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Dynamic Monitoring of Kidney Injury Over 3 Days in Intensive Care Unit in Patient with Sepsis and Its Association with ICU Mortality

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ABSTRACT

Introduction: Acute Kidney Injury (AKI) is a common complication in septic patients, significantly contributing to ICU mortality. The dynamic changes in kidney function over the initial days of ICU admission remain a crucial factor in determining patient outcomes. **Objective:** This study aimed to assess the association between changes in kidney injury markers and ICU mortality in septic patients. Additionally, it evaluated the predictive value of dynamic biomarker fluctuations over three days and the potential benefits of early biomarker-based interventions. **Methodology:** A retrospective observational study was performed at Aga Khan University Hospital (Karachi). A total of 229 out of 772 ICU admissions were selected based on predefined inclusion criteria. Patients were categorized into normal, improved, and deteriorated groups based on AKI progression from day 1 to day 3. Key biomarkers such as serum creatinine and urine output were analyzed. Statistical analyses, including correlation and multivariate regression, were performed to assess mortality predictors. **Results:** The deteriorated group had significantly higher APACHE II ($p = 0.02$) and SOFA scores ($p < 0.001$). CKD (G4-G5) was more prevalent in this group (55.9%, $p < 0.001$). ICU mortality was significantly higher in the deteriorated group (26.5%, $p = 0.021$), with a steep decline in survival by day 56 (45.2% vs. 62.9% in non-deteriorated patients). Multivariate analysis identified worsening AKI as an independent predictor of mortality. **Conclusion:** Dynamic changes in kidney injury markers over the first three days of ICU admission are strong predictors of mortality in septic patients. Early identification of deteriorating kidney function and timely interventions can potentially improve survival rates.

INTRODUCTION

Acute kidney injury (AKI) is a widespread and serious complication affecting a substantial proportion of critically ill patients admitted to intensive care units (ICUs), with reported incidence rates ranging from 20% to 50% [1][2]. The rapid reduction of kidney function causes electrolyte problems along with excessive fluid storage and waste accumulation that advanced disease states because of AKI [3]. The KDIGO criteria serve as the established standard for AKI diagnosis because they use urine output measurements and serum creatinine tests as primary indicators [4]. Hospital stays become longer and severe AKI raises mortality risks significantly for ICU patients and research shows 50% mortality exists when patients need renal replacement therapy [3,5]. Medical progress in critical care has not made AKI management straightforward because the condition develops from multiple causes including sepsis and hypovolemic shock and nephrotoxic drug effects and unstable blood pressure conditions [5,6].

Dynamic monitoring of kidney injury has become a promising strategy for improving early detection as well as timely initiation of treatment of AKI in ICU settings [7]. Early diagnosis is usually difficult, due to delays in traditional markers such as serum creatinine to the development of kidney injury [8]. Novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), cystatin C, and tissue inhibitor of metalloproteinases-2 (TIMP-2) have more recently been developed and introduced in nephrology and have proven to be more sensitive and specific compared to the use of traditional biomarkers for early diagnosis of renal injury [9][10]. Serial monitoring of these renal biomarkers comparing them to urine output measures allows for the accurate tracking of

renal changes and the potential for earlier intervention [11]. The approach is able to identify subtle change in renal function that could precede overt AKI, which would then lead to timely interventions, like fluid resuscitation, elimination of the nephrotoxic drugs and hemodynamic optimization to prevent progression of AKI and reduce the risk of complications associated with the latter.

The dynmaic renal damage monitoring serves as a critical indicator for risk evaluation and clinical outcome prediction of critical patients with AKI [13]. Various research investigations have confirmed a direct relationship between ICU mortality and AKI severity thus making immediate recognition and treatment essential [14-16]. The death rates of patients with AKI were significantly higher for those exhibiting persistent renal dysfunction compared to patients showing recovery from AKI based on a meta-analysis report [17]. Medical personnel can enhance critical care by identifying treatment strategies that fit patient needs based on established associations between clinical conditions and mortality rates. Biomarker screening to detect AKI at an early stage shows potential to cut down ICU mortality through enhanced treatment methods according to recent findings [18].

This study examines changes in renal damage during three days in ICU sepsis patients in relation to their hospital survival. Sepsis-induced acute kidney impairments cause considerable ICU admissions because of systemic inflammation combined with endothelial dysfunction and microvascular damage thus increasing the risk for negative clinical outcomes. The study analyzes renal biomarker changes together with their mortality prediction to generate new insights about critical care acute kidney damage management for developing evidence-based patient outcome improvement methods. This study stands uniquely among all research conducted in Aga Khan University Hospital. The research results from this study will establish fundamental knowledge for future studies that aim to develop effective strategies to reduce mortality rates in sepsis-related AKI patients in intensive care units.

OBJECTIVES

The purpose of this study is to assess the relationship between dynamic changes in kidney injury markers and ICU mortality in septic patients, to monitor kidney injury status for three days to evaluate the predictive value of biomarker fluctuations, and to determine the potential benefits of early biomarker-based interventions in reducing ICU mortality among those with AKI.

MATERIALS AND METHODS

The research took place at a solitary center through retrospective observational methods. The research examined how sepsis patients admitted to the ICU experience evolving kidney function during their critical illness. The study included patients through predefined criteria to ensure relevant cases were part of the analysis. The selection process included 229 patients from a total of 772 ICU admissions through rigorous screening to identify subjects who met the inclusion criteria and had sufficient medical records for assessment. The researchers designed their approach to guarantee that their study results applied to a specific group of critically ill septic patients.

Patients aged over eighteen who had been hospitalized to the ICU with a confirmed sepsis diagnosis in the past year comprised the inclusion criteria. Sepsis-3 criteria—which describe sepsis as life-threatening organ malfunction caused by a dysregulated host response to infection, recognized by an increase in the Sequential Organ Failure Assessment (SOFA) score by ≥ 2 points—formed the basis for the diagnosis of sepsis. Patients who had pre-existing end-stage renal disease (ESRD), died within three days of ICU admission (to exclude early death cases where kidney injury progression could not be assessed), or had no instance of sepsis during admission were excluded from the study since these patients already had irreversible kidney dysfunction that could compromise the results. Establishing these inclusion and exclusion rules helped the study to guarantee uniformity in the patient group and improve the validity of the results.

The study was place in Aga Khan University Hospital's tertiary care critical care unit, Karachi, which has a well-established ICU arrangement. Retracted from electronic health records, patient charts, and medical files, prior year data were retrospectively gathered. Changes in renal function and AKI development from day 1 to day 3 of ICU admission helped patients diagnosed with sepsis to be divided into many groups. The justification for selecting this three-day observation period was based on earlier studies implying that early renal function changes within the first 72 hours may be quite important in determining patient outcomes. Three groups were incorporated into the classification system: the normal group (patients with no AKI at both day 1 and day 3), the improved group (patients whose AKI stage showed improvement over the three-day period), and the deteriorated group (patients whose AKI stage worsened over the three-day period). This division made it possible to have a dynamic knowledge of renal damage development and its correlation with ICU death.

Data collecting included a thorough examination of demographic features, pre-existing comorbidities, initial and serial SOFA scores, APACHE II Score, demand for renal replacement therapy (RRT), presence of sepsis-related sequelae including multiorgan failure, and ICU mortality. Key biomarkers—urine output and serum creatinine levels—were used to evaluate renal function;

these were noted as part of daily laboratory activities from day 1 through day 3 of ICU admission. To offer a larger background for changes in renal function, other indicators like fluid balance, vasopressor needs, and nephrotoxic drugs were also recorded.

SPSS (version 27.0) statistical analysis was used to investigate relationships between ICU outcomes and kidney damage development. Relationships between dynamic kidney damage indicators and ICU mortality were found by correlation study. Independent predictors of ICU mortality were found by multivariate regression analysis, which adjusted for possible confounding variables like age, concomitant diseases, degree of sepsis, and baseline renal function. To guarantee strength in the results and evaluate the effect of missing data, sensitivity studies were carried out.

Ethical approval was obtained from the Institutional Review Board (IRB), ensuring that the study adhered to ethical guidelines for research involving human subjects. Patient confidentiality were strictly maintained, with all identifiable information anonymized. ICU charts and medical records were reviewed solely for research purposes, and data access was restricted to authorized study personnel. Since this was a retrospective observational study with no direct patient interaction, informed consent was not required; however, institutional ethical guidelines were followed rigorously to ensure compliance with best research practices.

RESULTS

The study population comprised 229 patients classified into Normal (n = 155), Improved (n = 40), and Deteriorated (n = 34) groups. The mean age was similar across the groups (p = 0.631), and there were no significant differences in BMI (p = 0.121) or sex distribution (p = 0.347). However, disease severity scores, including APACHE II (p = 0.02) and SOFA (p < 0.001), were significantly higher in the deteriorated group, indicating greater illness burden. The presence of CKD at advanced stages (G4-G5) was also markedly higher in the deteriorated group (55.9%, p < 0.001), suggesting that baseline renal dysfunction may influence AKI progression. These findings highlight that while demographic factors remain consistent, disease severity and pre-existing renal impairment strongly correlate with AKI deterioration.

Table 1

Distribution of Patients According to Dynamic AKI Stage

	Total (N = 229)	Grouping Normal Group (n = 155)	Improved Group (n = 40)	Deteriorated Group (n = 34)	p-value
Basic Data					
Age (years)	66.7 ± 15.1	66.9 ± 15.7	69.1 ± 14.0	69.1 ± 13.3	0.631
BMI (kg/m²)	22.1 ± 4.8	21.8 ± 4.9	22.8 ± 4.3	22.4 ± 4.3	0.121
Sex, male (%)	141 (61.6)	94 (60.6)	23 (57.5)	24 (70.6)	0.347
APACHE II Score	23.6 ± 8.1	22.7 ± 8.0	25.8 ± 7.3	25.0 ± 8.3	0.02
SOFA Score	8.2 ± 3.6	7.1 ± 3.1	10.7 ± 2.9	10.1 ± 4.0	<0.001
Comorbidities (%)					
Coronary Artery Disease	54 (23.6)	34 (21.9)	12 (30.0)	8 (23.5)	0.359
Hypertension	118 (51.5)	74 (47.7)	24 (60.0)	20 (58.8)	0.095
Diabetes Mellitus	94 (41.0)	61 (39.3)	18 (45.0)	15 (44.1)	0.49
CKD Stage (G1-G5) (%)					
G1 - G2	75 (32.8)	58 (37.4)	12 (30.0)	5 (14.7)	0.002
G3a - G3b	92 (40.2)	64 (41.3)	18 (45.0)	10 (29.4)	0.021
G4 - G5	62 (27.0)	33 (21.3)	10 (25.0)	19 (55.9)	<0.001
Infection Sources (%)					
Lungs	151 (66.0)	109 (70.3)	22 (55.0)	20 (58.8)	0.031
UTI	58 (25.3)	37 (23.9)	14 (35.0)	7 (20.6)	0.22
Organ Support (%)					
Mechanical Ventilation	212 (92.6)	144 (92.9)	37 (92.5)	31 (91.2)	0.315
Vasopressor Therapy	63 (27.5)	32 (20.6)	17 (42.5)	14 (41.2)	<0.001
Receiving Hemodialysis (HD)	9 (3.9)	1 (0.6)	2 (5.0)	6 (17.6)	<0.001

"AKI: Acute Kidney Injury; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; G2: eGFR ≥ 60 mL/min/1.73 m²; G3a: eGFR 45–J59 mL/min/1.73 m²; G3b: eGFR 30–44 mL/min/1.73 m²; G4: eGFR 15–29 mL/min/1.73 m²; G5: eGFR <15 mL/min/1.73 m²; ICU: Intensive Care Unit; UTI: Urinary Tract Infection; HD: Hemodialysis"

Mortality rates increased significantly among the deteriorated group compared to others, with 7-day mortality at 20.6% (p = 0.003) and hospital mortality at 47.1% (p = 0.041). ICU mortality was also significantly higher in this group (26.5%, p = 0.021), indicating that

dynamic AKI progression is associated with worse survival outcomes. The trends observed across different mortality time points reinforce the prognostic impact of AKI worsening in septic patients. These results emphasize the need for early intervention to prevent AKI progression and reduce mortality risks.

Table 2

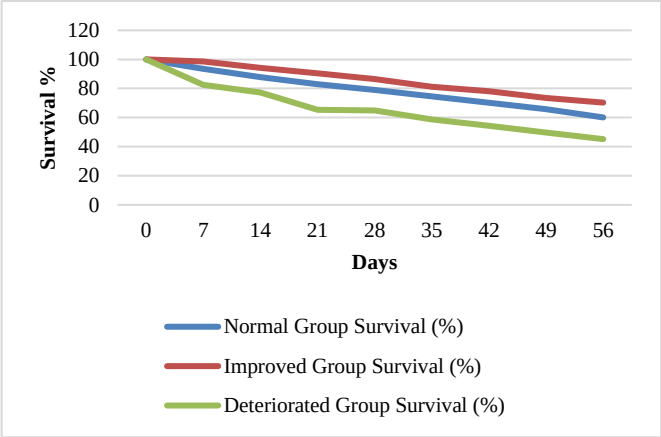
Mortality Outcomes of Patients with Sepsis

		Grouping				
Mortality Analysis	**Total (N = 388)**	**Normal Group (n = 263)**	**Improved Group (n = 68)**	**Deteriorated Group (n = 57)**	**p-value**	**p-value for Trend Test**
7-day	28 (7.2)	17 (6.5)	1 (1.5)	10 (17.5)	0.003	0.012
14-day	49 (12.6)	32 (12.2)	4 (5.9)	13 (22.8)	0.018	0.07
28-day	88 (22.7)	55 (20.9)	13 (19.1)	20 (35.1)	0.053	0.034
ICU	78 (20.1)	45 (17.1)	14 (20.6)	19 (33.3)	0.021	0.007
Hospital	150 (38.7)	92 (35.0)	28 (41.2)	30 (52.6)	0.041	0.012
Mortality Analysis	**Total (N = 388)**	**Non-Deteriorated Group (n = 331)**		**Deteriorated Group (n = 57)**	**p-value**	
7-day	28 (7.2)	18 (5.4)		10 (17.5)	0.003	
14-day	49 (12.6)	36 (10.9)		13 (22.8)	0.017	
28-day	88 (22.7)	68 (20.5)	20 (35.1)	0.018		
ICU	78 (20.1)	59 (17.8)	19 (33.3)	0.009		
Hospital	150 (38.7)	120 (36.3)	30 (52.6)	0.027		

Patients in the deteriorated group exhibited significantly lower survival rates over time. By Day 56, survival in the non-deteriorated group was 62.9%, compared to 45.2% in the deteriorated group. These findings further support the notion that AKI progression is a strong predictor of poor outcomes and mortality in septic patients.

Figure 1

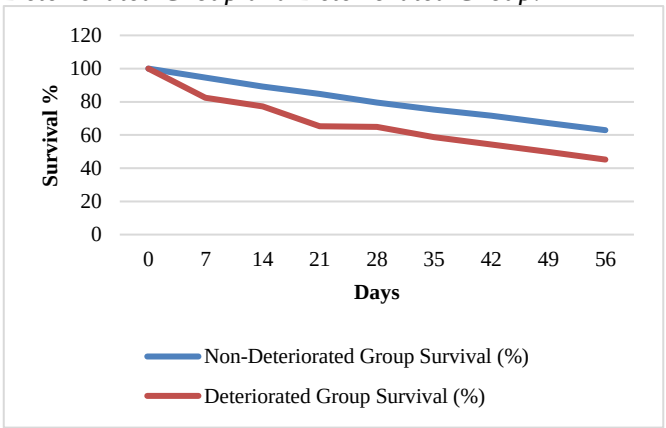
Hospital survival curve for patients in Normal Group, Improved Group and Deteriorated Group.



Survival declined over time in all groups, with the steepest decline observed in the deteriorated group. By Day 56, survival was 60.1% in the normal group, 70.3% in the improved group, and only 45.2% in the deteriorated group. This trend highlights the significant impact of AKI progression on long-term survival, reinforcing the importance of early intervention.

Figure 2

Hospital survival curve for patients in Non-Deteriorated Group and Deteriorated Group.



Multivariate analysis identified cancer (HR: 2.225, p < 0.001) and belonging to the deteriorated AKI group (HR: 1.702, p = 0.011) as independent predictors of hospital mortality. Other factors, such as history of stroke (p = 0.072), approached significance but did not meet statistical thresholds. These results indicate that among critically ill patients with sepsis, AKI progression significantly impacts survival, reinforcing the need for aggressive monitoring and management of renal function to improve outcomes.

Table 3

Univariate and Multivariate Cox Regression Analyses of the Predictors of Hospital Mortality

Variable	**Univariate Cox Regression Analysis**			**Multivariate Cox Regression Analysis (Likelihood Ratio)**		
	Hazard Ratio	**95% CI**	**p Value**	**Hazard Ratio**	**95% CI**	**p Value**
Hospital Mortality						
Age >65	1.074	0.785–1.470	0.656	-	-	-
Gender, male	0.882	0.660–1.180	0.398	-	-	-
APACHE II	0.994	0.978–1.011	0.494	-	-	-
BMI	0.99	0.962–1.019	0.49	-	-	-

Coronary heart disease	0.753	0.527–1.077	0.121	-	-	-
History of stroke	0.774	0.528–1.135	0.189	0.671	0.434–1.036	0.072
Hypertension	1.117	0.810–1.538	0.5	-	-	-
COPD	1.044	0.683–1.598	0.841	-	-	-
Cancer	2.032	1.511–2.731	<0.001	2.225	1.591–3.111	<0.001
Liver cirrhosis	2.218	1.434–3.431	<0.001	-	-	-
Diabetes mellitus	0.928	0.688–1.253	0.627	-	-	-
CKD	0.937	0.608–1.442	0.766	-	-	-
Deteriorated group (vs. all other groups)	1.65	1.102–2.471	0.015	1.702	1.131–2.560	0.011

DISCUSSION

Our study findings align with and expand upon previous research highlighting the prognostic implications of Acute Kidney Injury (AKI) progression in septic patients. The significantly higher APACHE II and SOFA scores in the deteriorated group underscore the role of disease severity in AKI outcomes, similar to prior studies that have identified these scores as strong predictors of mortality in critically ill patients with AKI [20, 21]. These scoring systems quantify the degree of organ dysfunction and severity of illness, reinforcing the notion that patients with higher scores are at an increased risk of mortality.

The marked association between advanced CKD (G4-G5) and AKI deterioration further reinforces existing evidence suggesting that baseline renal impairment predisposes patients to worse renal outcomes and increased mortality [22]. Patients with pre-existing CKD often exhibit a reduced renal reserve, making them more susceptible to acute insults and progression to end-stage renal disease. This finding supports the growing consensus that early recognition and intervention in high-risk patients could mitigate AKI progression and improve survival rates.

Research findings demonstrate that hospital and intensive care unit mortality increases directly with worsening acute kidney injury. The research results of Mehta et al. [23] show that septic patients with worsening AKI experience higher 28-day mortality rates and hospital deaths. The patients who experienced deterioration in our study demonstrated increased mortality at both the intensive care unit and hospital levels which emphasizes the importance of immediate treatment interventions.

Research shows that patients with deteriorating AKI experience early mortality at a rate of 20.6% which matches previous findings that AKI patients with unresolved or worsening kidney function have elevated death rates [24]. The high early mortality rate emphasizes the need for continuous renal function monitoring combined with timely intervention to minimize AKI complications. Further research needs to explore delayed or insufficient resuscitation methods for treating septic patients whose AKI condition worsens because these practices produce adverse effects.

The findings align with previous studies that have demonstrated the significant impact of AKI progression on survival in septic patients. Research has consistently shown that worsening AKI correlates with higher mortality rates, as seen in the study by Sahiba et al. [25], which reported that patients with deteriorating renal function had a nearly twofold increased risk of death compared to those with stable or improving kidney function.

Ahmed et al. [26] found that AKI severity was directly linked to reduced long-term survival, emphasizing the need for early detection and intervention. AKI progression contributes to systemic complications that worsen sepsis outcomes, reinforcing the importance of aggressive renal management [24]. AKI in critically ill patients significantly increases mortality risk, particularly in those with multi-organ dysfunction. The present study builds on these conclusions, demonstrating that the deteriorated AKI group had the lowest survival rates (45.2% by Day 56) and was a significant predictor of mortality.

Compared to earlier studies, the present findings further highlight the critical role of comorbidities such as cancer in worsening outcomes for septic patients with AKI. Previous research by Munch et al. [27] identified cancer as a major risk factor for AKI-related mortality, with hazard ratios comparable to those reported in this study. Nazzal et al. [28] confirmed that AKI patients with malignancies face significantly poorer outcomes due to increased vulnerability to sepsis and multi-organ failure. Moreover, a study by Mizushima et al. [29] emphasized that patients with improving renal function exhibit better long-term survival, as seen in the present study where the improved group had a 70.3% survival rate.

These results collectively emphasize the urgent need for proactive renal monitoring and aggressive management in septic patients, supporting ongoing calls for early AKI detection strategies to mitigate long-term mortality risks. The inability to restore immune homeostasis in these patients could serve as a therapeutic target for future interventions. Additionally, our findings suggest that serial monitoring of cytokine profiles may provide valuable prognostic information and guide personalized therapeutic approaches in septic patients with AKI.

Clinical Implications and Future Directions

Our study confirms that AKI progression in septic patients is strongly associated with increased mortality and immune dysregulation. The findings suggest that monitoring dynamic changes in renal function, and immune response could enhance early risk stratification and guide more personalized interventions. Future research should explore targeted immunomodulatory therapies to mitigate immune suppression and improve outcomes in patients with worsening AKI. Additionally, prospective interventional trials assessing early renal support strategies in high-risk groups may help refine clinical management protocols for septic AKI patients.

CONCLUSION

The study found that dynamic changes in kidney function significantly impact ICU mortality among septic patients, with those experiencing worsening AKI exhibiting the highest mortality rates (26.5% ICU mortality, p = 0.021) and poorest survival outcomes (45.2% survival by Day 56). Disease severity scores (APACHE II and SOFA), advanced CKD stages, and vasopressor use were strongly associated with AKI progression. Patients in the deteriorated group had a significantly higher risk of adverse outcomes, emphasizing the prognostic value of early renal function monitoring. Future research should focus on biomarker-driven early interventions to mitigate AKI progression and improve patient survival in sepsis-induced kidney injury.

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