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CARDIORENAL SYNDROME TYPE 1: CLINICAL PROFILE AND HOSPITAL OUTCOMES

General Medicine

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ABSTRACT

Type 1 Cardiorenal syndrome (CRS 1) in which an acute cardiac condition leads to secondary acute kidney injury is frequently encountered in critical care settings. In CRS 1 has a multifactorial pathophysiology and presents with sudden onset decrease in urine output and raised serum BUN and creatinine levels and also worsening of acute cardiac disease. CRS type 1 is a challenge to the treating physician because it results in increased morbidity and mortality of the cardiac patients.

Aim: To study the clinical profile of patients with cardiorenal syndrome type 1 and their in-hospital outcome

Methods: In this cross sectional prospective study, 50 consecutive subjects suffering from acute cardiac conditions were screened for CRS I and enrolled .They were assessed clinically, evaluated as per Performa and followed up for in hospital outcome in form of survival and hospital stay. The primary outcome was in-hospital mortality and secondary outcome was duration of hospital stay. During the study period all patient received standard line of management as per the clinical diagnosis.

Result: Mean age for all 50 patients with CRS 1 was 56 ± 14 years, with 56% males and 44% females. The Mean age for male patients was 53 ± 14 yr and for female patients was 61 ± 12 years. The primary diagnosis in33 (66%) patients was ACS with acute heart failure, in 10(20 %) ACS alone, and in 7(14%) uncontrolled hypertension with acute heart failure. The commonest co-morbidity was CAD, present in 44 patients (86%) followed by hypertension in 28 patients (56%), COPD in 19 (38%), CKD in 13 patients (26%) and diabetes in 12 (24%). Mean SBP in study population was 120±27 mm of Hg and DBP was 78±15 mm of Hg. Mean urine output in study population at first 6 hours was 65±21 ml/kg/hr which has decreased to 49±17 ml/kg/hr after 48 hours. Mean GFR in study population at admission was 81.3±27.9 ml/min. After 48 hour GFR was reduced to 47.4±18.96 ml/min. Total 50 patients of CRS 1 were included in the study, 11 patients (22%) expired during hospital stay and 39 patients (78%) survived. Mean age of survivors was 52±11.53 yrs that of non survivors was 73.5±8.18 years. The mean duration of hospital stay in the survivors was 8.97+/-1.72 days. CKD as a co morbid condition was significantly associated with mortality. There were significantly higher levels of blood urea, serum creatinine and serum potassium in patients with in-hospital mortality. Higher stage of AKI was significantly associated with in-hospital mortality.

CONCLUSION: From the above study we conclude that the in patients of CRS 1, males were affected at early age compared to females. ACS with heart failure is the commonest primary diagnosis leading to CRS 1. Patients with higher age, pre existing CKD and higher stage of AKI during hospital stay are at risk of poor outcome.

KEYWORDS

CRS,Cardiorenal syndrome,ACS,AKI.

Introduction

The heart and the two kidneys perform the vital functions of tissue perfusion and maintenance of normal hemostasis of body tissues. Disease and dysfunction of either organ significantly impacts the health status of an individual. In clinical practice cardiac failure and renal dysfunction have frequently been found to coexist. The Heart, Lung and Blood Institute coined the term Cardiorenal Syndrome to describe their interdependent relationship which results in disorder of one organ leading to disordered function of the other organ in acute or chronic form and dysfunction of either organ can initiate the syndrome. Five subtypes of CRS initially described by Ronco et al in 2005 were accepted by the Acute Dialysis Quality Initiative in 2008. [1]

Type 1 also known as acute CRS: Acute kidney injury due to sudden decrease in cardiac function e.g. acute coronary syndrome, arrhythmias, acute heart failure or valvular dysfunction.

Type 2 also known as chronic CRS: Chronic abnormality in cardiac function causing chronic kidney disease e.g. ischemic heart disease and cardiomyopathies.

Type 3 also known as acute renocardiac syndrome: Primary abrupt worsening of renal function leading to acute cardiac disorder (e.g. heart failure, arrhythmia, or pulmonary edema) e.g. in the setting of Glomerulonephritis or acute kidney injury.

Type 4 also known as chronic renocardiac syndrome: Primary chronic kidney disease leading to left ventricular hypertrophy, decrease in cardiac function and increased incidence o of adverse cardiovascular events.

Type 5 also known as Secondary cardiorenal syndrome: meaning a systemic process which affects both cardiac and renal function which were previously normal examples are diabetes mellitus, sepsis and systemic lupus erythmatosis.

Type 1 CRS in which an acute cardiac condition leads to secondary acute kidney injury is frequently encountered in critical care settings and contributes to their mortality and morbidity [2,3,4,5]. Risk factors like old age, hypertension, obesity, diabetes mellitus, cachexia, proteinuria, and anemia predispose patients suffering acute cardiac events to CRS1. Acute cardiac illness results in characteristic hemodynamic changes leading to systemic venous congestion[6] and renal venous congestion[6], activation of RAAS, hypothalamic-pituitary stress reaction, systemic oxidative stress[7,8], immune cell signaling, exposure to endotoxins from ischemic intestine, superimposed infections, and iatrogenesis[9] all contributing to development of CRS type 1.

CRS 1 is further divided into 4 subtypes. (1)

1) Acute cardiac injury leading to acute kidney injury
2) Acute cardiac injury leading to acute-on-chronic kidney injury
3) acute-on-chronic cardiac decompensation leading to acute kidney injury; and
4) acute-on-chronic cardiac decompensation leading to acute-on-chronic kidney injury.

Management approach includes attempts to improve cardiac function by reducing cardiac workload through the judicious use of diuretics, sympatholytic agents and RAAS blockade, vasodilators and ionotropes, some of which are known to produce worsening of renal parameters. Thus it is important to identify patients of acute cardiac conditions who are at risk of developing CRS1 so they can be managed optimally.

The present study was done in MMIMSR, Mullana, Ambala. It aims to document the clinical and biochemical profile of Cardiorenal Syndrome type 1, to define its risk factors and assess its impact on in-

hospital mortality with the objective to identify those patients who are at greater risk to develop CRS1, so that preventive strategies can be formulated to improve outcomes.

Aim: To study the clinical profile of patients with Cardiorenal Syndrome type 1 and their in-hospital outcome

Methods: All the patients who presented to medicine emergency with a diagnosis of acute cardiac event, acute left ventricular failure or cardiogenic shock were screened for AKI as defined by KDIGO criteria [10] by monitoring serum creatinine and urine output for a period of 48 hours post admission. Those patients in whom creatinine level rose by 0.3mg/dl or more or with decrease in urine output by at least 0.5ml/kg/hr were diagnosed to be CRS I and considered for enrolment. 50 consecutive subjects who met the inclusion criteria were enrolled for study Patients who were suffering from ESRD, on renal replacement therapy, with active infection, malignancy, chronic liver disease, hepatic failure and those who had undergone contrast administration in the previous 30 days were excluded. The enrolled patients were subjected to a detailed history and clinical examination and investigated according to a designed Performa. Patients were subjected to biochemical profile, echocardiography and other investigations as per the working diagnosis. X ray chest, urine routine microscopy, complete haemogram and cultures (wherever indicated) were obtained to rule out any focus of infection. Ultrasonography abdomen and liver function tests were done at baseline to rule out chronic liver disease. All enrolled patients followed up for outcome events the primary outcome being in-hospital mortality and secondary outcome the duration of hospital stay. The results were subjected to statistical analysis using SPSS 20 and chi square test to correlate findings with variables and risk factors with the level of significance as $p<0.05$.

Tables and Figures:

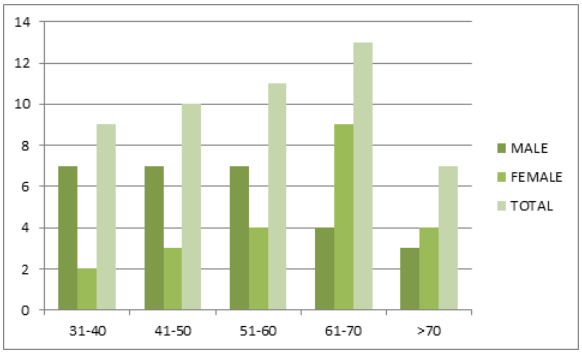

Figure 1: Bar diagram showing age distribution of cases.

Results and Observations

The present study was conducted to describe the clinical profile, biochemical profile and the hospital outcome of patients with Cardiorenal Syndrome type 1. A total number of 50 patients who met the inclusion criteria were included in the study. All our patients were from rural lower and lower middle socio-economic status. Out of a total number of 50 patients there were (28 males and 22 females) of mean age 56.76 ± 14.06 yrs. Mean age for males was 53.07 ± 14.73 yrs and for females mean age was 61.45 ± 11.9 years, with 18% of patients in 31-40 yr ,20% in 41-50, 22% in 51-60,26% in 61-70 and 14% in 70 + age group. Out of 50 patients of CRS I, 33 (66 %) had a primary diagnosis of ACS with LVF, 10 (20%) had ACS and 7(14%) presented with hypertension with LVF. The co-morbidities observed were hypertension in 28(56%), coronary artery disease in 44(33%) , COPD in 19(38%), pre-existing CKD in 13 (26%) diabetes mellitus in 12 (24%), DCMP in 6% and atrial fibrillation, hypothyroidism and old CVA each in 1 patient (2%). The mean SBP was 120 ± 27.61 mm of Hg and the mean DBP was 78 ± 15 mm of Hg.Mean urine output within 6 hours of admission in l patients with CRS 1 was 65.2 ± 21.59 ml/hr and fell to 49.6+/- 17.43 ml/hr at48 hours, i.e. It decreased by 25 % from baseline. The mean blood urea concentration rose by 48% from 30+/-13mg/dl at admission to 57.5 ± 30 mg/dl at 48 hours. Mean serum creatinine concentration at time of admission in all 50 patients of CRS 1 was 0.94 ± 0.26 mg/dl and rose by 42% to 1.6 ± 0.765 mg/dl at 48 hours. The mean GFR (calculated by MDRD equation) decreased by 42% from 81.3+/-27.9ml/min to 47.4+/-18.96ml/min at 48 hours. Mean serum potassium (K^+) concentration increased from 4.35 ± 0.68 mEq/L to 4.642 ± 0.74 mEq/L .(7% rise over baseline)

Out of 50 patients of CRS I, 39 (78%) survived (22 males and 17 females) and 11 patients (22%) succumbed (6 males and 5 females).The mean hospital stay in the 39 survivors was 8.97 ± 1.72 days. The mean age of the 39 survivors was 52.05 ± 11.53 yrs whereas that of 11 patients who expired was 73.5 ± 8.18 yrs. Mean age was significantly higher in those who did not survive (p value of 0.000013).Comparing the contribution of co-morbidities , Coronary artery disease was present in 34 (87%) out of 39 survivors and 10 (91%) out of 11 non survivors, hypertension was present in 21 (54%) out of 39 survivors and 7 (64%) out of 11 non survivors,CKD was present in 7(18%) of survivors and in 6 (55%) of non survivors and COPD was present in 15 (38%) out of 39 survivors and 4 (36%) out of 11 non survivors. Hence CKD was significantly higher in those who expired ($p<0.05$). Diabetes was present in 8 (21%) out of 39 survivors and 4 (36%) out of 11 non survivors. AF was present in 1(2.5%) out of 39 survivors and none of the non survivor had AF. DCMP was present in 3 (7.6%) survivors and in none of the non survivors. Hypothyroidism was present in 1 (2.5%) survivor only and in none of the non survivor. Stroke was present in only one non survivor and in none of the survivors.

In 39 survivors mean urine output at 48 hours of admission was 57.18 ± 9.58 ml/hr and in non survivors mean urine output at 48 hours of admission was 22.72 ± 10.81 ml/hr this was statistically significant (p value 0.0425).

In 39 patients who survived the mean blood urea concentration at 48 hours of admission was 54.95 ± 33.38 mg/dl whereas those who did not survive mean blood urea concentration was 66.54 ± 12.33 mg/dl. This was statistically significant (p value 0.0012).In 39 surviving patients mean serum creatinine concentration at 48 hours of admission was 1.48 ± 0.78 mg/dl where as in those who did not survived it was 2.03 ± 0.54 mg/dl this was statistically significant (p value 0.0009).In 39 survivors of CRS 1 mean serum potassium (K^+) concentration at 48 hours after admission was 4.47 ± 0.74 mEq/L where as in those who did not survive it was 5.2 ± 0.4 mEq/L this difference was statistically significant (p value 0.0002).Mean GFR (calculated by MDRD equation) of total 39 survivors patients with CRS 1 at admission was 85.2 ± 28.45 ml/min and fell to 52+/-18.3mi/min at 48 hours whereas in 11 non-g survivors mean GFR at time of admission was 66+/-20.59ml/min and fell to 30+/- 10.23mi/min at 48 hours. Thus AKI stage 1 was present in 37 (94%) of survivors and 7 (63%) non-survivors. Stage 2 AKI was in 1 (2.5%) survivors and 3 (27%) of non-survivors stage. Stage 3 AKI was in 1 (2.5%) survivors and in 1 (9%) patient of non-survivors. Advanced stage of AKI (i.e. stage 2 and 3) was significantly present in non survivor group with p value <0.05.The mean ejection fraction in survivors (n=39) with CRS 1 patients calculated on echocardiography at admission was 41.74 ± 12 %. In non survivors EF was 32.3 ± 12.15%.

DISCUSSION

In the present study 50 patients (28 males and 22 females) suffering from cardiorenal syndrome type 1 was studied for clinical and biochemical profile and hospital outcome. The mean age of the patients was 56 ± 14 yrs. Mean age for males was 53 ± 14 yr and for females was 61 ± 12 yrs. In the study conducted by González RP [11] et al reported mean age for CRS1 patients was reported as 70.3 ± 12.1 and a study by Eren Z et al[12]reported mean age of 72.3 ± 10.5 yrs where as Fabbian F et al[13] reported mean age of 79.9 yrs and Gigante A et al[14] also reported mean age of 79.9 yrs. In our study patients were significantly younger than the above mentioned studies. This difference of mean age reflects that in our population patients at younger age are at risk for developing CRS 1 in the setting of acute cardiac events in comparison to western population. In our study there were 56% males and 44% females. Studies conducted by Virendra C Patil[15], Fabbian F et al[13] and Eren Z et al[12] also reported male preponderance in CRS 1 patients, which was similar to our study. In our study males were younger compared to females. González RP [11] et al reported that on average, women are 5 years older than men at the time of first episode of ACS. This observation is similar to our study.

In our study 33 (66%) patients were having a primary diagnosis of ACS associated with AHF and 10 patients (20%) were having ACS not associated with heart failure leading to CRS 1, while in 7 patients (14%) patients primary diagnosis was uncontrolled hypertension with AHF. Eren Z et al[12] also reported 36 patients of ACS and 35 patients of

acute heart failure in their study of 71 CRS 1 patients. However their study did not mentioned the cause of acute heart failure in the non ACS group.

In our study coronary artery disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease and chronic kidney disease were the major co morbidities present in CRS 1 patients. A study conducted by Eren Z et al[12] in 2012 on CRS 1 patients also concluded that hypertension, CKD and decreased levels of Hemoglobin were independent predictors of AKI in ACS patients and Fabbian F et al[13] reported the significant association of smoking and CAD with CRS 1. González RP et al[11] reported significant association of CKD, smoking history, hypertension, diabetes mellitus and COPD with CRS 1. In our study 44 patients (86%) had CAD, 28 patients (56%) had hypertension, 19 (38%) had COPD, 13 patients (26%) had CKD and 12 (24%) had diabetes. However the significance of these co-morbidities in causation of CRS 1 in acute cardiac patients is not clear due to lack of controls in our study.
Mean Systolic BP in our study patients was 120±27 mm of Hg and DBP was 78±15 mm of Hg. This is comparable to study by Eren Z et al [12] who reported mean SBP of 110 ± 16 and DBP 66 ± 10 mm of Hg in CRS 1 patients.

In our study mean GFR (calculated by MDRD equation) in patients at admission 81.3±27.9 ml/min. After 48 hour GFR was reduced to 47.4±18.96 ml/min. Thus 42% reduction in GFR was documented in first 48 hours. Eren Z et al [12] reported the GFR 52±18 ml/min in patients of CRS 1. Gigante A et al [14] reported GFR 42.75±21.31 in 61 patients of CRS 1. Fabbian F et al [13] reported GFR 34±12 in 211 patients of CRS 1.

Out of 50 patients of CRS 1, in our study 11 patients (22%) expired during hospital stay and 39 survived. A study conducted by Eren Z et al [12] in 71 CRS 1 patients, reported 16 (22%) in-hospital mortalities similar to our study whereas Arguelles E et al [16] reported 11% in-hospital mortality in CRS 1 patients. González RP et al[11] reported that 216 out of 1912 patient of ACS developed CRS 1 and 30 patients with CRS 1expired during hospital stay i.e. 14%.

In patients those who survived and were discharged the mean duration of hospital stay was 8.97±1.72 days. Cowie et al [17] reported a mean duration of 11 days hospital stay in CRS 1 and Forman DE et al [18] reported the hospital stay of average 10 days in patients of CRS 1. Fabbian F et al [15] reported the mean duration of hospital stay 9.8±6.3 days. Logeart D et al [19] reported mean duration of 10 days of hospital stay. Our findings were comparable to above mentioned studies.

In our study the mean age of survivors was 52±11.53 yrs and of the non survivors 73.5±8.18 yrs. Thus advanced age was associated significantly with mortality in CRS 1 with p value <0.01. Study conducted by Eren Z et al [14] and Hu W et al [20] also concluded similar results.

In our study out of all co morbidities CKD was significantly associated with mortality (p value <0.05). A study conducted by Forman DE et al [10] and Eren Z et al [12] concluded the same result. Zhang W et al [21] concluded that CKD was not significantly associated with mortality.

In our study there was significantly (p value <0.05) higher levels of blood urea, serum creatinine and serum potassium in non survivors as compared to survivors and there was lower GFR and ejection fraction in non survivors as compared to survivors.

Higher stage (2 and 3) of AKI was associated with increased in-hospital mortality. Zhang W et al[21] reported no significant variation in these parameters in survivors and non survivors.

Conclusion

This was a hospital based, cross-sectional, prospective study on 50 patients of Cardiorenal syndrome I which aimed to document their clinical and biochemical parameters and correlate them with in hospital outcomes. We conclude that in patients of CRS 1, males were affected at early age compared to females. ACS with heart failure is the commonest primary diagnosis leading to CRS 1. Patients with higher age, pre existing CKD and higher stage of AKI during hospital stay are at a significantly higher risk of poor outcome in this condition. The present study highlights the need of large population based case-control studies so as to identify the risk factors independently responsible for development and progression of CRS 1 which lead to poor outcomes so that preventive strategy can be formulated in such patients.

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