



ORIGINAL RESEARCH PAPER

Nephrology

TO STUDY THE EPIDEMIOLOGY AND INCIDENCE OF RENAL REPLACEMENT THERAPY IN PATIENTS WITH CARDIO- RENAL SYNDROME ADMITTED TO A TERTIARY CARE INTENSIVE CORONARY CARE UNIT (ICCU). – ORIGINAL ARTICLE

KEY WORDS:

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ABSTRACT Cardiorenal syndrome (CRS) is a disorder of the heart and kidney whereby interactions between the two organs can occur. The Acute Dialysis Quality Initiative (ADQI) Working Group has developed a classification for the CRS into the five discrete subtypes. Knowledge of the epidemiology and incidence of heart-kidney interaction stratified by the proposed CRS subtypes is increasingly important for understanding the overall burden of disease for which CRS subtype, along with associated morbidity and mortality.

INTRODUCTION

Cardiovascular disease (CVD), including heart disease and stroke, is the leading cause of death in the United States, regardless of self-determined race/ethnicity (1). The rising prevalence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) is a global medical and epidemiological problem worldwide seen both in developed and even in the third world countries. Chronic kidney disease (CKD) is a worldwide public health problem affecting 10-16% of the adult population.

Various epidemiological studies have shown that renal impairment is a common and independent risk factor of morbidity and mortality (2) in patients with cardiac disease, either in asymptomatic (3) or symptomatic (4) congestive heart failure (CHF) patients. Moreover, chronic kidney disease (CKD) plays a significant role in the progression of cardiovascular disease regardless of the status of the heart (5).

The strong connection between renal and cardiovascular disease has revived interest in the complex interactions between heart and kidneys. The term cardiorenal syndromes (CRS) was coined by Ledoux in 1951 and referred to combined heart and kidney failure (6).

CRS is a common but under recognized condition which has a profound prognostic implications and has an adverse effect on both morbidity and mortality of cardiac and renal disease occurring alone. This has been shown in various studies done worldwide. Impaired renal function is consistently found to be an independent risk factor for 1-year mortality in acute HF patients, including those with ST segment elevation myocardial infarction (7).

Since Indian data is lacking this study will help us to understand the epidemiology and incidence and risk factors for the development of cardiorenal syndrome in our population. It will help in developing awareness and will help improve the outcome of these complex patients using a multidisciplinary approach, combining the expertise of cardiology, nephrology and critical care physicians.

AIMS AND OBJECTIVES

To study the epidemiology and establish the Incidence of Cardio-Renal Syndrome in patients admitted to a tertiary care Intensive Coronary Care Unit (ICCU).

MATERIAL AND METHODS

This was a prospective, observational study done to define the incidence of Cardio-Renal syndrome in an inpatient population and to study the complications and disease outcomes of patients presenting with cardiac disease and renal failure.

Inclusion criteria

- All consecutive patients admitted to the Intensive coronary

care unit (ICCU) at Christian Medical College and Hospital (CMCH), Ludhiana, during the one year study period between 1st March 2013 till 28th February 2014 were included in the study.

- All patients above the age of 18 years willing to participate in the study after giving prior informed consent were included.

Exclusion Criteria

- Age less than 18 years
- Pregnancy
- Patients unwilling to participate in the study or give informed consent
- Patients discharged against medical advice before a definitive diagnosis is made or three days.

Methodology

The study was conducted in the in-patients admitted to the Intensive Coronary Care Unit of the Cardiac Research Centre at CMC, Ludhiana. All the patients willing to participate in the study were included. Demographic data was collected according to the proforma. History and clinical examination was done and blood and urine samples were collected as per protocol. Blood samples were collected at admission and included complete blood profile, blood urea, creatinine, electrolytes, total protein, albumin and cardiac enzymes. Serum creatinine levels were repeated at least for three consecutive days and later as per requirement. Daily intake output, blood pressure were recorded till discharge. The patients were studied for etiology, recovery, progression, intervention including hemodialysis, outcome at discharge. Mortality was defined as death during in patient care. Incidence was estimated from the proportion of confirmed patients with cardio-renal syndrome admitted to ICCU and total number of patients admitted with cardiac diseases during the study period. Patients were described with clinical presentation, laboratory profile and outcome of the disease.

STASTICAL ANALYSIS

The incidence of cardio- renal syndrome was estimated from the proportion of confirmed cases of Cardio- renal syndrome divided by the total number of patients admitted in ICCU during the study period.

RESULTS AND ANALYSIS

This study was a one-year prospective study done among the in-patient population admitted in Intensive Coronary Care Unit (ICCU) of Christian Medical College and Hospital, Ludhiana. The study period was from 1st March 2013 till 28th February, 2014 During the study period a total of 1524 patient were admitted in ICCU. Among these 126 patients were not found to have a cardiac disease, 26 deaths and 39 patients were discharged against medical advice within first three days, 133 patients did not give consent to participate in the study. All these patients were not included for analysis as per our study proforma. Data collection

was not complete for another 78, these were also excluded from the final analysis. 1122 patients were finally included for analysis. The following were the results from the study.

TOTAL ADMISSIONS	1524
DEATHS (FIRST 72HRS)	26
LAMA (FIRST 72HRS)	39
NON-CARDIAC DIAGNOSIS	126
NOT GIVEN CONSENT	133
MISSING DATA	78
INCLUDED FOR ANALYSIS	1122

BASELINE CHARACTERISTICS

Sex distribution

Table 1 and Figure 1 shows the sex distribution of the study population. There were a total of 1122 patient, out of which 691 (61.59%) were males and 431 (38.41%) were females, with male to female sex ratio of 1.6: 1.

Table 1 : Sex distribution

Sex distribution	Frequency	Percentage (%)
Females	431	38.41
Males	691	61.59
Total	1122	100.00

Table 2 : Age Distribution

Age (Years)	Frequency	Percentage (%)
≤20	1	0.09
21-30	18	1.60
31-40	56	4.99
41-50	218	19.43
51-60	329	29.32
61-70	306	27.27
71-80	159	14.17
81-90	33	2.94
91-100	2	0.18
Total	1122	100.00

Table 2 shows the distribution of the patients according to their age. Majority of the patients 635 (56.65%) were between 51 to 70 years of age. The mean age of the study population was 59.24 ± 12.22 years. The youngest and oldest patient enrolled were 17 years and 99 years respectively.

Table 3 : Co-morbidities

Co-morbidity	Frequency	Percentage (%)
Diabetes Mellitus	456	40.64
Hypertension	623	55.53
Infection	155	13.81
Chronic Kidney disease	104	9.2

Table 3 and Figure 3 shows the presence of various common co-morbidities in our study population. Hypertension was the most common seen in 623 (55.53%) patients. In our study population 456 (40.64%) of the population was diabetic. In 155 (13.81%) there was evidence of infection at time of hospital admission. Chronic Kidney disease was present in 104 (9.2%).

Table 4 : Cardiac diagnosis at admission

Cardiac Diagnosis	Frequency	Percentage (%)
Acute Coronary syndrome (ACS)	570	50.80
Acute heart Failure (AHF)	110	9.80
ACS + AHF	265	23.61
ACS + AHF + Arrhythmia	47	4.19
Chronic Heart disease	40	3.57
Tachy-arrhythmia	55	4.90
Brady-arrhythmia	35	3.12
Total	1122	100.00

Table 4 shows the distribution of patients on the basis of their admitting cardiac diagnosis. Acute Coronary syndrome (ACS) was

the most common admitting diagnosis. Out of the 1122 patients, 882 (78.60 %) had ACS alone or in combination of acute heart failure and arrhythmias. A total of 570 (50.80%) had ACS alone, 265 (23.61%) had ACS along with acute heart failure and 47 (4.19 %) had ACS with both acute heart failure and arrhythmias.

Table 5 : Presenting symptom

Symptom	Frequency	Percentage (%)
Angina	636	56.68
Dyspnea	437	38.94
Palpitation	213	18.98
Syncope	80	7.1
Orthopnea	42	3.74
Edema	18	1.6

This table 5 shows the distribution of patients on the basis of the various presenting symptoms. The symptoms were seen in various combinations. Angina was the most common symptom seen in 636 (56.68%) of the patients, with dyspnea being the second common symptom seen in 437 (38.94%) of the patients. Other presenting symptoms included palpitations in 213 (18.98 %), syncope in 80 (7.1%) and edema in 18 (1.6%) of the study population.

Table 6 : Admission estimated Glomerular filtration rate (eGFR)

eGFR (ml/min/1.73 m ² BSA)	Frequency	Percentage (%)
< 15	31	2.76
15 - 29	87	7.75
30- 59	249	22.19
60-89	389	34.67
≥90	366	32.62
Total	1122	100.00

Table 6 shows the distribution of admission eGFR in our study population. The mean eGFR in this study population was 73.89 ± 31.94 ml/min. The maximum e GFR being 191.1 ml/min / 1.73 m² body surface area and minimum being 3.9 ml/min / 1.73 m² body surface area. Only 366 (32.62%) had a normal eGFR at the time of presentation to the hospital. Whereas 756 (67.37%) had different degree of renal dysfunction even on admission.

Table 7: Incidence of Cardio-renal syndrome

Cardio- renal syndrome	Frequency	Percentage
Absent	536	47.77
Present	586	52.23
Total	1122	100.00

Table 7 shows the incidence of cardio- renal syndrome in the study population. According to this table out of the total 1122 study population, cardio- renal syndrome was seen in 586 (52.23 %) of the patients.

Table 8 : Types of Cardio-renal syndrome

Types of Cardio-renal syndrome (CRS)	Frequency	Percentage (%)
Absent	536	47.77
CRS type 1	396	35.29
CRS type 2	23	2.05
CRS type 4	79	7.04
CRS type 5	88	7.84
Total	1122	100.00

Table 8 shows the frequency of various types of Cardio-renal syndrome in the study population. In our study out of the total 1122 patients, cardio- renal syndrome was seen in 586 (52.23%). Cardio-renal syndrome type 1 was the most common, seen in 396 (35.29%) of the total population. CRS type 5 was the second most common seen in 88 (7.84%) of the total study population. About 79(7.04%) and 23 (2.05%) were CRS type 4 and CRS type 2

respectively. None of the patients had type 3 CRS in our study population.

Table 9: Presenting Symptoms and Development of Cardio-renal Syndrome

Symptoms	Cardio-renal syndrome Absent		Cardio-renal syndrome Present		P value	OR (95% CI)
	Number	Percentage	Number	Percentage		
Angina (n=636)	354	66.04	282	48.12	< 0.005	0.477 (0.37-0.60)
Dyspnea (n=437)	113	21.0	324	55.3	<0.0005	4.62 (3.55-6.02)
Palpitation (n=213)	117	21.8	96	16.3	0.02	0.70 (0.52-0.94)
Syncope (n=80)	35	6.5	45	7.6	0.455	1.19 (0.75-1.83)
Orthopnea (n=42)	5	0.93	37	6.3	<0.0005	7.15 (2.7-18.3)
Edema (n=18)	1	0.001	17	2.9	<0.0005	15.98 (2.12-120.2)

Table 9 describes the occurrence of cardio-renal syndrome according to the various presenting symptoms. Amongst the total of 1122 patients various presenting features included syncope (n=80), angina (n=636), palpitation (n=213), dyspnea (n=437), orthopnea (n=42) and edema (n=18) patients in different combinations. Out of these presenting symptoms presence of dyspnea (55.3% vs 21% - p value < 0.005), orthopnea (6.3% vs 0.93% - p value < 0.0005) and edema (2.9% vs 0.001% - p value < 0.0005) at the time of hospitalization predicts the development of cardio-renal syndrome.

There was no difference in the development of cardio-renal syndrome in patients presenting with syncope (7.6% vs 6.5%, p value of 0.455). Angina (48.1% vs 66.04%) and palpitation (16.3% vs 21.8%) were more common in the group of patients who did not develop cardio-renal syndrome.

DISCUSSION

Many patients with heart failure have underlying renal dysfunction, and similarly, patients with kidney failure are prone to cardiac failure. Primary disorders of one of these two organs can cause dysfunction to the other, determining the pathophysiological basis for the cardiorenal syndrome (CRS). Although it was defined and classified several years ago (8), only in 2008 was this syndrome unanimously accepted in a consensus conference by experts in nephrology, critical care, cardiac surgery and cardiology, under the auspices of the Acute Dialysis Quality Initiative (ADQI) (9). Moreover, mortality, morbidity and cost of care greatly increase when cardiac and renal diseases coexist.

Our study was a prospective, observational study conducted at Christian Medical College and Hospital, Ludhiana, during the one-year study period between 1st March 2013 till 28th February 2014. The study was done to define the incidence of Cardio-Renal syndrome in an inpatient population and to study the complications and disease outcomes in these patients.

Incidence of Cardio-renal syndrome:

In our study out of the total 1122 study population cardio-renal syndrome was seen in 586 (52.23 %) of the patients. Acute Coronary syndrome (ACS) was the most common admitting diagnosis. Out of the 1122 patients, 882 (78.60 %) had ACS alone or in combination of acute heart failure and arrhythmias. Acute heart failure was the second most common admitting

diagnosis, seen in 110 (9.80%), Tachy-arrhythmias and Brady-arrhythmias were seen in 55(4.90%) and 35 (3.12%) of the patients respectively.

The incidence of cardio-renal syndrome was higher in diabetic as compared to non-diabetic population with p value being < 0.005 (the odds ratio being 2.150 with 95% CI 1.684-2.745). There was an increased chance of developing cardio-renal syndrome in patients who were hypertensive in comparison with normotensive population and this difference is statistically significant with p value of 0.009 (with odd's ratio 1.368 with 95% CI 1.080 – 1.732).

Among the 586 patients diagnosed with cardio-renal syndrome, CRS type 1 was the most common, seen in 396 (35.29%) of the total population. CRS type 5 was the second most common seen in 88 (7.84%) of the total study population. About 79 (7.04%) and 23 (2.05%) were CRS type 4 and CRS type 2 respectively. None of the patients had type 3 CRS.

In our study CRS type 1 was the most common as our study was done on patients admitted in Cardiac intensive care unit, whereas patients presenting primarily with sepsis and renal failure were admitted in medical and nephrology specialities respectively.

In a study done by Krumholz (10), on Medicare beneficiaries with HF, it was demonstrated that worsened renal function (WRF), defined as a rise in serum creatinine of 0.3 mg/dl (26.5 micromol/l) during hospitalization, occurred frequently with incidence of 28% of the study population. Analysis of data by Nohria (11), from the multicentric ESCAPE trial (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) which included 433 patients with low ejection fraction admitted with ADHF, the incidence of worsening renal function defined by increase in serum creatinine by 0.3 mg /dl was found to be as high as 29.5%.

As seen with ADHF, various studies have shown that acute coronary syndrome is also associated with increased incidence of worsening renal failure. In the analysis of data by Jose (12) from the Survival and Ventricular Enlargement (SAVE) trial in which 1854 patients with Myocardial infarction were enrolled during early post Myocardial infarction period, the incidence of worsening renal function was found to be as high as 12%. We found an incidence of WRF which was slightly higher than that reported in many previous studies. This difference is likely caused by our protocol with frequent (daily) reassessments of serum creatinine as well as by the higher prevalence of patients with advanced HF. Our study highlights the importance of frequent reassessments of renal function as the early detection of WRF has a prognostic significance.

CONCLUSIONS

Cardio-renal syndrome is a common condition in our population. Its incidence increases with presence of co-morbidities like Diabetes mellitus, hypertension, anemia and infection. Use of high dose diuretics especially infusion diuretics, inotropes, Angiotensin converting enzyme inhibitor and Angiotensin receptor blocker increases the incidence of cardio-renal syndrome. Occurrence of cardio-renal syndrome significantly increases the mortality. It also increases the complication rate and duration of hospital stay.

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