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Original Article

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Role of Uric Acid Albumin Ratio in Predicting Development of Acute Kidney Injury and Mortality in Intensive Care Unit Patients

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Abstract

Objective: This study aimed to evaluate the prevalence of hypoalbuminemia and hyperuricemia, and investigate uric acid albumin ratio association with mortality and acute kidney injury (AKI) in critically ill patients.
Materials and Methods: We evaluated 754 patients who were admitted to intensive care unit (ICU) between 2008 and 2014. We investigated the effects of hypoalbuminemia and uric acid / albumin ratio on mortality and AKI.
Results: A total of 754 critically ill patients (52.4% male and mean age 57.1±18.7 years) were enrolled in this study. Among them, 72.8% (549/754) patients had hypoalbuminemia during the admission to ICU. A total of 381/754 (50.5%) patients developed AKI. The 28-day mortality rate was significantly higher in hypoalbuminemia group than in normal plasma albumin group [35.7% (196) vs. 18.5% (38), p=0.01]. The uric acid level higher than 7 mg/dl was associated with AKI (p<0.001). Uric acid albumin ratio higher than 1.7 was significantly associated with AKI and 28-day mortality (p<0.001 and p<0.001).
Conclusion: This study successfully confirmed that hypoalbuminemia in ICU admission has been independently associated with increased early death and AKI in critically ill patients; and uric acid albumin ratio could be a marker to predict AKI and mortality.
Keywords: Hypoalbuminemia, uric acid, acute kidney injury, intensive care unit, mortality

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INTRODUCTION

Albumin is an important molecule under physiological and pathophysiological conditions. It is the main determinant of intravascular oncotic pressure and also major transporter of many hormones, drugs, bioactive elements, free fatty acids, calcium, iron, and bilirubin (1). Furthermore, previous studies have shown that albumin has much more complex functions, such as anti-inflammatory effects, protection from oxidative stress-induced injury, and anti-apoptotic effects, beyond being a transporter (1-3). Hypoalbuminemia is a common finding in patients with heart failure, nephrotic syndrome, liver cirrhosis, and malnutrition. At the time of admission to intensive care units (ICUs), the frequency of hypoalbuminemia is 21% in the critically ill patients (4). Hypoalbuminemia is a well-known risk factor for morbidity and mortality, and prolonged ICU and hospital stay in critically ill patients (5). In critically ill patients, plasma albumin level might be low due to capillary leakage during the inflammation, acceleration of catabolism, and decrease in synthesis by liver (6). It has been shown that decreased plasma albumin concentration in critically ill patients has a negative predictive value for increased pulmonary vascular permeability regardless of underlying disease and fluid status (7).

Uric acid is the end product of purine metabolism (8). Kidneys (two-thirds of total daily uric acid) and intestine (one-third of total daily uric acid) are responsible for uric acid removal from body (9). In adults, normal levels of blood uric acid levels range from 5 to 7 mg/dL (10). Many medical conditions and medicines such as chronic kid-

ney disease (CKD), hypertension, obesity, diabetes, diuretics, and anti-hypertensive drugs also affect blood uric acid levels (11). Studies in the last decade have shown that hyperuricemia increases the risk of CKD, cardiovascular mortality, and all-cause mortality (12-14). However, several studies have revealed opposite results (15, 16). Therefore, association between blood uric acid levels and mortality remains debatable.

Acute kidney injury (AKI) is a well-recognized clinical disorder in ICUs. Epidemiologic studies have shown that AKI is associated with increased disease severity, mortality, length of ICU stay, and prolonged mechanical ventilation (17-19). Although, there are well-known risk factors such as contrast agent, hypovolemia, hypervolemia, and CKD, there are currently no widely accepted markers to predict AKI development. Hyperuricemia and hypoalbuminemia are also associated with AKI (4, 20). Crystal precipitation and non-crystal pathways are proposed mechanisms in the hyperuricemia-related AKI development (21). Uric acid is a pro-inflammatory factor (13, 22). The pro-inflammatory effect of uric acid is more evident with high uric acid levels (22). The association of serum uric acid level with the development of AKI has been reported in the setting of cardiac catheterization and cardiovascular surgery (23). However, not all studies showed an independent association between AKI development and uric acid levels (24). And also, no comparative study of uric acid levels and AKI in ICU patients has been conducted. Over the past decade, many studies have focused on the independent risk factors (25-27) and early predictors for AKI (28, 29). Biomarkers such as neutrophil gelatinase associated lipocalin (NGAL) (30, 31) and cell cycle arrest markers tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP-7) (32) have been studied for AKI stratification and prediction. However, all these biomarkers are expensive, and their clinical values still appear to be limited (33).

High uric acid levels and hypoalbuminemia facilitate the development of AKI. On the other hand, both factors could be affected by many factors. This makes it difficult to use both parameters as markers of AKI. In this context, we aimed to measure the predictive value of the ratio of two important laboratory parameters associated with AKI and mortality.

MATERIALS AND METHODS

Study Population

The study was conducted in the nine-bedded internal medicine ICU at Hacettepe University, Ankara, Turkey, from January 2008 to April 2014. A total of 796 patients were admitted to ICU. The patients included in the study were older than 18 years. Patients were excluded if they had underlying disease that may have interfered with plasma albumin levels: severe (nephrotic) proteinuria, liver cirrhosis, second- and third-degree severe burns, and end-stage CKD. A total of 796 patients with available data were enrolled. Of 796 patients, 21 had end-stage CKD, 13 patients had cirrhosis, and 8 patients had no plasma albumin level at admission; and these 42 patients were excluded from the study. No patient had severe proteinuria or burns. A total of 754 patients were analyzed in the study. The ethics committee of Hacettepe University Hospital approved the study protocol in 2017. Informed consent is not necessary due to the retrospective nature of this study.

Clinical Outcomes

Hospital electronic medical records system was used to gather baseline information such as sex, age, co-morbidities, contrast agent exposure, and calculation of Charlson comorbidity index. The 28-day mortality rates and period of hospitalization in the ICU were determined for all patients. Also, chloride, phosphorus, potassium, sodium, creatinine, uric acid, and albumin levels were collected when patients were admitted to ICU. Hypoalbuminemia was defined as plasma albumin level of less than 3.5 g/dL; and hyperuricemia was defined as plasma uric acid level higher than 7 mg/dL. In the subgroup analysis, uric acid groups (low uric acid, normal uric acid, and high uric acid) and uric acid / albumin ratio were used to define the association between AKI and mortality. AKI was defined according to the definition of Kidney Disease Improving Global Outcomes (KDIGO) guidelines (34). CKD was defined according to KDIGO 2012 clinical practice guidelines (35). Comorbidity scores were determined using the Charlson comorbidity index (36). Other outcome variables were 28-day mortality and overall mortality.

Statistical Analysis

Symmetrically distributed variables in the text and tables were shown as means±standard deviation. If the distribution was heterogeneous, variables were shown as median (minimum- maximum). Categorical variables were expressed as percentage. Student's t test or the Mann-Whitney U test were used to compare continuous variables according to the data distribution. Data distribution was determined by using the Kolmogorov-Smirnov test. The chi-square test was used to compare categorical variables. Logistic regression was used to identify variables that predict AKI. Receiver operating curve (ROC) analyses were plotted to illustrate albumin and uric acid/albumin ratio cutoff levels at admission. The 28-day survival analysis was performed by means of the Kaplan-Meier curves. Cox-regression analysis was utilized to identify the albumin subgroups for mortality. P values less than 0.05 were considered statistically significant. Analyses were performed with the Statistical Package for the Social Science (SPSS) version 20.0.0, (IBM Corp.; Armonk, NY, USA) software for Windows.

RESULTS

A total of 754 critically ill patients (52.4% male and mean age 57.1±18.7 years) were enrolled in this study. These 754 patients were divided into two groups: those with hypoalbuminemia and those without it. Among them, 72.8% (549/754) patients had hypoalbuminemia during the admission to ICU. Between the two groups, there was no statistically difference in diabetes, hypertension, congestive heart failure, and CKD (p=0.64, p=0.54, p=0.67, and p=0.03, respectively). However, the mean age, median Charlson comorbidity score, and

malignancy frequency were higher in the hypoalbuminemia group (58.3±18.4 vs. 53.9±19.7, 3(0-10) vs. 2(0-8) and 24.4% vs. 13.3%, p=0.004, p=0.01, and p=0.001, respectively). Demographic characteristics of patients are shown in Table 1. A total of 381 (50.5%) of 754 patients developed AKI. A total of 55.2% (303/549) of patients, who had albumin levels under 3.5 g/dL, developed AKI compared with 38% (78/205) of patients with normal plasma albumin levels. The difference was found to be statistically significant (p<0.001). Twenty-four percent of total patients needed renal replacement treatment (RRT). Need for RRT was significantly higher in patients with hypoalbuminemia when compared to patients with normal albumin levels [75 (13.7%) vs. 13 (6.3%), p=0.008]. Admission reason to ICU such as sepsis was more frequent in patients with hypoalbuminemia (34.6% vs. 9.8%, p<0.001), whereas respiratory failure and toxicity were more frequent in those with normal albumin level (40.9% vs. 54.6%, p<0.001 and 1.8% vs. 18.5%, p<0.001). The 28-day mortality rate was significantly higher in hypoalbuminemia group, when compared to normal plasma albumin group [35.7% (196) vs. 18.5% (38), p=0.01]. However, overall mortality rate was similar between the two groups (p=0.9). The highest mortality rate (40.61%) was seen in the group of patients whose albumin levels were between 1.5 and 2.5 g/dL (Figure 1). Mortality rates decreased as the serum albumin levels increased (26.2% for 2.5-3 g/dl, 17.4% for 3-3.5 g/dL, 10.9% for 3.5-4 g/dL and 4.8% for >4 g/dL). Serum chloride, creatinine, and uric acid/albumin ratio were significantly higher in non-survivor group as compared to survivors (p=0.002, p=0.001, and p=0.03, respectively). Laboratory parameters of patients were summarized in Table 2.

Table 1. Demographic characteristics of patients

	Total patient (n=754)	Albumin at admission <3.5 g/dL (n=549)	Albumin at admission ≥3.5 g/dL (n=205)	p
Male	395 (52.4%)	301 (54.8%)	94 (45.9%)	0.028
Age (mean)(year)	57.1±18.7	58.3±18.4	53.9±19.7	0.004
18-35	128 (17%)	79 (14.4%)	49 (23.9%)	
36-65	313 (41.5%)	231 (42.1%)	82 (40%)	
>65	313 (41.5%)	239 (43.5%)	74 (36.1%)	
Charlson comorbidity score (median)	3 (0-10)	3 (0-10)	2 (0-8)	0.01
Diabetes mellitus	173 (22.9%)	124 (22.6%)	49 (23.9%)	0.645
Hypertension	192 (25.5%)	143 (26%)	49 (23.9%)	0.548
CHF (NYHA 3-4)	166 (22%)	123 (22.4%)	43 (21%)	0.674
Surgery	91 (12.1%)	70 (12.8%)	21 (10.2%)	0.343
CKD	103 (13.7%)	83 (15.1%)	20 (9.8%)	0.06
Malignancy	161 (21.4%)	134 (24.4%)	27 (13.3%)	0.001
AKI	381 (50.5%)	303 (55.2%)	78 (38%)	<0.001
Need for RRT total	88 (12%)	75 (13.7%)	13 (6.3%)	0.008
RRT within AKI	88 (23.1%)	75 (24.8%)	13 (17%)	0.2
ICU admission				
Sepsis	210 (27.5%)	190 (34.6%)	20 (9.8%)	<0.001
Respiratory failure	336 (44.6%)	224 (40.9%)	112 (54.6%)	<0.001
Hypervolemia	18 (2.4%)	14 (2.6%)	4 (2%)	0.49
Toxication	41 (5.4%)	10 (1.8%)	31 (15.1%)	<0.001
Others	149 (19.7%)	110 (20.1%)	39 (18.5%)	0.53
28-day mortality	234 (31%)	196 (35.7%)	38 (18.5%)	0.01
Overall morality	277 (36.7%)	201 (36.6%)	76 (37.1%)	0.9

CHF: Congestive heart failure; NYHA: New York Heart Association; CKD: Chronic kidney disease; AKI: Acute kidney disease; RRT: Renal replacement treatment; ICU: Intensive care unit

Table 2. Laboratory parameters of patients

	Total patient (n=754)	Non-survivor (n=242)	Survivor (n=512)	p
Chloride (mEq/L)	103±8	105.2±7.5	103.1±8.1	0.002
Phosphorus (mEq/L)	3.75±1.55	3.96±1.92	3.66±1.34	0.43
Potassium (mEq/L)	4.2±0.86	4.25±0.94	4.2±0.81	0.97
Sodium (mEq/L)	136.4±6.6	137.1±7	136±6.45	0.152
Uric acid day 1 (mg/dL)	5.6 (0.47-34.7)	5.86 (0.47-34.7)	5.47 (0.8-16.5)	0.46
Albumin day 1(g/dL)	3.04±0.79	2.79±0.72	3.14±0.8	<0.001
Albumin day 3	2.82±0.63	2.56±0.62	2.91±0.62	<0.001
Creatinine day 1 (mg/dL)	0.97 (0.1-9.1)	1.07 (0.1-9.1)	0.9 (0.2-6.34)	0.001
Creatinine day 3	0.88 (0.2-8.4)	1.25 (0.26-6.3)	0.84 (0.2-8.4)	<0.001
Uric acid/albumin	1.84 (0.19-12.6)	1.99 (0.19-12.6)	1.78 (0.25-8.99)	0.03

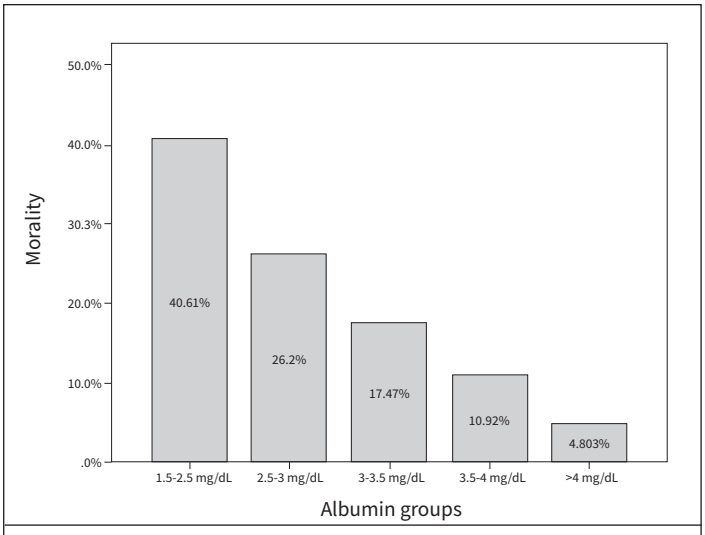

Figure 1. Mortality rate in relation to the serum albumin concentration on admission to intensive care unit. Numbers above the bars indicate mortality rate percentage.

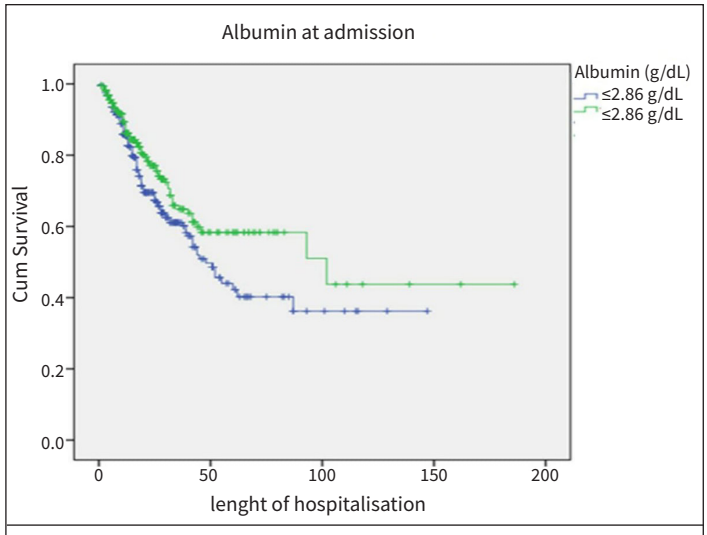

Figure 2. ROC curve for best cutoff value of albumin levels associated with mortality. 2.86 g/dl with sensitivity=60% and 40%, specificity=60%, UAC=0.629 Kaplan–Meier survival analysis for albumin at admission (log rank p=0.001).

Univariate and multivariate logistic regression was used to analyze independent risk factors for AKI (Table 3). Contrast agent [odds ratio (OR) 0.695, 95% confidence interval (CI) 0.492-0.983], nephrotoxic medication (OR:2.125, 95% CI 1.488-3.303), CKD (OR:5.217, 95% CI 3.362-11.498), and uric acid level higher than 7 mg/dL (OR:4.235, 95% CI 3.039-5.902) were significantly associated with AKI. Albumin levels were divided into four groups (group 1: albumin levels ≤2 g/dL, group 2: albumin levels between 2 and 2.99 g/dL, group 3: albumin levels between 3 and 4 g/dL, and group 4: albumin levels ≥4 g/dL). When group 4 was taken as a reference, all the groups were significantly associated with AKI in univariate logistic regression analysis [4.029(1.937-8.380), p<0.001, 2.572(1.508-4.384), p=0.001 and 2.251(1.175-3.872), p=0.03, respectively]. However, male gender (OR:1.003, 95% CI 0.729-1.337), diabetes mellitus (OR:1.151, 95% CI 0.784-1.690), hypertension (OR:0.749, 95% CI 0.491-1.140), surgery (OR:0.902, 95%CI 0.563-1.444), congestive heart failure (OR:1.093, 95% CI 0.700-1.707), and malignancy (OR:0.846, 95% CI 0.597-1.199) were not significantly associated with AKI. Nephrotoxic medication, CKD, uric acid level higher than 7 mg/dL, albumin level between 2 and 3 g/dL and under 2 g/dL were maintain statistical significance in multivariate logistic regression analysis [1.814 (1.215-2.710), p=0.004, 3.756 (2.115-6.465), p<0.001, 3.858 (2.653-5.160), p<0.001, 2.144 (1.204-3.820), p=0.01 and 2.945 (1.323-6.559), p=0.008, respectively].

ROC was used to determine best cutoff value of albumin levels at admission associated with mortality. The value of 2.86 g/dL was the best plasma albumin value associated with mortality (sensitivity=60% and 40%, specificity=60%, UAC=0.629). The Kaplan-Meier survival analysis revealed that patients with albumin levels >2.86 g/dL at admission had increased 28-day sur-

Table 3. Logistic regression analysis for risk factors for AKI development

	Univariate Analysis		Multivariate Analysis	
Variable	**Odds ratio (95%CI)**	**p**	**Odds ratio (95%CI)**	**p**
Male	1.003 (0.729-1.337)	0.985		
Contrast agent	0.695 (0.492-0.983)	0.04	0.705 (0.482-1.031)	0.07
Nephrotoxic medication	2.125 (1.488-3.303)	<0.001	1.814 (1.215-2.710)	0.004
Chronic kidney (GFR<60)	5.217 (3.362-11.498)	<0.001	3.756 (2.115-6.465)	<0.001
Diabetes	1.151 (0.784-1.690)	0.473		
Hypertension	0.749 (0.491-1.140)	0.177		
Surgery	0.902 (0.563-1.444)	0.666		
Congestive heart failure	1.093 (0.700-1.707)	0.695		
Malignancy	0846 (0.597-1.199)	0.384		
Albumin ≤2 g/dL	4.029 (1.937-8.380)	<0.001	2.945 (1.323-6.559)	0.008
2-3 g/dL	2.572 (1.508-4.384)	0.001	2.144 (1.204-3.820)	0.01
3-4 g/dL	2.251 (1.175-3.872)	0.003	1.557 (0.867-2.797)	0.1
≥4 g/dL	Ref.			
Uric acid ≥ 7 mg/dL	4.235 (3.039-5.902)	<0.001	3.858 (2.653-5.160)	<0.001

Table 4. Cox-regression analysis of uric acid levels and uric acid/albumin ratio for AKI and mortality

	Uric acid level at ICU admission*			Uric acid / Albumin ratio
	U.A <5 (n=157)	**U.A 5-7(n=63)**	**U.A>7 (n=70)**	**UA/A >1.7*** **
	Yes p**	**Yes p****	**Yes p****	**p****
AKI	47 (30%) ref.	22 (35%) 0.06	43 (61%) <0.001	<0.001
28-day mortality	28 (18%) ref.	15 (24%) 0.08	15 (21%) 0.1	<0.001
Overall mortality	39 (25%) ref.	19 (30%) 0.04	15 (21%) 0.48	0.17

U.A: Uric acid; UA/A: Uric acid/albumin; AKI: Acute kidney injury
*Hypertension, congestive heart failure, chronic kidney disease, and malignancy were excluded (n=290)
** Cox-regression analysis was performed for each p value
***ROC analysis was performed to find the best cutoff uric acid /albumin ratio for AKI: 1.7, sens: 58%, spec: 63%, and UAC: 0.598

vival as compared to patients with albumin under this level (log rank test p=0.001, respectively) (Figure 2). In the Cox-regression analysis of albumin subgroups for mortality, albumin levels between 1.5 and 2.5 g/dL [hazard ratio (HR) 3.209, 95% CI 1.242-8.292] and albumin levels between 2.5 and 3 g/dL (HR:2.052, 95% CI 1.093-3.852) were identified as strong predictors of mortality (Figure 3). After exclusion of the diseases such as hypertension, congestive heart failure, malignancy, and CKD that may affect serum uric acid levels, subgroup analysis of serum uric acid levels showed that serum uric acid levels higher than 7 mg/dL were associated with AKI but not with 28-day and overall mortality. ROC was used to determine best cutoff value of uric acid/albumin ratio associated with AKI. With 58% sensitivity and 63% specificity, 1.7 ratio was the best value. Higher than 1.7 ratio was associated with AKI and 28-day mortality (Log rank <0.001 and <0.001) (Table 4).

DISCUSSION

Our results show that more than 70% patients had a low plasma albumin levels at the time of ICU admission. Moreover, hypoalbuminemia was associated with increased mortality and AKI risk when compared with normal plasma albumin levels. Hypoalbuminemia is a common finding in critically ill patients, and its incidence is reported between 30% and 82% in the literature (37-39). The proposed mechanisms to hypoalbuminemia in critically ill patients are increased albumin losses from bleeding via gastrointestinal tract, increased capillary permeability, and dilution from intravenous fluid administration (5). Whatever the

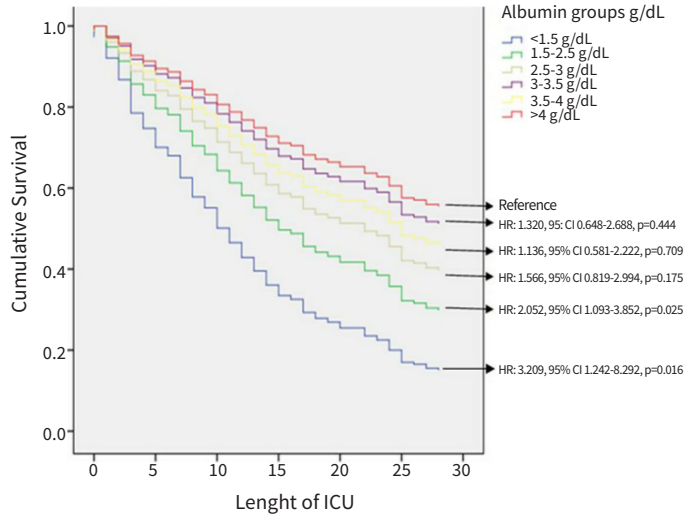

Figure 3. Cox-regression analysis of possible predictor albumin levels for mortality.
ICU: intensive care unit

proposed mechanism, hypoalbuminemia is strongly associated with increased mortality and adverse outcome in critically ill patients (2, 40-42).

Shao M et al. (4) reported that plasma albumin level under 3.5 g/dL was an independent risk factor for AKI and also AKI-associated mortality on ICU admission. Wiedermann CJ, in 2010, reported a meta-analysis of 17 observational clinical study. Both of this studies were confirmed that hypoalbuminemia is an independent predictor of AKI and AKI-related mortality (43). These results are compatible with our findings. Our results also suggested that nephrotoxic medication and CKD were independent risk factors for AKI. These results were similar to literature (44-46). On the contrary, contrast agent exposure was a statistically significant protector factor for AKI development. We found this relation because our study was not an intervention study, and clinicians might take precautions such as hydration or N-acetylcysteine administration not to develop AKI before contrast agent exposure (47, 48).

Several studies show that hypoalbuminemia is associated with mortality. Magnussen B et al. (49) reported a cohort study with community-acquired bacteremia. They found that albumin level status had a strong negative correlation with mortality, and this correlation was stronger than sepsis severity scores based on the systemic inflammatory response syndrome and organ dysfunction parameters (49). Ñamendys-Silva SA et al. (37) showed that albumin levels under 2 g/dL at the day of admission to the ICU might be associated with increased morbidity and mortality. Similar to the literature, our study presents two important findings for mortality in critically ill patients. Firstly, hypoalbuminemia is strongly associated with 28-day mortality, and length of ICU and hospital stay similar to the literature. Secondly, contrary to literature, hypoalbuminemia is not associated with overall mortality. There are several possible explanations by which plasma albumin levels are not associated with overall mortality. (a) Long hospital stay might be cause to more severe conditions such as multidrug-resistant infections and stress ulcer bleeding (50, 51), and this can explain why we did not find association between overall mortality and hypoalbuminemia. Because our measurements have done only during the ICU admission and we did not know the albumin levels during the new situation that caused death. (b) Also, threshold for hypoalbuminemia have been variable in the studies ranging from 3 g/dL to 3.5 g/dL. (c) Nutritional status of patients might directly affect plasma albumin levels (52). Despite the fact that the low plasma albumin level is an independent predictor for mortality and worse outcome in critically ill patients, it is unclear if hypoalbuminemia directly contributes to mortality. There is no evidence to support the use of albumin to treat hypoalbuminemia (5, 37, 53). Because of the retrospective design of our study, it is difficult to distinguish high mortality due to hypoalbuminemia or hypoalbuminemia in disease with high mortality risk such as sepsis.

Gaipov A et al. (54) designed a study in 2014 to find out a biomarker for AKI after open heart surgery. They found that high serum uric acid levels after surgery had high sensitivity and specificity as popular potential biomarkers such as NGAL to predict AKI. A study conducted in 2015 showed similar result in severe burns (55). There were low number of patients in both study, and a limited patient population was represented. The number of patients in our study is higher than both studies; and this is the first study to show this relation in ICU patients. In subgroup analysis, we showed that hyperuricemia is an important and independent risk factor for AKI after excluding hypertension, CKD, and congestive heart failure that may cause hyperuricemia. Apart from the well-established reason of AKI, crystal precipitation, hyperuricemia can cause to AKI via non-crystal mechanism such as renal vasoconstriction, increased inflammation, and apoptosis (56). Both albumin and uric acid are associated with AKI in critically ill patients. However, common conditions in critically ill patients such as malnutrition, sepsis, inflammation, congestive heart failure, and CKD can affect level of both parameters. Therefore, we used uric acid albumin ratio to determine risk of AKI. The ROC curve analysis revealed that 1.7 ratio was the best cutoff value to predict AKI with 58% sensitivity and 63% specificity. This ratio was also a predictor for 28-day mortality in ICU patients. Odden et al. (57) showed that high uric acid level is associated with cardiovascular and all-cause mortality. But this relationship was no longer significant after accounting for kidney disease. Although, we could not show the uric acid level and mortality association on the contrary of literature, we suggest a potential biomarker to predict mortality and AKI in critically ill patients.

Our study had some limitations. Firstly, we cannot generalize our findings outside critically ill patients. Secondly, we have no detailed information on some interventions and medical conditions (e.g., dosage of diuretic usage, urinary tract infection)

that could induce AKI and increase uric acid level. Thirdly, the retrospective nature of the study might have affected the quality of evidence. Therefore, our findings should be supported by randomized controlled prospective studies. Finally, we have had no data on the nutritional status, which is associated with hypoalbuminemia.

CONCLUSION

This study successfully confirmed that hypoalbuminemia in ICU admission has been independently associated with increased early death and AKI in critically ill patients. To our knowledge, this is the largest study that shows that hyperuricemia could be associated with AKI in ICU patients. It is also the first study in the literature to show that uric acid albumin ratio may be predictor for mortality and AKI even in patients without hypertension, congestive heart failure, or CKD. This low-cost biomarker may be useful in the identification of AKI development and mortality that could benefit from intensive management.

Ethics Committee Approval: Ethics Committee approval was received for this study from the Ethics Committee of Hacettepe University Hospital in 2017.

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.H.Y., S.C., T.Y., O.F.A.; Design - H.H.Y., T.P., D.E.; Supervision - H.H.Y., T.Y., O.F.A.; Resource - S.C., D.E., O.F.A., T.P.; Materials - T.P., S.C., O.F.A., D.E.; Data Collection and/or Processing - H.H.Y., O.F.A., D.E.; Analysis and/or Interpretation - H.H.Y., T.Y., D.E.; Literature Search - H.H.Y.; Writing - H.H.Y., T.Y.; Critical Reviews - T.Y., O.F.A.

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

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