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ORIGINAL ARTICLE

Assessment of Serum Uric Acid to Albumin Ratio as A Prognostic Indicator for short-mortality in Acute Kidney Injury: A Prospective Study

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Abstract

Background: Acute kidney injury is diagnosed via a rapid increase in renal function parameters. Hyperuricemia has been associated with acute kidney injury and results in increased mortality.

Objective: To assess the uric acid to albumin ratio as a prognostic indicator for short-term mortality in acute kidney injury.

Material and Methods: This observational prospective cohort study was conducted in the Department of Nephrology at Akbar Niazi Teaching Hospital from November 2023 to February 2024. 80 patients, aged 18 and above who presented to the emergency service, developed acute kidney injury and subsequently received follow-up and treatment.

Results: 80 patients having a mean age of 58.35±14.18 years (35% female and 65% male) were assessed. The mean uric acid to albumin ratio was 3.57±1.6 mg/g in the non-survivor group and 2.84±1.2 mg/g in the survivor group (p=0.001). The optimal cutoff for the uric acid to albumin ratio correlated with mortality was found to be 2.5 mg/g, with specificity 82% and sensitivity 78%. The 30-day cumulatively survival rate for the low was 88.1% ± 3% and the high uric acid to albumin ratio was 66.3% ± 4%. The assessed survival time was 25.6 days (95% CI: 24 to 30) for the low uric acid to albumin ratio group and 21.5 days (95% CI: 20 to 23) for the high uric acid to albumin ratio group.

Conclusion: The study observed a clear relationship between 30-day mortality and the uric acid to albumin ratio at the initial manifestation in AKI patients, independent age, and clinical findings.

Keywords: Acute kidney injury; Albumin; Hyperuricemia; Hypoalbuminemia; Uric acid.

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Introduction

Apart from its role as the primary driver of oncotic pressure within blood vessels, albumin plays a crucial role in the defensive mechanism of the body, contributing to anti-inflammatory, antioxidant, and anti-apoptotic functions.1In addition to these critical roles, albumin serves as a transporter for numerous hormones, bioactive substances, drugs, calcium, bilirubin, iron, And free fatty acids.[2] Albumin levels can decline due to increased malnutrition, metabolism, impaired absorption, reduced synthesis in the liver, or leakage in capillaries resulting from inflammation.[3] Hypoalbuminemia, a common occurrence in chronic conditions like nephritic syndrome, heart failure, and cirrhosis are linked tolonger hospital stays and higher mortality rates.[4]Uric acid, a

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significant byproduct of purine breakdown, is primarily eliminated by kidneys, with a minor portion excreted straight through intestines.[5]Conditions like diabetes, hypertension, obesity, chronic kidney disease, and gout along with certain medications, notably diuretics, elevate uric acid level in body.6Some studies have associated hyperuricemia with heightened mortality risks.[7]

Acute kidney injury (AKI) is typically identified by sudden rise in creatinine, reduction in urinary excretion, or both, indicating a rapid decline in kidney functions.8Hyperuricemia and hypoalbuminemia are linked to AKI and associated with higher mortality rates.[9]As per a study, a uric acidtoalbumin ratio exceeding 1.7 was markedly linked to both AKI and 28days mortality.[10]

The diagnosis of AKI was adjudicated as per guidelines from Kidney Disease Improving Global Outcomes (KDIGO), the following any one criterion when fulfilled: creatinine increase by 0.3 mg/dL in 48 hrs, creatinine increase to1.5 times from initial value in 7 days, or a decrease of 0.5 mL/kg/hr urine output in 6 hrs.11The definition of hypoalbuminemia was albumin level of ≤ 3.5 g/dL, while hyperuricemia was as elevated uric acid level ≥ 7 mg/dL.

The study null hypotheses were the predictive performance of uric acid to albumin ratio is not associated with short term mortality in AKI patients through ROC curve analysis, it is also not compared the survival probability of high uric acid to albumin ratio vs low uric acid to albumin ratio in AKI patients through Kaplan-Meier survival analysis. Similarly, Cox regression model shows no cause-effect relationship between uric acid and albumin ratio. The study objective was to assess the correlation between the uric acid to albumin ratio and short-term mortality in AKI patients through:

1. Determining the predictive performance of uric acid to albumin ratio for short term mortality in AKI patients through ROC curve analysis.
2. Comparing the survival probability of high uric acid to albumin ratio vs low uric acid to albumin ratio in AKI patients through Kaplan-Meier survival analysis.
3. Determining the effect of uric acid to albumin ratio on short term mortality in AKI patients through Cox regression model.

Material and Method:

Study design: Observational prospective cohort study.

Setting & Duration: This study was conducted in the Department of Nephrology at Akbar Niazi Teaching Hospital from November 2023 to February 2024. The patients provided written informed consent and acquisition of required ethics committee approval.

Inclusion criteria: In this study included a total of 80 patients, aged 18 and above who presented to the emergency service, developed AKI, and subsequently received follow-up and treatment at the internal medicine Department. The detailed history and physical examination together with appropriate and relevant clinical investigations were ordered by a nephrologist. The treatment was also advised by the same nephrologists to all the patients recruited for the study. The mortality was signed off by the nephrologists based on the guidelines of reporting death of the institution. The sample size for cohort was determined using the OpenEpi calculator, with the following parameters: 95% confidence interval, 80% power of test, and a uric acid toalbumin ratio of 3.3±1.5 mg/g in survival group and 2.5±1.0 mg/g in non-survival group; alpha error of < 5% ($p < 0.05$) was taken to be significant.[10]

Exclusion criteria: Patients who were not fulfilled the AKI criteria, excluded from study.

Sampling technique: The study employed a non-probability consecutive sampling technique.

Data collection procedure: The study-specific report forms documented the demographic details, comorbidities, and clinical manifestations of all study participants. Additionally, stay of hospital duration was noted from admission to hospital discharge. Mortality was recorded in 30 days from preliminary admission. Serum creatinine levels (including baseline levels from last 3 months, if available), albumin, urea, potassium, sodium, calcium, chloride, phosphorus, hemoglobin level, uric acid, pH, and bicarbonate (determined through venous blood gases) at the time of admission were documented. Additionally, to the presence of hematuria, proteinuria, and pyuria detected in urinalysis using a urine dipstick, albumin levels were measured in spot urine samples using the turbid metric method (mg/L). Levels of albumin and creatinine in spot urine were equaled to one another,

and the ratio of albumin to creatinine in urine was measured as a value in mg/g.

Statistics analysis: After assessing the data distributions, quantitative parameters were presented as mean and SD. Qualitative parameters were presented as frequency and percentage. The descriptive statistics including age, gender, and comorbid, were presented as mean and percentages. The demographics and comorbid of patients in survivor and non-survivor group were compared by independent t test for statistically significance differences in these parameters. To identify optimal uric acid to albumin cutoff level for predicting 30days mortality, diagnostic odd ratio (calculated as the ratio of (+) likelihood to (-) likelihood ratios), the index ratios (calculated as % sensitivity + specificity - 100), and the area under curve (ROC; calculated as sensitivity + specificity / 2) were utilized. Survival analysis for 30days period was conducted using Kaplan-Meier curve. Analysis of Cox regression was employed to determine the correlation between uric acid to albumin ratio and mortality. The probability p-value of 0.05 or less was deemed significantly. The datawas analyzed at SPSS v 25.

Results:

The patients mean age was58.35±14.18 years. Among them, 35% were female and 65% were male. Among the patients, 32.5% had hypoalbuminemia, and 75% had hyperuricemia. Comorbidities included hypertension (HTN) in 60% of patients, chronic kidney disease (CKD) in 47.5%, diabetes mellitus (DM) in 30%, malignancy in 20%, coronary artery disease (CAD) in 20%, congestive heart failure (CHF) in 15%, COPD in 10%, stroke history in 5%, and liver cirrhosis in 2.5% (Table 1), these difference between the two groups are not statistically significant.

Total mortality was15% of patients (n=12) during 30 days period, with 12.5% (n=10) expiring during their hospital stay.

Table 1: Demographics statistics and comorbidities, n=80

Variables	Survivor (n=68)	Non-survivor (n=12)	p value
Ages (years)	57.96±13.44	61.44±10.89	.458
Male	43 (63.2%)	9 (75%)	.394
Females	25 (36.8%)	3 (25%)	.394
DM	20 (29.4%)	4 (33.3%)	.573
HTN	41 (60.3%)	8 (66.7%)	.621
CKD	32 (47.1%)	5 (41.7%)	.601
Malignancy	13 (19.1%)	5 (41.7%)	.072
Liver cirrhosis	2 (2.9%)	1 (8.3%)	.115

The uric acidtoalbumin ratio was significantly higher in non-survivor compared to survivor (3.57±1.6vs2.84±1.2, p=0.001) groups. The ROC curve analysis was performed to evaluate the diagnostic accuracy of the model. The Area under the Curve (AUC) was 0.85 (95% CI: 0.80–0.90), indicating good discriminatory ability. At the optimal cutoff point of 0.45, the sensitivity was 0.78 and the specificity was 0.82. The ROC curve is shown in Figure 1.

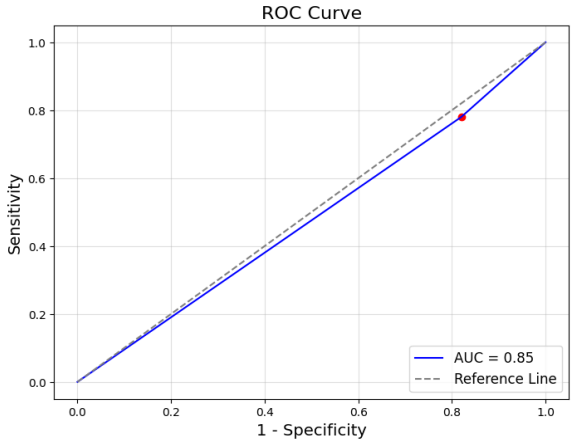

Figure 1: ROC curve of AUC based on ratio of uric acid to albumin (specificity and sensitivity)

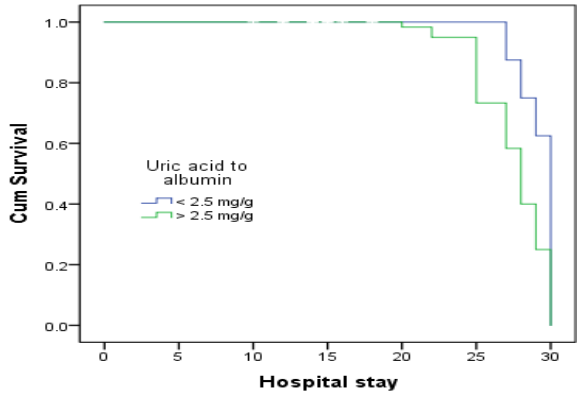

Figure2: Survival curve of Kaplan-Meier based on uric acidtoalbumin ratio.

In Kaplan-Meier curve (Fig. 2), the ratio ofuric acidtoalbumin> 2.5 was significantly high in 30days mortality (test of logrank, p=0.001).There was a noticeable difference in 30days cumulative rate of survival between the low uric acidtoalbumin ratio group (88.1%±3%) and the high uric acidtoalbumin ratio group (66.3%±4%).The estimated survival time for the low uric acidtoalbumin ratio group was 25.6 days (95% CI: 24-30), while the high uric acidtoalbumin ratio group had an estimated survival time of 21.5 days (95% CI: 20-23).

The Cox regression model included age, proteinuria, malignancy status, respiratory rate, albumin level, uric acid level, and uric acid to albumin ratio. The hazard ratio (HR) for uric acid to albumin ratio was 1.48 (95% CI: 1.10–2.10, $p < 0.01$), indicating a significant increase in risk associated with 30 days mortality. The overall model fit was assessed using the likelihood ratio test, which was significant ($\chi^2 = 15.23$, $p < 0.001$). The concordance index (C-index) for the model was 0.72, suggesting good predictive accuracy.

Table2: Cox regression hazard ratio for 30 days mortality, n=80

Variable	Attributes	Mortality			Univariate analysis		Multivariate analysis	
		Yes	No	RowTotal	HR(95%CI)	p-value	HR(95%CI)	p-value
UAAR	High	10	34	44	1.5 (1.2 – 1.9)	.001	1.48 (1.1 – 2.0)	.03
	Low	2	34	36	Reference		Reference	
Sex	Men	9	43	52	1.6 (0.7 – 1.9)	.555	1.55 (0.8 – 1.9)	.651
	Women	3	25	28	-		-	
Age	< 60 years	6	38	44	1.1 (0.9 – 1.2)	.017	0.8 (0.7 – 1.1)	.636
	> 60 years	6	30	36	-		-	
DM	Yes	4	20	24	2.2 (1.3 – 4.5)	.022	1.9 (1.0 – 5.0)	.162
	No	8	48	56	-		-	
HTN	Yes	8	41	49	3.0 (1.6 – 6.0)	.002	2.8 (1.3 – 7.0)	.432
	No	4	27	31	-		-	
Malignancy	Yes	5	13	18	2.0 (1.1 – 3.0)	.016	1.5 (0.7 – 3.0)	.262
	No	7	55	62	-		-	
IHD	Yes	4	12	16	2.9 (1.6 – 7.0)	.002	2.6 (1.1 – 4.5)	.321
	No	8	56	64	-		-	
COPD	Yes	1	7	8	1.2 (0.9 – 1.3)	.001	1.2 (1.1 – 1.3)	.021
	No	11	61	72	-		-	
CCF	Yes	2	10	12	1.0 (0.7 – 1.1)	.001	-	-
	No	10	58	68	-		-	
Stroke	Yes	1	3	4	0.6 (0.4 – 0.9)	.01	-	-
	No	11	65	76	-		-	

Discussion:

The study investigated the role of uric acidtoalbumin ratio in AKI patients and its association with 30days mortality. The correlation in mortality and the uric acidtoalbumin ratio was found to be independent of age, respiratory rate, malignancy, and as cites in multivariate analysis. In present study, the optimal ratio of uric acidtoalbumin cutoff for predicting 30days mortality in AKI patients was identified as 2.5 mg/g, sensitivity 78%, and specificity82%.

In a study, the ratio of uric acidtoalbumin was 1.78 observed to be associated with AKI, but its association with mortality is not ascertained.10Inpresent study, correlation between the ratio of uric acidtoalbumin identified and an elevated risk of 30days mortality in

patients who develop AKI. Hypoalbuminemia has long been recognized as an indicator of both morbidity and mortality. The study by Shao et al discovered that hypoalbuminemia is a risk factor for both the occurrence of AKI and long-term mortality.12A meta-analysis revealed that hypoalbuminemia is an indicator of both AKI occurrence and mortality.[13]Thepresent study was unable to identify the risk factors for occurrence of AKI as focused on patients who occurred AKI at the beginning of the study. Nonetheless, hypoalbuminemia is linked to heightened mortality rates in AKI patients.It's worth noting that patients who died within 30 days had significantly lower albumin levels compared with survivors throughout their hospitalization. Malnutrition could be a potential explanation, as it can directly affect the albumin level.[14]While, there is no evidence supporting the use of albumin therapy to address hypoalbuminemia to improve survival rate.[15]

In diabetic patients, there is a correlation between uric acid and albumin in urine, which is linked to the presence of Microalbuminuria and atherosclerosis.[15,16]Uric acid has also been suggested as a potential biomarker in occurrence of diabetic nephropathy.[17]It is recognized that albumin in urine contributes to hypoalbuminemia in patients with both CKD and AKI.[18]Furthermore, albuminuria is associated with an increased risk of mortality in cardiovascular, even among individuals in general population.[19]The notable findings in present study were the disparity in albumin, despite no change being observed in albumin in urine between the groups based on 30days mortality and the ratio of uric acidtoalbumin.This indicates that the development of hypoalbuminemia may be due to it being a negative acute-phase reactant rather than through loss in urine.

Previous research has demonstrated associations between low albumin and high uric acid with the occurrence of AKI and high mortality. By integrating these two closely linked factors identified in previous research, we have established a more powerful indicator of mortality. In our analysis of short-term mortality, we identified optimal sensitivity and specificity, ROC, and HR, along with determining the best cutoff level. When dividing patients in two groups based on cutoff level, we found that a high uric acidtoalbumin ratio was significantly correlated with a higher mortality and shorter survival time.

Although this study had several strengths, it also had some limitations. One limitation is that we did not consider patient treatments medical conditions that emerged post-hospitalization, which could have influenced mortality outcomes. Another limitation is that our findings may not be generalizable to other diseases, as it was conducted solely in patients with AKI. Despite this limitation, our study can serve as a template for future research in different diseases and broader populations.

Conclusion:

This study concluded that ages of the patients and clinical findings of uric acid to albumin ratio to be associated with a heightened risk of short-term mortality in acute kidney injury patients. Therefore, the study provides a practical, outcome-oriented approximation without delving into etiological distinctions.

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