

ORIGINAL RESEARCH

CARDIORENAL SYNDROME AND HEART FAILURE: WHAT'S ASSOCIATION?

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ABSTRACT:-

INTRODUCTION: - Heart failure is among key reasons of hospitalizations throughout the world. Prevalence is 1% among the ages of 50 and 59 years, gradually growing to >10% over age of 80 years. In patients with heart failure, concomitant and notable renal impairment is prevalent. Heart failure is increasingly being classified as a type of cardiorenal failure, in which there are contemporaneous cardiac and renal dysfunctions, each of which accelerates the progress of the other.

AIMS AND OBJECTIVES:-To study the etiology, risk factors and clinical outcomes of heart failure and cardiorenal syndrome.

MATERIALS AND METHODS: - The present study is an observational study conducted at Sri Aurobindo medical college and Post Graduate Institute, Hospital, Indore on 75 patients admitted in Medicine ward, Medicine emergency and Medicine ICU.

RESULTS:- The major risk factor which associated with mortality was coronary artery disease 73.5%. Type 2 diabetes mellitus was present in 62.5% patients while hypertension in 42.7%. Smoking was the risk factor in 46.2% and alcohol in 41.7% patients, COPD was present in 8.2% cases. NYHA grade 4 was more common and was seen in 79.2% while NYHA grade 3 in 22.8% cases.

CONCLUSION: Cardiorenal syndrome is very common in people who have heart failure. Patients with heart failure who have had two or more previous hospitalizations, sepsis, history of CAD and hypothyroidism are more likely to develop cardiorenal syndrome. The development of cardiorenal syndrome is an independent predictor of frequent readmissions, In addition to longer hospitalization and slower recovery, under treatment of the cardiorenal syndrome has the potential to be fatal on an individual level and have massive public health repercussions.

KEYWORDS: - CAD, cardiorenal syndrome, heart failure.

INTRODUCTION:-Heart failure is among key reasons of hospitalizations throughout the world. Prevalence is 1% among the ages of 50 and 59 years, gradually growing to >10% over age of 80 years. In patients with heart failure, concomitant and notable renal impairment is prevalent. Heart failure is increasingly being classified as a type of cardiorenal failure, in which there are contemporaneous cardiac and renal dysfunctions, each of which accelerates the progress of the other. One-fourth of patients

admitted to the hospital for treatment of ADHF will have notable impairment of renal function, which is linked to worse outcomes. It stays uncertain whether or not worsening renal function particularly contributes to poor consequences or whether it is simply a marker of advanced cardiac and renal dysfunction. In spite of the fact that the definition of diuretic resistance, its prevalence, and prognostic consequences are less well understood, diuretic resistance, without or with decreasing renal function, is not uncommon in ADHF¹.

The term cardiorenal syndrome is linked with cardiorenal failure, decreasing renal function, and diuretic resistance, but it is now more broadly defined as a condition of severe cardiorenal dysregulation manifested by one or more of those specific symptoms. The etiology of cardiorenal syndrome is unknown, however it is thought to involve interconnected hemodynamic and neurohormonal pathways. Mechanical fluid elimination using ultra filtration, hemofiltration, or hemodialysis may be required for resistant hypervolemia when usual treatment for acute decompensated heart failure fails². While ultra-filtration helps deal with diuretic resistance, it's unclear whether treatment can help individuals with cardiorenal syndrome avoid worsening renal function or enhance their outcomes. Newer treatment drugs, such as nesiritide, vasopressin antagonists, and adenosine antagonists, have shown promise in clinical trials, and more are in the works. In this observational study we are going to assess the risk factors, etiology and clinical outcome of cardiorenal syndrome. Renal impairment in sufferers with HF is more and more identified as an important risk factor for morbidity and mortality. In an evaluation of sufferers enrolled within side the CHARM study (2003) (Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity) Hillege et al. confirmed that the extent of renal dysfunction was a potent unbiased predictor of death or HF admission³.

The Acute Decompensated Heart Failure National Registry (ADHERE) year 2001, a massive database of 105,388 sufferers with HF requiring hospitalization with inside the United States, stated that 30% had a further analysis consistent with continual kidney disease. Approximately 20% of sufferers had serum creatinine (Cr) >2.0 mg/dL, 9% had creatinine >3.0 mg/dL, and 5% were receiving dialysis therapy. Smith et al. carried out a scientific evaluation and meta-analysis of 16 research characterizing the affiliation among renal impairment and mortality in 80,098 hospitalized and non-hospitalized⁴.

Owan et al. lately reported on secular tendencies with inside the severity of renal dysfunction in sufferers with ADHF in 6,440 consecutive precise sufferers hospitalized for HF remedy at Mayo Clinic Hospitals, Rochester, MN, from January 1, 1987, to December 31, 2002. Over the 16-yr time period, age and admission Cr increased, EGFR decreased, and hemoglobin decreased. The greater dominant role of renal dysfunction in HF became additionally stressed with inside the current Evaluation Study of Congestive Heart Failure and pulmonary Artery Catheterization Effectiveness (ESCAPE) trial (2013), wherein it changed into emphasized that episodes of HF decompensation were much less commonly related to uncorrected vasoconstriction and more usually related to renal dysfunction with requirement of better diuretic doses at discharge than traditionally noted. Thus, the severity of cardiorenal failure in sufferers hospitalized for HF is increasing. Importantly, cardiorenal failure is similarly widespread in patients with HF and normal ejection fraction (diastolic HF) or decreased ejection fraction (systolic HF)⁵.

Several researches have established that >70% of patients will reveal an increase in creatinine at some point of hospitalization for HF, with about 20% to 30% of HF patients experiencing an increase growth of >0.3 mg/dL. Worsening renal function takes place relatively early during the hospitalization. Any increase in creatinine has been proven to be associated with longer duration of stay, extended costs, and elevated short-term and long term mortality. The affiliation of worsening renal function with poorer consequences is unbiased of the degree of baseline renal dysfunction and lots of different pertinent covariables. Nonetheless, it remains doubtful whether or not the worsening renal function itself contributes to the elevated mortality or whether it simply serves as a marker of more extreme cardiac and/or renal dysfunction. Importantly, worsening renal function is usual in diastolic HF as it is in systolic HF. While the severity of underlying renal dysfunction in ADHF patients has multiplied over time, Owan et al. did not locate any proof of increases in the occurrence of worsening renal function over time. In patients with ADHF related to volume overload, preliminary therapy specializes in sodium and fluid restriction and diuretics. Diuretic resistance has been described as chronic pulmonary congestion without

or with worsening renal function regardless of tries at diuresis. The prevalence of diuretic resistance (DR) relies upon in element on the aggressiveness of the diuretic dosing. While worsening renal function usually develops with inside the absence of chronic congestion while diuretic dosing has been too high (termed over diuresis), worsening renal function additionally frequently happens regardless of chronic pulmonary congestion in patients with diuretic resistance. Both diuretic resistance and aggravating renal function are more common in patients with underlying renal dysfunction, and the triad of cardio-renal failure, diuretic resistance, and worsening renal function in spite of marked chronic volume overload represents the most extreme manifestation of the cardio-renal syndrome⁶.

Importantly, blood volume was closely correlated with pulmonary capillary wedge pressure (PCWP) and independently anticipated 1-year risk of demise or urgent cardiac transplantation, both substantially more with inside the hypervolemic patients. Observational statistics in patients with ADHF confirmed that pre-discharge reduction of PCWP <16 mm Hg, instead of an extended Cardiac index anticipated improved 2-year survival. Interestingly, with inside the Dutch study, extended CVP on admission, in addition to inadequate reduction of CVP throughout hospitalization, were the strongest determinants for the development of WRF. In contrast, impaired CI on admission and development in Cardiac index after intensive medical therapy had little impact on Worsening renal function. These intriguing observations raise questions on our contemporary management approach for acute HF, which has been to decrease cardiac filling pressures while preserving or enhancing Cardiac index. What are the mechanisms by which venous congestion worsens renal function, and why is vigorous diuresis alone so frequently ineffective⁶.

AIMS AND OBJECTIVES:-To study the etiology, risk factors and clinical outcomes of heart failure and cardiorenal syndrome.

MATERIAL AND METHODS:- The present study is an observational study conducted at Sri Aurobindo medical college and Post Graduate Institute, Hospital ,Indore on 75 patients admitted in Medicine ward, Medicine emergency and Medicine ICU.

Inclusion Criteria

- All patients aged > 18 years admitted with cardiac failure (including heart failure of any etiology with a duration of hospital stay more than 24 hours with or without renal dysfunction).
- Those patients/guardian (in case of unconscious patient) who give consent.

Exclusion Criteria

- Patients known case of chronic kidney disease.
- Patients with history of chronic NSAID abuse.

Data collection and statistical analysis:-

Especially designed pre-structured proforma will be used for collecting the relevant data. The data will be obtained from patient's history, Physical examination Blood investigations, radiological investigations & ECG.

All the data analysis were performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare the tables. Quantitative data is expressed as mean and standard deviation whereas categorical data is expressed as percentage. Paired sample t test was used to compare the means. Chi Square test was used to compare the categorical data. P value of <0.05 is considered as significant.

RESULTS:-In our study total patients were 75 of which maximum number of patients were in the age group 51-60yrs (36%) followed by 61-70yrs (25.3%), and minimum in 21-30yrs (4.0%) as shown in **Table 1.**

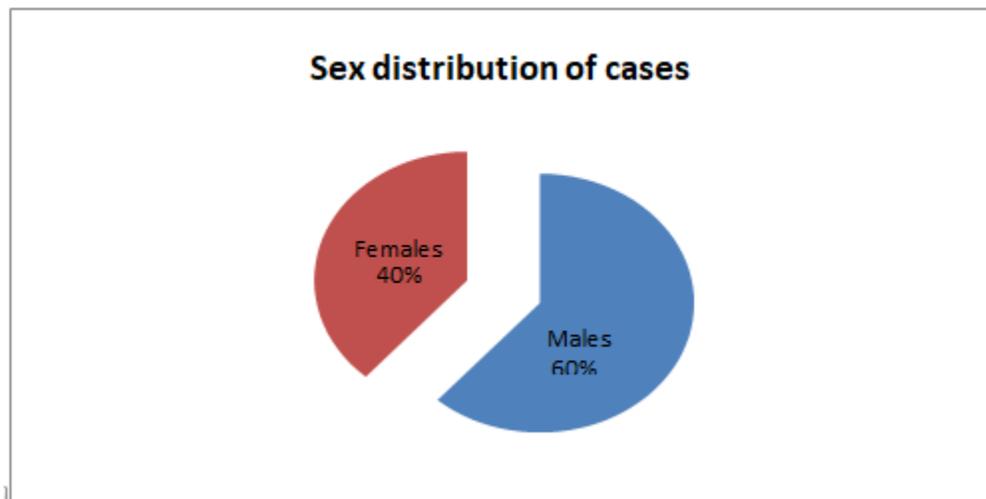
Age Group	No. of patients	Percentage%
21-30	3	4.0%
31-40	5	6.7%

41-50	8	10.7%
51-60	27	36.0%
61-70	19	25.3%
71-80	9	12.0%
81-90	4	5.3%

Table 1:-Distribution of patients according to age groups

In our study, 60 % patients were males and 40% were females (Fig-1). Among 21 to 30 years 2 males was there whereas 1 female was the patient .Among 31 to 40 years 5 males was there whereas no female was the patient. Among 41-50 years 5 males and 3 females had been included. Among 51 to 60 yrs, 16 males and 11 females were included. Among 61 to 70 years 10 males and 9 females had been included, whereas among 71-80 years 4 males and 4 female have been included. Among 81 to 90 years 3 males and 2 females had been included as shown in Table 2.

Age Group	Males		Females	
	No. of patients	Percentage	No. of patients	Percentage
21-30	2	4.4%	1	3.3%
31-40	5	11.1%	0	0.0%
41-50	5	11.1%	3	10.0%
51-60	16	35.6%	11	36.7%
61-70	10	22.2%	9	30.0%
71-80	4	8.9%	4	13.3%
81-90	3	6.7%	2	6.7%
Total	45	100%	30	100%

Table 2:-Sex distribution of patients according to age groups**Figure 1:- Sex distribution of cases**

Among the etiology, acute coronary syndrome was the main contributor and it was the cause in 60% of the patients followed by dilated cardiomyopathy in 28% cases and sepsis in 12% cases as shown in Table-3.

Etiology	Cases	Percentage
Acute Coronary Syndrome	45	60.0%
Sepsis	9	12.0%
Dilated Cardiomyopathy	21	28.0%

Table 3:-Etiology among to cases

Risk factors		Heart Failure		Type of Cardiorenal Syndrome					
		Present		1		2		5	
		Cases	%	Cases	%	Cases	%	Cases	%
ThyroidStatus	Normal	58	89.2%	36	92.3%	17	94.4%	5	62.5%
	Hypo	7	10.8%	3	7.7%	1	5.6%	3	37.5%
HF-NYHA	Grade 3	14	21.5%	7	17.9%	5	27.8%	2	25.0%
	Grade 4	51	78.5%	32	82.1%	13	72.2%	6	75.0%
COPD	Yes	5	7.7%	3	7.7%	1	5.6%	1	12.5%
	No	60	92.3%	36	92.3%	17	94.4%	7	87.5%
CAD	Yes	47	72.3%	35	89.7%	9	50.0%	3	37.5%
	No	18	27.7%	4	10.3%	9	50.0%	5	62.5%
Sepsis	Yes	8	12.3%	0	0.0%	0	0.0%	8	100.0%
	No	57	87.7%	39	100.0%	18	100.0%	0	0.0%
HTN	Yes	25	38.5%	19	48.7%	6	33.3%	0	0.0%
	No	40	61.5%	20	51.3%	12	66.7%	8	100.0%
TypeII DM	Yes	27	41.5%	17	43.6%	8	44.4%	2	25.0%
	No	38	58.5%	22	56.4%	10	55.6%	6	75.0%
Dys- lipidemia	Yes	7	10.8%	4	10.3%	3	16.7%	0	0.0%
	No	58	89.2%	35	89.7%	15	83.3%	8	100.0%
History of smoking	Yes	29	44.6%	21	53.8%	8	44.4%	0	0.0%
	No	36	55.4%	18	46.2%	10	55.6%	8	100.0%
History of Alcoholism	Yes	26	40.0%	18	46.2%	8	44.4%	0	0.0%
	No	39	60.0%	21	53.8%	10	55.6%	8	100.0%

Table-4 Risk factor association with type of cardio-renal syndrome

The major risk factor was coronary artery disease seen in 72.3%. Type 2 diabetes mellitus was present in 58.5% patients while hypertension in 38.5%. Smoking was the risk factor in 44.6% and alcohol in 40% patients. Sepsis was the risk factor in 12.3% cases and dyslipidemia in 10.8%. Hypothyroidism was present in 10.8% cases and COPD was present in 7.7% cases. NYHA grade 4 was more common and was seen in 78.5% while NYHA grade 3 in 21.5% cases as shown in **table 4**. Heart failure was present in 40 Males and 25 females. Type 1 cardiorenal syndrome was present in 25 Males and 14 females whereas type 2 cardiorenal syndrome was present in 13 males and 5 females. Type 5 cardiorenal syndrome was present in 2 males and 6 females. On admission, the average values of EGFR, urea, and creatinine were 46, 68mg/dl and 1.74mg/dl while after 48hrs the values were 38, 85mg/dl and 1.73mg/dl. The average Hemoglobin was 11.8g/dl.

The major risk factor which associated with mortality was coronary artery disease 73.5%. Type 2 diabetes mellitus was present in 62.5% patients while hypertension in 42.7%. Smoking was the risk factor in 46.2% and alcohol in 41.7% patients, COPD was present in 8.2% cases. NYHA grade 4 was more common and was seen in 79.2% while NYHA grade 3 in 22.8% cases as shown in **table 5**.

Risk factors		Mortality		χ^2 value	p value
		Yes	No		
Thyroid Status	Normal	19	45	0.017	0.900
	Hypothyroidism	4	7		
NYHA	Grade 3	7	11	1.115	0.332
	Grade 4	17	40		
COPD	Yes	3	6	0.217	0.900
	No	21	45		
CAD	Yes	16	35	0.115	.776

	No	8	16		
Sepsis	Yes	3	9	0.153	0.900
	No	21	42		
Hypertension	Yes	10	19	0.567	0.583
	No	14	32		
Type II DM	Yes	11	20	0.899	0.495
	No	13	31		
Dyslipidemia	Yes	2	9	1.112	0.467
	No	22	42		
History of smoking	Yes	11	22	0.453	0.612
	No	13	29		
History of Alcoholism	Yes	11	19	1.133	0.522
	No	13	25		

Table-5 Association of risk factors with mortality

DISCUSSION: - In our study, 60 % patients were males and 40% were females in the study done by Shah et al which was done on 50 ICU patients who had Cardio-renal syndrome, the study reported 67% males and 33% females(n=50). Study done by Salim et al which was done on total 563 who had chronic heart failure, in this study male patients were 56 % and female patients were 44%. In our study total patients were 75 of which maximum number of patients were in the age group 51-60yrs (36%) followed by 61-70yrs (25.3%), and minimum in 21-30yrs (4.0%).similar results were found in the study done by Abdullah et al which has reported maximum patients in the age group of 51-60 years of age(30%) . In the study done by Babu et al on patients with dilated cardiomyopathy and renal failure, maximum number of patients were in 41-50 age group(33.335)(n=54)^{7,8}.

Among the etiology, acute coronary syndrome was the main contributor and it was the cause in 60% of the patients followed by dilated cardiomyopathy in 28% cases and sepsis in 12% cases similar results were found in the study done by Prothasis et al which has reported 49%(maximum) patients with acute coronary syndrome 23% patients with dilated cardiomyopathy and 5 percent patient with sepsis. In the study done by Salim et al 68.3 % patients had acute coronary syndrome and 24% patients had dilated cardiomyopathy. In our study The major risk factor was found to be coronary artery disease, which was present in 72.3% of cases as compared to other studies like Babu et al in which the incidence of coronary artery disease was 63%.In the observational study done by shah et al CAD was the associated risk factor in the 48% of the patients (n=50) Type 2 Diabetes mellitus-in our study group diabetes mellitus was present in 58.5% of the patients^{9,10}.

While compared to other studies done by Babu et al it was 63% and in Shah et al it was 64%, which was found to be similar. In the observational study done by shah et al type 2 diabetes mellitus was the associated risk factor in the 64% of the patients.(n=50).Hypertension- in our study group 38.5% patients had hypertension .while compared study done by Babu et al it was 31.5%,which is found to be similar. In the observational study done by shah et al hypertension was the associated risk factor in the 68% of the patients.(n=50)¹¹.

Smoking was the associated risk factor in 44.6% of our study group patients while compared to the study done by Prothasis et al it was present in 42.04% of the patients, which was found to be similar. Similarly it was present in 35% patient group of study done by Abdullah et al.in the observational study done by Salim et al 33% patients (563) had smoking as a risk factor. Alcohol - was present in 40% patients of our study group patients, while compared to other studies it was 20.83 in the study done by Prothasis et al- and it was 14% in the observational study done by Salim et al¹².

Dyslipidemia-found to be risk factor in 10.8% patients of our study group. Similarly in the study done by Prothasis et al it was present in 14.58% patients of the study population. In the study done by Shah et al dyslipidemia was the associated risk factor in 44%(n=50) of the patients. Sepsis became the risk factor in 12.3% cases of our study patient group while compared to other observational study done by Prothasis et

al in which it was 19.79%.Hypothyroidism was present in 10.8% cases of our study population group. Similarly it was 13.54 % in the study done by Abdullah et al.COPD was present in 7.7% cases of our observational study population. While in the observational study done by Bhatnagar et al it was 38 % .In the Indian study done by Shah et al COPD was associated risk factor in 9%(n=50) of the study group patients¹³.

NYHA- in our observational study population out of 65 patients, 75.8% presented with NYHA4 symptoms and 21.5% patients presented with NYHA3 symptoms. In the Indian study done by Shah et al 48% patients presented with NYHA4 symptoms and 40% patients presented with NYHA3 symptoms in the observational study done by Abdullah et al patients most commonly presented with NYHA 2 symptoms(48%)¹⁴.

In our observational study CAD, sepsis and hypothyroidism was significantly associated with the incidence of Cardio-renal syndrome. Similarly in the study done by Prothasis et al CAD and sepsis were associated with the incidence of Cardio-renal syndrome in the observational study done by Abdullah et al most common risk factors were hypertension followed by diabetes mellitus and dyslipidemia¹⁵.

In our observational study there were no significant association between risk factors and mortality in comparison study done by Babu et al showed significant correlation between mortality with NYHA4symptoms and CAD. In the Indian study done by Shah et al anemia and reduced ejection fraction were associated with increased risk of mortality.

In our observational study mortality was 29 % which was significantly associated with decreased EGFR and raised urea levels (done on admission and after 48 hours of admission). Similarly In the study done by Shah et al mortality was 28 % which was significantly associated with decreased EGFR and raised UREA levels, in the study done by Bhatnagar et al mortality was 22%, which was significantly associated with decreased EGFR and raised urea levels, in the observational study done by Salim et al 33% patients (563), chronic renal failure diabetes and hypertension were associated with increased risk of mortality¹⁶.

CONCLUSION: - Cardiorenal syndrome is very common in people who have heart failure. Patients with heart failure who have had two or more previous hospitalizations, sepsis, history of CAD and hypothyroidism are more likely to develop cardiorenal syndrome. The development of cardiorenal syndrome is an independent predictor of frequent readmissions, In addition to longer hospitalization and slower recovery, under treatment of the cardiorenal syndrome has the potential to be fatal on an individual level and have massive public health repercussions. The breadth of knowledge and complexity of care required to provide the optimal treatment for these patients need a multidisciplinary approach integrating cardiology, nephrology, and critical care expertise. More research is needed to understand its pathophysiology and develop effective management strategies. Individualization of each patient with prudent drug use is the best line of care till then. New medicines offer promise for better outcomes for these difficult patients.

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