ORIGINAL ARTICLE

IN-HOSPITAL MORTALITY IN HEART FAILURE PATIENTS WITH ACUTE KIDNEY INJURY

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Objectives: Acute kidney injury (AKI) is frequently present co-morbid condition in patients admitted with acute heart failure (AHF). This study aimed to determine the frequency of in-hospital mortality in AHF patients presenting with AKI.

Methodology: This descriptive case series of AHF patients with AKI was conducted at a tertiary care cardiac hospital in Karachi, Pakistan. In accordance with the "Risk, Injury, Failure, Loss, and End-Stage Renal Disease (RIFLE) scale," the AKI was defined as a 3.0-fold increase in serum creatinine (sCr) or sCr > 4.0 mg/dL within 48 hours. All the patients were followed for seven days in order to assess the outcome variable, i.e., in-hospital mortality.

Results: A total of 149 patients were included with a mean age of 59.7 ± 11.03 years, and 80 (53.7%) patients were male. Hypertensive patients were 59.1% (88) of the sample, and 38.9% (58) of the patients were diabetics. In-hospital mortality was found in 11 (7.4%) patients. The mortality rate was 14.1% vs. 2.4%; p=0.008 among patients >60 and 40 to 60 years, respectively. The mortality rate was 12.5% vs. 3.5%; p=0.038 among diabetic and non-diabetic patients. Similarly, the mortality rate was 11.4% vs. 1.6%, p=0.022, among hypertensive and non-hypertensive patients.

Conclusion: It is to conclude that AKI in AHF patients carries a significant burden of in-hospital mortality. The mortality rate was significantly higher for patients with older age and co-morbid conditions such as hypertension and diabetes.

Keywords: ACS, coronary catheterization, trans-radial route, loss of radial pulse

Citation: Bhatti KI, Imdad M, Ali G, Khan NU, Zada S, Kumari S. In-hospital Mortality in Heart Failure Patients with Acute Kidney Injury. Pak Heart J. 2023;56(02):179-183. DOI: https://doi.org/10.47144/phj.v56i2.2543

INTRODUCTION

Heart failure (HF) is a prevailing condition with high rates of recurrent hospitalization due to decompensation and fatality, especially in the aging population.[1] It is a condition characterized by systemic or pulmonary congestion due to functional or structural cardiac abnormalities.[2] It is estimated to affect over 64.3 million individuals globally and with an upward trajectory over the coming years due to the aging population as a result of longer life expectancy in general and improved survival in diagnosed cases due to the availability of modern evidence-based life-saving treatment options.[3] Among many other co-morbid conditions associated with poor prognosis of patients with acute HF, acute kidney injury (AKI) is a common co-morbid condition associated with an increased risk of adverse outcomes.[4,5] It is a well-established interplay between acute HF and AKI, known as the "cardio-renal syndrome",[6] the aggravated HF and renal dysfunction increase the risk of AKI increases the risk of mortality and recurrent hospitalization in these patients.[7,8]

The occurrence of AKI among patients with acute HF ranges from 9 to 43%.[9,10] It has been observed to be a good predictor of in-hospital mortality and a significant predictor of 1-year mortality.[8,11] In-hospital mortality among acute HF patients with AKI is reported to be 10.8%,[12] In addition to mortality, it is consistently associated with prolonged hospitalization and high treatment cost. An increased cost of care can be a real challenge for the healthcare systems of low and middle-income countries. Although, our knowledge of this bi-directional relationship between the two vital organs has immensely improved in recent years, and fundamental pathophysiological bases for this relationship have been partly established.[13]

However, the body of evidence is skewed to the Western population; data from our part of the world are very limited, and the share of samples from developing and under-developing countries is very small as against their population share. Additionally, there is a need for more nationally representative studies from Pakistan.[14] Therefore, the current study was designed to assess the in-hospital mortality among

acute HF patients presenting with AKI at the largest tertiary care cardiac center in Karachi, Pakistan.

METHODOLOGY

After obtaining approval from the relevant department, this descriptive case series study was conducted as part of the College of Physicians and Surgeons Pakistan (CPSP) fellowship program. The study was conducted at the National Institute of Cardiovascular Diseases (NICVD) in Karachi, Pakistan, during the period from October 5, 2021, to April 4, 2022. The study included consecutive patients diagnosed with acute heart failure (AHF) in the emergency department who also developed acute kidney injury (AKI). Patients of either gender, aged between 40 and 80 years, diagnosed with AHF, and developed AKI were eligible for inclusion. However, patients with chronic renal failure, chronic liver disease, a history of blood transfusions within the last three months, and non-consenting patients were excluded from the study.

AHF was diagnosed based on the presence of any two of the following criteria: left ventricular ejection fraction (LVEF) ≤ 35% determined by echocardiography, New York Heart Association (NYHA) class II to IV determined clinically, and/or left bundle branch block (LBBB) with a QRS duration ≥120 ms determined by electrocardiography (ECG). AKI was defined according to the Risk, Injury, Failure, Loss, and End-Stage Renal Disease (RIFLE) scale as a 3.0-fold increase in serum creatinine (sCr) or sCr > 4.0 mg/dL within 48 hours.[15] Patients with an HbA1c > 6.5% or on anti-diabetic medication for at least six months were considered diabetic, while patients on anti-hypertensive medicines for at least six months were classified as hypertensive.

All patients underwent a detailed history taking, followed by a routine examination and baseline investigations. Body mass index (BMI) was calculated using weight in kilograms measured on a standard weighing scale and height in meters measured on a stadiometer at the time of presentation. Patients were treated according to the standard protocol of NICVD. The principal investigator followed all included patients during their hospital stay, up to seven days, to assess the outcome variable, which was in-hospital mortality. All demographic information, including age and gender, was recorded in a pre-designed proforma.

The sample size was calculated using the WHO sample size calculator, considering an in-hospital mortality rate of 10.8% in AHF patients presenting with AKI, with a 95% confidence level and a margin of error of 5%. The calculated sample size was n=149.

Data were entered and analyzed using SPSS version 23. The normality of continuous data was assessed using the Shapiro-Wilk test. Mean ± standard deviation (SD) was calculated for normally distributed continuous variables such as age, weight, height, and BMI. Frequency and percentages were calculated for gender, hypertension, diabetes mellitus, and the outcome variable, which was in-hospital mortality. Age, gender, BMI, hypertension, and diabetes mellitus were stratified with respect to in-hospital mortality, followed by appropriate chi-square or Fisher's exact test. A two-sided p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 149 patients were included in the study, with a mean age of 59.7±11.03 years. Among the patients, 80 (53.7%) were male. Hypertension was present in 88 (59.1%) patients, and 58 (38.9%) patients had diabetes (Table 1).

Table 1: Distribution of clinical and demographic characteristics of AHF patients with AKI

Characteristics	Total
Total (N)	**149**
Gender	
Female	80 (53.7%)
Male	69 (46.3%)
Age (years)	59.7 ± 11
40 to 60 years	85 (57%)
>60 years	64 (43%)
Body mass index (kg/m^2)	26.8 ± 5.3
18 to 24 kg/m^2	69 (46.3%)
>24 kg/m^2	80 (53.7%)
Diabetes	58 (38.9%)
Hypertension	88 (59.1%)

The in-hospital mortality rate was 7.4%, with 11 patients experiencing mortality. A significant difference in mortality rates was observed between patients aged >60 and those aged 40 to 60 years, with 14.1% and 2.4% rates, respectively (p=0.008).

The mortality rate was also significantly higher in diabetic patients than in non-diabetic patients, with 12.5% and 3.5% rates, respectively (p=0.038). Similarly, hypertensive patients had a higher mortality rate of 11.4% compared to non-hypertensive patients, with a rate of 1.6% (p=0.022) (Table 2).

Table 2: In-hospital mortality rate among AHF patients with AKI by several clinical and demographic characteristics

	Total (N)	In-hospital Outcome		P-value
		Mortality	Survived	
Total (N)	149	11 (7.4%)	138 (92.6%)	-
Gender				
Female	80	7 (8.8%)	73 (91.3%)	0.358
Male	69	4 (5.8%)	65 (94.2%)	
Age (years)				
40 to 60 years	85	2 (2.4%)	83 (97.6%)	0.008
>60 years	64	9 (14.1%)	55 (85.9%)	
Body mass index (kg/m^2)				
18 to 24 kg/m^2	69	3 (4.3%)	66 (95.7%)	0.159
>24 kg/m^2	80	8 (10%)	72 (90%)	
Diabetes				
Diabetic	64	8 (12.5%)	56 (87.5%)	0.038
Non-diabetic	85	3 (3.5%)	82 (96.5%)	
Hypertension				
Hypertensive	88	10 (11.4%)	78 (88.6%)	0.022
Non-hypertensive	61	1 (1.6%)	60 (98.4%)	

DISCUSSION

Considering the clinical significance of AKI in patients with acute HF, we conducted this study to estimate the mortality rate among these patients. We observed 149 patients with acute HF who developed AKI, and an in-hospital mortality rate of 7.4% was observed, which was further aggravated by the co-existence of co-morbid conditions such as hypertension and diabetes, and older age.

The prognostic role of AKI in acute HF patients has been well established. In a study by Shamagian LG et al.[16] evaluated the prognostic role of renal failure in patients with congestive heart failure. In a study of 552 patients, kidney failure was found to be an independent predictor of mortality, and this association was independent of the presence of hypertension, diabetes, age, and other risk factors of mortality, as observed in our study. Another registry-based study by Löfman I et al.[13] included 47,716 HF patients, and renal dysfunction (eGFR <60 mL/min/1.73 m^2) was observed in 51% of the patients. It was found to be a strong predictor of short- and long-term mortality. The probability of death was reported to be more the 80% and more than 60% in patients with severe and moderate renal dysfunction after five years of follow-up. This association persisted regardless of functional class, age, presence of diabetes, and duration of HF. Gudsoorkar PS et al.[9] had a similar observation regarding the association of AKI with early death or readmissions regardless of AKI's sustained or transient nature. Chen JJ et al.[10] found AKI in 9% of 7,519 admitted with acute decompensated HF; 39.4% of these patients subsequently developed acute kidney disease during 90 days of follow-up.

Multiple mechanisms are at work to strengthen this clinical association, such as volume overload due to net sodium retention, increased "renin–angiotensin–aldosterone system (RAAS) activation", and/or poor systolic function.[17] In contrast to the popular belief, the "cardio-renal syndrome" may not be the sole reflection of the impaired renal plasmatic flow due to low cardiac output state,[18] but evidence of multiple other pathophysiological mechanisms has surfaced in recent literature. In these patients, sodium reabsorption and raised glomerular afferent arteriole resistance are active mechanisms to maintain renal hemodynamics. These are mediated by multiple neuro-hormonal factors such as activation of RAAS and sympathetic nervous system resulting in endothelin release, vasopressin, and arginine, which in turn lead to preservation of glomerular filtration rate (GFR) and glomerular hydrostatic pressure, systemic vasoconstriction, and water and salt retention.[19] In addition to the acute response of the renal system to the low cardiac output state, both renal and cardiac diseases share multiple pathways. The bidirectional cross-talk between these two important organs involves hormonal and stress-mediated mechanisms, nutritional and metabolic changes, cellular immune-mediated and/or inflammatory responses, acid–base status and fluid alterations, and anemia.[4]

Interestingly, initiation or titration of heart failure medications such as "mineralocorticoid receptor antagonists," "angiotensin-converting enzyme inhibitors," diuretics, and β-blocker, leads to a marginal increase in serum creatinine in response to their effects on renal hemodynamics.[20] Not every increase in serum creatinine is adverse, and it is important to differentiate pseudo- and ture-worsening of renal function; hence serum creatinine should not be evaluated in isolation instead it is important to consider the entire clinical context.[6] Rising serum creatinine can be a less sensitive indicator of AKI as a rise in serum creatinine is a common clinical finding

after initiation or titration of HF medication; hence, rising serum creatinine can be merely a reflection of renal hemodynamics rather than intrinsic kidney injury.[21] Nonetheless, the AKI on admission has been reported to be a prognostic factor regardless of lack of worsening renal function during five years following admission.[22]

Even though this study was conducted at the country's largest cardiac care hospital, certain limitations limit the generalizability of study findings, including a small sample size and single-center coverage. These results emphasize the importance of timely identification and management of AKI in the context of AHF. Early recognition and appropriate therapeutic interventions for AKI can help optimize heart failure treatment and mitigate the risk of adverse outcomes, including the development of chronic kidney disease (CKD), end-stage renal disease, and mortality. Healthcare providers must prioritize the early detection and management of AKI in AHF patients, particularly those older or with comorbidities such as hypertension and diabetes. By doing so, healthcare professionals can potentially improve patient outcomes, reduce the burden of complications, and enhance overall prognosis.

CONCLUSION

The findings of this study demonstrate that acute kidney injury (AKI) in patients with acute heart failure (AHF) is associated with a substantial burden of in-hospital mortality. Moreover, the mortality rate was significantly higher among patients with older age and co-morbid conditions such as hypertension and diabetes.

AUTHORS' CONTRIBUTION

KIB and MI: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. GA, NUK, SZ, and SK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

Acknowledgment: The authors wish to acknowledge the support of the staff members of the Clinical Research Department of the National Institute of Cardiovascular Diseases (NICVD) Karachi, Pakistan.

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