildi. Yoğun bakım ünitesinde AKI gelişimi RIFLE kriterleri ile değerlendirildi. AKI gelişen hastalarda renal replasman tedavisi endikasyonu olup olmadığına bakıldı. Bilinci kapalı kişiler ve COVID-19 hastaları dahil yoğun bakım ünitesindeki tüm hastalar analize dahil edilmiştir.

Bulgular: Bireylerin %27,1'inde (n=271) AKI görüldü. AKI'lı hastaların %44.3'üne (n=120) hemodiyaliz uygulanmıştı. Hemodiyaliz nedenleri olguların %36'sında iskemi, %32'sinde sepsis ve multifaktöriyel nedenler idi. Potasyum dışındaki tüm parametrelerde (üre, kreatinin, ürik asit ve sodyumda) başlangıca göre artmıştı ($p<0,001$) ve başlangıç ölçümlerine göre istatistiksel olarak anlamlı bir fark bulundu. Tanı anında başlangıca göre tüm değerler artarken, GFR değerinde azalma gözlendi ($p<0,001$). Hemodiyalize giren hastaların ürik asit ölçümleri arasında istatistiksel olarak anlamlı fark vardı ($p<0,05$) ve ürik asit ölçümleri başlangıca göre arttı.

Sonuç: Bu çalışmanın sonuçlarına göre serum ürik asit düzeyinin azalmış böbrek fonksiyonu için bağımsız bir risk faktörü olduğu gösterilebilir. Ek olarak, yüksek ürik asit seviyeleri yoğun bakım ünitesinde hemodiyaliz, morbidite ve mortalitenin artmasına neden olur.

Anahtar Kelimeler: Hemodiyaliz, akut böbrek yetmezliği, hiperürisemi, ürik asit, yoğun bakım ünitesi

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Received/Geliş: 25.08.2022 **Accepted/Kabul:** 12.09.2022

INTRODUCTION

The mortality rate of patients with end-stage renal disease ARF requiring RRT exceeds 50% in intensive care unit patients (1). In study of 1800 intensive care unit patients, ARF has been detected in 57% of the individuals and 39% of these subjects developed stage 2-3 ARF according to Kidney Disease Improving Global Outcomes (KDIGO) criteria and 13.5% of them required RRT (1). Regarding the severity of the situation several studies on treatment alternatives and predictive bio-markers are still ongoing due to high morbidity and mortality rates in the ICU. Molecules such as calprotectin, cystatin-C, netrin-1, kidney injury molecule-1 have been studied for this purpose, but it has been stated that more studies are needed (2). In addition, the fact that, cost of these molecules are very high and they cannot be investigated in every center is another obstacle.

Uric acid is the end product of the catabolism of the purine nucleotides, guanylic acid, inosinic acid, adenylic acid and adenosine triphosphate in the human body. Endogenous source is from liver, muscle, small intestine, kidney and vascular endothelium tissues (3, 4). Exogenous source, on the other hand, is mostly animal foods, but it is also formed from fruit fructose (3). It consists of a heterocyclic structure with a molecular weight of 168 daltons and is a weak acid with a pKa of 5.8 at physiological pH. Hyperuricemia is identified as plasma uric acid concentrations are higher than 7.0 mg/dL (4). When uric acid level it is higher than 6.8 mg/dL it crystallizes and collapses. Although high uric acid has become more commonly associated with gout, its importance in some other diseases is undeniable. Hyperuricemia is associated with hypertension, vascular diseases, renal disease and cardiovascular events. In addition, there is an antioxidant and pro-inflammatory mechanism of action for uric acid (3). While it is reported that it clears toxic reactants and protects the tissue against oxidative stress at normal levels (4), serum uric acid levels are also decreased when oxidative stress is present.

The uric acid in the serum is saturated at environmental conditions in 6.4-6.8 mg/dL, and 7.0 mg/dL is the upper limit of solubility. When it exceeds this value, uric acid crystallizes and begins to precipitate. Uric acid suppresses the production of nitric oxide, which plays an active role in glucose transport (5). It causes renal vaso-constriction, systemic hypertension, tubulointerstitial damage, decrease in nitric oxide synthase production and deterioration in afferent arteries (6-8). It suppresses nitric oxide bio-activity and insulin resistance via inflammatory factors and adipokines (9). It has been shown to be associated with blood glucose level (7). Şengül et al. (8) reported that HbA1C, which reflects the long-term metabolism and elevation of glucose, is also positively associated with glucose and uric acid elevation.

Increased uric acid levels cause systemic cytokine production, tumor necrosis factor α, local increase in chemokines, monocyte chemotactic protein 1 and cyclooxygenase 2 in blood vessels (3). The majority of the daily excretion (2/3) of uric acid occurs through the kidneys and 1/3 is via the gastrointestinal system (1). In normal and non-diabetic individuals, uric acid is completely filtered from the glomerulus and almost completely reabsorbed from the proximal tubules (7). In the presence of hyperuricemia, uric acid crystals accumulate in the joints and kidneys (10).

Study Hypothesis

Hyperuricemia is a condition seen in chronic renal failure (CRF). While there are studies stating that the level of uric acid increases mainly due to the decrease in GFR in CRF (3), there are also studies stating that hyperuricemia causes chronic kidney failure (7) and causes progression of the disease (5,6). Chonchol et al. (11) stated that the increase in serum uric acid level in CRF was mainly due to the decrease in GFR and that hyperuricemia played a minor role in the progression of the disease. On the contrary, there are studies stating that GFR decrease is observed more rapidly in hyperuricemia patients (5) and that end-stage renal failure develops more frequently in those with hyperuricemia (6). There is also a study stating that CRF develops more in healthy populations with high serum uric acid levels (7).

ARF is one of the most important factors affecting mortality in intensive care patients. Some of these studies are also in the direction of whether uric acid levels are related to AKI. In this study, we aimed to evaluate whether there was a relationship between uric acid levels and AKI and RRT requirement, hence it is a cost-effective and easy to obtain parameter.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara City Hospital No:1 Clinical Researches Ethics Committee (Date: 20.04.2022, Decision No: E1-22-2565). The study complied with the Declaration of Helsinki and informed consent has been obtained from all participants.

A total of 1000 individuals who were admitted to ICU of our institution between 01.03.2020-01.01.2022, without any prior renal disease and GFR of 80-120 ml/minutes, have been enrolled in this retrospective analysis.

Patients with an estimated glumerular filtration rate (e-GFR) between 80-120 ml/minutes, calculated with the MDRD formula (Modification of diet in renal disease) were included in this retrospective analysis. Demographic data, age, gender and comorbidity, length of stay in the ICU, duration of mechanical ventilation, mortality rate were obtained from patient files. Since the study was retrospective in nature, all patients in the ICU including the unconscious indivuduals and Coronavirus disease 2019 (COVID-19) patients have been included in the analysis.

Hospitalization urea, creatinine, GFR, uric acid, Na, K data were recorded from the laboratory data of electronic hospital database. The development of AKI in the ICU were evaluated via RIFLE criteria. In patients who developed AKI, it was checked whether there was an indication for RRT. The uric acid level of the patients who needed RRT at that time was also recorded.

Inclusion Criteria

Individuals between 18-90 yars old, that are followed up in the ICU. Additionally, these patients did not have any chronic renal disease at the time of admission.

Exclusion Criteria

Patients <18 and >90 years old, who have diabetes mellitus and chronic renal disease at the time of admission. Pregnant women were also excluded from the study.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences, version 22 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation and/or (Median-IQR) values and as numbers or percentages where appropriate. The homogeneity of variances between the groups was evaluated with the Levene test, and the distribution of continuous variables was evaluated by using Shapiro Wilk and Kolmogorov-Smirnov tests. According to the results of normality tests, differences between independent groups were analyzed by using the Mann-Whitney U test or Student's t-test. The chi-square and/or Fisher's exact test were used to compare groups among the categories of variables. Before ran regression, correlations between variables were obtained by using Spearman or Pearson correlation coefficient and evaluated with rho and relevant p values.

In order to define risk factors of outcome variable ARF (-) or (+), multiple logistic regression analysis and adjusted odds ratios with their confidence intervals were calculated. All covariates with missing data in less than 20% of observations and a p-value <0.05 in univariate testing were considered for inclusion in the final multiple regression model and retained if the p-value was <0.05 or if they demonstrated evidence of significant confounding (>10% change in effect size). Highly collinear covariates (defined as correlation coefficient >0.6) were not included together in the final multiple model and these variables are shown in the regression table). The model fit was assessed by Hosmer-Lemeshow Test. A p-value of less than 0.05 was considered statistically significant for all statistical processes.

RESULTS

A total of 1000 individuals were enrolled within the scope of this study. Patients were segmented into 2 groups as subjects who did and did not develope ARF. In terms of gender difference 63.4% (n=634) of them patients were male, 36.6% (n=366) were female, and there was a correlation between the diagnostic groups in terms of gender distribution (p<0.05). ARF was more common in male patients.

The distribution of demographic and clinical findings by diagnosis groups were given in **Table 1**. When the statistically significant variables among the diagnostic groups were examined, it was seen that the mean laboratory values of patients who developed ARF were higher in all parameters except the neurological disease and the initial GFR value. In terms of their final status of the study group, 79.3% (n=215) of patients with ARF and 18% (n=131) of patients without acute failure had deceased. Additionally, diabetes, hypertension, coronary artery disease (CAD), cancer and neurological diseases were higher in patients with ARF.

ARF was observed in 27.1% (n=271) of the individuals. The laboratory and hemodialysis evaluation results of the patients with ARF at the time of diagnosis were given in **Table 2**. Hemodialysis had been administered in 44.3% (n=120) of patients with ARF. The reasons for hemodialysis were ischemia in 36%, sepsis and multifactorial reasons in 32% of the subjects.

The distribution of laboratory parameters at the onset and at the time of diagnosis of patients with ARF was given in **Table 3.** When the table was examined, it was observed that there was a statistically significant difference compared to the initial measurements in urea, creatinine, uric acid and Na increased compared to baseline (p<0.001) as all parameters except K. All values from baseline increased at the time of diagnosis, while a decrease was observed in the GFR value (p<0.001).

Table 1. Distribution of clinical findings of patients with acute renal failure

Characteristics (n=1000)	Total	ARF (-) (n=729)	ARF (+) (n=271)	P-value
	n (%) or Median±SD	n (%) or Median±SD	n (%) or Median±SD	
Age, years	63±16	62±17	67±14	<0.001
Gender				0.007
Female	366 (36.6)	285 (39.1)	81 (29.9)	
Male	634 (63.4)	444 (60.9)	190 (70.1)	
Day of admission	14±9.1	13±8.2	16.7±10.8	<0.001
Day of intubation	5±9	3±7	10±10	<0.001
HFNO	644 (64.4)	451 (61.9)	193 (71.2)	0.006
NIMV	158 (15.8)	113 (15.5)	45 (16.6)	0.67
IMV	432 (43.2)	202 (27.7)	230 (84.9)	<0.001
Comorbidity				
Diabetes mellitus	251 (25.1)	163 (22.4)	88 (32.5)	0.001
Hypertension	412 (41.2)	280 (38.4)	132 (48.7)	0.003
CAD	238 (23.8)	161 (22.1)	77 (28.4)	0.037
COPD	142 (14.2)	103 (14.1)	39 (14.4)	0.916
Renal	2 (0.2)	1 (0.1)	1 (0.4)	0.469
Cancer	166 (16.6)	108 (14.8)	58 (21.4)	0.013
Neurologic	212 (21.2)	170 (23.3)	42 (15.5)	0.007
APACHE score	8.1±4.7	7.4±4.3	9.9±5	<0.001
SOFA score	3.7±2.2	3.3±1.9	4.7±2.7	<0.001
Baseline urea	45.2±19.5	42.5±18.1	52.5±21.2	<0.001
Baseline creatinine	0.8±2.7	0.8±3.2	0.7±0.2	0.596
Baseline GFR	99.3±18.2	101.3±19.7	93.9±11.5	<0.001
Baseline Na+	138.3±9	138.3±8.5	138.3±10.3	0.961
Baseline K+3	4.1±1.3	4.1±1.4	4±0.6	0.51
Baseline uric acidt	4.4±1.8	4.3±1.7	4.6±1.8	0.021
Procalcitonin	1.2±6.3	1.2±6.5	1.1±5.7	0.938
Inotrope				<0.001
None	631 (63.1)	580 (79.6)	51 (18.8)	
Nor-adrenaline	359 (35.9)	144 (19.8)	215 (79.3)	
Nor-adrenaline+Dopamine	10 (1)	5 (0.7)	5 (1.8)	
Steroid				<0.001
No	394 (39.4)	315 (43.2)	79 (29.2)	
250 Mg Methylprednisolone	202 (20.2)	129 (17.7)	73 (26.9)	
>250 Mg Methylprednisolone	123 (12.3)	90 (12.3)	33 (12.2)	
80 Mg Methylprednisolone	145 (14.5)	99 (13.6)	46 (17)	
6 Mg Dexamethasone	84 (8.4)	60 (8.2)	24 (8.9)	
Hydrocortisone	1 (0.1)	0 (0)	1 (0.4)	
40 Mg Metilprednizolon	51 (5.1)	36 (4.9)	15 (5.5)	
Final Status				<0.001
Discharged	346 (34.6)	131 (18)	215 (79.3)	
Exitus	654 (65.4)	598 (82)	56 (20.7)	

HFNO: High flow nasal oxygen, NIMV: Non invasive mechanical ventilation, IMV: İnvasive mechanical ventilation, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease

Table 2. Acute renal failure related features

Characteristics (n=271)	n (%) or Median±SD
What day did ARF develop?	10±7
Urea when ARF developed	106.9±47.9
Creatinine when ARF developed	1.5±0.5
GFR when ARF developed	45.7±14.9
Sodium when ARF developed	143.1±8
Potassium when ARF developed	6.5±30.3
Uric acid when ARF develops	6.1±3.2
Hemodialysis	120 (44.3)
Reason for hemodialysis	
Ischemic	97 (36)
Sepsis	86 (32)
Multifactorial	86 (32)
Uric acid at the entrance to hemodialysis	8.7±2.7

ARF: Acute renal failure, GFR: Glomerular filtration rate

Table 3. Evaluation of laboratory findings of patients with acute renal failure

Variables (n=271)	Median±SD	P-Value
Baseline urea	52.6±21.2	<0.001
Urea when ARF developed	106.9±47.9	
Baseline creatinine	0.7±0.2	<0.001
Creatinine when ARF developed	1.5±0.5	
Baseline GFR	93.8±11.4	<0.001
GFR when ARF developed	45.7±14.9	
Baseline sodium	138.3±10.3	<0.001
Sodiumwhen ARF developed	143.1±8	
Baseline potassium	4±0.6	0.187
Potassium when ARF developed	6.5±30.3	
Baseline uric acid	4.6±1.8	<0.001
Uric acid when ARF developed	6.1±3.2	

ARF: Acute renal failure, GFR: Glomerular filtration rate

The distribution of uric acid measurements at the beginning, time of diagnosis and during hemodialysis among patients who developed AFR were given in **Table 4.** When the table was examined, it was observed that there was a statistically significant difference between the uric acid measurements of the patients undergoing hemodialysis ($p<0.05$) and uric acid measurements were increased compared to baseline.

Table 4. Uric acid distribution of patients undergoing hemodialysis

Variables (n=120)	Mean±SD	P value
Baseline Uric acid	4.5±2.0	
Uric acid when ARF developed	6.3±3.9	<0.001
Uric acid at the entrance to hemodialysis	8.7±2.7	

ARF: Acute renal failure

DISCUSSION

The most common causes of ARF in the hospital conditions can be stated as prerenal events and acute tubuler necrosis (ATN) (13). In a multicenter study, ATN was reported in 45% of cases, prerenal events in 21%, acute attack due to prerenal causes on the basis of CRF in 12.7%, and postrenal causes in only 10% of cases (14). In an early research by Brivet et al. (15), prerenal causes were found in 17% of the cases, intrinsic renal causes (mostly ATN) in 78%, and postrenal causes in 5% of the individuals. In another single-center study of 81 patients, sepsis was the primary cause of ARF (44%) followed by drug toxicity in 14%, and obstructive uropathy in 11% of cases (16).

Major surgical procedures are an important risk factor for the development of AFR in hospitalized patients, thus it increases the length of hospital stay, cost, morbidity and mortality. Cardiac, vascular and major abdominal surgeries are the ones with the highest risk among surgical procedures. Prerenal azotemia and ATN are usually responsible for perioperative ARF(17). In a study examining 2672 patients who underwent coronary artery by-pass surgery (CABG), it was reported that 8% of the patients developed ARF in the post-operative period, 14% of them resulted in death, and on the contrary, the mortality rate was 1.8% in patients who did not develop ARF (18). Abelha et al. (19), examined 1597 patients in the post-anaesthetic ICU and the incidence of ARF was found to be 7.5%. In the same study, it was observed that the mortality rate in patients with ARF was approximately four times higher than in patients without ARF.

Factors that increase the risk of perioperative ARF can be listed as age, history of CRF, heart disease, use of nephrotoxic agents (radiocontrast, NSAID, ACEI, ARB and diuretics), hypertension, diabetes mellitus, peripheral vascular disease, emergency surgery, type and procedures of surgery (20).

In previous research it was shown that serum creatinine value is not a good predictor for the diagnosis of renal failure in the elderly. Since body muscle mass decreases with increasing age, the creatinine value is low as long as the actual GFR is measured. In addition, when there is a sudden decrease in GFR in the elderly, a rapid and parallel increase in serum creatinine does not occur, since muscle mass is reduced. For this reason, the search for new predictive markers that are not affected by age, muscle mass, diet and physical activities that can be used in the diagnosis of ARF continues. Herget et al. (21) reported that the serum cystatin-C level in elderly patients increased by 50% before clinical ARF has observed. In another study conducted in intensive care patients, serum cystatin C level was found to have a good positive predictive value for ARF (22). Apart from the serum cystatin-C level, there are also studies on some new markers (such as KIM-1, urinary interleukin-18 level, NGAL) in urine and serum (2). In this study, a statistically significant difference was found compared to the initial measurements in urea, creatinine, uric acid and Na increased compared to baseline ($p<0.001$) as all parameters except K. All values from baseline increased at the time of diagnosis, while a decrease was observed in the GFR value ($p<0.001$).

The most important cause of death in patients with ARF are infection (especially sepsis), cardiovascular and pulmonary dysfunction. Although it usually depends on the underlying cause, ARF has a mortality rate of 20-70% despite advances in medical care (23).

In the study of Nash et al. (24), the rate of ARF was found to be 7% in patients admitted to the hospital, while this rate was 23% in ICU. In the study conducted by Medve et al. (25) in 7 ICU between October and November 2009 in Hungary, ARF was detected in 24.4% of patients. The mean age of these patients was 64.9 years. Liano et al. (26) evaluated 740 ARF patients who applied to 13 tertiary health institutions and found ATN in 45% of the patients, prerenal causes in 21% and postrenal causes in 10%.

In the study conducted in Northern Italy, ARF has been found in 25.6% of diabetes patients, 58.5% of hypertension patients, 12.8% of NSAID users, 19.2% of ACEI and ARB users, 5.1% of contrast material administered 5.1% individuals and 25.6% of subjects with sepsis. In the study of Liangos et al. (13), diabetes was 10.6%, hypertension was 13.6%, cancer was 2.9%, and sepsis was 1.7% in ARF patients. The rate of those who needed dialysis was 5.7% (13,15). In the study of Uchino et al. (19) based on multicenter intensive care data, the etiology of 1738 ARF patients was 10% sepsis, 25.6% hypovolemia, 19% drug use, and 2.6% obstructive uropathy. Continuous hemodialysis was required in 80%

of the patients, intermittent hemodialysis was required in 16.9% and peritoneal dialysis was required in 3.2%. In the study conducted by Barrantes et al. (23) of 735 ARF patients, 72.3% of patients had drug use (ARB, ACEI, NSAID, contrast, etc.), 18.1% had infection, 35.8% had hypovolemia (nausea, vomiting, diarrhea, etc.) 12.9% of the patients required RRT (23). In the etiology of ARF patients followed in ICU in Hungary, 44% had septic shock, 39% had hypovolemia, 2% were drug users (25). In our country, 541 ARF patients (mean age 64.9±15.6) were evaluated between 2008 and 2012 in Central Anatolia. The underlying etiology was several diseases in 78%, acute gastroenteritis in 35.1%, drug use in 14.8%, heart failure in 9.6%, use of contrast material in 7% and sepsis in 5.4% (26). In the current study it was seen that the mean laboratory values of patients who developed ARF were higher in all parameters except the neurological disease and the initial GFR value. Additionally, diabetes, hypertension, coronary artery disease, cancer and neurological diseases were higher in patients with ARF.

Uchino et al. (27), reported that mortality was 52% in ARF patients with a mean age of 67 years in ICU. The mortality rate in the hospital excluding intensive care patients was 8%. Among the risk factors, the use of vasopressor agents, mechanical ventilation, and septic shock were more common. In the study of Barrantes, the mortality rate was found to be higher (15.2%) especially in ARF patients over the age of 60 (27). Medve et al. (25), published that mortality was 49% in intensive care ARF patients, and risk factors wereage, sepsis, and mechanical ventilation. In a study conducted from Turkey, the mortality rate was found to be 7.4%, and among the causes of death, cardiopulmonary failure was 70%, and sepsis and myocardial infarction were 10% (28). In this study 79.3% of patients with ARF and 18% of patients without acute failure had deceased.

Elevated uric acid level is a common finding in renal failure. In the past, it was stated that uric acid elevation developed only due to decreased excretion from the kidneys, but today it has been shown that uric acid also plays an active role in the formation and progression of kidney damage. It has been shown that hyperuricemia causes renal vasoconstriction, systemic hypertension, tubulointerstitial damage, decreased nitric oxide synthase production, and afferent arteriolopathy. In this study the presence of diabetes mellitus, hypertension, coronary artery disease was higher in patients with ARF.

Uric acid suppresses nitric oxide bioactivity, affects insulin resistance via inflammatory factors and adipocytokines (22). In this study, uric acid levels were higher in patients with ARF and even higher in individuals who underwent hemodialysis.

CONCLUSION

Regarding the results of this study one can conclude that serum uric acid level has been shown to be an independent risk factor for decreased renal function. Additionally, elevated uric acid levels lead to increased hemodialysis, morbidity and mortality in the ICU. This outcome has been confirmed with published studies.

Abbreviations

ACEI: Angiotensin converting enzyme inhibitors, **AKI:** Acute kidney injury, **ARB:** Angiotensin renin blockers, **ARF:** Acute renal failure, **ATN:** Acute tubuler necrosis, **CABG:** Coronary artery by-pass surgery, **CAD:** Coronary artery disease, **COPD:** Chronic obstructive pulmonary disease, **CRF:** Chronic renal failure, **e-GFR:** Estimated glumerular filtration rate, **GFR:** Glomerular Filtration Rate, **HFNO:** High frequency nasal oxygen, **ICU**: Intensive care unit, **IMV:** Invasive mechanical ventilation, **KDIGO:** Kidney disease improving global outcomes , **MDRD:** Modification of diet in renal disease, **NIMV:** Non-invasive mechanical ventilation, **RRT:** renal replacement therapy, **SD:** Standard deviation, **SPSS:** Statistical package for the social sciences,

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No:1 Clinical Researches Ethics Committee (Date: 20.04.2022, Decision No: E1-22-2565).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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