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Original Research Article

A Study of Characteristics and Outcome of Cardiorenal Syndrome in Heart Failure

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Abstract:

Aim & Objectives: The objective of this study is to assess the prevalence, predictors, and outcomes of Cardiorenal syndrome (CRS) in patients hospitalised with heart failure (HF) in the medical wards of a tertiary care hospital.

Material & Methods: The study employed a cross-sectional design. Patients who were 18 years of age or older and met the specified criteria for inclusion were recruited in a sequential manner over a span of 15 months. A comprehensive medical history and physical examination were conducted, together with appropriate baseline blood tests including blood chemistry, complete blood count, urinalysis, estimated glomerular filtration rate (eGFR), electrocardiography (ECG), echocardiogram, and renal ultrasound scan. The urinary protein creatinine ratio was measured in individuals who had proteinuria. At the time of initial presentation, serum levels of creatinine, urea, and electrolytes were determined. These measurements were then repeated once over the course of heart failure treatment. Heart failure and CRS were precisely characterised and categorised based on suitable criteria. Statistical analysis conducted with the SPSS software.

Results: Of the 100 patients studied, 62 are male 38 are female, mean age 50.64 ± 13.4. Out of them 47 patients are under heart failure alone group, 53 patients developed cardiorenal dysfunction. Among CRS group, 86.8% are above 40years, (p 0.04) and have high frequency of diabetes whereas in non CRS group 76% are non-smoker. Majority of patients have type1 CRS and 72.5% CRS patients are classified under mild CRS. Serum Creatinine >1.91mg/dl and serum urea >120mg/dl are predictors of mortality. Patients diagnosed with CRS exhibited a significantly elevated mortality rates compared to those who did not present the illness.

Conclusion: Patients with heart failure had a substantial incidence of CRS. The independent predictors of CRS were found as NYHA class 4 and age more than 40 years. Patients with CRS experience a considerably higher duration of hospital stay compared to those without CRS. Within a hospital setting, individuals with CRS experience a notably elevated death rate. Serum creatinine & serum urea are significant indicators of mortality.

Keywords: Cardiorenal syndrome; Creatinine; GFR; Heart failure; Urea.

Introduction

Heart failure (HF) is now recognised as a worldwide public health issue that impacts nations with varying financial levels. The significant burden of high HF and the requirement for resource-intensive interventions can result in health system crises in areas with limited resources. [1] The INDUS research estimated the prevalence of the condition to be around 1.2 per 1000 individuals in India. After its onset, heart failure has a 1-year death rate of 7.2% and a 1-year hospitalisation rate of 31.9% in individuals with chronic heart failure. However, for patients admitted to the hospital due to acute heart failure, these rates rise to 17.4% and 43.9% respectively. Globally, the prevalence of heart failure has risen to around 23 million individuals. [2] Cardiorenal syndrome (CRS) is a pathological condition in which the heart and kidneys have sudden or chronic dysfunctions, leading to dysfunctions in the other organ. The interaction between the failing heart and the kidneys, and vice versa, in terms of blood flow dynamics, as well as changes in neuro-hormonal markers and inflammatory molecular fingerprints that are specific to its clinical characteristics.[3] The development of cardiorenal syndrome is linked to changes in the renin-angiotensin-aldosterone system

(RAAS), an imbalance between nitric oxide (NO) and reactive oxygen species (ROS), the sympathetic nervous system, and inflammation. These factors serve as the connections between the cardiovascular and renal systems.[2] In heart failure, there is a drop in renal perfusion pressure which leads to the narrowing of the blood vessels that provide blood to the kidneys (afferent arterioles). This results in a further reduction in renal blood flow and glomerular filtration rate (GFR). When heart failure (HF) occurs, the effects become more pronounced because there is an increased release and decreased removal of catecholamines. [4]

Renal impairment (RI) is common in patients with heart failure (HF), and around 20% - 40% of patients admitted to the hospital for acute heart failure syndromes (AHFS) also have concurrent renal impairment (RI).[5] Renal impairment, characterized by a minimum 25% rise in serum creatinine or levels equivalent to or exceeding 2mg/dl, has been seen to be prevalent among patients with heart failure who are having intensive therapy.[6] Progressive renal failure patients now acknowledge cardiovascular disease as the primary cause of mortality.[7] The simultaneous presence of renal impairment and heart failure is becoming increasingly acknowledged as separate risk factors that contribute to illness and death.[8] The convergence of these factors has significant implications for the treatment and prediction of outcomes in individuals with heart failure.[9] Even a slight impairment in kidney function, shown by an elevation in blood creatinine or a reduction in estimated glomerular filtration rate (GFR), significantly affects the risk of cardiovascular disease.[10] Research has demonstrated that patients have a 1% rise in mortality for every 1ml/min decline in creatinine clearance. Additionally, individuals with a small drop in kidney function face a cardiovascular risk similar to that associated with diabetes mellitus.[11,12] The correlation between renal insufficiency and unfavorable outcome in individuals with HF is not just an indicator of advanced cardiac illness, but rather it is directly linked to morbidity and death regardless of standardized indices of HF severity. Research has demonstrated that baseline renal impairment (RI) can elevate the chances of both morbidity and death in individuals who are hospitalized for acute heart failure syndrome (AHFS). [5-15] Based on a thorough examination of data from 1,129 patients, it was shown that having a serum creatinine level more than 2.5mg/dL at the time of release was the strongest independent predictor of readmission for any cause. The interval [5,16] A multivariate Cox regression analysis was conducted using data from 541 individuals, revealing a significant association between all-cause mortality and increasing quartiles of xv Blood urea nitrogen (BUN). [5,17] An analysis of data from the SOLVD trial revealed that patients with both renal dysfunction and left ventricular systolic dysfunction (LVSD) were more prone to experiencing more severe symptoms of heart failure, as indicated by their higher NYHA Class, in comparison to patients with normal renal function and LVSD. [19] HR Shah et al. conducted a study in North India to examine the clinical characteristics and outcomes of individuals with CRS. Therefore, there is a lack of research on the frequency and variables that contribute to different forms of CRS, as well as their impact on health and death rates in Central India. Furthermore, there is a growing prevalence of cardiovascular disorders resulting in heart failure and renal ailments among the rural population, which are addressed by primary care physicians. The interval [4,9] Therefore, we undertook this study to determine the prevalence, classifications, and outcomes (mortality and length of hospitalization) of individuals with CRS. Furthermore, to ascertain the risk variables linked with mortality in individuals with CRS. Timely detection of these risk factors can help decrease the incidence and mortality rates associated with CRS.

Aims and Objectives:

The research aimed to ascertain the prevalence and consequences of CRS among patients hospitalised with HF to the outpatient department, with the following objectives:

1. To identify the characteristics that might predict and etiological contributors to the development of chronic respiratory symptoms (CRS) in patients hospitalised with heart failure (HF).
2. To assess the length of hospital stay and mortality rate among patients with CRS who are hospitalised for heart failure (HF). Additionally, the study aims to identify the variables that contribute to mortality in CRS patients admitted for HF.

Materials and Methods:

The study was done in a Medical college with a bed capacity of 422 in the department of medicine. The study has a cross-sectional design. Included in the study were patients aged 18 years and older who were hospitalised with a diagnosis of heart failure, as determined by the Framingham criteria. Patients who were already receiving regular dialysis treatment before to admission and declined to give consent to participate in the trial were not included in the study. The study received approval from the institutional Ethical Committee, and informed permission was acquired from every patient. The HELSINKI declaration was followed. Patients who met the specified criteria were enrolled in successive order until the desired sample size was reached.

Patients who had been suspected to have heart failure were questioned using a standardised Proforma in order to gather demographic

information, clinical history, general and cardiovascular evaluations, including anthropometric measures.

The patients had the following diagnostic tests: serum creatinine [SCr], urea and electrolytes [U/E/], a complete blood count, blood glucose, serum uric acid, lipid profile, urinalysis, electrocardiogram (ECG), and echocardiogram. The urinary protein-creatinine ratio was measured to assess the amount of protein excreted in a 24-hour urine sample in individuals who had protein in their urine during urinalysis. A renal ultrasonography scan was performed on all individuals. The Cockcroft-Gault equation, which has been globally verified and proven to accurately estimate the glomerular filtration rate (GFR), was used to predict the GFR in Indian patients. [20-22] During the therapy, serum creatinine [SCr], urea, and electrolyte levels [U/E] were reassessed either on day seven or at the time of discharge. The diagnosis of heart failure was made based on the modified Framingham Criteria. [23] The diagnosis of renal impairment in heart failure (cardiorenal syndrome) was made based on an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73m2. The interval [4,9] The evaluation of the severity of clinical symptoms was conducted using the New York Heart Association (NYHA) functional class.[20]

Methodology

Bilateral blood pressure assessment was conducted using a conventional mercury sphygmomanometer on both the left and right arm. The arm exhibiting the highest blood pressure measurement was documented. The stadiometer was used to measure height in meters and the weight measurements were taken in kilogram using a weight-based scale twelve lead surfaces ECG was used to record electrical activity of the heart. The investigator conducted ECG recordings on all enrolled patients using ECG equipment. The researcher conducted transthoracic echocardiography on all patients. The measurements were conducted in accordance with the American Society of Echocardiography (ASE) guidelines, using the leading-edge to leading-edge convention and simultaneous ECG recording. [19] Continuous-wave refers to a type of signal or transmission that is uninterrupted and continuous. The Doppler technique was employed to investigate the valves in cases where there was suspicion of any valvular abnormality. Tissue Doppler imaging was employed to distinguish between normal and pseudo-normal left ventricular filling in cases with diastolic dysfunction. EDTA blood collection container was to estimate the haemoglobin and count the White blood cells. A volume of 10ml venous blood was collected following an overnight fast of 8-12 hours in order to measure fasting plasma glucose (FPG) and lipid profiles, including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TGL). The serum levels of urea, electrolytes, and creatinine were analysed using an automated analyzer. The central laboratory conducted the analysis of all samples.

Data Analysis: The data collected was compiled, verified, and analyzed using the computerized statistical software package for social sciences [SPSS] version 16.0. The mean and standard deviation were used to characterize quantitative variables. A P value below 0.05 was deemed statistically significant.

Observation and Results

A total of 100 patients who satisfied the inclusion criteria were studied over the period of 18 months (May 2021 to October 2022). They consisted of62 (62%) males and 38 (38%) females giving male to female ratio of 1.6:1. The mean age of the patients was 50.64 ± 13.4 (range 18-90 years).

Table 1: Baseline characteristics of patients

Variables	N (%)
Age (years)	50.64±13.44
Gender Male	62 (62)
Female	38 (38)
Hypertension	57 (57)
Diabetes	49 (49)
Dyslipidemia	46 (46)
Smoking	37 (37)
Alcoholic	39 (39)
Hypothyroidism	16 (16)
Systolic dysfunction	51 (51)
Diastolic dysfunction	49 (49)
Clinical aetiology of HF Hypertensive heart disease	37 (37)
Dilated cardiomyopathy	35 (35)
Peripartum cardiomyopathy	10 (10)
Rheumatic heart disease	10 (10)
Ischemic heart disease	2 (2)

Cor-pulmonale	3 (3)
Systolic blood pressure (SBP) (mm Hg)	127.6±33.04
Diastolic blood pressure (DBP) (mm Hg)	74.73±10.9
Haemoglobin (Hb) (mg/dl)	10.46±1.9
Serum urea (mg/dl)	50.7±24.8
Serum creatinine (mg/dl)	2.1±3.1
eGFR (ml/min)	59.35±33.3
Total cholesterol (TC) (mg/dl)	193.8±57.8
Left ventricular ejection fraction (LVEF) (%)	44.9±11.8

Figure-1 shows the sex and age distribution of the study population and Figure-2 shows sex distributions among study groups. The most frequent age group was that

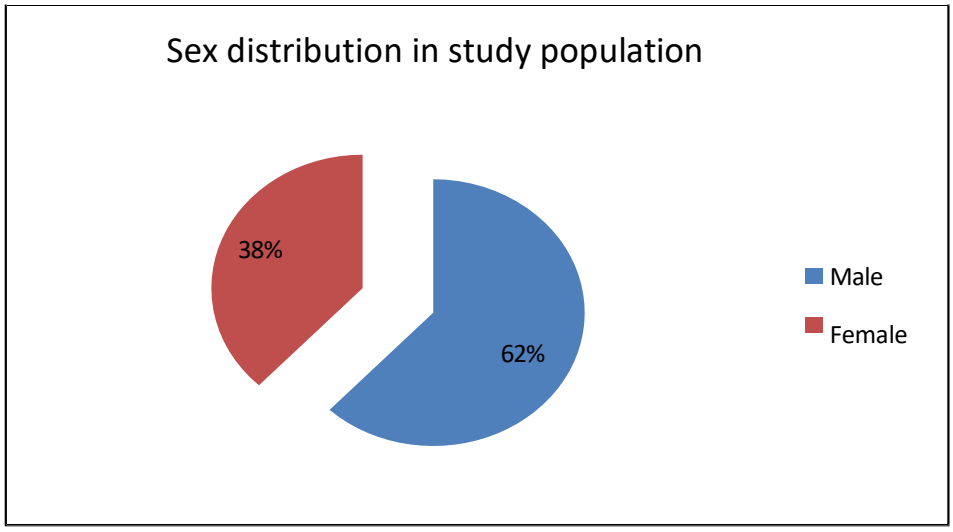

Figure 1: shows the sex and age distribution

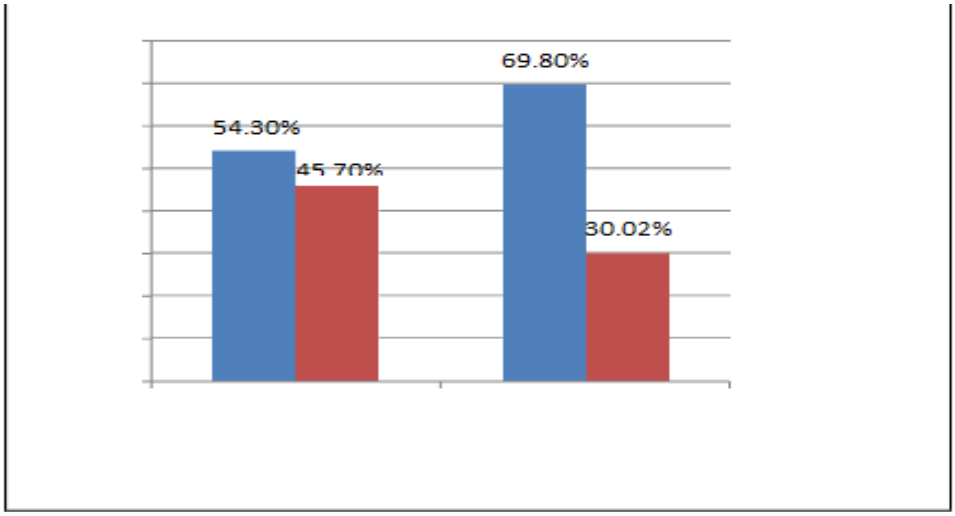

Figure 2: Sex distribution among study population

Majority of patients have dyspnoea of grade 4. Compared to the group without CRS, those with CRS, 86.8% were above 40 years (86.8% vs. 69.6% p <0.04), had higher frequency diabetes (62.3% vs. 34.8% p= 0.009) (Table-2).

Table 2: Comparison of the clinical characteristics and echocardiographic findings among the patients

Variables	Total	CRS present	CRS absent	P-value
	n=100 (%)	n=53 (%)	n=47 (%)	
Gender-Male	62(62)	37(69.8)	25(54.3)	0.146
Female	38(38)	16(30.2)	22(45.7)	
Age(years)	50.64±13.44	53.51±13.59	47.33±12.59	0.02
BMI	23.09±2.6	23.28±2.20	22.88±3.02	0.45

Hypertension	57(57)	34(64.2)	23(50.0)	0.221
Diabetes	49(49)	33(62.3)	16(34.8)	0.009
Paroxysmal nocturnal dyspnoea (PND)	81(81)	50(94.3)	31(67.4)	0.001
Orthopnoea	80(80)	50(94.3)	30(66.7)	0.001
Jugular venous pressure (JVP)	76(76)	45(84.9)	31(67.4)	0.04
Cardiomegaly	83(83)	49(92.5)	34(73.9)	0.01
Third heart sound (S3)	75(75)	47(88.7)	28(60.9)	0.001
Systolic Dysfunction (SD)	51(51)	24(44.28)	27(55.72)	0.37
Diastolic Dysfunction (DD)	58(58)	34(58.07)	24(41.93)	0.45
LVEF <50	72(72)	37(69.81)	35(74.46)	0.339

According to Figure-3, 72.2% of the CRS group had mild grades, 18.5% had moderate, and 9.3% had severe grades. The majority of the patients with CRS, namely 41 individuals (77.35%), were diagnosed with type I CRS. Type II CRS was observed in 8 patients (15.09%), while the remaining 4 patients (7.5%) were diagnosed with type IV CRS (Figure-4). None of the patients included in the research exhibited type III and V CRS.

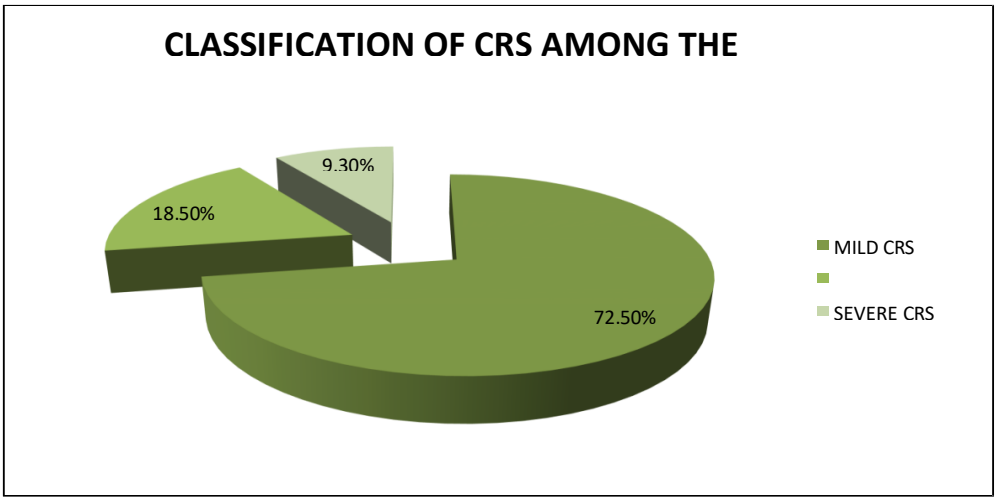

Figure 3: Classification of CRS among the CRS group. Mild: HF+ eGFR 30– 59mL/min/1.73m^2, Moderate: HF+eGFR 15-29mL/min/1.73m^2, Severe: HF+eGFR <15mL/min/1.73m^2 or dialysis

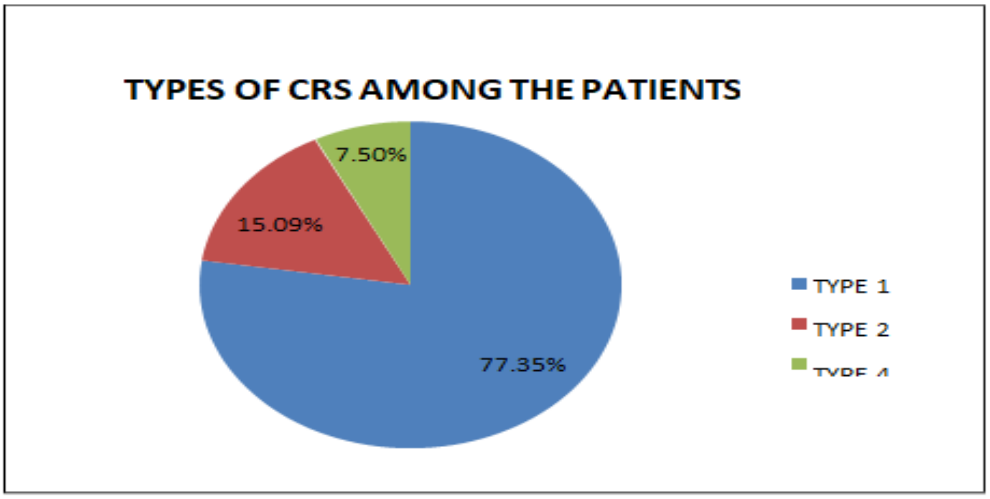

Figure 4: Types of CRS found among the patient

Figure-5 shows comparisons of risk factors among study groups where in CRS groups 64.2% were hypertensive, 62.3% were diabetic, 47.2% had dyslipidaemia, 49.1% were smoker, 43.4% were alcoholic,15.1% had hypothyroidism and 45.3% had anemia, compared to non CRS group where 50.0% were hypertensive, 34.8% were diabetic, 45.7% had dyslipidaemia, 23.9% were smoker, 34.8% were alcoholic, 17.4% were hypothyroid and 37% were anemic (p value 0.221, 0.009, 1.000, 0.01, 0.416, 0.790, 0.421 respectively).

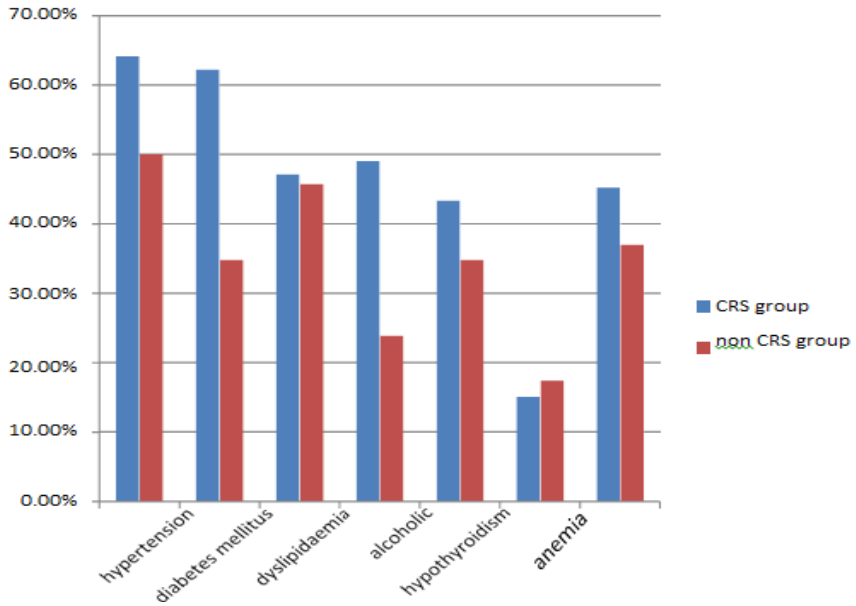

Figure 5: Comparison of risk factors among study groups

In comparison to the group without CRS, the CRS 2 group exhibited a considerably higher average level of serum urea (59.51mg/dl vs. 39.61mg/dl, p=<0.0001) and creatinine (3.13mg/dl vs. 1.01mg/dl, p=<0.0001). Conversely, the mean eGFR was significantly lower in the CRS group (34.99 ml/min vs. 87.40 ml/min, p<0.0001) (Table-3). Proteinuria was detected in 75 individuals, accounting for 75% of the study population. Out of the total number of patients, 66.66% of them with proteinuria had CRS, whereas only 33.33% of those without CRS had proteinuria. This difference was shown to be statistically significant with a p-value of 0.017.

Table 3: Comparison of the laboratory parameters among patients with & without CRS

Variables	CRS present	CRS absent	P-value
	Mean±SD	Mean±SD	
Hb (mg/dL)	10.323±1.74	10.613±2.10	0.455
Total cholesterol (mg/dl)	191.68±64.13	196.15±50.09	0.703
eGFR (ml/min)	34.99±11.98	87.40±27.36	<0.0001
Urea (mg/dl)	59.51±26.45	39.61±17.68	<0.0001
SCr (mg/dl)	3.13±3.75	1.01±1.23	<0.0001

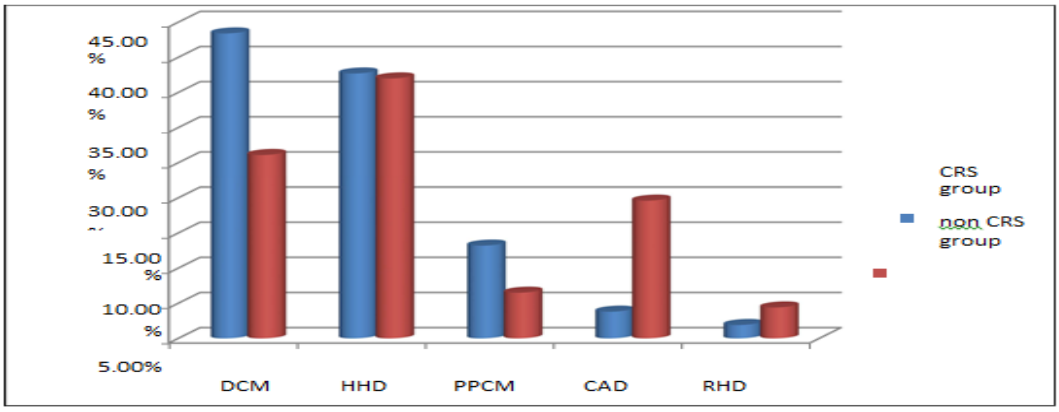

Figure 6: Aetiology of HF among the study patients

Figure-6 shows the etiology of heart failure among the study participants. The most common etiology was dilated cardiomyopathy found in 43.4% CRS group and hypertensive heart disease (37%) in non CRS group.

Table 4: Comparison of clinical variables among patients with and without cardiorenal syndrome

Variables	CRS present	CRS absent	P-value
	n=53 (%)	n=47 (%)	
Age (>40years)	46(86.8)	32(69.6)	0.04
SBP >160mmHg	15(28.3)	5(10.9)	0.04
Diabetes	33(62.3)	16(34.8)	0.009
NYHA IV	33(62.3)	15(32.6)	0.007
Anaemia	24(45.3)	17(37)	0.421

Table 5: Mortality and duration of hospital stay

Variables	Total patients	CRS present	CRS absent	P-value
	n=100 (%)	n=53 (%)	n=47 (%)	
Death	35(35)	31(58.5%)	4(8.7%)	<0.0001
Duration of stay (days)	9.41±7.09	10.42±3.70	8.26±9.51	<0.0001

Table-5 shows the outcomes (death and duration of hospital stay) among patients. Of the 100 patients, 35 (35%) died. Among CRS group 31(58.5%) are died whereas in non CRS group, 4 (8.7%) are died (p value <0.0001), suggesting significantly higher mortality rate in those with CRS. The mean length of hospital stay for CRS group was 10.42 ± 3.70days and in non CRS group was 8.26±9.55 days (P value<0.0001).Figure-7 shows comparison of outcome among CRS and non CRS group.

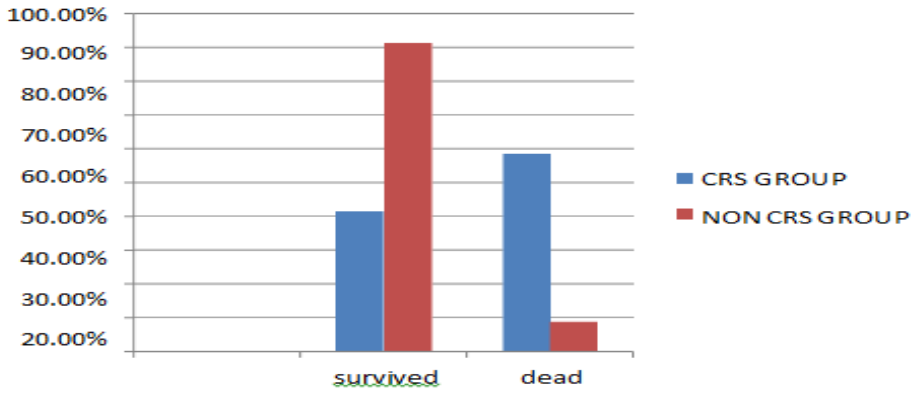

Figure 7: Comparison of outcome among CRS and non CRS group

Table 6: Comparison of Deceased and Survivors of CRS

Variables	Deceased	Survivors	P-value
	n=31(%)	n=22(%)	
NYHA class IV (%)	20 (64.51)	11 (50)	0.009
DM	722.8	418.18	0.90
SBP <160mmHg	15 (48.38)	18 (90.6)	0.000
DBP <60mmHg	4 (11.4)	10 (15.6)	0.76
SCr >1.91mg/dl	20 (64.51)	10 (45.45)	0.001
Urea >120mg/dl	13 (41.93)	5 (22.72)	0.001
eGFR <53ml/min	31 (100)	19 (86.36)	0.042
Cholesterol >200mg/dl	14 (40.0%)	28 (43.8)	0.83

Table-6 presents a comparison of clinical and laboratory data between those who died and those who survived CRS. The deceased had a considerably larger percentage of patients with SCr levels of ≥1.91mg/dl, urea levels of >120mg/dl, eGFR levels of <53ml/min, and NYHA class IV (p=0.001, 0.001, 0.045, and 0.009 respectively). On the other hand, the survivors had a higher percentage of patients with systolic blood pressure (SBP) levels below 160mmHg (p=0.000).

Discussion

The condition was prevalent in 53.5% of the study population. The prevalence rate observed in the present study is marginally greater than that reported in several local studies on the occurrence of renal impairment in patients with heart failure. [7,8] The incidence of renal dysfunction in patients hospitalised with heart failure varied between 7% and 50% in the trials. The divergent results may be attributed to disparities in the research methodology

and the demographic composition of the study participants. Nevertheless, several prior investigations have documented a significant frequency of CRS. [22-24] within a particular investigation, it was shown that 60% of patients diagnosed with acute decompensate heart failure (ADHF) exhibited a moderate level of cardiorenal syndrome (CRS). [24] The participants in the present study were comparatively young, with a mean age of 50.64 ± 13.44 years. This observation aligns with the findings of a prior research conducted on patients with heart failure at the study centre, as well as another study with heart failure patients from western Odisha, South-Western Nigeria. The average age of the participants in both studies was 45.53 ± 8.61.[7] However, these findings contradict the higher average ages found in the research conducted in Maharashtra (71.357± 6.48 years) and in the United States of America (USA) (61 ± 18 years) and Europe (71.3 ± 12.7 years).The age disparity may be attributed, at least in part, to the earlier onset of some factors that contribute to heart failure, including peripartum cardiomyopathy and rheumatic heart disease, within the Indian population. [26] The factors that were shown to be associated with CRS in this study were individuals with heart failure who were classified as NYHA class IV and were over the age of 40 years. McAliter et al discovered that within their group, 39% of patients in NYHA class IV and 31% of patients in NYHA class III with symptoms of heart failure exhibited a significant level of renal impairment.[13] The death rate of 58.5% seen in this research among CRS patients was much greater compared to the rates reported in other investigations. [17] In the Cardiorenal research conducted by HR Shah et al, the clinical outcome study reported a total death rate of 16%. [4] In our study, we mostly enrolled patients with severe heart failure, which might account for the elevated fatality rates observed in previous investigations. Patients with CRS had a significantly longer hospital stay compared to those without CRS (10.42±3.703 vs. 8.26±9.551, p value-0.000). A research conducted in the United States of America found that acute renal damage led to a threefold increase in the duration of hospitalisation and a 22% higher death risk among patients with heart failure who were over the age of 65. Nevertheless, a research conducted in Nigeria on the exacerbation of renal dysfunction in patients with heart failure found no notable disparity in the length of hospital stay between patients with and without worsened renal dysfunction.[8] The sole factors that indicated the likelihood of death in this investigation were a serum creatinine level of 1.9mg/dl or higher and a blood urea level above 120mg/dl. Renal dysfunction measurements have been discovered to be more potent indicators of mortality compared to markers of LV dysfunction (LVEF and NYHA) in patients with CRS. [11,18]The study conducted by HR Shah et al revealed a significant correlation between blood creatinine levels and mortality in patients with heart failure.[4] Elevated serum creatinine (SCr) and urea levels were determined to be substantial and autonomous indicators of death or re-hospitalization in the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbation of Chronic Heart Failure research. [27] In a study that looked back at 1004 consecutive patients who were admitted to 11 different hospitals for heart failure, it was found that a decline in kidney function was linked to a 7.5 times higher chance of death during the hospital stay, after adjusting for other factors. [28]

Conclusion

CRS was very prevalent in patients with heart failure. The independent predictors of CRS were found as NYHA class IV and age more than 40 years. Patients with CRS experience a considerably longer duration of hospitalisation compared to those without CRS. The mortality rate is notably elevated among people with CRS in hospital settings. The predictors of death were discovered as measures of renal function, namely a serum creatinine (SCr) level greater than 1.91mg/dl and a urea level greater than 120mg/dl. Identifying the major failing organ (either the heart or kidneys) proved challenging in certain individuals, which might have impacted the categorization of CRS into various subgroups. The exclusion of other populations of heart failure patients, particularly those attending outpatient clinics, may have influenced the prevalence of CRS.

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