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Impact of Acute Kidney Injury in Patients with Acute Decompensated Heart Failure: Cardiorenal Syndrome

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Abstract

Introduction: Cardiorenal syndrome (CRS) is a complex interdependent relationship between the heart and kidneys, prevalent in hospitalized patients with acute decompensated heart failure (ADHF). The main aim of this study is to evaluate cardiac and renal function, treatment factors, and outcomes because of mortality and persistent renal dysfunction in acute decompensated heart failure (cardiorenal syndrome type 1) patients.

Methods: We studied 100 patients hospitalized with ADHF and acute kidney injury (AKI). Patients were evaluated clinically, biochemically, ultrasonographically, and echocardiographically to assess demographics, etiologic and risk factors, cardiac and renal function, and outcomes because of mortality and persistent renal dysfunction. The study monitored the patients until discharge and followed up with three months to one year. Record information about functional improvement, worsening symptoms, and mortality.

Results: The majority of the patients were males (72%), with dyspnea being the most common symptom (92%) followed by decreased urinary output (82%). The mean age of the patients was 62.60 years. Low level of Mean arterial pressure (MAP) 18.97 (95% CI 4.59 to 78.37, P 0.0001), estimated glomerular filtration rate (eGFR) 0.92(95% CI 0.87 to 0.99; P 0.02), maximum creatinine 3.08 (95% CI 1.67 to 5.67, P 0.0001), maximum level of urea 1.02(95% CI, P 0.001), lower Left ventricular ejection fraction (LVEF) 1.05 (95% CI 0.15 to 0.84, P 0.04) were independently predictors of in-hospital mortality. CRS-1 is associated with an increased risk of mortality (25%), and residual renal dysfunction (16%) at one-year follow-up. .

Conclusion: Persistent renal dysfunction, renal replacement therapy possibly improve the treating persistent renal dysfunction, and recurrent HHF (more than 2 admissions) post-hospitalization index within twelve months were predictors of mortality (25%) at one year.

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Keywords: Cardiorenal syndrome, Acute decompensated heart failure, Acute kidney injury, Worsening renal function, Mortality.

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Introduction

Acute decompensated heart failure (ADHF) carries high mortality and its prevalence is increasing in India.1 It is a prevalent condition in hospitalized patients with acute decompensated heart failure (ADHF) and is associated with increased morbidity, mortality, and healthcare costs.[2]

Cardiorenal syndrome (CRS) is a complex and interdependent relationship between the heart and kidneys, in which dysfunction of one organ contributes to the dysfunction of the other. There are five types of CRS, and in this study, we focus on CRS type 1, which is characterized by acute kidney injury (AKI) occurring as a result of ADHF. AKI in ADHF is associated with an increased risk of short- and long-term all-cause and cardiovascular mortality, increased length of stay, readmission rates, and healthcare costs. The pathophysiological mechanisms leading to AKI in ADHF are complex and involve alterations in cardiac output, systemic hemodynamics, and compromised kidney perfusion, as well as increased systemic venous hypertension.[3]

In the ADHF setting, worsening renal function (WRF) is a prevalent condition, affecting 10% to 40% of patients.4 The definition of WRF commonly used in clinical practice is an absolute increase in serum creatinine value by > 0.3 mg/dL.5 A meta-analysis of 23 cohort, registry, and randomized controlled studies found that ADHF patients with WRF had an almost two-fold higher rate of all-cause mortality than those without WRF.[7]

Managing CRS type 1 presents several challenges, including comorbidities, diuretic resistance, and the use of diuretics associated with "pseudo-AKI." There have been recent advances in the understanding of CRS type 1, including the emergence of newer markers of kidney injury, but their role in prognostic outcomes is not clear. AKI in patients with acute decompensated heart failure is a serious complication that contributes to worse clinical outcomes and increased mortality rates. Timely recognition, aggressive management, and a multidisciplinary approach are essential to improve patient outcomes in this complex cardiorenal syndrome.[8] The aim of this study is to the evaluation of cardiac and renal function, treatment factors, and outcomes because of mortality and persistent renal dysfunction in acute decompensated heart failure (cardiorenal syndrome type 1) patients.

Material and Methods

We enrolled one hundred patients in this prospective observational study with acute decompensated heart failure patients who were selected from admitted to the tertiary cardiac care hospital during the period of 12 months from May 2017 to May 2018. Patients were diagnosed with heart failure based on a combination of symptomatology and associated echocardiographic evaluation.

Inclusion Criteria:

Inclusion criteria included all patients admitted with cardiac failure with LVEF ≤ 40% of any etiology with a duration of hospital stay of more than 24 hours with acute kidney injury. Acute kidney injury was diagnosed using the RIFLE criteria proposed by the acute dialysis quality initiative group, with worsening of renal failure defined by an increase in the absolute serum creatinine value by >0.3 mg/dL.[5] Cardiorenal syndrome- I was defined as a quick decline in cardiac function that results in an acute decrease in renal function. ADHF was defined as either new-onset HF or decompensation of chronic HF with symptoms enough to warrant hospitalization leading to decreases in glomerular filtration. Patients with documented chronic kidney disease including renal artery stenosis.

Enclusion Criteria:

The exclusion criteria of the study were patients with first-time detected chronic kidney disease as evidenced by smaller kidney size. Patients with diabetic nephropathy (proteinuria >300mg/24 hrs). Patients with a history of Non-steroidal anti-inflammatory drugs (NSAID) abuse. Patients not satisfying the above criteria (hospital stay <24 hrs). Patients with terminal illnesses/life expectancy less than one year.

Patient Evaluation:

Patients were evaluated clinically, biochemically, ultrasonographically, and echocardiographically.

Table 1. Demographic and clinical details of total population.

Variables	Total N=100 or mean ± SD
Age (years) (mean ± SD)	62.60±12.20
Male	72
Symptomatology	
Chest pain	57
Dyspnoea	92
Reduced urine output	82
Altered sensorium	5
NYHA Class	
II	13
III	64
IV	23
Etiology	
ACS-HF	47
NICMP-WHF	28
ICMP-WHF	18
VHD-WHF	7
Pre-existing comorbidities	
Diabetes	35
Hypertension	69
Obesity	67
Smoking/Tobacco	25
Alcohol	14
Thyroid illness	6
Pre-existing AF	3
Family history of Cardiomyopathy	2
Previous Medications history	
Loop diuretics	61
ACEI/ARB	39
ARNI	26
BB	50
MRA	26
SGLT2i	11
Hemodynamic variables	
Heart rate (/min) (mean ± SD)	103.14± 19.20
Systolic blood pressure (SBP) (mean ± SD)	101.76± 19.11
Mean arterial pressure (MAP) <60mmHg (%)	23
LBBB (%)	5
LVEF (%) (mean ± SD)	26.95±8.30
Functional Severe MR (%)	12
Laboratory parameters	
Haemoglobin < 12gm% (%)	28
Maximum creatinine (mean ± SD)	2.69 ± 0.76 (1.5-7.62)
Maximum urea (mean ± SD)	95.16± 38.65
Potassium (mean ± SD)	4.71 ± 0.79 (1-7.7)
SGPT (mean ± SD)	228.21 ± 595 (12-3295)
In-hospital outcome (index hospitalization)	Total (N=100)
Revascularisation	34
Inotrope infusion	37
Need for renal replacement therapy	24
IABP for Hemodynamic support	19
Invasive mechanical ventilation	10

ACS- Acute coronary syndrome, HF-heart failure, NICMP-WHF- Non-ischemic cardiomyopathy- worsening heart failure, ICMP-WHF- Ischemic cardiomyopathy- worsening heart failure, VHD-WHF-Valvular heart disease- worsening heart failure, LVEF- left ventricular systolic function, MR-mitral regurgitation, SGPT- Serum glutamate pyruvate transaminase, IABP- intra-aortic balloon pump.

Evidence of coronary artery disease, rheumatic heart disease, hypertension, diabetes mellitus, dyslipidemia, sedentary lifestyle, obesity, current active smoking, current alcohol abuse, and family history of risk factors including cardiomyopathy were obtained. A clinical examination of heart failure was performed; the clinical diagnosis of heart failure was made based on ACC/AHA guidelines consisting of the pyramid approach to heart failure stages, including a relevant general examination, vital signs, and cardiovascular system.[8]

Biochemical investigations:

Biochemical investigations included admission blood glucose, fasting, and postprandial blood glucose, admission blood urea and serum creatinine, myocardial

Table 2. Results of multivariate analysis of confounding variables using the backward. model.

Variables	Total N=100	Survivors N=87 (%)	Non-survivors N=13 (%)	P-value
Age (years) (mean ± SD)	62.60±12.20	62.58±11.96	62.69±13.65	0.98
Male	72	62(71.26)	76.92% (10)	0.93
BMI	25.93±2.95	25.74±2.78	27.21±3.73	0.09
Symptomatology				
Chest pain	57	49(56.32)	8(61.53)	0.96
Dyspnea	92	81(93.10)	11(84.61)	0.61
Reduced urine output	82	71(81.6)	11(84.61)	0.90
Altered sensorium	5	3(3.44)	2(15.38)	0.25
NYHA Class				
II	13	13(14.9)	0	0.29
III	64	61(70.11)	3(23.07)	0.003
IV	23	13(14.94)	10(76.92)	<0.0001*
Pre-existing comorbidities				
Diabetes	35	29(33.33)	6(46.15)	0.55
Hypertension	69	59(67.81)	10(76.92)	0.73
Obesity	67	58(66.66)	69.23 (9)	0.89
Alcohol	14	10(11.49)	4(30.76)	0.15
Thyroid illness	6	5(5.74)	1(7.69)	0.73
Pre-existing atrial fibrillation	3	2(2.29)	1(7.69)	0.85
Family history of Cardiomyopathy	2	1(1.14)	1(7.69)	0.61
Etiology				
ACS-HF	47	40(45.97)	7(53.84)	0.82
NICMP-WHF	28	25(28.73)	3(23.07)	0.93
ICMP-WHF	18	16(18.39)	2(15.38)	0.90
VHD-WHF	7	6(6.89)	1(7.69)	0.63
Hemodynamic variables				
Heart rate (/min) (mean ± SD)	103.14± 19.98	102.09±20.32	110.15±15.93	0.18
Systolic blood pressure (SBP) (mean ± SD)	101.76±19.11	104.79±18.42	81.46±8.13	<0.0001*
Mean arterial pressure (MAP) <60mmHg	23	13(14.94)	10(76.92)	<0.0001*
LBBB	5	3(3.44)	2(15.38)	0.25
LVEF (mean ± SD)	26.95±8.30	27.93±8.15	20.38±6.03	0.001*
Functional Severe MR	12	9(10.34)	3(23.07)	0.39
Laboratory parameters				
Haemoglobin < 12gm	28 (28)	21(24.13)	7(53.84)	0.058
Maximum creatinine (mean ± SD)	2.69±1.12	2.47±0.76	4.18±1.81	<0.0001*
Maximum urea (mean ± SD)	95.16±38.66	89.63±32.91	132.21±51.66	0.0001*
SGPT (mean ± SD)	228.21± 594.9	179.82±517.45	552±899.91	0.03*
SGOT	250.29±867.82	211.25±854.26	511.54±947.76	0.25
eGFR	41.63±18.99	45.47±19.54	29.77±9.60	0.006*
S.creatinine	2.74±1.15	1.84±0.72	2.88±1.54	<0.0001*
TC	12886.7±5368.78	13101.49±5350.58	11449.23±5481.89	0.3
Alkaline PO4	85.83±32.61	87.21±32.84	76.62±30.65	0.28
S.Bilirubin	2.06±1.36	2.13±1.39	1.56±0.93	0.16
Outcome variables (index hospitalization)				
Revascularisation (n)	34	30(34.48)	4(30.76)	0.96
Inotrope infusion (n)	37	24(27.58)	13(100)	<0.0001*
Need for renal replacement therapy (n)	24	12(13.79)	12(92.3)	<0.0001*
IABP for Hemodynamic support (n)	19	12(13.79)	7(53.84)	0.002*
Invasive mechanical ventilation (n)	10	3(3.44)	7(53.84)	<0.0001*

BMI- Body mass index, ACS- Acute coronary syndrome, HF-heart failure, NICMP-WHF- Non-ischemic cardiomyopathy-worsening heart failure, ICMP-WHF- Ischemic cardiomyopathy- worsening heart failure, VHD-WHF-Valvular heart disease-worsening heart failure, LVEF- left ventricular systolic function, MR- mitral regurgitation, LBBB- Left bundle branch block, SGPT- Serum glutamic pyruvic transaminase, SGOT- serum glutamic-oxaloacetic transaminase, eGFR- Estimated glomerular filtration rate, IABP- intra-aortic balloon pump, *P value <0.05 shows statistically significant

enzyme assay for acute coronary syndromes, fasting lipid profile, thyroid function test, and repeat serum creatinine periodically. Bedside chest roentgenogram in standard AP view and bedside ultrasonogram was also done for most patients since they were admitted in ICU settings.

Creatinine clearance was estimated using the Cockroft- Gault formula. Echocardiography was done for all these patients. Both 2D and color Doppler echocardiography were done by a single experienced cardiologist. Left ventricular systolic performance was quantified as the LV ejection fraction. The operational definition of systolic dysfunction for study purposes is an ejection fraction of less than 40%. The left ventricular diastolic performance was quantified by Doppler and graded from I to III.[9]

Follow up:

All 100 of the study's participants were monitored until discharge, and a follow-up is scheduled for 3 months to one year to find out persistent renal dysfunction and predictors of mortality at one year. In-hospital outcome and mortality was recorded. Follow-up details regarding functional improvement, readmission, worsening symptoms, and death were carefully recorded. Information about deceased patients was obtained.

Written informed consent was taken from patients or their relatives before the procedure. The study protocol was approved by the institutional ethics committee (UNMICRC/CARDIO/2016/11).

Statistical analysis:

Using SPSS 26.0 software (IBM, Inc., Chicago, IL, USA), the categorical variables were expressed as frequencies (percentages), and the continuous variables were expressed as the mean ± standard deviation. The Chi-square test and independent t-test were used for categorical variables Univariate and multivariate analysis models were used to find out the predictors of persistent renal dysfunction at follow-up. A P-value <0.05 was considered statistically significant.

Results:

A total of 100 patients with acute decompensated heart failure and acute kidney injury were included in this study. The mean age of the patients was 62.60± 12.26. years. Most of the patients (75%) were in the age group of 50-75 years. The majority of the patients were males, constituting 72% of the total population, while females constituted 28%.

The baseline characteristics of the study population are mentioned in Table 1. The most common symptom in the patients with cardiorenal syndrome was dyspnea, which was present in 92% of the patients. Decreased urine output was the second most common symptom, present in 82% of the patients, followed by chest pain, which was present in 57% of the patients. In most of the patients, this was the first time they had these complaints, while 25% of the patients had a history of similar complaints in the past. Most of the patients were on NYHA class III (64%) followed by NYHA class IV (23%) and class II (13%).

The most common etiology of presentation in the patients was acute myocardial infarction, which was present in 47% of the patients. Among patients with myocardial infarction (MI), 27% had anterior wall MI, while 20% had inferior wall MI. Dilated cardiomyopathy was the next most common presentation, which was present in 46% of the patients. 28% had non-ischemic and 18% of patients had old acute coronary syndrome with ischemic cardiomyopathy as a cause of presentation, while 7% of patients had valvular heart disease as an etiology.

29% of patients had a history of previous myocardial infarction. 35% of patients had a history of type 2 diabetes mellitus, while 69% of patients had a history of hypertension. 25% of patients (all males) were smokers, 14% of patients were chronic alcoholics, 6% of patients had a history of thyroid disease, 3% had pre-existing atrial fibrillation (AF) and 2% of patients had a family history of cardiomyopathy. According to the previous medication history of all patients, 61% of Patients had a history of diuretic use, 39% had a history of ACE inhibitor use, 50% were on beta blockers, 26% were on antiplatelets, 24% were on statins, 11% on sodium-glucose cotransporter-2 inhibitors and 26% were using aldosterone inhibitors.

On presentation, 50% of the patients had tachycardia, while only 3% of patients had bradycardia. Most patients had systolic blood pressure (SBP) between 100-120 mmHg (38%), 35% had SBP <100

Table 3. Regression analysis to predictors of mortality.

Variables	Odds	95 CI	P value
NYHA class- IV	1.20	0.27-5.34	0.007*
Lower eGFR	0.93	0.88-0.98	0.02*
Systolic blood pressure (SBP) (mean ± SD)	0.85	0.78-0.93	0.001*
Mean arterial pressure (MAP) <60mmHg	18.97	4.59-78.37	0.0001*
LVEF (mean ± SD)	1.05	0.15-0.84	0.04*
Functional Severe MR	2.60	0.60-11.23	0.20
Anaemia	3.67	1.10-12.12	0.03*
Maximum creatinine (mean ± SD)	3.08	1.67-5.67	0.0001*
Maximum urea (mean ± SD)	1.02	1.01-1.04	0.001*
SGPT (mean ± SD)	1.001	1-1.001	0.06

NYKA- New York Heart Association, eGFR- estimated glomerular filtration rate, LVEF- left ventricular systolic function, MR- mitral regurgitation, SGPT- Serum glutamate pyruvate transaminase, *P value <0.05 shows statistically significant

mmHg, 20% had SBP between 120-140 mmHg, and 7% patients had SBP above 140 mmHg. All patients had bilateral lung crepitation and 13% of patients had abdominal distention.

In terms of laboratory investigations, the mean hemoglobin value was 11.13±2.18 g/dL. The mean serum creatinine level was 2.03± 0.94 mg/dL, the mean eGFR was 41.63 ±18.99 mL/hr, the mean SGPT was 228.21± 597.89 U/L. The mean total WBC count was 12886.70±5368.78/ mm3, and the average platelet count was 1.08±1.17 lacs/ml. SGPT with a mean of 228.21 ± 597.89 U/L, and SGOT with a mean of 250.29 ± 867.82 U/L. The mean serum bilirubin level was 2.06 ±1.36 mg/dl, and the mean alkaline phosphatase level was 85.83 ± 32.61 U/L.

Chest X-ray showed changes of pulmonary congestion in 97 patients while 3 patients had normal chest X-ray. Echocardiography showed severe LV dysfunction (LVEF <35%) in 90 patients while 10 had LVEF >35%. USG KUB showed that the mean right kidney size was 10.2±1.32 cm, the mean left kidney size was 10.1 ± 1.32 cm, and the mean cortico-medullary differentiation was 3.24± 0.62 mm.

Revascularisation was performed in 34% of the total population, 37% had inotrope infusion, 24% of patients needed renal replacement therapy, 19% had required intra-aortic balloon pump (IABP) for hemodynamic support and 10% of patients had invasive mechanical ventilation. Out of them, 13% had in-hospital mortality.

In-hospital mortality and outcome measures in expired and discharged patients **(table 2)** However, in hospital admitted maximum patients had NYHA class IV (76.92% vs 14.94%, P <0.0001), systolic blood pressure was significantly lower (81.46±8.13 vs 104.79±18.42 mmHg, P <0.0001) and mean arterial pressure (MAP) was <60mmHg also significantly lower [10(76.92%) vs 13(14.94%), P <0.0001] in expired patients. The mean eGFR was significantly lower in expired patients (29.77 ± 9.60 vs 45.47±19.54, P 0.006), lower LVEF (20.38± 6.28 vs 27.93± 8.2, P 0.001), serum creatinine levels were significantly higher in expired patients (2.88 ± 1.54 vs 1.84±0.72, P <0.0001), maximum creatinine (4.18± 1.81 vs 2.47± 0.76, P <0.0001) and maximum urea (132.21± 51.66 vs 89.63± 32.91, P 0.0001) also significantly increased in in-hospital expired patients. According to these variables, NYHA class IV, lowering of systolic blood pressure and MAP, anemia, maximum creatinine, and urea, and lowering in eGFR and LVEF had significant effects on patients with acute decompensated heart failure and acute kidney injury in mortality. However, the variables such as BMI, total count, platelets, potassium, SGOT, alkaline phosphatase, and S. Bilirubin did not show any significant difference between the expired and discharged patients or alive and expired patients **(table 2).**

All expired patients need inotrope infusion and most of them also need renal replacement therapy (92.3%). Half of them (53.84%) required IABP for hemodynamic support and invasive mechanical ventilation.

According to binary logistic regression model

Table 4. Predictors of Persistent renal dysfunction for >3months.

Variables	Total N=87(%)	Normal renal functions N=61(%)	Persistent renal dysfunction for >3months N=26(%)	p-value
Age (years) (mean ± SD)	62.58±11.96	62.54±11.75	62.69±12.44	0.97
Male	62(71.26)	43(70.49)	19(73.07)	0.99
BMI	25.93±2.95	25.59±2.85	27.3±3.03	0.02*
NYHA Class				
II	13(14.94)	11(18.03)	2(7.69)	0.36
III	61(70.11)	45(73.77)	16(61.53)	0.52
IV	13(14.94)	5(8.19)	8(30.76)	0.01*
Pre-existing comorbidities				
Diabetes	29(33.33)	21(34.42)	8(30.76)	0.97
Hypertension	59(67.81)	40(65.57)	19(73.07)	0.49
Obesity	58(66.66)	41(67.21)	17(65.38)	0.86
Alcohol	10(11.49)	6(9.83)	4(15.38)	0.71
Etiology				
ACS-HF	40(45.97)	26(42.62)	14(53.84)	0.47
NICMP-WHF	16(18.39)	19(31.14)	6(23.07)	0.62
ICMP-WHF	18(20.69)	12(19.67)	6(23.07)	0.94
VHD-WHF	6(6.9)	6(9.83)	0	0.23
Hemodynamic variables				
Heart rate (/min) (mean ± SD)	102.09± 20.32	102.45± 20.41	101.23± 20.06	0.84
Mean arterial pressure (MAP) <60mmHg	13(14.94)	5(8.19)	8(30.76)	0.02*
LVEF (mean ± SD)	27.93± 8.15	27.86± 7.76	28.07±8.99	0.93
Functional Severe MR	9(10.34)	7(11.47)	2(7.69)	0.94
Laboratory parameters				
Haemoglobin < 12gm	21(24.14)	16.39 (10)	11(42.3)	0.02*
Maximum creatinine (mean ± SD)	2.47±0.76	2.35±0.65	2.74±0.92	0.06
Maximum urea (mean ± SD)	89.63±32.91	86.33±30.23	97.36±37.35	0.24
Outcome variables (index hospitalization)				
Revascularisation	30(34.48)	23(37.70)	7(26.92)	0.47
Inotrope infusion	24(27.59)	7(11.47)	17(65.38)	<0.0001*
Need for renal replacement therapy	12(13.79)	1(1.63)	11(42.30)	<0.0001*
IABP for Hemodynamic support	12(13.79)	6(9.83)	6(23.07)	0.19
Invasive mechanical ventilation	3(3.45)	0	3(11.53)	0.04*

ACS- Acute coronary syndrome, HF-heart failure, NICMP-WHF- Non-ischemic cardiomyopathy- worsening heart failure, ICMP-WHF- Ischemic cardiomyopathy- worsening heart failure, VHD-WHF-Valvular heart disease- worsening heart failure, LVEF- left ventricular systolic function, MR- mitral regurgitation, *P value <0.05 shows statistically significant

Table 5. Logistic regressions for predictors of persistent renal dysfunction at more than 3months to one-year.

Variables	Odds	95 CI	P value
NYHA Class IV	8.8	1.35-57.42	0.02*
Anaemia	3.74	1.33-10.49	0.01*
Maximum creatinine (mean ± SD)	1.72	0.94-3.12	0.07
Maximum urea (mean ± SD)	1.01	0.99-1.02	0.16
Mean arterial pressure (MAP) <60mmHg	4.98	1.44-17.15	0.01*
LVEF (mean ± SD)	1.003	0.95-1.06	0.91
Functional Severe MR	1.56	0.30-8.05	0.598

LVEF-Left ventricular ejection-fraction, LVEF- left ventricular systolic function, MR- mitral regurgitation, *P value <0.05 shows statistically significant.

Table 6. Predictors of mortality at 1 year.

Variables within 12months post index hospitalization	Total N=87(%)	Survivors N=75(%)	Non-Survivors N=25(%)	p-value
Revascularisation	12(13.79)	11 (14.67)	1(4)	0.29
Persistent renal dysfunction for >3months	26(29.89)	14 (18.67)	12(48)	0.01*
Renal replacement therapy for persistent renal dysfunction	12(13.79)	2 (2.67)	10(40)	<0.0001*
Recurrent HHF (>2 admission)	27(31.03)	15 (20)	12(48)	0.01*
New-onset AF	5(5.74)	3 (4)	2(8)	0.79

HHF-hypertensive heart failure, AF-Atrial fibrillation, *P value <0.05 shows statistically significant.

NYHA class-IV 1.20(95% CI 0.27 to 5.34, P 0.007), lowering in MAP 18.97 (95% CI 4.59 to 78.37, P 0.0001) and systolic blood pressure 0.85(95% CI 0.78 to 0.93; P 0.001), anemia 3.67(95% CI 1.10 to 12.12; P 0.0.3), lowering in eGFR value 0.92(95% CI 0.87 to 0.99; P 0.02), maximum creatinine 3.08 (95% CI 1.67 to 5.67, P 0.0001), maximum level of urea 1.02(95% CI 0.99 to 1.02, P 0.001), lower LVEF 1.05 (95% CI 0.15 to 0.84, P 0.04) were independently predictors of in-hospital mortality **(table 3).**

We assessed a discharged total of 87 patients for predictors of persistent renal dysfunction at more than 3 months follow-up (table 4). After discharge 26(29.89%) patients had renal dysfunction. Out of 26 patients, 30.76% had NYHA class IV, MAP also decreased significantly (P 0.02) in 30.76% of patients, and lower hemoglobin (<12%) was significantly seen in 42.3% of patients (P 0.02). Renal dysfunction and factors associated with it were responsible for the rehospitalization of patients after discharge. Maximum creatinine and urea don't show a significant difference between renal dysfunction and normal renal function patients (P 0.06, 0.24) at more than 3 months to one-year follow-up. Revascularisation was needed in 26.92% out of 26 patients, 65.38% population needed inotrope infusion, 42.30% population needed renal replacement therapy, and 23.07% needed IABP for hemodynamic support. 11.53% of patients need invasive mechanical ventilation support.

According to binary logistic regression NYHA class-IV 8.8(95% CI 1.35 to 7.42; P 0.02), Anaemia 3.74(95% CI 1.33-10.49; P 0.01), and lower mean arterial pressure 4.98(95% CI 1.44 to 7.15; P 0.01) were independently predictors of persistent renal dysfunction **(table 5)**.

In terms of patient outcome and predictors of mortality at one year (N=87 patients) as post-index hospitalization **(table 6)**. Out of 87 living patients 25 (28.74%) patients had died at 3 months to one-year outcome. Out of 87 living patients 12 patients had revascularisation out of them 1 patient had died (P 0.29) other 12 patients had renal replacement therapy

for persistent renal dysfunction out of them 10 patients died (P <0.0001), 26 patients had persistent renal dysfunction for more than 3 months out of them 12 patients were died (P 0.01). 27 patients had recurrent HHF (>2 admissions) out of them 12 patients died and a new onset of AF was seen in 5 patients out of 2 patients were died within 12 months post index hospitalisation.

In summary, lowering in MAP and systolic blood pressure, anemia, eGFR value and LVEF, maximum creatinine, and maximum level of urea were independent predictors of in-hospital mortality. NYHA class-IV, anemia, and lower mean arterial pressure were independent predictors of persistent renal dysfunction at 3 months to one-year outcome. Persistent renal dysfunction, renal replacement therapy for treating persistent renal dysfunction, and recurrent HHF (more than 2 admissions) post-hospitalization index within 12 months were predictors of mortality (25%) at one year.

Discussion

This prospective observational study provides valuable insights into the demographic and clinical characteristics of ADHF patients with AKI, including the high prevalence of comorbidities such as coronary artery disease, hypertension, and diabetes mellitus. This highlights the importance of identifying and addressing risk factors and comorbidities in the management of CRS type 1. The study underscores the significant impact of AKI on the outcomes of ADHF patients, including increased mortality and persistent renal dysfunction.

The results are consistent with previous studies that have shown the high prevalence and negative impact of renal dysfunction on heart failure outcomes. Yang et al and Shai et al have demonstrated a significant association between worsening renal function and poor outcomes in heart failure patients.[10,11] Mullen et al have also highlighted the importance of cardiorenal syndrome in decompensated heart failure.[12]

In our study population, the most common age group was 50 to 75 years. In general, most of the studies have shown that the incidence of AKI is higher with increasing age. Most of the patients in our group were males; this is consistent with most of the studies where the male population predominates (72%). A similar finding was observed in the Indian College of Cardiology National Heart Failure Registry.[1]

The most common symptom in acute decompensated heart failure is dyspnoea (92%), which is also the most common presentation in our study. Among dyspnoea, 41 % of patients had NYHA class-IV dyspnoea, while 29 % had NYHA class-III dyspnoea. All patients had B/L crepitations of variable degrees on lung auscultation. The second most common symptom in our study was decreased urinary output. It occurred in a total of 82% of patients during indexed admission. The decreased urine output is also considered to be a criteria for diagnosing acute kidney injury.

Acute decompensated heart failure (ADHF) carries high mortality and its prevalence is increasing in India. Our study reported 25% mortality in patients with acute decompensated heart failure and acute kidney injury in AMI. Similar results were noted in a study by Hsing-Shan Tsai et al which showed mortality rates of 30% among patients of MI with AKI.11 This finding shows AKI as an important prognostic marker in cases of AMI as its presence increases mortality of AMI by 2 to 3 times. The present study reported 13% mortality during hospitalization. Acute worsening of renal function during hospitalization for ADHF is a strong and consistent independent predictor of adverse outcomes.[12]

Zhang et al. analyzed the one-year survival and renal function recovery of acute kidney injury patients with chronic heart failure. Our study also emphasizes the importance of renal function in determining immediate short-term and long-term outcomes in patients with heart failure.[13]

In our study, we found that parameters like Low hemoglobin, baseline creatinine, and urea levels, baseline eGFR, maximum levels of urea and creatinine, and lower LVEF have shown a consistent relationship with mortality during hospitalization. This effect continued for 3 months as well as 6 months of mortality. Mean hemoglobin levels were 11.13 gm/dl at presentation and 9.65 gm/dl in mortality group. The term "Cardiorenal Anemia Syndrome (CRAS)", coined by Silverberg et al defined as a condition induced by dysfunction of either organ exacerbating dysfunction of either organ.14 In our study anemia was significantly associated with increased mortality. It is consistent with other studies showing that anemia is frequently linked to poor outcomes in people with CRS-1.[1,15]

Studies have shown the benefits of multidisciplinary

care, including optimal medical therapy, fluid management, and renal replacement therapy when necessary, in improving outcomes in these patients which was also seen in our study as improving renal function did improve the prognosis in our patients. [16,17]

Fonarow et al reported that BUN, SBP, and creatinine levels were the three variables most predictive of in-hospital mortality in the Acute Decompensated Heart Failure National Registry (ADHERE).18 Our study had significantly higher values of serum Creatinine and Blood Urea in the Mortality group as compared to the survivor group at all points of follow-up.

In our study, the statistically significant lower EF values occurred in the mortality group as compared to the survivor group. Jepth Curtis et al have shown that mortality linearly decreases as LVEF increases to 45%.[19] Many other studies have shown low EF and association of worse outcomes.[1,19,20] Indian College of Cardiology National Heart Failure registry data suggests higher serum creatinine levels and poor LVEF contributed to 30-day mortality and rehospitalization in ADHF. 1 Our study's findings are highly consistent with the studies conducted in this setting.

On 3 months of follow persistent renal dysfunction occurred in 23 patients. At the end of the 6-month follow up total of 16 patients had persistent worsening of Renal function. Zhang et al studied AKI in heart failure with a one-year follow-up. He found a total of 35% of patients had non-recovery of renal function. Different rates in our studies could be due to smaller numbers of patients with CRS-1 in this study (n=60).[13]

These findings support the need for early detection and management of AKI in ADHF patients, including the use of appropriate diuretic strategies to avoid worsening renal function. Overall, the study provides useful information on the clinical characteristics of patients with acute decompensated heart failure and acute kidney injury, but further research is needed to explore the optimal management strategies for this population.

The study underscores the significant impact of AKI on the outcomes of ADHF patients, including increased mortality and persistent renal dysfunction. The findings emphasize the importance of identifying risk factors and addressing comorbidities to improve the management of CRS type 1.

This study's results are limited by several important factors. First and foremost is the sample size. For a disease that has a very high prevalence, it may be essentially difficult to conclude a small group of the population, especially considering the nature of the study center. Population behavior is to seek health care only when the functional limitation becomes severe enough to disturb day-to-day activities. This study was a single-center experience study. The second factor is the patients received treatment from different physicians and the treatment protocol was individualized. So, the outcome difference would have had some impact due to these factors.

Conclusion

The most common presenting complaint in patients with acute decompensated heart failure and acute kidney injury was dyspnea on exertion, followed by decreased urine output. Managing cardiorenal syndrome remains complex. In this population, impaired renal function is associated with increasing mortality and morbidity. CRS-1 is linked to a 25% increased risk of mortality. Lowering in MAP and systolic blood, eGFR value, severe LVEF, anemia, high maximal serum creatinine, and urea level were independently associated with worse mortality outcomes.

Abbreviations

CRS	:	Cardiorenal syndrome
ADHF	:	Acute Decompensated Heart Failure
AKI	:	Acute Kidney Injury
MAP	:	Mean Arterial Pressure
eGFR	:	Estimated Glomerular Filtration Rate
LVEF	:	Left ventricular ejection fraction
WRF	:	Worsening Renal Function
NSAID	:	Non-steroidal anti-inflammatory drugs
NYHA	:	New York Heart Association
MI	:	Myocardial infarction
AF	:	Atrial fibrillation
ACE	:	Angiotensin Converting Enzyme
SBP	:	Systolic blood pressure
SGPT	:	Serum glutamate pyruvate transaminase
WBC	:	White blood cell

SGOT	:	Serum glutamic-oxaloacetic transaminase
USG KUB	:	Ultrasonography (kidney, ureter, and bladder)
BMI	:	Body mass index
IABP	:	Intra-aortic balloon pump
AMI	:	Acute Myocardial Infarction
CRAS	:	Cardiorenal Anemia Syndrome
BUN	:	Blood Urea Nitrogen

References

1. Jayagopal PB, Sastry SL, Nanjappa V, et al. Clinical characteristics and 30-day outcomes in patients with acute decompensated heart failure: Results from Indian College of Cardiology National Heart Failure Registry (ICCNHFR). *International Journal of Cardiology*. 2022 Jun 1;356:73-8. Int J Cardiol. 2022 Jun 1;356:73-78.
2. Njoroge JN, Teerlink JR. Pathophysiology and therapeutic approaches to acute decompensated heart failure. *Circulation research*. 2021 May 14;128(10):1468-86.
3. Viswanathan G, Gilbert S. The cardiorenal syndrome: making the connection. *Int J Nephrol*. 2010 Oct 4;2011:283137.
4. Palmer JB, Friedman HS, Waltman Johnson K, et al. Association of persistent and transient worsening renal function with mortality risk, readmissions risk, length of stay, and costs in patients hospitalized with acute heart failure. *Clinicoecon Outcomes Res*. 2015 Jun 19:357-67.
5. Lopes JA, Jorge S. The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review. *Clin Kidney J*. 2013 Feb;6(1):8-14.
6. Damman K, Valente MA, Voors AA, et al. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. *Eur Heart J*. 2014 Feb;35(7):455-69.
7. Chen JJ, Lee TH, Kuo G, et al. Acute Kidney Disease After Acute Decompensated Heart Failure. *Kidney Int Rep*. 2022 Jan 3;7(3):526-536.
8. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2019 Jul 9;74(1):104-132.
9. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015 Jan;28(1):1-39.e14.
10. Yang YH, Wang L, An F, et al. Renal dysfunction and survival in hospitalized patients with chronic heart failure: a retrospective analysis. *Chinese Journal of Cardiovascular Diseases,* 2009,37(08):729-733.
11. Tsai HS, Chen YC, Chu PH. The Influence of Acute Kidney Injury on Acute Cardiovascular Disease. *Acta Cardiol Sin*. 2014 Mar;30(2):93-7. doi: 10.1136/hrt.2009.166256.
12. Tang WW, Mullens W. Cardiorenal syndrome in decompensated heart failure. *Heart*. 2010 Feb 1;96(4):255-60.
13. Zhang W, Wen D, Zou YF, et al. One-year survival and renal function recovery of acute kidney injury patients with chronic heart failure. *Cardiorenal Med*. 2015 Feb;5(1):40-7.
14. Silverberg DS. The role of erythropoiesis stimulating agents and intravenous (IV) iron in the cardio renal anemia syndrome. *Heart Fail Rev*. 2011 Nov;16(6):609-14.
15. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. 2009 Aug;(113):S1-130.
16. Cowie MR, Komajda M, Murray-Thomas T, et al. Prevalence and impact of worsening renal function in patients hospitalized with decompensated heart failure: results of the prospective outcomes study in heart failure (POSH). *Eur Heart J*. 2006 May;27(10):1216-22.
17. Goldberg A, Kogan E, Hammerman H, et al. The impact of transient and persistent acute kidney injury on long-term outcomes after acute myocardial infarction. *Kidney Int*. 2009 Oct;76(8):900-6.
18. Fonarow GC, Abraham WT, Albert NM, et al;

OPTIMIZE-HF Investigators and Hospitals. Influence of a performance-improvement initiative on quality of care for patients hospitalized with heart failure: results of the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF). *Arch Intern Med*. 2007 Jul 23;167(14):1493-502.

19. Curtis JP, Sokol SI, Wang Y, et al. The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure. *J Am Coll Cardiol*. 2003 Aug 20;42(4):736-42.
20. Toma M, Ezekowitz JA, Bakal JA, et al. The relationship between left ventricular ejection fraction and mortality in patients with acute heart failure: insights from the ASCEND-HF Trial. *Eur J Heart Fail*. 2014 Mar;16(3):334-41.

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