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Acute Kidney Injury Severity And Its Impact On Clinical Outcomes In Critically Ill Patients.

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ABSTRACT
Acute kidney damage (AKI), which is linked to higher morbidity, mortality, and the need for organ support, is a frequent consequence in critically sick patients. This study evaluated AKI severity and its relationship with major clinical outcomes. A retrospective secondary-data-based observational study was conducted using data from 144 critically ill patients. Patients were classed as either AKI or non-AKI, and KDIGO Stages 1-3 were used to classify the severity of AKI. In-hospital mortality, mechanical ventilation, usage of vasoactive drugs, dialysis, ARDS, and length of hospital stay were among the clinical outcomes. Binary logistic regression, correlation analysis, independent t-test, chi-square test, frequency, and percentage were all used. AKI occurred in 41 patients (28.5%), with KDIGO Stage 3 being the most frequent severity category. Patients with AKI were older and had significantly higher APACHE II and IGS2/SAPS II scores. Mortality, mechanical ventilation, vasoactive drug use, dialysis requirement, and ARDS were significantly more frequent among AKI patients. Dialysis requirement increased significantly with advancing KDIGO stage. KDIGO severity correlated positively with AKI creatinine and negatively with urine output. AKI continued to be independently linked to in-hospital mortality in adjusted regression (adjusted OR=3.657, 95% CI: 1.225–10.915, p=0.020). Higher mortality, more organ support needs, and a more severe disease were all linked to AKI. Identification of critically sick individuals at increased risk of unfavorable outcomes may be aided by early detection and careful monitoring of renal impairment.

Keywords: Acute kidney injury; KDIGO; Critical illness; Mortality; Dialysis

1. Introduction

It has been demonstrated that acute kidney damage (AKI), a prevalent and clinically relevant disease in critically sick patients, increases morbidity, mortality, health care use, and length of hospital stay. AKI can occur rapidly in critical illness due to multi-faceted factors of systemic inflammation, changes in renal perfusion, hemodynamic instability, infection, organ dysfunction and therapeutic interventions. Renal function changes that occur in the intensive care unit (ICU) may significantly impact prognosis, and worsening or improvement of AKI status are linked to clinical outcomes in critically ill patients, including those with septic patients [1]. As a result, early detection and evaluation of AKI are essential for critical care management. In intensive care units (ICUs), AKI is a serious issue. The multinational AKI-EPI study showed that AKI is common in the critically ill and that the worse the severity of the AKI, the worse the outcome [2]. Due to the diversity of patient populations, underlying disease processes, diagnosis and management, healthcare resources, and exposure to causative factors in each clinical setting, there is considerable variation in the epidemiology of AKI. However, AKI is still a significant clinical issue worldwide and a significant contributor to the adverse short and long-term outcomes [3]. It is also seen in various age groups with critically ill children and young adults having substantial morbidity and mortality due to AKI [4].

Generally, AKI is multifactorial in critical illness. Renal injury may be caused by reduced renal perfusion, circulatory shock, systemic inflammation, endothelial dysfunction, and/or sepsis, potentially nephrotoxic agents, and/or multiorgan failure. Patients can have multiple of these factors at the same time and become vulnerable to renal dysfunction [5]. These mechanisms are especially applicable in cases of severe systemic conditions, such as severe COVID-19, which can present with respiratory failure, inflammatory response, hemodynamic abnormalities, infection-related complications, and/or multiple organ involvement. A pre-existing chronic renal illness may further impair the

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prognosis. Renal impairment is linked to poor outcome in septic patients in the ICUs, suggesting the need for baseline renal status in critically ill populations, with both AKI and chronic kidney disease being linked to poor outcome [6].

The severity of AKI is important to assess, as renal dysfunction is not an either/or phenomenon. The Kidney Disease: Improving Global Outcomes (KDIGO) classification establishes a standardized approach for evaluating AKI in relation to elevated blood creatinine and urine production. categorizes AKI into three stages, each of which is more severe than the last. This classification can be used to assess disease progression, compare patient populations, and identify those most likely to experience poor outcomes. Modern evidence highlights that the severity of AKI is the result of complex pathophysiological processes with renal perfusion, inflammatory factors, microcirculatory abnormalities, tubular injury, and interactions with other organs [7].

The clinical effect of AKI is not limited to renal failure. But the modern understanding of renal failure is that relatively small amounts of renal deterioration can have important consequences, even when dialysis is not required, as traditional concepts would have suggested. Therefore, in the most severe cases, AKI should be considered as a part of an evolving illness, and the length, level, course, and associated systemic abnormalities are all associated with prognosis [8]. This idea is used when different outcomes are being compared between renal failure stages (KDIGO) to assess how the various stages differ from one another.

AKI can have a number of clinical repercussions, including death, the need for mechanical breathing, the need for vasopressors, renal replacement treatment, and duration of hospital stay. Importantly, even mild- or moderate-severity AKI has been linked to increased mortality and morbidity in the critically ill patient, indicating that early signs of renal dysfunction should not be ignored as a minor clinical concern [9]. Patients may experience worsening metabolic and fluid abnormalities as AKI worsens and might need dialysis or other renal replacement therapies. For patients with severe AKI, the timing and initiation of renal replacement therapy (RRT) is an important part of critical care management and may be a determinant of clinical outcomes [10]. Although it is a well-known and serious consequence of critical illness, the degree of the negative consequences can vary greatly based on the patient's clinical state and the degree of renal damage. The fact that the diagnosis of AKI is simply binary could thus underestimate the prognosis of progressive renal dysfunction. The KDIGO classification can give a more detailed understanding of the association between renal injury and clinical outcomes. Using the mortality rate, dialysis dependency, mechanical ventilation, and use of some vasopressors as indicators to evaluate the severity of AKI and its association with specific hospitalizations can help identify patients at high risk, and help guide timely clinical action. Thus, this study's primary goal is to evaluate the degree of acute renal damage and how it affects the critically sick patient's clinical outcome.

Objectives

1. To use KDIGO staging to assess the prevalence and severity of acute renal damage in critically ill patients.
2. To contrast the results and clinical features of individuals with and without acute renal damage.
3. To evaluate the relationship between the severity of AKI and unfavorable clinical outcomes, namely death, length of hospital stay, dialysis, and mechanical ventilation.

2. Methodology

2.1 Study Design

This study used a pre-existing clinical dataset of critically sick patients for a retrospective observational analysis based on secondary data. The purpose of the study was to evaluate the prevalence and severity of AKI and its relationship with the most important clinical outcomes [11].

2.2 Study Population

Fourteen patients were selected for the study from a total of 144 critically ill patients available in the data-set. Patients were categorized as either having AKI or not. Severity-based analysis was performed by further categorizing the patients with AKI into KDIGO Stage 1, 2, and 3.

2.3 Eligibility Criteria

Those patients with available data for AKI status, renal parameters and major clinical outcomes were included. Records which did not have enough information to conduct a certain analysis were omitted from that specific analysis only.

2.4 Study Variables

Demographic variables (age, sex, BMI), comorbidities (HTN, DM, CVD) and clinical severity indices (APACHE II, IGS2/SAPS II) were measured. Renal variables included were the status of AKI, serum creatinine, urinary output, KDIGO stage, cause of AKI, and dialysis requirement. Clinical outcomes were mortality, mechanical ventilation, length of mechanical ventilation, requirement for vasoactive drugs, dialysis, and length of hospital stay.

2.5 Assessment of AKI Severity

The AKI status was determined using the data in the dataset. Using the Kidney Disease: Improving Global Outcomes (KDIGO) categorization system, the severity of AKI was categorized as Stage 1, Stage 2, and Stage 3. Both the existence of AKI and its rising severity (based on KDIGO criteria) were examined in the patients.

2.6 Outcome Measures

In-hospital fatalities were the primary result. The need for dialysis, the use of invasive mechanical ventilation, the use of vasoactive agents (VVAs), mechanical ventilation (MV) days, and inpatient days were secondary outcomes.

2.7 Statistical Analysis

Categorical variables were summarized using frequency and percentage, whereas continuous variables were summarized using mean and standard deviation. Continuous variables were compared between the two study groups (AKI vs non-AKI) by independent-samples t-test. Association between categorical variables such as AKI status, KDIGO stage, mortality,

mechanical ventilation, dialysis and requirement for vasoactive drugs was assessed using the chi-square test. Correlation analysis was used to analyze the relationships between renal parameters and the relevant continuous clinical variables. The data were analyzed using binary logistic regression to find variables linked to hospital deaths, and the results were displayed as odds ratios with 95% confidence intervals. Statistical significance was defined as a p-value of less than 0.05.

3. Results

3.1 Baseline Demographic and Clinical Characteristics

Baseline demographic data, comorbidities and severity of illness scores were analyzed to assess if there were clinical differences observed between those who developed AKI and those who did not. Pre-existing characteristics and general disease severity are relevant for the development of AKI and outcomes as these factors may influence the overall disease severity and progression. Age, BMI, sex, significant comorbidities, and validated critical illness ratings were therefore compared between the AKI and non-AKI groups. Table 1 provides a summary of the findings.

Table 1. Baseline demographic and clinical characteristics according to acute kidney injury status

Characteristic	Overall	Non-AKI	AKI
Age, years	58.21 ± 13.76	56.39 ± 14.35	62.78 ± 11.02
BMI, kg/m²	29.24 ± 5.38	29.44 ± 5.78	28.73 ± 4.22
IGS2/SAPS II score	29.85 ± 13.07	28.56 ± 13.49	33.10 ± 11.46
APACHE II score	12.75 ± 6.43	11.70 ± 5.97	15.39 ± 6.84
Male sex	80 (55.6%)	57 (55.3%)	23 (56.1%)
Hypertension	55 (38.2%)	33 (32.0%)	22 (53.7%)
Diabetes mellitus	56 (39.4%)	34 (33.7%)	22 (53.7%)
COPD	4 (2.9%)	2 (2.0%)	2 (5.0%)

Patients who had developed AKI had significantly higher IGS2/SAPS II and APACHE II scores and were older. Other factors significantly related with the development of AKI were hypertension and diabetes mellitus. However, body mass index, sex distribution and COPD did not have a significant difference between groups.

3.2 Frequency and Severity of AKI

The incidence of AKI in the entire study group was examined to ascertain the renal load in all critically sick individuals. Patients identified as having AKI were then classified by the KDIGO system to describe the distribution of disease severity. This step enabled the identification of mild, moderate and severe renal injury, and was used to make comparisons to the outcomes after AKI. The distribution is displayed in Table 2.

Table 2. Distribution of AKI and KDIGO severity

AKI/KDIGO category	n	Percentage	Reference population
Non-AKI	103	71.5%	Total study population
AKI	41	28.5%	Total study population
KDIGO Stage 1	5	12.2%	Patients with AKI
KDIGO Stage 2	16	39.0%	Patients with AKI
KDIGO Stage 3	20	48.8%	Patients with AKI

As shown in Table 2, a significant number of critically ill patients developed AKI. The majority of patients with AKI had more severe stages, with KDIGO Stage 3 being the most severe subgroup. Stage 2 was also a large proportion and there was a relatively small proportion of Stage 1. Overall distribution of patients by AKI status can be seen in Figure 1.

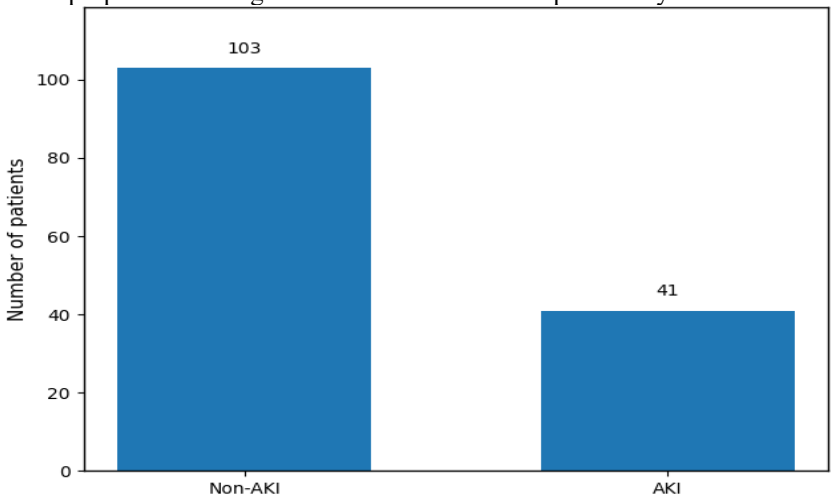

Figure 1. Distribution of patients according to acute kidney injury status

A lower but clinically significant proportion of the study's participants suffered AKI, but the majority of individuals did not acquire the condition (Figure 1). This distribution indicates that a considerable percentage of critically sick individuals have AKI, which calls for more research on the severity of AKI and patient outcomes.

3.3 Clinical Outcomes According to AKI Status

The clinical significance of renal injury was assessed by comparing major outcomes between those with and without renal injury. The analysis was conducted on indicators of clinical deterioration relevant to clinical practice, such as mortality, respiratory support, vasoactive therapy, renal replacement therapy, ARDS, and outcomes related to duration. These metrics were selected because they reflect the severity of critical disease and the amount of resources required to present with AKI. The comparison is shown in Table 3.

Table 3. Comparison of clinical outcomes between patients with and without acute kidney injury

Clinical outcome	Non-AKI	AKI	Statistical test	p-value
In-hospital mortality	57 (55.3%)	36 (87.8%)	Chi-square	<0.001
Mechanical ventilation	50 (48.5%)	34 (82.9%)	Chi-square	<0.001
Vasoactive drug requirement	43 (44.3%)	32 (82.1%)	Chi-square	<0.001
Dialysis requirement	0 (0.0%)	13 (31.7%)	Fisher's exact test	<0.001
ARDS	61 (66.3%)	35 (92.1%)	Chi-square	0.005
Duration of hospitalization, days	12.98 ± 11.38	14.73 ± 13.05	Independent t-test	0.454
Duration of mechanical ventilation, days	5.05 ± 9.52	10.06 ± 9.73	Independent t-test	0.019

Table 3 shows that AKI was consistently associated with worse clinical outcomes. The rates of death, mechanical ventilation, vasoactive medication usage, dialysis, and ARDS were all considerably greater in patients with AKI. Additionally, the AKI group required mechanical ventilation for a notably longer period of time. However, there was no discernible difference in the total duration of hospital stay between the two groups (AKI and non-AKI). A survival curve graph is shown in Fig. 3 to further highlight the disparity in in-hospital mortality between the AKI and non-AKI groups.

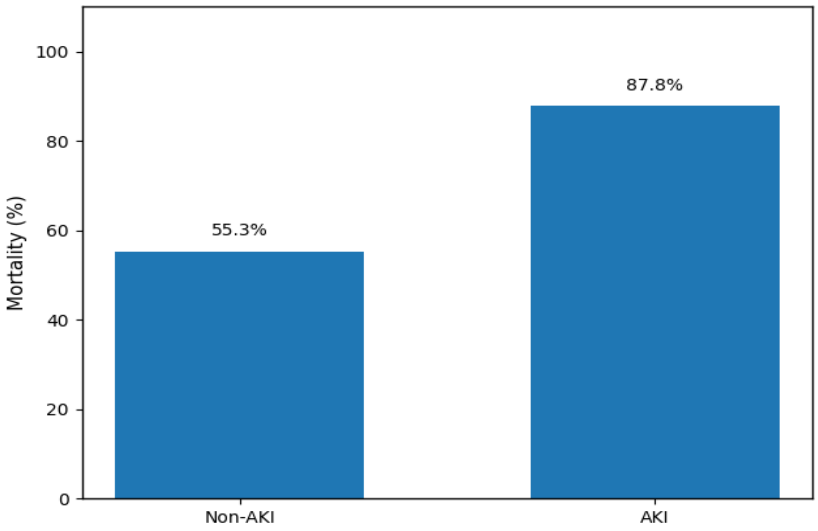

Figure 3. In-hospital mortality according to acute kidney injury status

In-hospital mortality was significantly greater in patients with AKI than in those without AKI (figure 3). Based on this finding, the development of AKI was associated with significantly worse short-term clinical outcome in critically ill patients.

3.4 Clinical Outcomes According to KDIGO Severity

Analysis of outcomes was extended to include the presence or not of AKI, as this is a spectrum of renal dysfunction. AKI patients were classified according to the KDIGO classification and compared for clinical outcomes to see if there was a progressive worsening of outcomes with worsening renal injury. The three stages were compared for mortality, mechanical ventilation, vasoactive support, dialysis and length of hospital stay. The outcome of this is reported in Table 4.

Table 4. Clinical outcomes according to KDIGO stage among patients with acute kidney injury

KDIGO stage	n	Mortality	Mechanical ventilation	Vasoactive drugs	Dialysis	Hospital stay, days
Stage 1	5	4 (80.0%)	4 (80.0%)	4 (80.0%)	0 (0.0%)	11.40 ± 6.58
Stage 2	16	12 (75.0%)	12 (75.0%)	12 (75.0%)	3 (18.8%)	21.13 ± 17.30
Stage 3	20	20 (100.0%)	18 (90.0%)	16 (88.9%)	10 (50.0%)	10.45 ± 7.49

The mortality rate and dialysis burden was greatest in the most severe AKI category, as summarized in Table 4. However, the overall association of KDIGO stage and mortality was not statistically significant. There was no significant difference across stages in mechanical ventilation and in the use of vasoactive drugs. Dialysis requirement was significantly associated with increasing KDIGO severity, however, in contrast. Less dialysis was needed among patients with Stage 1 disease, and more was needed among patients with Stage 2 disease and the most was needed among patients with Stage 3 disease. This suggests that with increasing severity of AKI there was a greater prevalence of increased renal replacement needs. The mortality rates by KDIGO stage are shown in Figure 4.

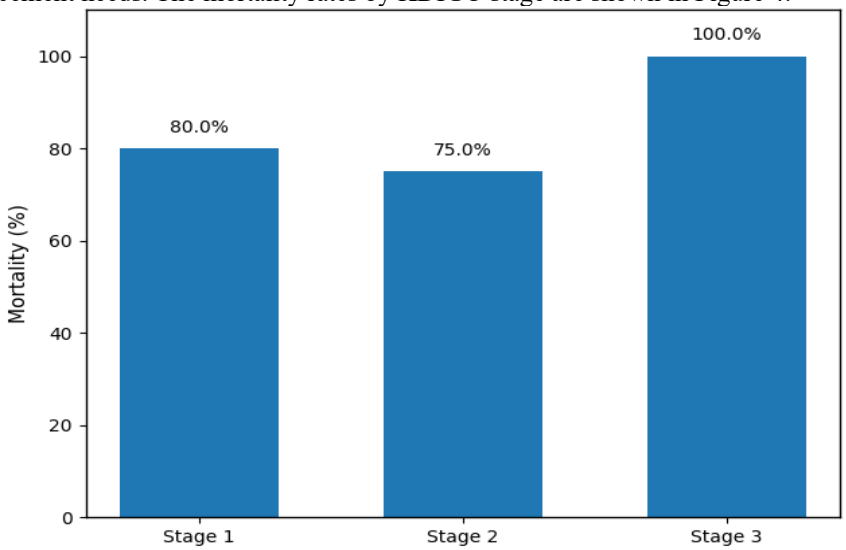

Figure 4. In-hospital mortality according to KDIGO stage

As seen in Figure 4, mortality rate was 100% among KDIGO Stage 3 patients, with a high mortality rate among patients of KDIGO Stage 1 and 2. The relationship between KDIGO stage and mortality was not statistically significant, but the trend appears to be worse prognosis for severe AKI.

3.5 Correlation Between Renal and Clinical Parameters

Correlation analysis was used to explore the relationships between renal function, physiological severity, urine output and variables related to hospitalization. For continuous variables, Pearson correlation was applied, and the correlation between the ordinal KDIGO stage with selected renal and clinical measure was evaluated using the Spearman correlation. The general correlation pattern of the main continuous variables is shown in Figure 6.

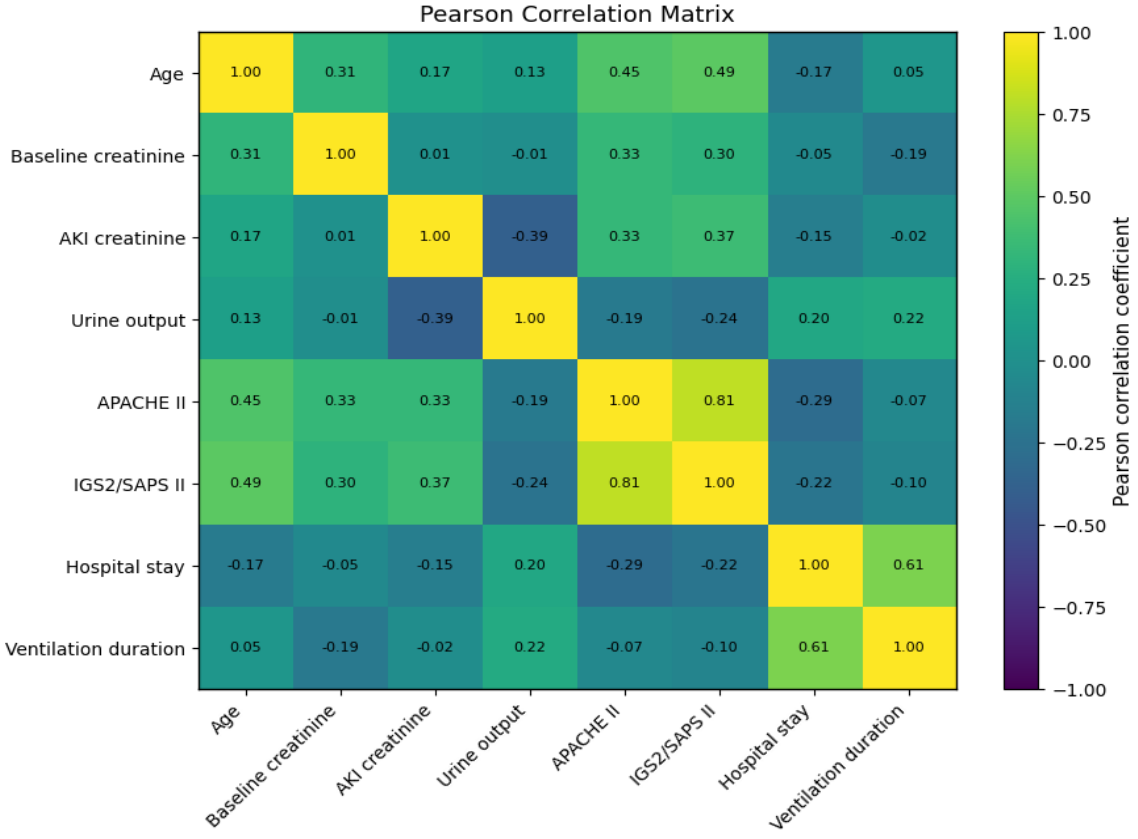

Figure 6. Correlation matrix of major renal and clinical variables

The highest correlation was noted between the APACHE II and IGS2/SAPS II scores (r = 0.81) that showed good agreement between the two measures of critical illness severity as shown in Figure 6. The duration of ventilation was also significantly associated with hospital stay (r = 0.61). Baseline and AKI-associated creatinine were positively correlated with APACHE II (r = 0.33 and 0.30, respectively) and IGS2/SAPS II (r = 0.33 and 0.30, respectively), and negatively correlated with urine output (r = −0.39 and −0.39, respectively). Further Spearman analysis showed that the KDIGO stage was positively correlated with creatinine level for AKI ($\rho = 0.526$, $p<0.001$) and negatively correlated with urine output ($\rho = -0.720$, $p<0.001$). Increased severity of AKI was associated with more significant increases in creatinine and decreased urine output, confirming these findings.

3.6 Predictors of In-Hospital Mortality

AKI was significantly correlated with in-hospital mortality, according to the uncorrected logistic regression. Diabetes mellitus and dialysis were not statistically significant in relation to death, although age, APACHE II score, IGS2/SAPS II score, mechanical ventilation, vasoactive medication usage, and hypertension were. AKI continued to be an independent predictor of in-hospital mortality even after controlling for age and APACHE II score. The APACHE II score and age continued to have separate correlations with mortality. Overall, our results show that, in addition to the overall severity of critical illness, AKI independently increases the chance of death.

4. Discussion

In the current investigation, it was found that patients with acute kidney injury had a significantly poorer clinical profile in the critical care setting. The patient cohort with AKI was significantly older and more often had longer stays in the hospital ward, hypertension, and diabetes mellitus. AKI was also linked to increase in-hospital mortality, increased use of mechanical ventilation and vasoactive drugs, increased need for dialysis, increased incidence of ARDS and longer duration of mechanical ventilation. The present results are in line with the general knowledge that highly complicated patients with high physiological and nutritional risk have more severe organ dysfunction and worse prognosis [12]. Our results corroborate that there is a strong link between AKI and mortality, suggesting that AKI is not just a temporary phenomenon of the kidney, but an important prognostic event. There is prior evidence that AKI can have long-term consequences such as ongoing renal dysfunction, chronic kidney disease, recurrent admission, cardiovascular complications and mortality [13]. When considering all other variables, AKI remained a significant independent risk factor for in-hospital mortality in the present analysis. This indicates that the presence of AKI adds some extra prognostic information to overall severity of illness and is a potential independent marker of adverse outcome.

The pathophysiological link between critical illness and AKI is complex. Renal damage can occur in sepsis by changes in renal perfusion, inflammatory responses, endothelial dysfunction, microcirculatory changes, tubular damage, and immune dysfunction [14]. Severe COVID-19 may also involve similar mechanisms, as hypoxemia, systemic inflammation, hemodynamic instability, coagulopathy and multiorgan dysfunction can be associated with renal dysfunction. Severe AKI has been reported to have poor outcomes in patients with COVID-19, especially when it is complicated by death and need for renal replacement therapy [15]. Severe systemic consequences of progressive renal dysfunction are reflected by the high mortality rate seen in patients with advanced KDIGO stages in the current investigation. There was also a significant association between KDIGO severity and dialysis requirement. Needing dialysis increased with severity of AKI, which meant that the renal functional impairment was getting worse. Fluid management is also an important aspect in the prevention and management of AKI in critically ill patients. Randomized trials have emphasized the need for fluid choice and hemodynamic management in the ICU setting [16]. Similarly, in critically ill septic patients, previous studies have demonstrated that AKI is linked to more severe illness, increased need for organ support and adverse clinical outcomes [17]. Patients who are already receiving dialysis or are developing end-stage renal disease could be particularly at risk due to low renal reserve and increased systemic disease burden [18].

The correlation analysis also showed that renal dysfunction was closely related to the severity of critical illness. Creatinine level was positively correlated with APACHE-II and IGS2/SAPS-II scores, and negatively correlated with urine output when it came to AKI-related creatinine. KDIGO stage was also moderately correlated with AKI creatinine and strongly correlated with negative urine output. The present results suggest that a greater severity of AKI was related with greater biochemical renal dysfunction and decreased urine output. These patterns highlight the need for ongoing renal monitoring following an acute illness. The importance of structured follow-up after AKI for the detection of chronic renal impairment, for the optimization of medication use, for blood pressure and kidney function monitoring and reduction of long-term complications has been proposed [19].

Age was also independently related to death with the adjusted model. Critically ill older patients may also have diminished physiological reserve, more comorbidities and less tolerance of multiorgan dysfunction. There were also other differences in treatment decisions, preferences and outcomes among seriously ill older adults, as reported previously [20]. AKI is now known as a common and important complication of critically ill COVID-19 patients, and is associated with direct and indirect kidney injury pathways [21]. Similarly, mortality rates, respiratory failure, and multiorgan involvement have been shown to be high in critically ill patients with SARS-CoV-2 pneumonia [22]. A systematic review and meta-analysis also found that COVID-19 is linked to higher rates of serious illness, admission to an intensive care unit

(ICU), and mortality in patients with AKI [23].

The study's conclusions have significant therapeutic ramifications. Early detection of renal impairment, thorough monitoring of serum creatinine and urine output, optimal hemodynamics, avoidance of needless nephrotoxic drugs, and prompt management of complications may all assist to stop AKI from getting worse. But early detection may not be enough. Automated electronic AKI alerts have been shown to be ineffective when used randomly without an effective clinical response, and notification alone is not likely to increase the results of such alerts [24]. The study is subject to several limitations, such as being a retrospective secondary data design and the small number of patients in some KDIGO stages, especially KDIGO 1. Residual confounding also may occur. However, the clear links between AKI, disease severity, dialysis need and mortality reinforce the relevance of renal dysfunction in the critically ill.

5. Conclusion

AKI was common and clinically important and was strongly associated with adverse outcomes among critically ill patients. Patients with AKI were more likely to be sicker, to have hypertension and diabetes mellitus, and had significantly worse clinical outcomes than those without AKI. AKI was linked to increase in-hospital mortality, increased need for mechanical ventilation and vasoactive support, increased incidence of ARDS, longer duration of mechanical ventilation and increased requirement for dialysis. Severity-based analysis also revealed that more advanced KDIGO stages were related to higher renal dysfunction and dialysis need. The grades of AKI were correlated with creatinine, with higher creatinine levels associated with higher severity, and correlated with urine output, with lower urine output associated with more severe AKI, indicating progressive worsening of renal function as the severity of the AKI increased. Significantly, even after controlling for age and APACHE II score, AKI remained an independent predictor of in-hospital mortality, indicating that it is a prognostically significant condition that goes beyond overall illness severity. These findings emphasize the significance of early renal dysfunction identification, meticulous serum creatinine and urine output monitoring, hemodynamic status adjustment, and prompt treatment of complications in critically sick patients. The significance of AKI severity as a risk and outcome measure in the clinical context is supported by the study's limited sample size and retrospective design.

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