Exploring the Rate of Mortality in Critically Ill Patients with Acute Kidney Injury: A Comprehensive Analysis Stratified by Rifle Classification

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Abstract

Objective: To determine the rate of mortality among critically ill patients with acute kidney injury using the RIFLE classification.

Material and Methods: This comprehensive analysis of cross-sectional study was done in Intensive Care Unit between April 2022 and April 2023 in a tertiary care hospital, Akbar Niazi Teaching Hospital, Islamabad Pakistan. Total 350 patients were admitted in the ICU of the hospital, ages 18 years and above, presented with critical illness. The RIFLE classification was employed to assess patient mortality, revealing that individuals in the R, I, and F classes had higher mortality rates than those with normal kidney function. Regression model and odd ratio analysis was conducted to measure the association between the maximum RIFLE stage and mortality.

Results: The patients mean age was 48.58±17.12 years. Among 350 patients, 65.1% (n=228) developed AKI, whereas 34.9% (n=122) had normal kidney functions. The mean urine output value was 40.04±48.09 ml/hr, with 43% patients was anuric and creatinine was 4.37±3.52 mg/dl. Patients in the RIFLE classes R, I, and F exhibited hospital mortality rate was 2.2%, 4.8%, and 11.4%, respectively. The odd ratio for in-hospital mortality associated with AKI and RIFLE classes R, I, and F was 1.9 (1.56-2.40, p = 0.0001), 1.1 (0.80-1.40, p = 0.231), 1.5 (1.1-2.00, p ≤ 0.001), and 4.0 (3.50-4.50, p = 0.0001), respectively.

Conclusion: Hospital mortality is elevated in cases of AKI as per the RIFLE classification. Notably, patients falling into RIFLE class R face a heightened risk of advancing to either stage I or F.

Keywords: Acute kidney injury; Critical illness; Hospital; Intensive care units; Mortality.

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Introduction

Critically ill patients often encounter the common complication of acute kidney injury (AKI).[1] The reported incidence of AKI in hospitals have more than doubled, encompassing a notable increase in cases requiring dialysis.[2] Additionally, there is an observed correlation between AKI and high-income countries, with AKI developing in more than 20% of the hospitalized population. This statistic includes around 50% of admitted patients in intensive care unit (ICU).[3] In an analysis, persistent AKI was associated with a 30-day mortality odds ratio (OR) of 2.4 and a 1-year mortality OR of 2.1, based on the RIFLE classification's three grades (R, I, and F).[4]

AKI necessitating dialysis (AKI-D) is linked to a significantly elevated mortality rate, surpassing that of other critical illnesses such as myocardial infarction (MI) or acute respiratory distress syndrome

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(ARDS). Among patients experiencing AKI-D, the overall hospital mortality stands at 33%, and those in the ICU confront a mortality rate ranging within 50-60%.[5]

Currently, numerous studies have aimed to enhance our comprehension of AKI definition and diagnostic criteria. Previously, AKI definitions, primarily relying on creatinine or it's clearance level, were used. The standard classification and definition of AKI, the RIFLE (Risk, Injury, Failure, Loss, and End-stage)[5]. Currently, this criterion is employed for AKI classification, incorporating both serum creatinine levels and urine output volume. The RIFLE criteria, emphasizing alterations in creatinine levels within 24 hours.[6]

A total cessation of renal function lasting at least 4 weeks characterizes end-stage kidney disease, necessitating renal replacement therapy (RRT) for a minimum of 3 months.[7] The RIFLE classification defines three escalating grades of AKI severity – risk ®, injury (I), and failure (F) classes, along with two outcome categories: loss and end-stage kidney disease. A distinctive aspect of RIFLE classification is that it offers three severity grades for AKI, determined by changes in either creatinine levels or urine output relative to baseline condition. This approach enables the classification of patients with AKI into one of the three RIFLE severity categories.[8]

The severity of AKI was assessed using the RIFLE staging system. AKI severity was categorized as follows: [Stage 1: creatinine increases 1.5 times or reduce GFR $\geq$ 25%, urine output was 0.5 ml/kg/h in 6 hours, and diuresis], [Stage 2: creatinine increases 2 times or reduce GFR $\geq$ 50%, urine output remained 0.5 ml/kg/h in 12 hours, and diuresis], and [Stage 3: creatinine increases 3 times or reduce GFR $\geq$ 75%, urine output was failure and anuric].[8]

The study hypothesized that the odds of mortality in critically ill patients with AKI at the R, I, and F stages of the RIFLE classification are comparable to the odds of mortality in critically ill patients with normal kidney function in our population.

Therefore, the study aim was to determine the rate of mortality among critically ill patients with acute kidney injury using the RIFLE classification.

Material and Methods

A comprehensive analysis of prospective cross-sectional observational study was done in Intensive Care Unit between April 2022 and April 2023 in a tertiary care hospital, Akbar Niazi Teaching Hospital, Islamabad Pakistan. After taken the Ethical Approval (Ref. No. 69/IMDC/IREB-2022, Dated: 22 March, 2022). Total 350 patients were recruited through non-probability consecutive sampling, utilizing the WHO sample size calculator with a 95% confidence interval, 5% alpha error, and an incidence of AKI was 67%.[9] The inclusion criteria encompassed individuals of both genders (male/female), aged 18 years and above, presented with critical illness. Exclusion criteria involved individuals with preexisting chronic kidney disease, hemodialysis, and malignancy. Additionally, individuals who had not completed a 24-hour duration in the ICU. Upon receiving approval from ethical committee of the institutes and obtaining informed verbal consent from each patient, data collection was initiated. A structured proforma was employed to gather information from the medical records of the patients. To account for variations in patient characteristics, we concurrently considered factors such as age, gender, mortality, and the maximum RIFLE stage. The RIFLE classification was assessed, and the duration of the patient's hospital stay in the ICU was also documented. Every patient was followed up until reaching the ultimate outcome, which could be either discharge or death.

Continuous data's central tendency is represented as mean ± standard deviation. To evaluate the influence of various baseline characteristics on AKI occurrence and maximum RIFLE stage, univariate logistic regression was conducted. The multivariate regression and odds ratio analysis were employed to investigate the association between maximum RIFLE stage, AKI incidence (defined as patients meeting any RIFLE stage), and mortality. Significance was determined with a probability (p-value) of $\leq$ 0.05. The analysis was conducted utilizing SPSS v 23.

Results

Total 350 patients with critical illness were enrolled from the ICUs. The patients mean age was 48.58±17.12 years. Among 350 patients, 70% (n=245) were male and 30% (n=105) were females. Among 350 patients, 65.1% (n=228) developed AKI,

whereas 34.9% (n=122) had normal kidney functions. The mean urine output value was 40.04±48.09 ml/hr (range; 0-200 ml/hr), with 43% patients was anuric and creatinine was 4.37±3.52 mg/dl. 26% (n=91) patients were referred from surgical ICU, whereas 66.9% (n=234), and 7.1% (n=25) were referred from medical and gynecological ICUs, respectively. The patients' baseline characteristics are organized and presented based on the maximum RIFLE stage (Table 1).

Table 1: *Baseline characteristics of patients according to RIFLE stages, n=350*

Variables		Stage 1: Risk	Stage 2: Injury	Stage 3: Failure
n=228 with AKI		46 (13.1%)	88 (25.1%)	94 (26.9%)
Age (years)	Mean ± SD	49.87±16.48	48.21±17.14	47.67±17.75
Gender	Male	28 (60.9%)	57 (64.8%)	58 (61.7%)
	Female	18 (39.1%)	31 (35.2%)	36 (38.3%)

Total 228 patients whom developed AKI, in which majority 26.9% (n=94) were in RIFLE stage 3. As the severity of AKI escalated, there was a concurrent increase in the ICU stay and mortality. Mortality rates for patients with RIFLE stage R, I, and F were 2.2%, 4.8%, and 11.4%, respectively (Table 2). The regression analyses outcomes scrutinized how various characteristics influenced the occurrence of AKI and the attainment of maximum RIFLE class F (Table 3). Aging was correlated with a higher likelihood of experiencing AKI and reaching RIFLE stage F.

Notably, patients with RIFLE stage F on the basis of GFR criteria had slightly higher mortality in-hospital when compare with patients RIFLE stage F on the basis of urine output (30% vs. 23%, p = 0.002). The odd ratio for mortality associated with AKI and RIFLE stage R, I, and F was 1.9 (1.56-2.40, p = 0.0001), 1.1 (0.80-1.40, p = 0.231), 1.5 (1.1-2.00, p ≤ 0.001), and 4.0 (3.50-4.50, p = 0.0001), respectively. Even after adjusting for covariates, AKI continued to be associated with risk of hospital mortality, it was almost increased in twofold (Table 4).

Table 2: *Mortality rate based on RIFLE stages*

Variables	Risk (n=46)	Injury (n=88)	Failure (n=94)	Overall (n=228)
n=228 with AKI	46 (13.1%)	88 (25.1%)	94 (26.9%)	228 (65.1%)
Mortality	5 (2.2%)	11 (4.8%)	26 (11.4%)	42 (18.4%)

Table 3: *Characteristics impact on developing AKI, n=350*

Characteristics	Association (covariates) with developing AKI		Covariates with developing maximum RIFLE class F	
	Odds ratios (CI: 95%)	p	Odds ratios (CI: 95%)	p
Age (years)	1.47 (1.15-2.10)	1E-04	1.45 (0.98-2.00)	0.0001
Gender	1.0 (0.80-1.10)	1E-04	1.61 (0.79-3.28)	0.189
Mortality	1.95 (0.35-3.12)	0.02	1.14 (0.11-2.18)	0.03

** Logistic regression test with 95% confidence interval*

Discussion

Our study revealed a notably high incidence of AKI, according to RIFLE classification, at 65%, and this was linked to an elevated risk of hospital mortality. While this incidence of nearly 70% may appear inconsistent with current literature.[10] When focusing on cases classified as RIFLE stage F (30%), we identified a higher rate among ICU patients than is typically reported. Though still falling within the 20% range among ICU patients, aligning with previous findings.[11,12] Notably, milder form of kidney dysfunction, represented by RIFLE stage R or I, were statistically associated with increased mortality. Overall, RIFLE demonstrated its effectiveness as a well-balanced classification system, enabling the identification of patients with varying degrees of AKI severity. As expected, the incidence of AKI and reaching RIFLE stage F were linked to a higher baseline severity of illness and advancing age. Even when kidney dysfunction was not considered, patients developing AKI tended to be slightly older. However, the severity within the AKI group was not significantly influenced by age. Patients progressing to RIFLE stage I and F did not exhibit a greater age than those remaining in RIFLE class R. Notably, while Chen et al have previously discussed the progression of AKI in a meta-analysis,[13] our study, is also examine the progression of AKI in our hospital's ICU patients.

In a comparative study assessing outcomes, a reported 11% mortality was attributed to AKI.[14] In contrast, our study observed a higher mortality rate of 18.4% among all AKI cases. A separate study in Sri Lanka demonstrated a substantial prevalence of AKI

during ICU stays, reaching approximately 60.2%. Notably, the most prevalent RIFLE class was class 3 or F, accounting for 58.8% of the total AKI cases in that study.[15] In our research, the incidence of AKI was slightly higher at 65%, and the most common RIFLE classes were I and F, constituting 38% and 41%, respectively, of all patients developing AKI.

The findings that a moderate degree of renal impairment poses a most significant risk of death is particularly noteworthy, considering the limited understanding of the underlying reasons. Subsequent studies should explore the alternative management approaches for patients with mild kidney dysfunction could impact outcomes. If the issue indeed lies with the kidney, potential mechanisms contributing to the heightened mortality associated with AKI may lie in the pathophysiological changes stemming from kidney insufficiency. These changes could include salt and water retention leading to volume overload, hyperkalemia, and acid base imbalances,[16] potentially leading to reduced blood pressure, cardiac output, and blood flow to the liver and kidneys[17], insulin resistance, protein breakdown, and even modifications in innate immunity.[18] Additionally, patients with AKI often experience a heightened occurrence of infectious complications and are prone to developing anemia.[19-21] This study comes with some limitations. Firstly, we did not endeavor to compare RIFLE with alternative classification systems, nor did we evaluate the differences between urine output and creatinine criteria. It remains a possibility that the criteria of urine output and creatinine offer opposite information, and combining these criteria might result in a loss of such nuanced distinctions.

Conclusion

The study concluded that hospital mortality is elevated in cases of AKI as per the RIFLE classification. Notably, patients falling into RIFLE class R face a heightened risk of advancing to either stage I or F. Even after accounting for baseline severity of illness, gender, and age, patients classified as RIFLE stage I or F still undergo a significantly prolonged length of stay and face an increased risk of in-hospital mortality.

Conflict of Interest *None*

Funding Source *None*

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Authors Contribution

JKK, ZUAK, AA: Conceptualization of Project

JKK, ZUAK, AA: Data Collection

SAAS, RY : Statistical Analysis

SAAS, RY, AM: Writing of Manuscript