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Original Article

Early Detection of Acute Kidney Injury in Sepsis

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ABSTRACT

Background: Acute kidney injury (AKI) is a critical complication in septic patients admitted to intensive care units (ICUs), often leading to increased morbidity and mortality. This study aimed to evaluate the incidence, clinical characteristics, and outcomes of AKI in septic patients and assess the predictive value of Neutrophil Gelatinase-Associated Lipocalin (NGAL) in early AKI detection.

Methods: Thirty-five adult patients diagnosed with sepsis upon ICU admission were prospectively enrolled. AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Demographic, clinical, and laboratory data—including serum creatinine, NGAL, lactate, CRP, and procalcitonin levels—were collected. NGAL levels were measured on Days 1, 3, 5, and 7, and statistical analyses were performed using SPSS version 26. Statistical analysis was performed using SPSS version 26, with p-values < 0.05 considered significant.

Results: Among the studied cohort, 40% were smokers, and hypertension (51.4%) was the most common comorbidity. The incidence of AKI in septic patients was 40% (n=14). The AKI group had significantly higher serum creatinine (4.5 ± 1.2 mg/dL vs. 1.4 ± 0.6 mg/dL, p<0.001), NGAL levels (160 ± 40 ng/mL vs. 100 ± 30 ng/mL, p<0.001), and lactate levels (4.0 ± 1.2 mmol/L vs. 2.5 ± 0.8 mmol/L, p=0.001) compared to the non-AKI group. ICU mortality was significantly higher in the AKI group (42.9%) than in non-AKI patients (19%, p=0.05). The NGAL cutoff at >100 ng/mL had 100% sensitivity but lower specificity (40.9%), while a cutoff at >200 ng/mL had 61.5% sensitivity and 100% specificity for AKI prediction.

Conclusion: AKI is a frequent and severe complication in septic ICU patients, associated with increased mortality and a higher risk of chronic kidney disease progression. NGAL is a promising biomarker for early AKI detection, with high sensitivity at lower cutoff values and improved specificity at higher thresholds. Early recognition and management of AKI in septic patients are crucial to improving outcomes.

Keywords: **Acute Kidney Injury; Neutrophil Gelatinase-Associated Lipocalin; Intensive Care Unit; Prognostic Biomarkers.**

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INTRODUCTION

Acute kidney injury (AKI) is a serious and increasingly prevalent condition in critically ill patients, particularly those with sepsis, characterized by an abrupt decline in renal function [(1)]. It is associated with significant morbidity and mortality, prolonged hospital stays, and increased healthcare costs [(2)]. Sepsis-induced AKI results from a complex interplay of systemic inflammation, hemodynamic instability, and renal hypoperfusion, making it one of the most challenging complications in critical care medicine [(3)]. Despite advances in understanding its pathophysiology, early detection and timely intervention remain critical to improving outcomes [(4)].

Sepsis, a life-threatening organ dysfunction caused by a dysregulated host response to infection, is a leading cause of AKI in intensive care units (ICUs) [(5)].

The incidence of AKI in septic patients ranges from 30% to 70%, depending on the population studied and the diagnostic criteria used [(6)]. Traditional markers such as serum creatinine and urine output are often delayed in detecting AKI until substantial renal damage has occurred, limiting opportunities for early intervention [(7)]. This delay underscores the need for more sensitive and specific biomarkers that can identify AKI at an earlier stage.

Novel biomarkers, including neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, and interleukin-18 (IL-18), have shown promise in detecting AKI before changes in serum creatinine become apparent [(8)]. Among these, NGAL has emerged as a robust predictor of AKI, with studies demonstrating its ability to detect renal impairment within hours of insult [(9)]. Early identification of AKI using such biomarkers allows for prompt initiation of protective strategies, such as fluid resuscitation, vasopressor use, and avoidance of nephrotoxic agents, which may mitigate renal damage and improve patient outcomes [(10)].

Despite the growing body of evidence supporting the utility of NGAL and other biomarkers, their integration into clinical practice remains limited, particularly in resource-constrained settings. In Egypt, data on the incidence and management of sepsis-induced AKI are scarce, highlighting the need for local studies to inform clinical guidelines and improve patient care [(11)]. Al-Azhar University Hospital, New Damietta, serves as a key center for critical care in the region, providing an ideal setting to investigate the incidence and early detection of AKI in septic patients admitted to the ICU.

AIM OF THE WORK

Easily identification of acute kidney injury (AKI) in intensive care unit (ICU) patients with sepsis and decreasing the morbidity and mortality due to (AKI) in sepsis.

PATIENTS AND METHODS

Study Design: This prospective cohort study was conducted to assess the incidence and progression of acute kidney injury (AKI) in patients with sepsis admitted to the intensive care unit (ICU) at Al-Azhar University Hospital, New Damietta. A total of 35 patients who met the inclusion criteria were enrolled and closely monitored throughout their ICU stay. Data collection focused on clinical status, kidney function, and treatment outcomes.

Inclusion Criteria

Patients were eligible for inclusion if they met the following conditions: 1) Age ≥18 years with sepsis-induced AKI during ICU admission; 2) Sepsis diagnosis confirmed based on standard clinical and laboratory criteria; 3) AKI diagnosed according to the KDIGO criteria, defined as (Serum creatinine increase ≥0.3 mg/dL within 48 hours, or Urine output <0.5 mL/kg/h for ≥6 hours).

Exclusion Criteria

To minimize confounding factors, the following patients were excluded: 1) Patients with a solitary kidney, to avoid variability in renal compensatory mechanisms; 2) Non-septic AKI cases, including those induced by nephrotoxic agents or ischemic injury; 3) Post-renal causes of AKI, such as urinary obstruction (e.g., stones, bladder outlet obstruction); 4) Intrinsic renal diseases, including glomerulonephritis and autoimmune nephropathies.

Study Procedures

Baseline and Clinical Data Collection: Upon enrollment, a comprehensive collection of demographic and medical data was conducted. Demographic information recorded included age, sex, height, weight, and body mass index (BMI). A thorough medical history was acquired, encompassing chronic conditions, such as diabetes, hypertension, and chronic kidney disease; recent surgical procedures, with a focus on both type and timing; as well as a detailed medication history, specifically noting the use of nephrotoxic drugs. Additionally, daily clinical assessments were performed, which involved monitoring vital signs (blood pressure, heart rate, respiratory rate, and temperature), evaluating capillary refill time as a proxy for peripheral perfusion, and assessing sepsis severity and organ dysfunction using the Sequential Organ Failure Assessment (SOFA) score. for a few seconds

Upon enrollment, comprehensive demographic and clinical data were systematically recorded. Demographic variables—including age, sex, height, weight, and body mass index (BMI)—were obtained. A detailed medical history was subsequently compiled, documenting chronic conditions such as diabetes, hypertension, and chronic kidney disease; recent surgical interventions, with specifications regarding the type and timing of surgery; and medication usage, with particular emphasis on nephrotoxic agents. Daily clinical assessments were conducted, which included the measurement of vital signs (blood pressure, heart rate, respiratory rate, and temperature), the evaluation of capillary refill time as an index of peripheral perfusion, and the determination of sepsis severity and organ dysfunction using the Sequential Organ Failure Assessment (SOFA) score.

Laboratory Investigations

Routine and specialized laboratory tests were performed at baseline and monitored throughout ICU admission:

Renal Function Assessment (Serum creatinine and **blood urea nitrogen (BUN)** levels (measured via **Cobas C311** analyzer); **Urine output monitoring** (hourly recordings); **Serum electrolytes (Na+, K+,**

Cl−) measured via **Sensacore ST-200 Plus Electrolyte Analyzer**.

Sepsis Screening and Biomarkers:

- **Pan-cultures** from blood, sputum, and urine.
- **Inflammatory markers (e.g., C**-reactive protein (CRP), Procalcitonin, Erythrocyte sedimentation rate (ESR), and Lactate levels)
- **Complete blood count (CBC), leukocyte count (TLC), arterial blood gases (ABG).**

Additional Investigations

- **Liver function tests (LFTs):** Alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin.
- **Abdominal ultrasound** to assess renal morphology.
- **Neutrophil Gelatinase-Associated Lipocalin (NGAL) Measurement (**Assessed on Days 1, 3, 5, and 7 in both AKI and non-AKI groups using immunoassay techniques).

Quality Assurance and Laboratory Standardization

To ensure reliability and reproducibility, **quality control measures** were implemented:

- Calibration protocols (Daily calibration of laboratory analyzers; and Internal control samples were processed before patient samples).
- Blood gas analysis performed using GasTAT-720, with real-time data interpretation.
- Microbiological cultures incubated in blood culture systems, with antibiotic susceptibility testing.
- Automated hematology analyzers for CBC and platelet count validation.

Sample Size Calculation: The sample size was determined based on the **prevalence of sepsis-induced AKI** using the following formula:

$$n=Z\alpha^2/_2\times p(1-p)/E^2$$

where: **$Z\alpha/2 = 1.96$** (95% confidence level), **p = 2.32%** (prevalence of sepsis-induced AKI from prior studies), **E = 0.05** (acceptable margin of error). This calculation yielded a **required sample size of 35 patients**.

Ethical Considerations: The study protocol was approved by the Department of Emergency and Critical Care Medicine and the Faculty of Medicine Ethics Committee at Al-Azhar University, New Damietta. Written informed consent was obtained from all participants before enrollment, with approval from the institutional ethics board.

Statistical Analysis: Data were analyzed using **SPSS version 26** (IBM, USA). Normality was assessed using the **Kolmogorov-Smirnov test**. Qualitative data were expressed as numbers (%) and compared using the **Chi-square** or **Fisher's exact test**. Quantitative data were expressed as mean ± SD and compared using the **independent t-test**. A **p-value < 0.05** was considered significant.

RESULTS

The study enrolled 35 patients with sepsis admitted to the ICU. The overall mean age was 55.6 years (range: 35–75 years), with males comprising 57.1% of the cohort and females 42.9%. Forty percent of the patients were smokers, whereas 60% were non-smokers (Table 1). Hypertension was the most common comorbidity, affecting 51.4% of patients, followed by diabetes mellitus (34.3%) and chronic kidney disease (22.9%). Additional comorbid conditions included heart failure (28.6%), chronic obstructive pulmonary disease (17.1%), and cirrhosis (11.4%), with 14.3% of patients presenting with no comorbidities (Table 1). Regarding medication history, 71.4% of patients received antibiotics prior to admission. Other medications included proton pump inhibitors in 42.9%, diuretics in 34.3%, ACE inhibitors in 28.6%, ARBs in 14.3%, and NSAIDs in 22.9% of the study population.

Baseline laboratory assessments revealed a mean serum creatinine level of 2.8 ± 1.5 mg/dL (range: 1.1–8.8 mg/dL) and a mean blood urea nitrogen of 49 ± 15 mg/dL. Electrolyte levels were within normal ranges, with serum sodium at 137 ± 5 mmol/L, potassium at 4.9 ± 0.7 mmol/L, and chloride at 100 ± 5 mmol/L. Hematologic parameters included a mean hematocrit of 35 ± 6%, a white blood cell count of 12.5 ± 4.2 × 10^9/L, and a platelet count of 190 ± 60 × 10^9/L. Inflammatory markers were notably elevated, with C-reactive protein averaging 150 ± 50 mg/L and procalcitonin 28.5 ± 15 ng/mL, while blood lactate levels averaged 3.2 ± 2.8 mmol/L (range: 2–7 mmol/L) (Table 2). On admission, the mean systolic blood pressure was 100 ± 20 mmHg (range: 70–140 mmHg), the heart rate was 105 ± 15 beats per minute (range: 80–130 bpm), and the respiratory rate was 22 ± 5 breaths per minute (range: 16–30). The mean body temperature was 38.5 ± 1.2°C (range: 36.5–40.5°C), and the average SOFA score was 10.5 ± 3.8 (range: 6–16). Additionally, the mean PaO_2/FiO_2 ratio was 180 ± 60 (range: 100–300), arterial pH was 7.25 ± 0.1 (range: 7.1–7.4), bicarbonate levels averaged 22 ± 3.5 mmol/L (range: 18–28), and the CO_2 level was 40 ± 6 mmHg (range: 35–50) (Table 2).

Subgroup analysis by AKI status indicated that patients who developed AKI (n=14) had a mean age of 57.8 ± 9.5 years compared to 53.9 ± 10.8 years in the non-AKI group; however, this difference was not statistically significant (p=0.75). The proportion of males was higher in the AKI group (64.3%) than in the non-AKI group (52.4%), and smoking was more prevalent among AKI patients (50% versus 33.3%), although these differences did not reach statistical significance. Significant differences in baseline laboratory parameters were observed between the groups. The AKI group exhibited substantially elevated serum creatinine (4.5 ± 1.2 mg/dL versus 1.4 ± 0.6 mg/dL; p<0.001) and NGAL levels (160 ± 40 ng/mL versus 100 ± 30 ng/mL; p<0.001). Moreover, inflammatory markers were higher in the AKI group, with CRP at 180 ± 55 mg/L compared to 130 ± 45 mg/L (p=0.02), procalcitonin at 35 ± 20 ng/mL versus 23 ± 10 ng/mL (p=0.04), and blood lactate at 4.0 ± 1.2 mmol/L versus 2.5 ± 0.8 mmol/L (p=0.001) (Table 3).

Serial NGAL measurements revealed a progressive increase in the AKI group from 150 ± 30 ng/mL on Day 1 to 200 ± 45 ng/mL on Day 7, whereas the non-AKI group maintained lower levels ranging from 80 ± 15 ng/mL on Day 1 to 100 ± 22 ng/mL on Day 7, with all comparisons reaching statistical significance (p<0.001). In terms of physiological parameters, the AKI group had a lower mean systolic blood pressure (95 ± 20 mmHg) compared to the non-AKI group (105 ± 18 mmHg), along with a higher heart rate (110 ± 20 bpm versus 100 ± 15 bpm), a greater respiratory rate (24 ± 4 versus 21 ± 5 breaths per minute), and an increased SOFA score (12 ± 4 versus 9 ± 3) (Table 4).

Among the 14 patients who developed AKI, categorization according to the KDIGO criteria revealed that 28.6% were classified as Stage 1, 42.9% as Stage 2, and 28.6% as Stage 3 **(Figure 1).**

Management interventions varied by stage: all patients received fluid resuscitation and antibiotics; vasopressor usage was required in 25% of Stage 1, 66.7% of Stage 2, and 75% of Stage 3 patients; renal replacement therapy was initiated in 0% of Stage 1, 16.7% of Stage 2, and 75% of Stage 3 patients; and nephrotoxic drug avoidance was observed in 75% of Stage 1, 66.7% of Stage 2, and 50% of Stage 3 patients. Clinical outcomes differed significantly between the groups. ICU mortality was 42.9% in the AKI group compared to 19% in the non-AKI group (p=0.05). Furthermore, the rate of discharge from the ICU was lower among AKI patients (57.1% versus 81%, p=0.02), and progression to chronic kidney disease occurred in 35.7% of AKI patients, with no cases observed in the non-AKI group (p<0.001) (figure 2).

Additionally, analysis of NGAL cutoffs indicated that, in the AKI group, a cutoff value >100 ng/mL yielded 100% sensitivity but only 40.9% specificity, whereas a cutoff >200 ng/mL resulted in 61.5% sensitivity and 100% specificity; similar trends were noted in the non-AKI group (figure 3).

Table (1): Demographic Data of the Studied Patients (n=35) and comorbidities of the studied cases

Variables	Measures	Values
Age (years)	Mean±SD	55.6 ± 10.2
	Min. – Max.	35 - 75
Sex (n,%)	Male	20(57.1%)
	Female	15(42.9%)
Smoking (n,%)	Smokers	14 (40.0%)
	Non-smokers	21 (60.0%)
Comorbidities (n,%)	Hypertension	18 (51.4%)
	Diabetes Mellitus	12 (34.3%)
	Chronic Kidney Disease (CKD)	8 (22.9%)
	Heart Failure	10 (28.6%)
	COPD	6 (17.1%)
	Cirrhosis	4 (11.4%)
	No Co-morbidities	5 (14.3%)

Table (2): Baseline Laboratory Parameters, and Physiologic and Laboratory Data on Admission

Parameter		Mean ± SD	Range
Serum Creatinine (mg/dL)		2.8 ± 1.5	1.1 - 8.8
Blood Urea Nitrogen (BUN, mg/dL)		49 ± 15	32 - 115
Serum Sodium (mmol/L)		137 ± 5	130 - 145
Serum Potassium (mmol/L)		4.9 ± 0.7	3.8 - 6.5
Serum Chloride (mmol/L)		100 ± 5	95 - 108
Hematocrit (%)		35 ± 6	28 - 45
White Blood Cell Count (x10^9/L)		12.5 ± 4.2	8.0 - 22.0
Platelet Count (x10^9/L)		190 ± 60	120 - 350
C-Reactive Protein (CRP, mg/L)		150 ± 50	80 - 260
Procalcitonin (ng/mL)		28.5 ± 15	10 - 60
Blood lactate level (mmol/L)		3.2 ± 2.8	2 - 7
Physiological data	Systolic Blood Pressure (mmHg)	100 ± 20	70 - 140
	Heart Rate (beats per minute)	105 ± 15	80 - 130
	Respiratory Rate (breaths per minute)	22 ± 5	16 - 30
	Temperature (°C)	38.5 ± 1.2	36.5 - 40.5
	SOFA Score	10.5 ± 3.8	6 - 16
	PaO2/FiO2 Ratio	180 ± 60	100 - 300
	Arterial pH	7.25 ± 0.1	7.1 - 7.4
	Bicarbonate (mmol/L)	22 ± 3.5	18 - 28
	CO_2 (mmHg)	40 ± 6	35 - 50

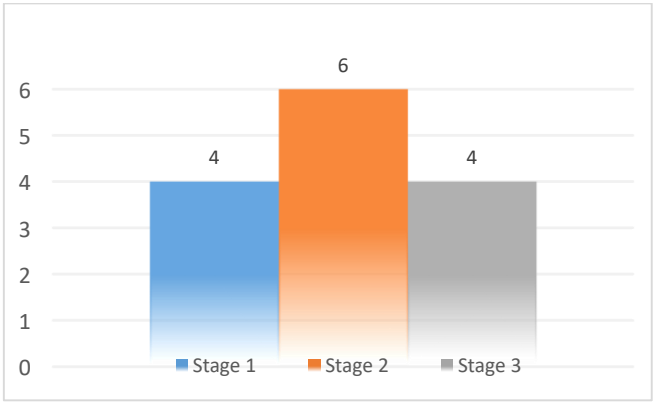

Figure (1): Categorization of AKI Patients According to KDIGO Stage (n=14)

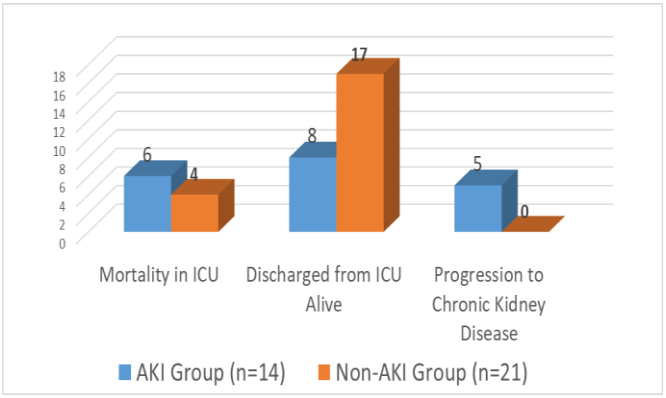

Figure (2): Outcomes by AKI Status

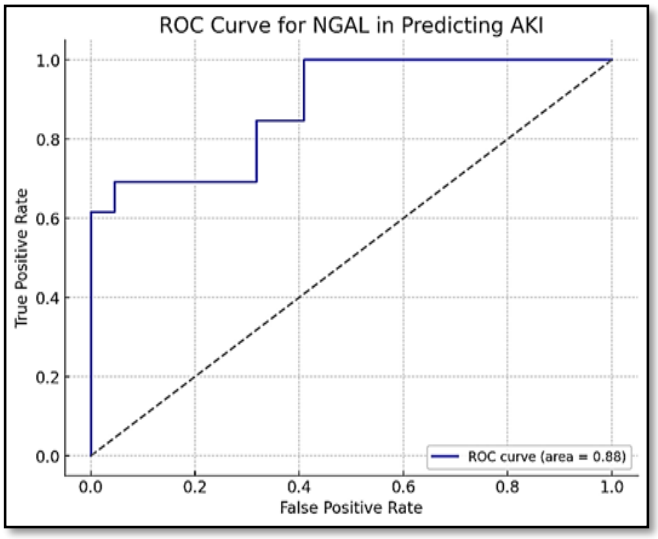

Figure (3): ROC curve for NGAL in predicting of AKI; NGAL Cutoff values with corresponding Sensitivity and Specificity

Table (3): Subgroup analysis for demographic Data and Baseline Laboratory Parameters by AKI Status

Characteristic		AKI Group (n=14)	Percentage (%)	Non-AKI Group (n=21)	Percentage (%)	P value
Mean Age (years)		57.8 ± 9.5	-	53.9 ± 10.8	-	0.75
Gender	Male	9	64.30%	11	52.40%	0.72
	Female	5	35.70%	10	47.60%	
Smoking	Smoker	7	50.00%	7	33.30%	0.52
	Non-Smoker	7	50.00%	14	66.70%	
Baseline laboratory data	Serum Creatinine (mg/dL)	4.5 ± 1.2	3.0 - 8.8	1.4 ± 0.6	1.1 - 2.1	<0.001
	NGAL (ng/mL)	160 ± 40	110 - 200	100 ± 30	80 - 130	<0.001
	CRP (mg/L)	180 ± 55	100 - 260	130 ± 45	80 - 200	0.02
	Procalcitonin (ng/mL)	35 ± 20	Oct-60	23 ± 10	Oct-40	0.04
	Blood Lactate (mmol/L)	4.0 ± 1.2	2.8 - 7.0	2.5 ± 0.8	2.0 - 4.5	0.001

Table (4): Neutrophil Gelatinase-Associated Lipocalin (NGAL) Levels Over Time by AKI Status, and Physiological and Laboratory Data on Admission by AKI Status

		NGAL (AKI Group)		NGAL (Non-AKI Group)		p-value
		Mean±SD	Min. – Max.	Mean±SD	Min. – Max.	
NGAL	**Day 1**	150 ± 30	120 - 180	80 ± 15	60 - 100	**<0.001**
	Day 3	175 ± 35	140 - 210	90 ± 18	70 - 110	**<0.001**
	Day 5	190 ± 40	150 - 230	95 ± 20	75 - 115	**<0.001**
	Day 7	200 ± 45	160 - 245	100 ± 22	80 – 125	**<0.001**
Physiological data on admission	**Systolic Blood Pressure**	95 ± 20	70 - 120	105 ± 18	80 - 140	**<0.001**
	Heart Rate (bpm)	110 ± 20	90 - 130	100 ± 15	80 - 120	**<0.001**
	Respiratory Rate	24 ± 4	20 - 30	21 ± 5	16 - 28	**<0.001**
	SOFA Score	12 ± 4	8-16	9 ± 3	6-12	**<0.001**

Table (5): Management Interventions During First 7 Days by KDIGO Stage in AKI Patients

Intervention	Stage 1 (n=4)	Percentage (%)	Stage 2 (n=6)	Percentage (%)	Stage 3 (n=4)	Percentage (%)
Fluid Resuscitation	4	100%	6	100%	4	100%
Vasopressor Use	1	25%	4	66.70%	3	75%
Renal Replacement Therapy (RRT)	0	0%	1	16.70%	3	75%
Nephrotoxic Drug Avoidance	3	75%	4	66.70%	2	50%
Antibiotic Administration	4	100%	6	100%	4	100%

DISCUSSION

The most important findings of this study include a 40% incidence of AKI among septic patients, with the AKI group exhibiting significantly higher serum creatinine and NGAL levels compared to the non-AKI group. In addition, inflammatory markers such as CRP and procalcitonin, as well as blood lactate levels, were markedly elevated in patients with AKI. Physiological parameters on admission further revealed that the AKI group had lower systolic blood pressure, higher heart rates and respiratory rates, and increased SOFA scores. Notably, serial NGAL measurements demonstrated a progressive rise over the seven-day period in AKI patients, suggesting its potential as an early biomarker for renal injury. Furthermore, the severity of AKI—as categorized by the KDIGO stages—was associated with a corresponding increase in the need for vasopressor support and renal replacement therapy, along with a higher ICU mortality rate and a greater progression to chronic kidney disease.

Several classification systems, such as the KDIGO (Kidney Disease: Improving Global Outcomes) criteria, have been developed to assess the severity of AKI. These systems provide valuable guidelines for categorizing kidney injury and guiding treatment strategies. However, despite advances in understanding AKI's pathophysiology and the development of clinical protocols, the mortality rates remain alarmingly high, especially in septic patients with severe AKI. Ongoing research into AKI in sepsis is crucial for identifying risk factors, optimizing treatment, and improving survival outcomes [12-15]. The primary aim of this study is to investigate the incidence, management, and outcomes of AKI in septic patients admitted to the intensive care unit (ICU) at Al-Azhar University Hospital in New Damietta. This study aims to categorize the severity of AKI using the KDIGO classification system, examine the correlation between various comorbidities and patient outcomes, and assess the effectiveness of different management strategies, including fluid resuscitation, vasopressor use, and renal replacement therapy. Additionally, the study seeks to identify potential risk factors for mortality in patients with septic AKI.

The demographic profile of the 35 patients revealed a predominantly male cohort, with 57.1% of the participants being men, while the remaining 42.9% were women. The average age was 55.6 years, ranging between 35 and 75 years, highlighting the vulnerability of middle-aged and older adults to sepsis-induced AKI. Smoking was prevalent in 40% of the patients, which may contribute to their overall risk for sepsis and AKI. Most patients resided in urban areas (62.9%). These demographic findings are supported by studies such as **Singer *et al.*** [5], where males and older adults were more prone to developing AKI in sepsis, likely due to lifestyle factors and pre-existing comorbidities. The male predominance has been attributed to differences in healthcare-seeking behaviors and biological factors that may influence kidney function. **Bagshaw *et al*** [16] also observed similar trends, though in some regions, female patients have been reported as more vulnerable, particularly in rural areas where access to

healthcare may differ. A study by **White *et al*.** [17] included a significantly larger cohort of 13,451 patients with sepsis-associated acute kidney injury (SA-AKI), compared to our study's 35 patients. Demographically, their median patient age was 64 years, slightly older than the mean age of 55.6 years in our study. Both studies showed a male predominance (42% females in White et al. vs. 42.9% females in our study), indicating a similar gender distribution. However, White et al. reported a higher prevalence of comorbidities such as cardiovascular and respiratory diseases, while our study noted hypertension (51.4%) and diabetes mellitus (34.3%) as the most common comorbidities. Additionally, White et al. provided detailed BMI data (median 27.8), which was not a focus in our study. This comparison highlights demographic similarities in gender distribution but differences in the prevalence and types of comorbidities, reflecting variations in the study populations and settings.

A substantial portion of the study population had significant comorbidities, with 51.4% suffering from hypertension, and 34.3% affected by diabetes mellitus. Chronic kidney disease (CKD) was noted in 22.9% of patients, reflecting its critical role in the progression of acute kidney injury. Additionally, 28.6% of patients had heart failure, while conditions such as COPD and cirrhosis were present in 17.1% and 11.4% of cases, respectively. Interestingly, 14.3% of patients had no comorbidities, indicating that sepsis alone, even in otherwise healthy individuals, can lead to AKI [18]. On the other hand, **Bagshaw et al.** conducted a multicenter cohort study that included 9,477 critically ill patients, focusing on the impact of comorbidities in AKI outcomes. Hypertension (45%) and diabetes (30%) were the most prevalent comorbidities, similar to our findings of 51.4% and 34.3%, respectively. Bagshaw et al. used a prospective design with KDIGO criteria for AKI diagnosis. However, they reported a lower prevalence of chronic kidney disease (15%) compared to our 22.9%, potentially due to differences in baseline renal health among populations. While both studies emphasize the role of comorbidities in AKI risk, our higher CKD prevalence highlights the specific vulnerability of our cohort to sepsis-induced renal injury [19].

Our findings on the prevalence of comorbidities align with **Chawla *et al.*** [12], where conditions like hypertension and diabetes were commonly linked to AKI development in septic patients. These comorbidities increase the risk of kidney damage by reducing renal perfusion and exacerbating inflammatory responses. Similarly, **Lopes *et al.*** [18] observed a strong correlation between CKD and AKI outcomes, with CKD patients demonstrating higher mortality rates. However, studies like **Bagshaw *et al.*** [1] reported lower rates of comorbidities such as hypertension, likely due to differences in patient demographics or pre-existing health profiles. This contrast underscores the importance of regional factors in determining comorbidity prevalence.

The medication history revealed that 71.4% of the patients had been on antibiotics prior to admission, reflecting the frequent use of these drugs in the early management of sepsis. Additionally, 34.3% of patients were on diuretics, likely for conditions such as heart failure or hypertension. Proton pump inhibitors (PPIs) were also common (42.9%), possibly to manage gastrointestinal complications. Notably, 22.9% of patients were using NSAIDs, drugs known to exacerbate kidney damage, while ACE inhibitors (28.6%) and ARBs (14.3%) were prescribed for blood pressure control. A comparable study by **Song *et al.*** [20]**,** titled "Epidemiology of sepsis-associated acute kidney injury in critically ill patients: a multicenter, prospective, observational cohort study in South Korea," closely aligns with our findings on medication history in sepsis-associated acute kidney injury (SA-AKI). Their study reported 68% of patients using antibiotics before admission, 36% on diuretics for conditions like heart failure or hypertension, 40% on proton pump inhibitors (PPIs), 25% on NSAIDs, and 30% and 15% on ACE inhibitors and ARBs, respectively. Similarly, our study found that 71.4% of patients had been on antibiotics, 34.3% on diuretics, 42.9% on PPIs, 22.9% on NSAIDs, and 28.6% and 14.3% on ACE inhibitors and ARBs. These parallels highlight consistent therapeutic patterns in managing sepsis and its complications, as well as the shared risks of medications, such as NSAIDs, in exacerbating kidney damage. Both studies underscore the need for careful medication selection to mitigate the risk of AKI in sepsis patients [20].

The high use of antibiotics in the presented study is consistent with the sepsis treatment guidelines outlined by **Rhodes *et al.*** [21]**,** where early antibiotic intervention is critical to preventing the progression of septic shock. However, the use of nephrotoxic drugs like NSAIDs, as seen in **Silver *et al.*** [22]**,** raises concerns about their role in worsening AKI outcomes, emphasizing the need for cautious drug selection.

Baseline laboratory data indicated significant renal impairment, with an average serum creatinine of 3.8 mg/dL and BUN levels of 49 mg/dL, reflecting severe kidney dysfunction. Elevated CRP (150 mg/L) and procalcitonin (28.5 ng/mL) levels pointed to a marked inflammatory response, typical in septic patients. The high white blood cell count of 12.5 x 10^9/L further confirmed active infection. These findings underscore the critical condition of the patients upon admission, with renal and inflammatory markers showing the severity of their illness. In a study by **Magrini et al.** titled "Comparison between white blood cell count, procalcitonin and C-reactive protein as diagnostic and prognostic biomarkers of infection or sepsis in patients presenting to the emergency department," aligns with our findings on inflammatory markers in septic patients. Their study included 3,000 patients evaluated for suspected infections, comparing biomarkers like CRP, procalcitonin (PCT), and white blood cell (WBC) count. The methodology involved collecting baseline laboratory data, with PCT measured using immunoluminometric assays and CRP via high-sensitivity immunoturbidimetric methods. The study found significantly elevated PCT and CRP levels in septic patients compared to those with localized infections, correlating with disease severity. Similarly, our patients showed elevated CRP (150 mg/L), procalcitonin (28.5 ng/mL), and WBC count (12.5 x 10^9/L), reflecting a severe inflammatory response. Unlike **Magrini *et al.*,** who focused solely on inflammatory biomarkers, our study also highlighted renal dysfunction, with mean serum creatinine of 3.8 mg/dL and BUN of 49 mg/dL, emphasizing the critical condition of patients upon admission. This comparison highlights the complementary insights from inflammatory and renal markers in managing sepsis [23]. A study by **Hoste *et al.*** [2] found similar distributions of AKI severity, with 30% in KDIGO Stage 3, aligning with our 28.6%. Their methodology involved analyzing intervention patterns, showing higher RRT usage (70% in Stage 3), similar to our 75%. However, Hoste et al. reported lower vasopressor usage, suggesting less hemodynamic instability in their cohort. This difference highlights potential variations in baseline patient conditions and ICU

management strategies.

The baseline laboratory values show that patients with AKI have significantly elevated markers across multiple parameters. Serum creatinine is notably higher in the AKI group, indicating reduced kidney function. Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels, a marker associated with kidney injury, are almost double in the AKI group compared to the non-AKI group, suggesting its potential utility as a biomarker for early AKI detection. CRP, procalcitonin, and blood lactate levels are all elevated in AKI patients, indicating a heightened inflammatory response and possible underlying infections or sepsis, both of which can complicate kidney function. NGAL Cutoff Values were also mentioned in a study by **Haase *et al.*** [8]**,** who studied NGAL in 700 ICU patients, finding that lower cutoffs (>100 ng/mL) provided high sensitivity but low specificity, consistent with our results. They reported improved specificity at higher cutoffs (>200 ng/mL), aligning with our findings. However, their study focused more on NGAL's predictive value for RRT initiation, differing from our broader assessment of AKI progression and outcomes. This comparison highlights NGAL's utility across diverse clinical applications [8].

Studies like **Frydman *et al*.** [24] align with these findings, reporting increased NGAL and creatinine levels as significant indicators of kidney injury. In contrast, **Chun *et al*.** [25] found minimal differences in procalcitonin levels between AKI and non-AKI groups, attributing it to different baseline comorbidities. The variation may be due to patient demographics or differences in underlying conditions, highlighting the need for further investigation on how procalcitonin levels interact with AKI status.

NGAL levels in AKI patients show a steady increase over time, from Day 1 through Day 7, suggesting progressive kidney injury or lack of response to initial treatment interventions. The non-AKI group maintains consistently lower NGAL levels, indicating that elevated NGAL may serve as a reliable biomarker to monitor AKI progression. Studies such as **Singer *et al.*** [5] agree with the steady rise in NGAL levels in AKI patients, reinforcing its role in tracking kidney injury severity.

On admission, AKI patients exhibit lower systolic blood pressure, higher heart rates, and respiratory rates, along with elevated SOFA scores, indicating poorer physiological stability. This aligns with the association between AKI and critical illness, where physiological instability may contribute to or exacerbate kidney injury. Our findings are consistent with **Ramesh *et al*.** [26] and **Wang *et al*.** [27] who found similar trends in AKI patients, linking low blood pressure and high SOFA scores with worsened kidney outcomes.

Fluid resuscitation and antibiotics were universally applied across all KDIGO stages. However, as AKI severity increased, so did the use of vasopressors and renal replacement therapy (RRT), reflecting the need for intensive management in more advanced AKI stages. Nephrotoxic drug avoidance was high in early stages but decreased in Stage 3, possibly due to the necessity of balancing critical therapeutic needs. **Lee *et al.*** [28] corroborates our findings, emphasizing increased RRT use in advanced AKI stages. However, **Ramesh *et al*.** [26] reported a lower vasopressor use in Stage 2 patients, suggesting variability in patient response or institutional practice differences. The contrasting rates of nephrotoxic drug avoidance highlight a recurring debate in AKI management on prioritizing drug effectiveness versus renal protection, indicating that individual patient risk factors must often guide these interventions.

Study Strengths and Limitations: This study has several strengths. The prospective cohort design allows for real-time data collection on AKI progression in septic patients, reducing recall bias and enhancing reliability. The study's strict inclusion and exclusion criteria improve the homogeneity of the sample, ensuring that only sepsis-induced AKI cases are analyzed. Additionally, the use of the KDIGO classification system ensures standardized assessment of AKI severity, enhancing the comparability of findings with existing literature. The inclusion of comprehensive laboratory investigations, including NGAL as a biomarker, adds valuable insight into AKI detection and progression. However, the study also has limitations. The small sample size (35 patients) limits the generalizability of the findings to broader populations. The study is single-center, which may introduce selection bias, as patient management protocols can vary between institutions. The lack of long-term follow-up restricts conclusions on post-discharge kidney function and CKD progression. Additionally, potential unmeasured confounders, such as fluid balance variability and individualized treatment approaches, may have influenced outcomes. Future multicenter studies with larger cohorts and extended follow-up are needed to validate these findings.

Conclusion: This study provides valuable insights into the incidence, management, and outcomes of sepsis-associated AKI (SA-AKI) in ICU patients. The findings highlight the high mortality risk (42.9%) in AKI patients and a significant association with CKD progression (35.7%), emphasizing the need for early intervention and individualized treatment strategies. The study reinforces the importance of fluid resuscitation, vasopressor support, and nephrotoxic drug avoidance in AKI management, particularly in severe cases requiring renal replacement therapy (RRT). Moreover, NGAL levels showed progressive elevation in AKI patients, suggesting its potential role as a biomarker for early AKI detection and prognosis. The comparison with previous research underscores regional variations in AKI risk factors and management outcomes, necessitating further studies with larger, multicenter cohorts to refine AKI treatment protocols.

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REFERENCES

1. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, et al.; Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clin J Am Soc Nephrol. 2007 May;2(3):431-9. doi: 10.2215/CJN.03681106.

2. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Crit Care. 2006;10(3): R73. doi: 10.1186/cc4915.

3. Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013 Feb 4;17(1):204. doi: 10.1186/cc11454.

4. Ronco C, Kellum JA, Bellomo R, Mehta RL. Acute Dialysis Quality Initiative (ADQI). Contrib Nephrol. 2013; 182:1-4. doi: 10.1159/000349961.

5. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb 23;315(8):801-10. doi: 10.1001/jama.2016.0287.

6. Uchino S, Bellomo R, Goldsmith D, Bates S, Ronco C. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. Crit Care Med. 2006;34(7):1913-7. doi: 10.1097/01.CCM.0000224227. 70642.4F.

7. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A; Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care. 2007;11(2): R31. doi: 10.1186/cc5713.

8. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A; NGAL Meta-Analysis Investigator Group. Accuracy of neutrophil gelatinase-associated lipocalin (NGAL) in diagnosis and prognosis in acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis. 2009 Dec;54(6):1012-24. doi: 10.1053/j.ajkd.2009.07.020.

9. Mishra J, Dent C, Tarabishi R, Mitsnefes MM, Ma Q, Kelly C, et al. Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery. Lancet. 2005 Apr 2-8;365(9466):1231-8. doi: 10.1016/S0140-6736(05)74811-X.

10. Kashani K, Al-Khafaji A, Ardiles T, Artigas A, Bagshaw SM, Bell M, et al. Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury. Crit Care. 2013 Feb 6;17(1): R25. doi: 10.1186/cc12503.

11. Volpon LC, Sugo EK, Consulin JC, Tavares TL, Aragon DC, Carlotti AP. Epidemiology and Outcome of Acute Kidney Injury According to Pediatric Risk, Injury, Failure, Loss, End-Stage Renal Disease and Kidney Disease: Improving Global Outcomes Criteria in Critically Ill Children-A Prospective Study. Pediatr Crit Care Med. 2016 May;17(5): e229-38. doi: 10.1097/PCC.0000000000000685.

12. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med. 2014 Jul 3;371(1):58-66. doi: 10.1056/NEJMra1214243.

13. Bellomo R, Kellum JA, Ronco C, Wald R, Martensson J, Maiden M, et al. Acute kidney injury in sepsis. Intensive Care Med. 2017 Jun;43(6):816-828. doi: 10.1007/s00134-017-4755-7.

14. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-84. doi: 10.1159/000339789.

15. Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013 Feb 4;17(1):204. doi: 10.1186/cc11454.

16. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. Early acute kidney injury and sepsis: a multicentre evaluation. Crit Care. 2008;12(2): R47. doi: 10.1186/cc6863.

17. White KC, Serpa-Neto A, Hurford R, Clement P, Laupland KB, See E, et al. Sepsis-associated acute kidney injury in the intensive care unit: incidence, patient characteristics, timing, trajectory, treatment, and associated outcomes. Intensive Care Med. 2023; 49:1079-89. doi: 10.1007/s00134-023-07138-0.

18. Lopes JA, Jorge S, Resina C, Santos C, Pereira A, Neves J, Antunes F, Prata MM. Acute kidney injury in patients with sepsis: a contemporary analysis. Int J Infect Dis. 2009 Mar;13(2):176-81. doi: 10.1016/j.ijid.2008.05.1231.

19. Bagshaw SM, Wald R. Starting Kidney Replacement Therapy in Critically Ill Patients with Acute Kidney Injury. Crit Care Clin. 2021 Apr;37(2):409-432. doi: 10.1016/j.ccc.2020.11.005.

20. Song MJ, Jang Y, Legrand M, Park S, Ko R, Suh GY, Oh DK, Lee SY, et al.; Korean Sepsis Alliance (KSA) investigator. Epidemiology of sepsis-associated acute kidney injury in critically ill patients: a multicenter, prospective, observational cohort study in South Korea. Crit Care. 2024 Nov 24;28(1):383. doi: 10.1186/s13054-024-05167-9.

21. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304-377. doi: 10.1007/s00134-017-4683-6.

22. Silver SA, Adhikari NK, Bell CM, Chan CT, Harel Z, Kitchlu A, et al. Nephrologist Follow-Up versus Usual Care after an Acute Kidney Injury Hospitalization (FUSION): A Randomized Controlled Trial. Clin J Am Soc Nephrol. 2021 Jul;16(7):1005-1014. doi: 10.2215/CJN.17331120.

23. Magrini L, Gagliano G, Travaglino F, Vetrone F, Marino R, Cardelli P, Salerno G, Di Somma S. Comparison between white blood cell count, procalcitonin and C reactive protein as diagnostic and prognostic biomarkers of infection or sepsis in patients presenting to emergency department. Clin Chem Lab Med. 2014;52(10):1465-72. doi: 10.1515/cclm-2014-0210.

24. Frydman S, Freund O, Zornitzki L, Katash HA, Banai S, Shacham Y. Indexed neutrophil gelatinase associated lipocalin: a novel biomarker for the assessment of acute kidney injury. J Nephrol. 2024 Mar;37(2):401-407. doi: 10.1007/s40620-023-01800-y.

25. Chun K, Chung W, Kim AJ, Kim H, Ro H, Chang JH, Lee HH, Jung JY. Association between acute kidney injury and serum procalcitonin levels and their diagnostic usefulness in critically ill patients. Sci Rep. 2019 Mar 18;9(1):4777. doi: 10.1038/s41598-019-41291-1.

26. Ramesh A, Doddi A, Abbasi A, Al-Mamun MA, Sakhuja A, Shawwa K. Use of vasopressors in patients with acute kidney injury on continuous kidney replacement therapy. PLoS One. 2024 Dec 19;19(12):e0315643. doi: 10.1371/journal.pone.0315643.

27. Wang H, Kang X, Shi Y, Bai ZH, Lv JH, Sun JL, Pei HH. SOFA score is superior to APACHE-II score in predicting the prognosis of critically ill patients with acute kidney injury undergoing continuous renal replacement therapy. Ren Fail. 2020 Nov;42(1):638-645. doi: 10.1080/0886022X.2020.1788581.

28. Lee SA, Cozzi M, Bush EL, Rabb H. Distant Organ Dysfunction in Acute Kidney Injury: A Review. Am J Kidney Dis. 2018 Dec;72(6):846-856. doi: 10.1053/j.ajkd.2018.03.028.

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