To Study the Clinical Outcome of Cardiorenal Syndrome in a Tertiary Care Hospital of Bihar

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ABSTRACT

Background: Cardiorenal syndrome (CRS) is defined as disorders of heart and kidney whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other. The exact mechanism of CRS is complex and multifactorial. **Objective of the study:** To identify and categorize various patients admitted with CRS into different subtypes and assess the clinical outcome at discharge and 3 months. **Material and methods:** We took 50 patients of CRS admitted in ICU of Medicine Department, Darbhanga Medical College and Hospital (DMCH), Laheriasarai, Darbhanga, Bihar. Outcome was addressed as favorable for stable patients at discharge and 3 month follow-up, whereas unfavorable for patients who expired or were put on hemodialysis. **Results:** Out of 50 patients, 30 patients (60%) were males, with mean ages of males and females being 65.15 and 66.48 years, respectively. Majority of patients had type 1 CRS (44%), followed by type 4 (28%), type 2 (24%) and type 5 (4%). There were no patients with type 3 CRS. At the end of the study, 25 (50%) patients were stable, 12 (24%) required dialysis and 13 (26%) patients expired. **Conclusion:** CRS occurs in all age groups, more commonly in elderly subjects, with male preponderance. CRS 1 is more prevalent than CRS 4. Prognosis was unfavorable in CRS 1, CRS 4 and CRS 5, bad prognostic factors being pre-existing renal impairment, anemia, decreased glomerular filtration rate (GFR) and decreased ejection fraction. Sepsis was the predominant cause of death in patients with CRS 5.

Keywords: Cardiorenal syndrome, sepsis, low GFR, low ejection fraction

Cardiorenal syndrome (CRS) is defined as disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other. The mechanism of CRS is quite complex and multifactorial, the factors being renin-angiotensin-aldosterone system (RAAS) activation, imbalance between nitric oxide (NO) and reactive oxygen species (ROS), sympathetic activation and chronic inflammation. CRS has been divided into 5 subtypes by Ronco et al in 2008. Type 1 CRS (acute CRS) is characterized by rapid worsening of cardiac function leading to acute kidney injury (AKI). Type 2 CRS (chronic CRS) is characterized by chronic heart failure leading to progressive decline in glomerular filtration rate (GFR) leading to chronic kidney disease (CKD). Type 3 CRS (acute renocardiac syndrome) manifests as AKI, which can occur as a primary event (e.g., acute glomerulonephritis) or a secondary event (e.g., radiocontrast dye, exogenous or endogenous nephrotoxins, post-surgical, etc.) followed by cardiac dysfunction. Type 4 CRS (chronic renocardiac syndrome) is a condition characterized by increased cardiovascular (CV) risk in CKD patients. Type 5 CRS (secondary CRS) is associated with multiple systemic conditions, either acute or chronic, such as sepsis, systemic lupus erythematosus (SLE), amyloidosis and diabetes mellitus. The co-existence of renal and cardiac involvement leads to increased morbidity and mortality, and also increased cost of the care.

MATERIAL AND METHODS

A total of 50 patients, above 18 years of age having both cardiac and renal involvement, were admitted in our hospital. Detailed history taking, examination and investigations were carried out, with special focus on comorbidities such as hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), dyslipidemia, hypothyroidism, chronic obstructive pulmonary disease (COPD) and nephrotoxic drug ingestion. Outcome was addressed as favorable

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(for stable patients at discharge and 3 months) and unfavorable (for patients who died or were put on hemodialysis). Investigations included complete blood count (CBC), kidney function tests (KFT), cardiac enzymes, pro–B-type natriuretic peptide (pro-BNP), lipid profile, thyroid profile, urine routine examination (R/E) and culture, electrocardiography (ECG), chest X-ray (CXR)-posteroanterior (PA) view, ultrasonography (USG)-whole abdomen. Heart failure was classified by New York Heart Association (NYHA) classification, whereas CKD as per Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines. Estimated GFR (eGFR) was calculated using the Modification of Diet in Renal Disease Study (MDRD) equation. All patients were classified into various subtypes of CRS as per Ronco guidelines (2008).

Statistical Analysis

All statistical analyses were performed using Chi-square test and student *t*-test. Differences with a probability of type 1 error <5% were considered statistically significant.

RESULTS

Demographic Profile

Out of 50 patients, 30 patients (60%) were males, with mean ages of males and females being 65.15 and 66.48 years, respectively. Majority of patients had type 1 CRS (44%), followed by type 4 (28%), type 2 (24%) and type 5 (4%).

Symptomatology

All patients presented with dyspnea, while pedal edema was noted in 38 patients, as shown in Table 1.

Laboratory Parameters

Out of 50 patients, 28 patients were known cases of CKD, whereas 30 patients had heart failure with reduced ejection fraction. Table 2 summarizes the findings for laboratory parameters at different study time points.

Table 1. Clinical Parameters

Parameters	No. of patients
Dyspnea	50
Dependent edema	38
Chest pain	25
Syncope	4
Decreased urine output	24

Comorbidities

In all, 40 patients were hypertensive, 34 were diabetic, 28 were known cases of CKD, 22 were having CAD and 20 had dyslipidemia.

Prevalence of CRS

Majority of patients had type 1 CRS (44%), followed by type 4 (28%), type 2 (24%) and type 5 (4%) (Table 3). At the time of discharge, 27 patients were stable, 16 required dialysis and 7 patients expired (Table 4). At the end of the study, 25 (50%) were stable, 12 (24%) required dialysis and 13 (26%) patients expired (Table 5). No patients were having CRS type 3.

Table 2. Laboratory Parameters

Lab parameters	No. of patients	Mean ± SD
Baseline		
Creatinine (mg/dL)	28	2.5 ± 1.32
eGFR (mL/min)	25	28.05 ± 10.52
EF (%)	30	46 ± 11.50
At admission		
Hemoglobin (>10)	22	
Hemoglobin (<10)	28	
Creatinine (mg/dL)	50	3.42 ± 1.9
eGFR (mL/min)	50	27.02 ± 15.50
EF (%)	50	32.8 ± 11.6
At discharge		
Creatinine (mg/dL)	43	3.26 ± 1.58
eGFR (mL/min)	43	25.12 ± 11/34
At 2 months		
Creatinine (mg/dL)	35	3.18 ± 1.68
eGFR (mL/min)	35	30.06 ± 14.45
EF (%)	35	36.45 ± 10.07

EF = Ejection fraction.

Table 3. Distribution of CRS Subtype

CRS subtypes	No. of patients
CRS type 1	22
CRS type 2	12
CRS type 4	14
CRS type 5	2

Table 4. Outcome at Discharge

Outcome	No. of patients
Stable	27
Dialysis	16
Death	7

Table 5. Outcome at 3 Months

Outcome	No. of patients
Stable	25
Dialysis	12
Death	13

DISCUSSION

CRS has emerged as a significant problem over a few decades as a result of increased prevalence of HTN, diabetes, dyslipidemia, etc. Western studies have shown a complex relationship between heart and kidneys, but in the Indian scenario, it remains an uncharted territory. Our study aimed at identifying and classifying patients with CRS into various subtypes and assessing outcomes at discharge and at 3 months follow-up.

There was a male preponderance in our study (M:F = 3:2), which might be due to increased number of risk factors in male population such as acute coronary syndrome (ACS), HTN, diabetes, dyslipidemia, etc.

Nearly half of the patients had unfavorable outcomes (as shown in Tables 4 and 5), which were significantly higher in CRS 1 and CRS 4, probably due to devastating presentation of CRS 1 with ACS, acute left ventricular failure (LVF) or AKI, resulting in further progression to end-stage renal disease (ESRD) and increased CV mortality. Co-existing renal insufficiency is one of the strongest independent risk factors and predictors of mortality.

Our study revealed more than half of the population had hemoglobin <10 g/dL (cardiorenal anemia syndrome). Anemia causes increase in oxidative stress and hypoxia to myocardium, leading to compensatory increase in heart rate and stroke volume, which activates RAAS and sympathetic nervous system (SNS), causing renal vasoconstriction and fluid retention. In a previous study, it was established that prevalence of anemia was high amongst patients with CRS; however, anemia was not the single contributory mortality factor as uremia and low ejection fraction were also contributing to adverse outcomes.

Three-fourth of the population had significant left ventricular dysfunction. All these people had unfavorable outcome at follow-up. This is possibly due to a complex interplay of various factors such as imbalance of failing heart, neurohormonal system activation, sympathetic overactivity, NO, renin-angiotensin system (RAS) and inflammatory cascade. Risk factors contributing towards worsening renal function during heart failure include old age, comorbidities, drugs like diuretics, angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), prior myocardial infarction and previous renal insufficiency.

In past also, it was determined that in patients with chronic heart failure, renal dysfunction is common, deteriorates over a relatively short period of time, is unlikely to recover substantially and augurs a poor prognosis.

Our study has limitations in terms of small sample size. Cystatin C could not be estimated at our center due to its nonavailability. Longer follow-up at 6 months or 1 year could derive better understanding and more accurate analysis of various CRS subtypes.

CONCLUSION

CRS is a common entity nowadays. There are five subtypes of CRS. The exact mechanism is multifactorial. CRS can occur in all age groups but is more common in elderly population with a male preponderance. CRS 1 was more prevalent followed by CRS 4. Unfavorable outcomes were noted with CRS 1, CRS 4 and CRS 5. Sepsis was the predominant cause of death in patients having CRS 5 with 100% mortality during hospital stay. Risk factors like pre-existing renal impairment, anemia, reduced ejection fraction and reduced eGFR were significantly associated with poorer outcome across all CRS subtypes. Therefore, large population-based studies are warranted to chart the prevalence of CRS subtypes and prognosticate each individually. Longer follow-up studies should be undertaken in order to understand the natural history of CRS.

SUGGESTED READING

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Make sure

DURING MEDICAL PRACTICE

SITUATION: A hypertensive patient with long-standing type 2 diabetes on a calcium channel blocker was found to have moderately increased albuminuria (between 30 and 300 mg/day).

LESSON: In the RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) study in patients with type 2 diabetes already receiving conventional antihypertensive therapy, the use of the ARB losartan significantly decreased the risk of end-stage renal disease. Losartan also significantly decreased the degree of proteinuria.

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