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STUDY OF CLINICAL PROFILE AND OUTCOME OF TYPE 1CARDIORENAL SYNDROMEAMONG HEART FAILURE PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: The most common presenting symptom for acute heart failure is shortness of breath and infections are most common precipitating events for failure.Patients of cardiorenal syndrome type 1 had comparatively higher mortality and morbidity among acute heart failure patients. Aim of this study is to determine the clinical profile and outcome of type 1cardiorenal syndrome among heart failure patients. **Material and Methods:** Total 92 patients of acute heart failure were included in the study. The clinical and laboratory profile and course in hospital were documented. **Results:** Cardiorenal Syndrome Type 1 was present in 16.3% patients. In our study, outof 15 CRS1 patients, 9(60%) were females and 6(40%) were males. Whereas other studies showed predominantly male sex involvement in CRS1. Highest number of patients 23 each (25.00%) were between 51-70 years of age. At presentation the main underlying predisposing factors for acute heart failure in patients were DCMP in 4.34% (P value - 0.001), Smoking in Twenty one 22.82%, Hypertension in 27.17% and Diabetes Mellitus in Twenty 21.73% patients. Various precipitating events were presentfor acute decompensation of stable heart failure or for acute heart failure. Among total 92 patients, infection in 43.47%, non compliance to treatment in 6.52%, naturalprogression of disease in 13.04%, anemia in 5.43%, ACS in 17.39%. TShe main underlying etiologies for acute heart failure were CAD, ACS in 13.33%, RHD in 13.33%, DCMP in 40% (P value- 0.043), High output failure and Diabetic cardiomyopathy in13.33 % each. Among patients of CRS1, 73.3 % had stage 1 acute kidney injury, 20 % had stage 2 acute kidney injury whereas 6.7 % had stage 3 acute kidney injury. Among CRS1 patients 20 % patients had inhospital mortality and6.6% patients were given dialysis support. 80% patients impoved and discharged from hospital. Average length of stay of patients among CRS1 group was higher compared toNCRS1 group (P value - <0.0001). **Conclusion:** The patients of Type 1 CRS are seen predominantly in females and elderlypopulations. Most of the patients have stage 1 AKI and recovered completely. Thus it is concluded that patients of type 1 CRS are associated with more mortality and more duration of hospital stay and DCMP is important underlying cause for development ofCRS1.

KEYWORDS: Cardiorenal syndrome, non cardiorenal syndrome, acute kidney injury, dilated cardiomyopathy, acute heart failure.

INTRODUCTION

Type 1 CRS (acute CRS) occurs in approximately 25% to 33% of patients admitted with ADHF, depending on the criteria used, and represents an important consequence of hospitalization with a myriad of implications for diagnosis, prognosis, and management. Cardiorenal syndrome type 1 (CRS1) is a syndrome characterized by a rapid worsening of cardiac function leading to acute kidney injury (AKI), causing high mortality rates, substantial loss in quality of life and high healthcare cost.

AKI is an independent risk factor for 1-year mortality in ADHF patients, including patients with ST-segment elevation myocardial infarction who develop signs and symptoms of HF or have a reduced left ventricular ejection fraction. This independent effect might be due to an associated acceleration in cardiovascular pathobiology due to kidney dysfunction through the activation of neurohormonal, cell signaling, oxidative stress, or exuberant repair (fibrosis) pathways. Upon initial recognition, AKI induced by primary cardiac dysfunction implies inadequate renal perfusion until proven otherwise.

The spectrum of acute cardiac events that may contribute to AKI includes acute decompensated heart failure (ADHF), acute coronary syndrome (ACS), cardiogenic

shock, and surgery-associated low cardiac output syndrome. Recent studies have emphasized the prognostic value of baseline renal dysfunction in a wide spectrum of acute coronary syndromes. Further cardiorenal syndrome divided into 5 subtypes according to the temporal sequence of organ failure as well as the clinical context.

Type 1 CRS (Acute CRS): HF resulting in AKI. Example - ACS resulting in cardiogenic shock and AKI, AHF resulting in AKI.
Type 2 CRS (Chronic CRS): Chronic HF resulting in CKD.

Type 3 CRS (Acute renocardiac Syndrome): AKI resulting in AHF. Example- HF in the setting of AKI from volume overload, inflammatory surge, and metabolic disturbances in uremia.
Type 4 CRS (Chronic renocardiac Syndrome): CKD resulting in chronic HF. Example- LVH and HF from CKD-associated cardiomyopathy.
Type 5 CRS (Secondary CRS) Systemic process resulting in HF and kidney failure.

Example-Amyloidosis, sepsis, cirrhosis However, in clinical practice, identifying the initial insult and subsequent events that result in decompensated acute or chronic CRS/renocardiac syndrome can be challenging.

AKIN classification can detect AKI with high sensitivity and specificity, while establishing different severity levels to predict the prognosis of affected patients. Incidence estimates for AKI associated with ACS and ADHF range from 9 to 19% and from 20 to 45%, respectively. It is of critical significance to determine the incidence of and outcomes associated with CRS for understanding the overall burden of the disease as well as its natural history, morbidity, and mortality.

AIM AND OBJECTIVES
Aim this study is to determine the clinical profile and outcome of type 1cardiorenal syndrome among heart failure patients.

MATERIAL AND METHODS
It was cross sectional observational study constitutes all the consecutive patients admitted with AHF in Department of Medicine in Indira Gandhi Medical College, Shimla (H.P.) from 1st July 2018 to 30th June 2019.

Cardiorenal syndrome type 1 (CRS1) is a syndrome characterized by a rapid worsening of cardiac function leading to acute kidney injury (AKI).

Framingham Criteria for Diagnosis of Heart Failure

- Major Criteria: PND, JVD, Rales, Cardiomegaly, Acute Pulmonary Edema, S3Gallop, Positive hepatic Jugular reflex, ↑ venous pressure > 16 cm H20.

- Minor Criteria: Lower limb edema, Night cough,

Dyspnea on exertion, Hepatomegaly, Pleural effusion,Reduced vital capacity by 1/3 of norma,l Tachycardia >120 bpm, Weight loss 4.5 kg over 5 days management.

AKI assessment was done according to AKIN classification. Stage Serum creatinine criteria.
Stage1 Increase in serum creatinine of ≥0.3 mg/dl (≥26.4 mmol/l) or increase to ≥150- 200% (1.5- to 2-fold) from baseline within 48 hours.
Stage 2 Increase in serum creatinine to >200–300 % (>2to3-fold) from baseline.
Stage 3 Increase in serum creatinine to >300% (>3 fold) from baseline [or S. creatinine. of ≥4.0mg/dl (≥354 mmol/l) with an acute increase of at least 0.5 mg/dl (44.21.mmol/l)]

INCLUSION CRITERIA
Patients ≥ 18 years old with a diagnosis of AHF.

EXCLUSION CRITERIA
Patients with known chronic kidney disease. Patients with other risk factors except for AHF that may cause AKI. Patients not willing to giveconsent.

METHODS
The data regarding clinical profile of patient was collected using pretested self- designed questionnaire including demographic profile, comorbidities. Various laboratory parameters noted including haematological, biochemical, BNP. Echocadiogaphy was perfomed in the Department of Cardiology at IGMC Shimla by th e cardiologist. The subjects were examined in the supine position and up lateral position with the use of a Philips i33 X-Matrix echocardiography machine. Two dimensional (2-D), Motion mode (M - Mode), Pulsed wave (Pw) Doppler, Continuous wave (Cw) Doppler, Doppler Tissue Imaging (DTI) were performed according to standard protocol .Images were taken according to the guidelines of the American Society of Echocardiography.]Parameters as given in the protocol were obtained in all the subjects.

STATISTICAL ANALYSIS
Data was entered on Microsoft excel spreadsheet on day to day basis. Results summarized in tables and percentages. The data analyzed using statistical Epi Info software. This study included 92 patients of acute heart failure admitted in Department of Medicine ward in Indira Gandhi Medical College and hospital, Shimla.

OBSERVATIONS AND RESULTS
DEMOGRAPHIC PRESENTATION
In studied population, among total 92 patients of acute heart failure 15 (16.3%) patients had acute kidney injury at admission or during hospital course and hence cardiorenal syndrome Type 1 whereas 77 (83.7%) had no kidney injury and were included in Non cadiorenal syndrome type 1. (Figure 1)
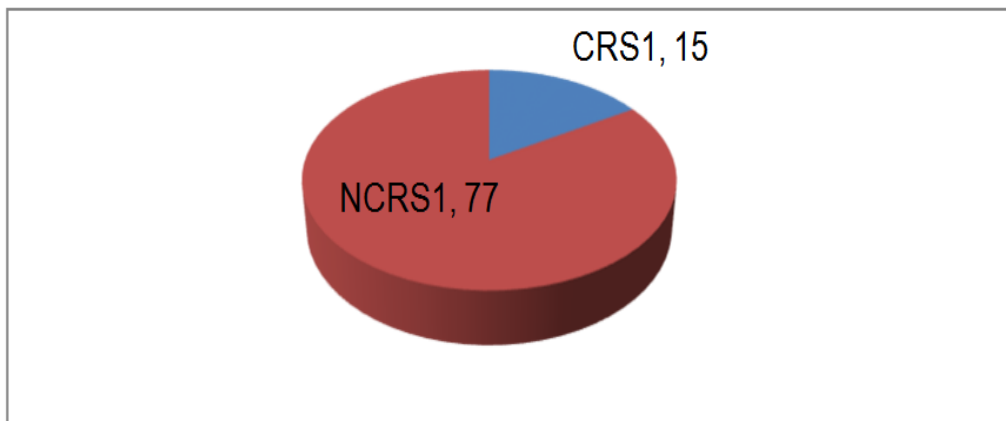
Figure 1: Distribution of patients among CRS1 and NCRS1.

GENDER WISE DISTRIBUTION OF HEART FAILURE PATIENTS

Of total 92 patients in the study group, 48 (52%) were females and 44 (48%) were male patients. Female to male ratio was 1.08:1.Out of 15 CRS1 patients, 9(60%) were females and 6(40%) were males. This shows that type 1 CRS were predominant in females. (Table 1, Table 2).

Table 1: Gender Wise Distribution Of Heart Failure Patients.

S. No		Frequency (n)	Percentage (%)
1.	MALE	44	52
2.	FEMALE	48	48

Table 2: Gender Wise Distribution Of Patients Of Crs Type 1.

S. No		Frequency (n)	Percentage (%)
1.	MALE	SIX	FORTY
2.	FEMALE	NINE	SIXTY

AGE WISE DISTRIBUTION

Among total 92 patients, highest number of patients 23(25.00%) were in two age group of 51-60 and 61-70 years. Eighteen (19.56%) were in the age group 71-80, Eleven (11.95%) in the age group 41-50 and 81-90 each. Five (5.43%) in age group 31-40 andone patient (1.08%) was in 11-20 years age group. It shows that with increase in age prevalence of cardiorenal syndrome also increases. Average age in study population was 63.38±14.47 years. (Table 3, Figure 2)

Table 3: Distribution of the Study Population by Age (n=92)

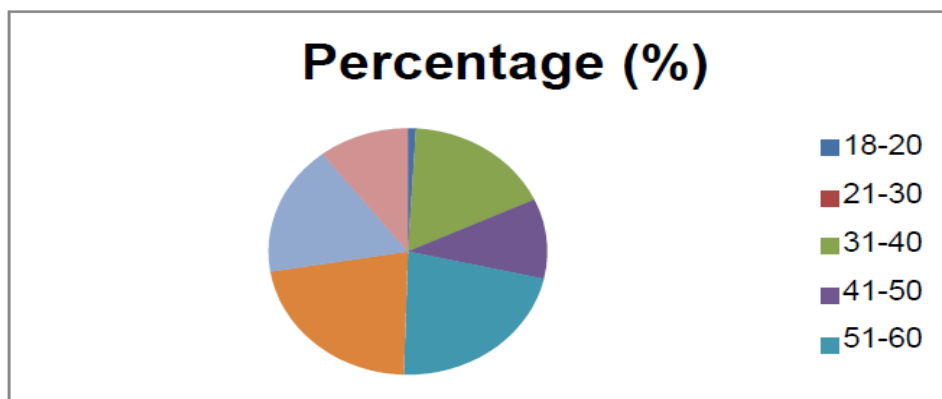| S. No.	Age group(years)	Frequency(n)	Percentage(%)
1.	18-20	1	1.08
2.	21-30	0	0
3.	31-40	5	19.56
4	41-50	11	11.95
5	51-60	23	25.0
6	61-70	23	25.0
7	71-80	18	19.56
8	81-90	11	11.95

Figure 2: Distribution of study population by age.

Distribution of CRS1 patients as per AKIN Stage
Among patients with CRS1, Eleven (73.3%) patients had AKIN Stage 1 acute kidney injury, Three (20%) patients had AKIN Stage 2 acute kidney injury and 1 (6.7%) patienthad AKIN Stage 3 acute kidney injury.(Table 4)
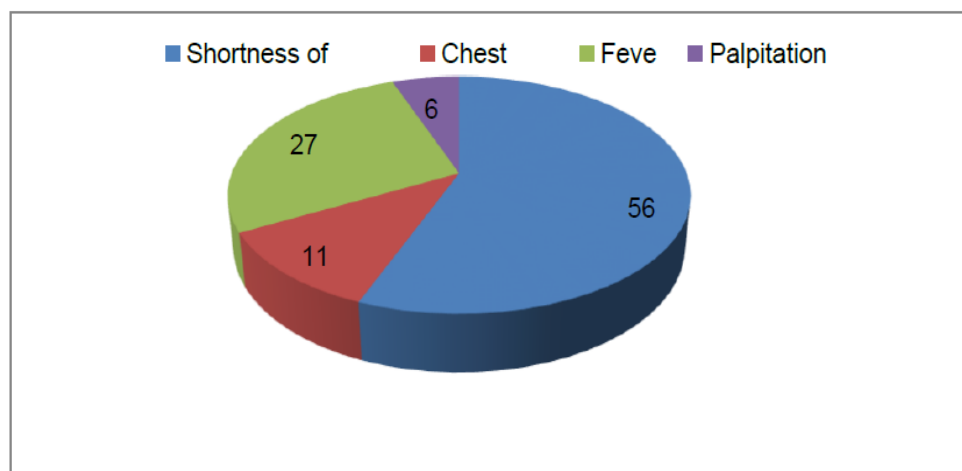
Table 4: Distribution ofCRS1 patients by AKIN Stage.

S. No	AKIN Stage	Frequency (n)	Percentage (%)
1.	1	11	73.3
2.	2	03	20
3.	3	01	6.7

Chief complaints at the time of admission
Shortness of breath was present in 86(93.47) patients, Chest pain was present in 16 (17.39%), fever in 39(42.39%), Palpitations in 8(8.69 %) patients. (Figure 3).

Figure 3: Symptoms at presentation(n=92)

Clinical features at Presentation
At presentation age of patients did not contribute difference to patient with or without AKI. The Mean systolic Blood Pressure in patients without AKI was110.11±12.95 and with AKI was 99.87 ± 11.98 which was statistically significant (P value0.006). Mean Diastolic Blood Pressure in patients without AKI was 68.55 ± 09.90 and with AKI was 57.73 ± 11.90 which was statistically significant (P value – 0.000). Mean Arterial Pressure in patients without AKI was82.40 ±10.31 and with AKI was 71.77 ± 11.16 which was statistically significant (P value - 0.001). Mean BMI of patients without AKI was22.609 ±2.58 and with AKI was 22.400 ± 2.58 which was statistically insignificant (P value - 0.771) (Table 5).

Table 5: Comparison of some demographic and clinical characteristics ofpatients with CRS1and with NCRS1

Characteristics/ Feature	CRS1n=15 mean±SD	NCRS1 n=77 mean±SD	p value
AGE(Yrs)	63.40±11.55	63.38±15.04	0.995
Sex Male	64±12.36	63.97±14.24	.996
Female	63±11.72	62.79±15.94	.969
SBP	99.87±11.98	110.11 ±12.95	**0.006***
DBP	57.73±11.90	68.55±9.90	**0.000***
MAP	71.77±11.16	82.40±10.31	**0.001***

* P value < .05 is significant

MAIN PREDISPOSING FACTORS FOR ACUTE HEART FAILURE AMONGCRS 1 AND NCRS 1
In studied population, at presentation the main underlying predisposing factors for acuteheart failure in patients were DCMP in Four (4.34%), Smoking in Twenty one(22.82%), Hypertension in Twenty Five(27.17%), Alcohol in Eight(8.69%), Anemia in Two(2.17%), Old MI in Fourteen(15.21%), Diabetes Mellitus in Twenty (21.73%) patients. (Figure 4).
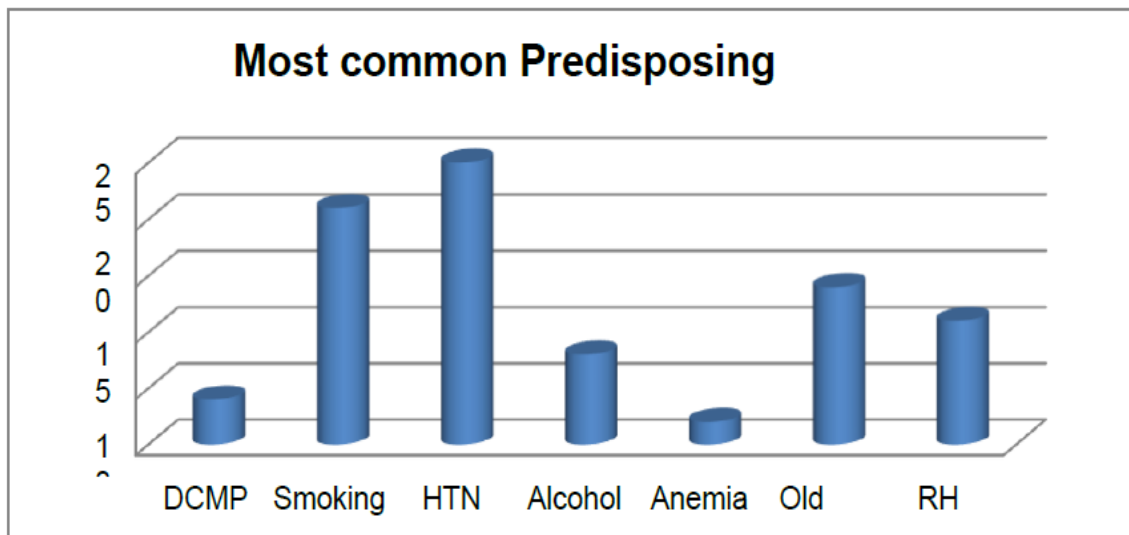
Figure 4: Predisposing Factors for Acute Heart Failure in study.

Population

This study found that some of these predisposing factors were associated with CRS1 like among patient with CRS1 20% were known case of DCMP whereas NCRS1 group had 1.29% patients with DCMP which was statistically significant (P value – 0.001). Among other CRS1 patients Smoking was in 26.66%, hypertension, alcohol and anemia was in 6.66% each, old Myocardial Infarction 0%, RHD was in 13.33 % and all of these were statistically insignificant when compared with Non CRS1 group.(Table 6)

Table 6: Main Predisposing factors for Acute Heart Failure in CRS 1 vs NCRS 1.

Predisposing Factor	CRS1	NCRS1	P Value
DCMP	20 %	1.29%	**0.001**
Smoking	26.66%	22.07%	0.698
HTN	6.66%	31.16%	0.051
Alcohol	6.66%	9.90%	0.760
Anemia	6.66%	1.29%	0.195
Old	0%	18.18%	0.073
MIDM	33.33%	19.48%	0.234
RHD	13.33%	11.68%	0.857

Distribution of the Study Population by Precipitating factors

In studied population, various precipitating events were present for acute decompensation of stable heart failure or for acute heart failure. Among total 92 patients, 40(43.47%) had infection, 6(6.52%) had non compliance to treatment, 12(13.04%) had natural progression of disease, 5(5.43%) had anemia, 16(17.39%) had ACS, 8(8.69%) had AF, 3 (3.26%) had no obvious precipitating cause, and 2(2.17%) had other precipitating causes including pericardial effusion and haemorrhoid bleed. (Table 7)

Table 7: Distribution of the Study Population by Precipitating event (n=92)

S. No	Precipitating event	Frequency (n)	Percentage (%)
1.	Infection	40	43.47
2.	Non compliancetotreatment	6	6.52
3.	Natural course	12	13.4
4.	Anemia	5	5.43
5	ACS	16	17.39
6	AF	8	8.69
7	Nil	3	3.26
8	other	2	2.17

Investigations

On investigations all the haematological parameters among both NCRS1 group and CRS1 group were comparable and were statistically insignificant (p value-0.675) except for mean TLC count which was 5.69 thou/μL in patient with CRS1 and 7.11 in NCRS1 group which was statistically significant (P value - 0.031).

Etiology of heart failure

In this study the main underlying etiology of heart failure were ACS in 2 patients of CRS1 group compared to 14 patients of NCRS1 group, RHD in 2 patients of CRS1

group compared to 9 patients of NCRS1 group, DCMP in 6 patients of CRS1 group compared to 13 patients of NCRS1 group, Ischemic cardiomyopathy in none of the patients of CRS1 group compared to 14 patients of NCRS1 group, Hypertensive Heart disease in none of the patients of CRS1 group compared to 11 patients of NCRS1 group, High output failure in 2 patients each among CRS1 group and NCRS1 group, Diabetic cardiomyopathy in 2 patients of CRS1 group compared to 6 patients of NCRS1 group and 9 patients had other diseases including Cor pulmonale, Congenital heart disease, Aortic valve disease etc.. (Figure 4)
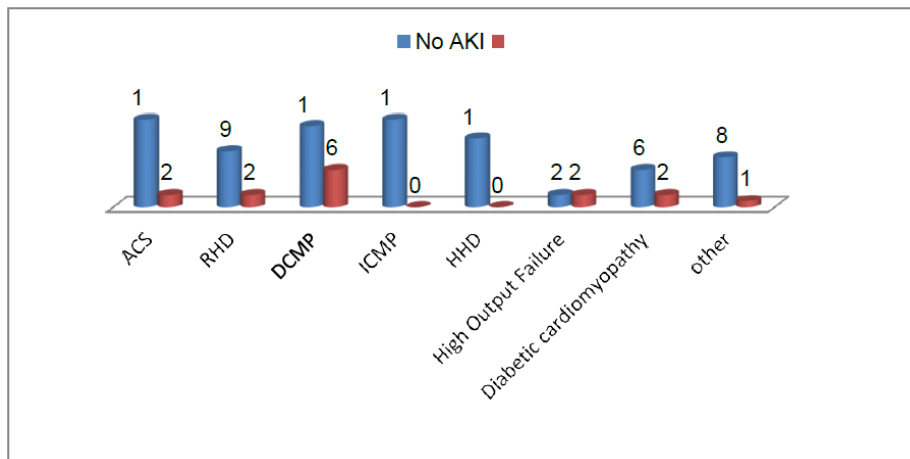

Figure 4: Distribution of Heart diseases among NCRS1 and CRS1 group.

Hospital course of CRS1 patients

Among patients of CRS1, 3 (20 %) patients had inhospital mortality and 1 (6.6%) patient was given dialysis support. 12 (80%) patients improved and

discharged from hospital. Average length of stay of patients among CRS1 group was 7.2 ± 2.04 andNCRS1 group was 5.4 ± 1.36 which was statistically significant.(P value - <0.0001)(Figure 5).
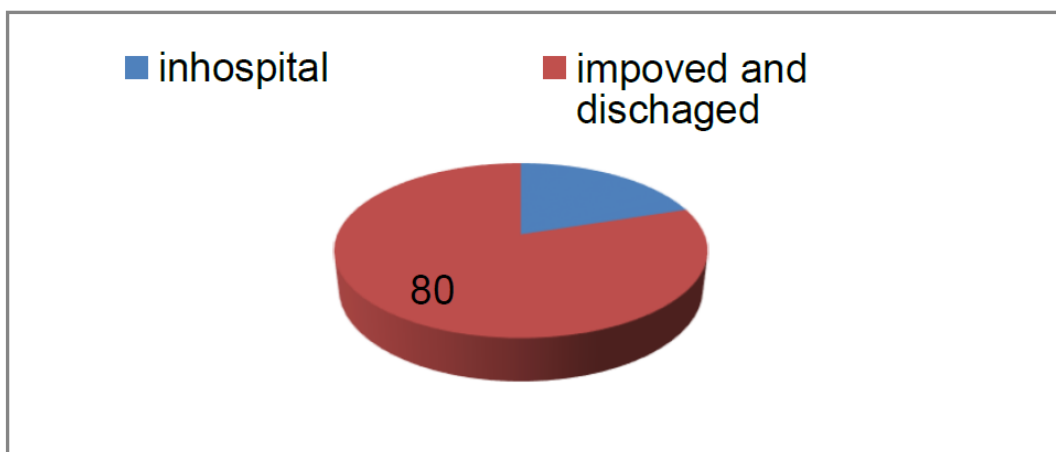

Figure 5: Hospital course of patients among CRS1 group.

Out of three (20%) patients died in CRS1 group, the main etiologies of heart failure were RHD in 2 (66.7%) and DCMP in 1(33.3%) patient.

DISSCUSION

This study constitutes total of 92 patients of acute heart failure, who presented to Department of Medicine at Indira Gandhi Medical College and hospital Shimla. This

study aimed to find out the clinical profile and outcome of type 1cardiorenal syndrome among heart failure patients. The prevalence of CRS1 in our study found to be 16.3 %.

In study conducted by Gigante A et al on 1,087 patients discharged from their unit during the study period, 190 (17.5%) were diagnosed with CRS and

CRS1 prevalence was found to be 32.1%. Most of CRS1 patients in our study were in Stage 1 and recovered completely and discharged. These wide ranges may be attributable to differences in the definitions used to determine worsening renal function and/or ethnic or geographical differences in the selected populations. As the reported incidences of worsening renal function in patients with ACS or ADHF lie on relatively broad limits, further studies with a large sample size are needed to clarify what contribution the AKIN criteria for AKI makes. In our study, out of 15 CRS1 patients, 9(60%) were females and 6(40%) were males. Whereas other studies showed predominantly male sex involvement in CRS1. In our study, patients who were already known case of DCMP had higher number of AKI and hence CRS1 which other studies have not shown.

Our study showed that at presentation average Systolic Blood pressure (99.87±11.98), average Diastolic blood pressure (57.73±11.90) were lower among CRS1 patients than those among NCRS1 patients. In study conducted by Eren Z et al also showed average systolic and diastolic blood pressures were lower in CRS 1 patients with statistical difference.

Our study showed that at presentation average TLC (5.69 ±1.15), was lower among CRS1 patients than those among NCRS1 patients. Whereas other parameters such as Hb, S. K^+, ejection fraction were not statistically different among CRS1 patients compared to NCRS1 patients as shown in study by Eren Z et al.

The most common precipitating factor for heart failure was infections (43.47 %) in our study. It may be seen as most of population is from rural background in our study and with low socioeconomic status and probably due to an aging population, an increasing number of immunocompromised patients and comorbidity conditions.

Our study found that the total length of hospital stay was average 5.76 ± 1.61 days in all patients .Length of stay was more in CRS1 patients with average 7.2 ± 2.04 days as compared to patients with NCRS1 in whom average stay was 5.4 ± 1.36 days. In study conducted by Metra M et al. on Worsening renal function in patients hospitalised for acute heart Failure also found that the total length of hospital stay was average 13±11 days in all patients. Length of hospital stay was higher in patients of acute heart failure with Worsening renal function patients with average 17±14 days as compared to patients without Worsening renal function. This was similar to our study. This may be important both with respect to quality of life and the cost of treatment. Increased length of hospital stay is likely an effect of AKI as it causes changes in treatment aimed at improving renal function. The total duration of stay was less in our study as compared to study by Metra M et al. This might be because of more number of non heart failure patients in our resource limited centre with limited number of beds in wards.

The 20% CRS1 patients died during hospitalization. These results were comparable in study conducted by Hu W et al. on Risk Factors and Prognosis of Elderly Patients with cardiorenal Syndrome Type 1 which showed 23.2 % mortality in CRS1 patients during hospitalization.

Limitations
This study was conducted in a single centre on a small sample size. Dosages of drugs used were not considered in the study. Average duration of hospital stay was less due to limited resources.

CONCLUSION

The most common presenting symptom for acute heart failure is shortness of breath and infections are most common precipitating events for failure. The overall prevalence of CRS1 is 16.3 % among various etiologies of acute heart failure. The incidence of CRS1 was higher in females as compared to males and occurs more in elderly accounting for associated increased comorbidities.

The patients with CRS1 have lower Total leukocyte count. No significant difference in other haematological parameters. Patient with known case of DCMP are more prone for development of CRS1 if decompensation occurs. Smoking, Diabetes mellitus, Hypertension do not contribute significantly for development of CRS1. Various medications used for management of heart failure during hospital course do not significantly contribute for development of CRS1. Among etiologies of heart failure, DCMP contribute significantly for development of heart failure. Patients of CRS1 had higher mortality and increased duration of hospital stay. Among CRS1 mortality patients, DCMP and RHD are important cause of heart failure.

Thus it is concluded that patients of type 1 cardiorenal syndrome are associated with more mortality and more duration of hospital stay and DCMP is important underlying cause for development of CRS1.

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