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ORIGINAL ARTICLE

Serum Fibrinogen to Serum Albumin Ratio as a prognostic Factor among Acute Kidney Injury Patients

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Abstract

Background: Acute kidney injury (AKI) is considered occurs frequently among the ICU patients, leading to longer hospital stays, more complications, as well as mortality. Inflammation plays significant role in AKI, the fibrinogen to albumin ratio (FAR), is an inflammation marker that could help in prediction of outcomes among these patients. We aimed in this work to assess the prognostic role of FAR for prediction of the hospital mortality among critically ill patients who had AKI.

Methods: This prospective cohort study was conducted on 120 adults who had AKI who were admitted to the ICU, we collected their medical history, laboratory investigations included fibrinogen and albumin levels, and calculated FAR, the Simplified Acute Physiology Score (SAPS), as well as Sequential Organ Failure Assessment (SOFA) scores. We tracked whether patients got discharged or died during their ICU stay.

Results: Out of the 120 patients, 31 (25.8%) died. We found that those who died had higher levels of FAR, fibrinogen, creatinine, and BUN (all with P<0.001). Smoking (P=0.009) and congestive heart failure (P=0.02) were also more common in the patients who didn't survive. FAR was positively linked to SOFA and SAPS II scores, as well as other laboratory markers. The ROC curve showed FAR had a strong ability to predict death, with an AUC of 0.856 at a cut-off of 0.79. In multivariate logistic regression analysis, FAR was identified as a significant independent predictor of mortality (odds ratio [OR] 1.36, 95% CI 1.48–1.52, P<0.001), along with other factors such as smoking (OR 3.04, 95% CI 1.29–7.16, P=0.01) and congestive heart failure (OR 3.06, 95% CI 1.26–7.43, P=0.01).

Conclusions: An elevated FAR has been linked to an increase in hospital mortality in critically ill patients with AKI, suggesting its potential utility as a prognostic indicator among these patients.

Keywords: Fibrinogen to Serum Albumin Ratio; Prognostic Factor ;Acute Kidney Injury.

INTRODUCTION

Acute kidney injury (AKI) is a common complication that occurs frequently during the course of critically ill patients, often resulting in prolonged ICU stays, higher rates of complications, and increased short- and long-term mortality. Survivors are also at elevated risk of

progressing to chronic kidney disease or end-stage renal disease [1,2].

Recent studies highlight that early detection and proactive management of AKI risk factors can reduce in-hospital mortality among critically ill patients [3,4]. As such, it's important to find cost-effective, reliable clinical markers that either outperform or meaningfully enhance current ICU scoring systems for predicting AKI outcomes.

Inflammation plays a central role in both the onset and progression of AKI, supported by growing mechanistic and experimental research [5,6]. In response, researchers have explored the utility of systemic inflammation markers as predictors of AKI, with promising results for combined indices like neutrophil-to-lymphocyte ratio and cell cycle biomarkers [7.8].

Similarly, serum fibrinogen, an acute-phase reactant produced by the liver, increases in response to inflammation and tissue injury. Elevated fibrinogen levels are often observed in critically ill patients and are linked to a prothrombotic state, increased microvascular dysfunction, and poor clinical outcomes. High fibrinogen concentrations have been independently associated with a higher risk of mortality and major adverse events in patients with AKI, likely reflecting the underlying inflammatory and coagulative disturbances present in this population [9].

Recently, the fibrinogen-to-albumin ratio (FAR) has gained attention as a new marker of inflammation and prognosis. FAR has demonstrated predictive value for outcomes in various malignancies and cardiovascular events [9–12]. Specifically related to renal injury, studies have linked elevated FAR to contrast-induced nephropathy and post-contrast AKI [13,14]. However, evidence remains limited regarding FAR's role in predicting general AKI prognosis across ICU populations.

While FAR has shown prognostic value in cancer and cardiovascular conditions, its utility in predicting outcomes in general ICU patients with AKI remains unclear. Most existing studies focus on specific subgroups, limiting broader applicability. This highlights the need for research evaluating FAR as a prognostic marker across diverse AKI cases in critical care settings. So, we aimed in this work to assess the prognostic role of FAR for prediction of the hospital mortality among critically ill patients who had AKI.

METHODS

This prospective cohort study was conducted at the Internal Medicine Department, Faculty of Medicine, Zagazig University over a period of six months from June 2024 to December 2024.

A comprehensive sampling technique was adopted, including all eligible patients admitted during the study period. Based on an estimated ICU admission rate of 20 cases per month and a 6-month duration, a total of 120 patients were expected to be enrolled. Sample size calculations were performed utilizing the OPEN-EPI software with a confidence interval of 95% utilizing a power of 80%.

Institutional Review Board (ZU-IRB#10667/9/4-2023) clearance was obtained and informed consent was collected from all patients who participated in the study. The research was conducted following the World Medical Association's Code of Ethics (Helsinki Declaration) for studies involving human subjects.

The study included patients aged 18 years or older who were diagnosed with acute kidney injury according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria: an elevation of serum creatinine (SCr) of at least 0.3 mg/dL (or 26.5 µmol/L) in the span of 48 hours; an increase of at least 1.5 times the baseline in SCr, either known or suspected to have happened within

the last 7 days; or urine output below 0.5 mL/kg/h for 6 hours, with patients admitted to the intensive care unit (ICU) for at least 48 hours during their initial admission [1]. For patients without a recent pre-admission creatinine, the lowest measured value during hospitalization was used as the baseline, consistent with KDIGO and critical care practice recommendations

Patients were excluded if they had chronic liver disease, chronic kidney disease, malnutrition, major burns, were pregnant, or had received albumin or fresh frozen plasma within the past month. Additional exclusions included those on steroid therapy and patients with more than 5% missing individual data.

Clinical Assessment

Upon inclusion, all participants underwent comprehensive clinical evaluations, including a detailed history and physical examination. Imaging studies, particularly ultrasonography, were reviewed. Routine laboratory investigations included complete blood count (CBC), renal and liver function tests, and coagulation profiles.

Outcome Measures

The primary outcome was in-hospital mortality. To assess illness severity, both SOFA as well as SAPS II were assessed within 24 hours of ICU admission.

The SOFA score has been calculated by assessing the function of six organ systems, involving respiratory, cardiovascular, coagulation, liver, central nervous system, as well as renal, each of them scored from 0 to 4, from less dysfunction based on clinical and laboratory criteria to more. The key input parameters included the PaO_2/FiO_2 ratio, platelet count, bilirubin level, mean arterial pressure or vasopressor use, Glasgow Coma Scale, and serum creatinine or urine output. Possible scores ranged from 0 to 24; the higher the value, the more the organ dysfunction and the higher the probability of mortality [15].

The SAPS II score was derived from 17 variables recorded within the first 24 hours of ICU admission, including 12 physiological measures, age, type of admission, and presence of chronic diseases such as AIDS or metastatic cancer. Each variable was weighted and summed to produce a total score, which was then applied to a logistic regression formula to estimate hospital mortality, with higher scores indicating more severe illness and increased risk of death [15].

Data Management and Extraction

Structured query language (SQL) was used for the data extraction purpose from the MIMIC-III database (PostgreSQL v9.6). Variables included demographic information, comorbidities (which included examples such as coronary artery disease (CAD),atrial fibrillation (AF), heart failure, diabetes, COPD, pneumonia, ARDS, and stroke), and laboratory data. The data that were taken into account for the study were from each patient's first ICU admission only [16].

Laboratory investigations

Venous blood samples were drawn aseptically via venipuncture on days 1, 3, and 7 after ICU admission. Two milliliters of blood were placed in EDTA tubes for CBC analysis using an automated cell counter (Sysmex XN-330, Japan). Three milliliters were collected in plain tubes, allowed to clot at 37°C for 10 minutes, and centrifuged at 1200 ×g. Another 2 mL were placed in sodium-citrated tubes for fibrinogen analysis, which was conducted using a Sysmex CA-1500 system, following established methods as previously described [17,18]. Serum albumin was measured using the Cobas 8000 autoanalyzer, as reported in earlier studies [17,18]. The fibrinogen-to-albumin ratio (FAR) was calculated accordingly. The 7-day follow-up period was selected as it encompasses the acute phase of critical illness and the majority of

ICU-related complications in AKI patients. This timeframe is commonly used in prognostic studies to capture early outcomes, allow for monitoring of dynamic laboratory changes, and provide a standardized window for outcome assessment.

Statistical analysis

Data analysis was performed with the assistance of SPSS software, version 23.0 (SPSS Inc., Chicago, IL, USA). The qualitative variables were presented as counts and percentages. At the same time, quantitative variables were presented as a mean ± SD or median (IQR) depending on the distribution of data. Group comparisons were carried out using Chi-square or Fisher's exact tests for categorical data, whereas independent sample t-test or Mann-Whitney U test was carried on continuous data. Correlations were established by either the Pearson or Spearman coefficient. Predictors of binary outcomes underwent logistic regression, whereas diagnostic accuracy was assessed using ROC curve analysis and AUC values contouring test performance. The value of p for statistical significance was ≤0.05.

RESULTS

The patients' ages ranged from 21 to 80 years, with a mean age of 66.1 ± 10.7 years. The majority of patients were male (71.7%), while females accounted for 28.3%. Regarding smoking status, 70% of the patients were non-smokers, and 30% were smokers. The most common comorbidity among the studied population was diabetes mellitus (DM), affecting 42.5% of patients, followed by hypertension (35%), congestive heart failure (CHF) (25%), CAD (22.5%), as well as atrial fibrillation (16.7%) (Table 1).

Baseline laboratory results showed a median TLC of $8.8 \times 10^3/mm^3$, hemoglobin of 9 gm/dL, and platelets of $115 \times 10^3/mm^3$, indicating common cytopenias. Liver enzymes were mildly elevated (AST 54.5 U/L; ALT 25 U/L), with a median bilirubin of 2 mg/dL. Median serum creatinine and BUN were 1.21 mg/dL and 28 mg/dL, respectively. The median INR was 1.5 and FAR was 0.065. ABG analysis revealed metabolic acidosis, with a median pH of 7.21, bicarbonate 22 mEq/L, and an anion gap of 15.5 mmol/L (Table 2).

Analysis of ICU outcomes revealed a statistically significant association between smoking status and mortality; 48.4% of non-survivors were smokers compared to 23.6% among discharged patients ($p = 0.009$). Additionally, CHF was significantly more prevalent among those who died (41.9%) than those discharged (19.1%) ($p = 0.022$) (Table 3).

Significant laboratory differences were exhibited between survivors and non-survivors. Patients who died had higher median serum creatinine (1.34 vs. 0.9 mg/dL, $p < 0.001$), BUN (35 vs. 26.4 mg/dL, $p < 0.001$), fibrinogen (3.5 vs. 2.3 g/dL, $p < 0.001$), and fibrinogen-to-albumin ratio (FAR) (0.064 vs. 0.89, $p < 0.001$). Regarding arterial blood gases, non-survivors had significantly higher pH (7.39 vs. 7.37, $p = 0.041$), PCO_2 (37 vs. 33 mmHg, $p = 0.007$), and bicarbonate levels (24 vs. 19 mEq/L, $p < 0.001$), suggesting compensated metabolic acidosis or mixed disturbances. (Table 4).

Table (5) exhibits a highly significant positive correlation between FAR with SOFA score (r=0.237, P=0.001), SAPS II (r=0.244, P=0.001), Pco2 (r=0.277, P=0.002), Hco3 (r=0.330, P<0.001), fibrinogen (r=0.841, P<0.001) and serum Creatinine (r=0.245, P=0.007). Furthermore, FAR exhibits a highly significant negative correlation with TLC (r=-0.201, P=0.03) and albumin (r=-0.356, P<0.001).

On conducting ROC curve analysis on FAR for discriminating between discharged and died patients, at cut off point of 0.79, it

shows sensitivity (64.3%), specificity (96.6%) and AUC 0.856 (Figure 1).

In logistic regression analysis, significant independent predictors of ICU mortality included FAR (OR 1.36, 95% CI 1.48–1.52, P<0.001), smoking (OR 3.04, 95% CI 1.29–7.16, P=0.01), and congestive heart failure (OR 3.06, 95% CI 1.26–7.43, P=0.01), as well as SOFA and SAPS II scores (Table 6).

Supplementary Table (1) shows a statistically significant correlation between FAR and associated comorbidities, as FAR levels were higher among diabetic patients (P<0.001), hypertensive patients (P=0.02), patients with CAD (P=0.04), patients with AF (P=0.02), and patients with CHF (P=0.04).

Table 1: Demographic data and comorbidities among studied patients

Variables	All patients (n=120)
Age *(years)* Mean ± SD Range	 66.1 ± 10.7 (21 – 80)
Sex *(N. %)* – Male – Female	 86 (71.7%) 34 (28.3%)
Smoking status *(N. %)* – Non smoker – Smoker	 84 (70%) 36 (30%)
Diabetes mellitus	51 (42.5%)
Hypertension	42 (35%)
Coronary artery disease	27 (22.5%)
Atrial fibrillation	20 (16.7%)
Congestive heart failure	30 (25%)

Table 2: Laboratory data and ABG findings among studied patients

	All patients (n=120)			
	Median	IQR	Minimum	Maximum
TLC *($10^3/mm^3$)*	8.8	6.4	3.4	30
Hb *(g/dL)*	9	3	4.1	15
PLT *($10^3/mm^3$)*	115	82.8	70	411
Bilirubin *(mg/dL)*	2	3.3	0.2	35
Albumin *(g/dL)*	3.7	0.5	3	4.5
AST *(U/L)*	54.5	80	15	177
ALT *(U/L)*	25	34	14	255
Creatinine *(mg/dL)*	1.21	1.55	0.5	7
BUN *(mg/dl)*	28	18	15	55
Na *(mEq/L)*	135	8.1	115	145
Ca+ *(mg/dL)*	7.9	0.73	7.2	11.1
K *(mmol/L)*	3.6	1.01	2.5	5.7
Mg *(mg/dL)*	2.1	0.5	1.72	4.6
Ph *(mg/dL)*	3.1	1.33	1.3	10.5

	All patients (n=120)			
	Median	IQR	Minimum	Maximum
INR	1.5	0.2	1.01	3.5
Fibrinogen	2.3	0.33	1.2	4.2
FAR	0.065	0.14	0.052	1.25
PH	7.21	0.12	7.09	7.5
Pco2 *(mmhg)*	32	10	14	45
Hco3 *(mEq/L)*	22	5	5	29
Anion gap *(mmol/L)*	15.5	8	5	25

TLC: Total Leukocyte Count, Hb: Hemoglobin, PLT: Platelets, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, BUN: Blood Urea Nitrogen, Na: Sodium, Ca^{+}: Calcium, K: Potassium, Mg: Magnesium, Ph: Phosphate, INR: International Normalized Ratio, FAR: Fibrinogen-to-Albumin Ratio, PH: Potential of Hydrogen (blood pH), Pco_2: Partial Pressure of Carbon Dioxide, Hco_3: Bicarbonate, ABG: Arterial Blood Gases.

Table 3: Association between ICU fate with different demographic data and different clinical data

Variables	**Discharged (n=89)**	**Died (n=31)**	**P value**
Age *(years)* Mean ± SD Range	 66.6 ± 9.26 (37 – 85)	 64.4 ± 14.1 (21 – 80)	 0.39[1]
Sex *(N. %)* – Male – Female	 64 (71.9%) 25 (28.1%)	 22 (71%) 9 (29%)	 0.92[2]
Smoking status *(N. %)* – Non smoker – Smoker	 68 (76.4%) 21 (23.6%)	 16 (51.6%) 15 (48.4%)	 **0.009[2]**
Diabetes mellitus	39 (43.8%)	12 (38.7%)	0.62[1]
Hypertension	31 (34.8%)	11 (35.5%)	0.95[1]
Coronary artery disease	19 (21.3%)	8 (25.8%)	0.61[1]
Atrial fibrillation	14 (15.7%)	6 (19.4%)	0.78[2]
Congestive heart failure	17 (19.1%)	13 (41.9%)	**0.02[2]**

ICU: Intensive Care Unit, CAD: Coronary Artery Disease, AF: Atrial Fibrillation, CHF: Congestive Heart Failure, P: P-value (statistical significance).

*[1]Mann-Whitney U test, [2]Chi-square test / Fisher's exact test, Non-significant: P >0.05, Significant: P ≤0.05

Table 4: Association between ICU fate and laboratory data among studied patients

Variables	Discharged (n=89)	Died (n=31)	P value
TLC *($10^3/mm^3$)*	9 (8.8)	7.3 (3.25)	0.33[1]
Hb *(g/dL)*	9 (3)	9.2 (2.25)	0.55[2]
PLT *($10^3/mm^3$)*	115 (81)	115 (84)	0.85[1]
Bilirubin *(mg/dL)*	2.1 (4.2)	1.6 (2.1)	0.06[1]
Albumin *(g/dL)*	3.7 (0.5)	3.7 (0.35)	0.62[2]
AST *(U/L)*	41 (81)	59 (80.5)	0.95[1]
ALT *(U/L)*	25 (37)	32 (25)	0.9[1]
Creatinine *(mg/dL)*	0.9 (0.4)	1.34 (1.7)	**<0.001**[1]
BUN *(mg/dl)*	26.4 (22)	35 (24)	**<0.001**[1]
Na *(mEq/L)*	134 (9)	134 (7.5)	0.79[1]
Ca+ *(mg/dL)*	7.8 (0.8)	8.2 (0.7)	0.09[1]
K *(mmol/L)*	3.9 (1.1)	3.9 (1)	0.87[1]
Mg *(mg/dL)*	2 (0.6)	1.9 (0.3)	0.64[1]
Ph *(mg/dL)*	3.1 (1.6)	3 (1.15)	0.69[1]
INR	1.5 (0.3)	1.4 (0.45)	0.17[1]
Fibrinogen *(g/dL)*	**2.3 (0.2)**	**3.5 (1.5)**	**<0.0011**
FAR	**0.064 (0.09)**	**0.89 (0.34)**	**<0.0011**
PH	7.37 (0.14)	7.39 (0.06)	**0.04**[1]
Pco2 *(mmhg)*	33 (12)	37 (7)	**0.007**[1]
Hco3 *(mEq/L)*	19 (8)	24 (7)	**<0.001**[1]
Anion gap *(mmol/L)*	16 (8)	15 (8)	0.45[1]

TLC: Total Leukocyte Count, Hb: Hemoglobin, PLT: Platelets, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, BUN: Blood Urea Nitrogen, Na: Sodium, Ca^+: Calcium, K: Potassium, Mg: Magnesium, Ph: Phosphate, INR: International Normalized Ratio, FAR: Fibrinogen-to-Albumin Ratio, PH: Potential of Hydrogen (blood pH), Pco_2: Partial Pressure of Carbon Dioxide, Hco_3: Bicarbonate, ICU: Intensive Care Unit, P: P-value (statistical significance).*[1]Mann-Whitney U test, [2]Student's T test, Non-significant: P >0.05, Significant: P ≤0.05

Table 5: Correlation of FAR with different laboratory data

Variable	FAR	
	r	*P*
Age	-0.086	0.35[2]
SOFA score	0.237	**0.001**[2]
SAPS II	0.244	**0.007**[2]
Length of ICU stay	0.241	0.12[2]
TLC	-0.201	**0.03**[1]
Serum Creatinine	**0.245**	**0.0072**
Pco2	**0.277**	**0.0022**
Hco3	0.330	**<0.001**[2]
Albumin	-0.356	**<0.001**[2]
Fibrinogen	0.841	**<0.001**[2]

FAR: Fibrinogen-to-Albumin Ratio, SOFA: Sequential Organ Failure Assessment, SAPS II: Simplified Acute Physiology Score II, TLC: Total Leukocyte Count, Pco_2: Partial Pressure of Carbon Dioxide, Hco_3: Bicarbonate. *[1]Pearson correlation, [2]Spearman rank correlation test, Non-significant: P >0.05, Significant: P ≤0.05

Table 6: Logistic regression analysis for predictors of mortality

Variables	P value	Odds (CI 95%)
Age	0.32	1.02 (0.98 – 1.06)
Sex	0.92	0.96 (0.39 – 2.36)
Smoking status	**0.01**	3.04 (1.29 – 7.16)
CHF	**0.01**	3.06 (1.26 – 7.43)
SOFA score	**<0.001**	1.39 (1.16 – 1.68)
SAPS II	**<0.001**	1.04 (1.09 – 1.69)
Bilirubin	**0.04**	1.12 (1.00 – 1.25)
Serum Creatinine	**0.003**	2.78 (1.4 – 5.52)
Pco2	**0.005**	0.89 (0.83 – 0.97)
Hco3	**<0.001**	0.85 (0.78 – 0.94)
Fibrinogen	**<0.001**	0.04 (0.013 – 0.15)
FAR	**<0.001**	1.36 (1.48 – 1.52)
Length of ICU stay	**0.03**	1.17 (1.012 – 1.35)

CHF: Congestive Heart Failure, SOFA: Sequential Organ Failure Assessment, SAPS II: Simplified Acute Physiology Score II, Pco_2: Partial Pressure of Carbon Dioxide, Hco_3: Bicarbonate, FAR: Fibrinogen-to-Albumin Ratio, CI: Confidence Interval, P: P-value (statistical significance).

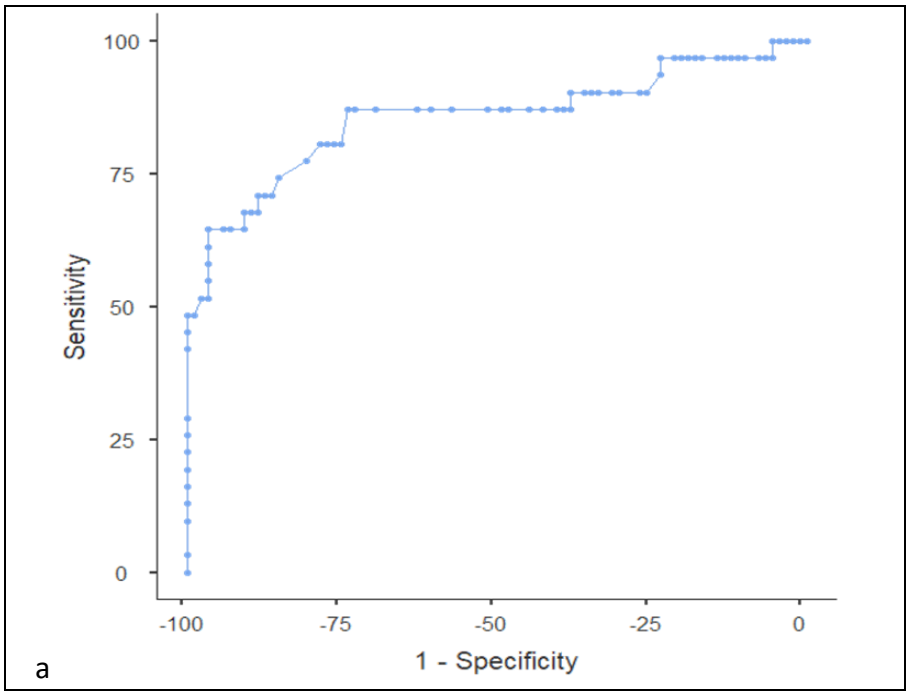

Figure (1): ROC curve analysis of FAR in differentiating discharged from died patients

DISCUSSION

Recent studies have emphasized the clinical utility of the fibrinogen-to-albumin ratio (FAR) in critically ill patients. Xia et al. [17] reported that elevated FAR levels were significantly correlated with increased mortality and multiorgan dysfunction in patients with acute kidney injury (AKI). Similarly, Kim et al. [18] identified FAR as an independent predictor of adverse outcomes in ICU patients with comorbidities such as diabetes, CAD, and chronic kidney disease. In patients with septic AKI, Zhan et al. [19] demonstrated that a high FAR on ICU admission was closely linked to poor clinical trajectories, highlighting its value in early risk stratification. Moreover, Xu et al. [20] extended these findings by showing that preoperative FAR predicted the development of postoperative AKI in patients undergoing cardiac surgery, supporting its role beyond traditional inflammatory indices.

In the current study, DM emerged as the most common comorbidity, affecting 42.5% of patients with AKI, followed by hypertension (35%), CHF (25%), CAD (22.5%), as well as the atrial fibrillation (AF) (22.5%). This was in line with recent research, which indicates a high prevalence of metabolic and cardiovascular disorders among AKI patients. DM has long been recognized as a major factor contributing to both the onset as well as the progression of AKI. Li et al. [21] found that patients with both DM and CHF frequently exhibit worse renal outcomes, underscoring the synergistic impact of these conditions. Similarly, Kuźma et al. [22] reported that DM and hypertension were among the most frequent comorbidities in patients at risk of contrast-induced AKI, which aligns with our observations.

Hypertension and CHF also featured prominently in our findings. This is in line with Go et al. [23], who found that cardiovascular comorbidities, including CHF and CAD, significantly increase the risk of poor outcomes following AKI. The role of hypertension and AF in heart failure progression was further reinforced by Bavishi and Patel [24], who emphasized their interconnected pathophysiology and

the frequent coexistence of renal dysfunction. While AF and CAD were the least prevalent conditions in our study, their impact remains clinically significant. Iacob et al. [25] identified AF as a major determinant in the risk stratification of patients with cardiorenal syndrome, and Horodinschi and Diaconu [26] noted that concurrent AF and CAD markedly increase mortality in patients with renal impairment.

The current study findings revealed a significant association between elevated FAR and several comorbidities: DM ($p < 0.001$), hypertension ($p = 0.02$), CAD ($p = 0.04$), AF ($p = 0.02$), and CHF ($p = 0.04$). These associations support the role of FAR as a marker of the underlying pro-inflammatory and pro-thrombotic milieu characteristic of chronic cardiometabolic diseases. The link between FAR and DM has been well established in literature. Chen et al. [27] found that patients with type 2 diabetes had significantly higher FAR levels, which correlated with increased arterial stiffness. This was supported by Wang et al. [28], who reported that FAR predicted adverse outcomes in diabetic patients undergoing percutaneous coronary interventions, and by Zhao et al. [29], who linked elevated FAR with cardiac autonomic neuropathy in diabetes.

Beyond diabetes, FAR has also been validated as a prognostic tool in cardiovascular disease. Xu et al. [30] demonstrated that FAR independently predicted outcomes in heart failure patients, irrespective of diabetic status. In CAD, Li et al. [31] showed that elevated FAR correlated with greater disease severity and poorer long-term prognosis among patients with non-ST elevation acute coronary syndrome.

In comparing laboratory data between ICU survivors and non-survivors, we observed that non-survivors had significantly higher levels of serum creatinine, blood urea nitrogen (BUN), fibrinogen, and fibrinogen-to-albumin ratio (FAR), all with strong statistical significance ($p < 0.001$). These elevated markers reflect both compromised renal function and systemic inflammation, underscoring their potential as prognostic indicators in critically ill patients with acute kidney injury (AKI). The observed rise in creatinine and BUN aligns with prior findings that identify these markers as reliable indicators of renal dysfunction and increased mortality risk in AKI patients [17,19].

Notably, FAR levels were consistently elevated among non-survivors, consistent with the results of Xia et al. [17] and Zhan et al. [19], who reported strong associations between high FAR and adverse clinical outcomes in AKI cohorts. This supports the utility of FAR as a surrogate marker for both inflammatory burden and disease severity in critical care settings.

In contrast, non-significant differences were revealed as regards hemoglobin, platelet count, or liver enzyme levels between survivors and non-survivors, suggesting limited prognostic value for these parameters in AKI-related mortality. These findings echo those of Kim et al. [18], who concluded that inflammation-based markers such as FAR were more closely associated with mortality risk than general hematological or hepatic indices.

We also found that patients who did not survive their ICU stay had significantly higher arterial pH, partial pressure of carbon dioxide (PCO_2), and bicarbonate (HCO_3^-) levels ($p < 0.05$ for all), suggesting a tendency toward metabolic alkalosis or compensated respiratory acidosis. These acid–base imbalances may signal ventilatory impairment, fluid shifts, or chronic hypercapnic compensation. Ko et al. [32] similarly found elevated arterial pH to be significantly associated with increased mortality in ICU patients with AKI and acute hypoxic respiratory failure.

A significant positive correlation was observed between FAR and SOFA score (r = 0.237, p = 0.001) and also with SAPS II (r = 0.244, p = 0.001), indicating that FAR mirrors the overall inflammatory status and severity of organ dysfunction, which aligns well with what the normal ICU scoring systems convey. Xia et al. [17] also arrived at a similar conclusion in their study, reporting that FAR values significantly correlated with SOFA and SAPS II scores in patients with AKI. Zhan et al. [19] further highlighted that FAR predicted poor outcomes particularly in patients with SOFA scores ≥7, reinforcing its role in multi-organ dysfunction assessment.

Interestingly, non-significant variations in anion gap values was found between survivors and non-survivors in our study (p = 0.451). This contrasts with reports by Sim et al. [33] and Lee et al. [34], who found higher anion gap values to be predictive of mortality in AKI patients, particularly in the context of acute poisoning or paraquat intoxication. These inconsistencies may be due to variations in AKI etiology, timing of arterial blood gas collection, or differences in fluid status and compensatory mechanisms. Achanti and Szerlip [35] have emphasized that acid–base imbalances in critically ill patients are often multifactorial and dynamic, and thus isolated markers such as the anion gap may not reliably indicate disease severity when interpreted in isolation.

In our study, the fibrinogen-to-albumin ratio (FAR) demonstrated statistically significant correlations with various physiological and biochemical parameters, including partial pressure of carbon dioxide (PCO_2) (r = 0.277, p = 0.002), bicarbonate (HCO_3^-) (r = 0.330, p < 0.001), fibrinogen (r = 0.841, p < 0.001), and serum creatinine (r = 0.245, p = 0.007). Despite extensive literature supporting FAR as a prognostic marker, there is a notable lack of studies exploring its direct relationship with acid–base variables such as PCO_2 and HCO_3^- in critically ill AKI patients. Ahmed et al. [36] described abnormal arterial blood gas (ABG) values in ICU patients but did not evaluate correlations with FAR. Similarly, the relationship between FAR and serum creatinine remains under-investigated in this context.

The observed associations between FAR and acid–base indicators suggest a possible link to respiratory or metabolic compensation states. Such patterns are consistent with inflammatory and ventilatory pathophysiology commonly seen in chronic critical illness, as described by Achanti and Szerlip [35]. In our study, we found a positive correlation between FAR and serum creatinine, indicating that as renal function worsens (higher creatinine), there is a concomitant rise in FAR, likely reflecting the dual impact of increased inflammation and declining kidney function in critically ill AKI patients. This is consistent with the established understanding that both elevated FAR and higher creatinine are associated with more severe disease and poorer prognosis [17,18].

A strong negative correlation was also observed between FAR and serum albumin (r = –0.356, p < 0.001), along with a weaker but significant inverse correlation with total leukocyte count (TLC) (r = –0.201, p = 0.03). These results are in line with previous work. Zhan et al. [19] and Kim et al. [18] showed that elevated FAR consistently coincided with reduced serum albumin in ICU patients with AKI. Xu et al. [20] further highlighted the role of preoperative hypoalbuminemia in contributing to elevated FAR and its association with postoperative AKI. Albumin, a negative acute-phase reactant, is often reduced in inflammation or malnutrition, enhancing the prognostic utility of the FAR.

Although evidence directly linking FAR with TLC is limited, Abd El Tawab [37] reported a similar inverse trend while examining the neutrophil-to-albumin ratio in AKI patients. They also noted leukocyte shifts associated with hypoalbuminemia in septic AKI, supporting our findings of altered inflammatory cell profiles in this population.

Receiver Operating Characteristic (ROC) curve analysis in our cohort demonstrated that FAR is a strong mortality predictor in ICU patients with AKI. At a cut-off value of 0.79, FAR achieved an area under the curve (AUC) of 0.856, with 64.3% sensitivity and 96.6% specificity. This indicates high specificity in identifying non-survivors, suggesting FAR's usefulness in excluding survival when elevated. Similar results were found by Xia et al. [17], who also demonstrated FAR's independent predictive value. Kim et al. [18] confirmed its role in long-term ICU mortality risk.

Further supporting its predictive strength, Xu et al. [20] identified FAR as a marker for postoperative AKI following cardiac surgery, they demonstrated its utility in post-contrast AKI among cardiovascular patients. Collectively, these studies validate the wide applicability of FAR in critical care prognosis.

Multivariate logistic regression in our study revealed several independent predictors of ICU mortality among AKI patients, including smoking status, CHF, SOFA and SAPS II scores, bilirubin, serum creatinine, PCO_2, HCO_3^-, fibrinogen, FAR, and ICU length of stay. These findings align with earlier reports identifying CHF as a mortality predictor, especially when coexisting with pulmonary or renal disease, as demonstrated by Shi et al. [38].

Biochemically, elevated bilirubin and creatinine levels were independently associated with higher mortality. Senju and Machado-Kayzuka [39] confirmed the prognostic value of bilirubin and renal markers in trauma patients.

Acid–base disturbances, particularly elevated PCO_2 and HCO_3^- levels, also emerged as significant mortality predictors. Majithia-Beet [40] reported similar findings in critically ill patients with severe respiratory dysfunction, reinforcing the clinical significance of these parameters.

Fibrinogen and FAR both demonstrated strong associations with poor outcomes. Elevated fibrinogen, as an acute-phase protein, reflects systemic inflammation, while hypoalbuminemia indicates nutritional decline. Their combination in the FAR offers a holistic view of the patient's physiological state. This dual prognostic value is further supported by Sawatani et al. [12], who validated FAR as a reliable indicator in acute heart failure patients.

Despite the meaningful insights offered by our study, some limitations should be acknowledged. First, it was performed at a single center with a relatively small sample size, which may affect the generalizability of the findings. Second, although comprehensive data were collected, potential confounders such as nutritional status and volume shifts were not fully accounted for. Third, the observational design limits causal interpretation, and longitudinal outcomes beyond hospital discharge were not evaluated. Future multicenter studies with larger sample sizes, more diverse populations, and extended follow-up are needed to validate these results.

CONCLUSIONS

An elevated FAR has been linked to an increase in hospital mortality in critically ill patients with AKI, suggesting its potential utility as a prognostic indicator among these patients.

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