Prevalence, types, risk factors, and outcomes of cardiorenal syndrome in a rural population of central India: A cross-sectional study

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ABSTRACT

Background and Objectives: Heart failure leading to renal dysfunction and vice-versa termed as Cardio-Renal Syndrome (CRS) has now been increasingly identified as a marker of higher morbidity and mortality. Till date, there is limited data available regarding clinical profile, associated risk factors and outcome of CRS in rural population of central India. This study was conducted to elucidate the prevalence, risk factors, and outcome of CRS and its types. Methods: This was a single-centric, cross-sectional study conducted amongst the patients admitted to medicine wards and ICCU from October 2017 to September 2019. Classification given by RONCO et al. in 2008 was used for classifying CRS patients into various types. Cross-sectional data was used to find the prevalence, risk factors and their inter-relationship with outcome and mortality. STATA software was used for statistical analysis. Results: Out of 96 CRS patients, 47(48.96%) were Type 1, 22 (22.92%) were type 2, 19(19.79%) were type 4 and 3 (3.13%) were type 3, and 5 (5.21%) were of type 5. Most common risk factor was Hypertension (HTN) found in 46 (47.92%), followed closely by Coronary Artery Disease (CAD) and anaemia. Mortality was seen in 44(45.83%) of CRS patients and it was significantly high. High mortality was common in patients of types 3 and type 5 CRS. Risk factors like HTN, CAD, smoking, reduced glomerular filtration rate, low ejection fraction and sepsis were significantly associated with worse outcomes across all CRS sub-types. Interpretation and Conclusions: There is high mortality among CRS. Prevention or optimal management of HTN, CAD and sepsis is required to decrease mortality. There is need for more population based studies for confirming our study findings.

Keywords: Cardio-renal syndrome, outcomes, risk factors, types

Introduction

Heart failure (HF) leading to renal dysfunction and vice-versa is termed as cardiorenal syndrome (CRS).¹ It is one of the poor prognostic indicators as CRS causes higher morbidity and mortality in patients suffering concomitantly from heart failure (HF) and acute kidney injury (AKI) or chronic kidney disease (CKD).²

Reduced renal function seen in patients suffering from acute or chronic HF increases cardiovascular morbidity and mortality.³ Acute dialysis quality initiative quotes the existence of some

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form of renal dysfunction, i.e., CRS in 25% to 63% of patients suffering from HF. Moreover, a majority of these patients develop varying levels of worsening renal function during the management of HF. In such patients, even a slight reduction in renal function is related to an exponential rise in mortality. Similarly, AKI or CKD may have a deleterious effect on cardiac performance through various factors such as volume overload, negative inotropy, uncontrolled hypertension, and electrolyte imbalance being some of them. Therefore, the patients having renal dysfunction are at a markedly higher risk for acute HF. It is found that in CKD patients, 43.6% of all deaths occur due to cardiac diseases. It is estimated that patients with CKD are found to have 10 to 20 times more likely possibilities to die from various cardiac diseases than their similar groups in the general population. CRS also carries its importance because there is an increase in the geriatric population due to increased longevity, increase in incidence and prevalence of various cardiovascular and renal risk factors and also because of more numbers of younger population suffering from cardiac and renal diseases.

Till date, few studies have been reported in western countries about the prevalence, types, and outcomes associated with mortality in patients of CRS. In India HR Shah et al., had studied the clinical profiles and outcomes of CRS patients in North India. Thus, there is still a paucity of studies regarding the prevalence and risk factors associated with various types of CRS and morbidity and mortality in Central India. Moreover, there is an increasing trend of cardiovascular diseases leading to heart failure and kidney diseases among rural population, which are catered by primary care physicians. Hence, we conducted this study to estimate the prevalence, types, and outcomes (mortality, dialysis requirement, and duration of hospital stay) of CRS patients. Also, to find out the risk factors associated with mortality among CRS. Early identification of these risk factors may aid in reducing the morbidity and mortality due to CRS.

**Material and Methods**

**Ethical approval**

This study was started upon approval by the institutional ethics committee (vide IEC/2017-18/6755).

**Study design**

This single-centered cross-sectional study was conducted between October 2017 and September 2019 in patients admitted to medicine wards and ICCU which cater to the rural population of central India. The patients were enrolled in study after giving informed consent. Cross-sectional data was used to find the prevalence, risk factors and their interrelationship with outcome and mortality.

**Data collection**

During the study period, 215 patients were admitted with HF diagnosed as per Framingham criteria. Of these, 69 patients had deranged renal function and were identified as having AKI or CKD based on the 2012 KDIGO guidelines for AKI and CKD and then were classified into type 1 and 2 CRS as per the classification of CRS given by Ronco et al. in 2008. Similarly, 254 patients were admitted with worsening renal function, of which 22 patients were diagnosed as having HF and then were classified into type 3 and 4 CRS. Fifty-six patients were admitted with systemic conditions such as sepsis (secondary to cellulitis, infections of lower respiratory tract, various infections of urinary tract), acute respiratory distress syndrome and systemic lupus erythematosus, out of which five patients were diagnosed as having simultaneous dysfunction of both heart and kidneys and were classified into type 5 CRS. Thus, a total of 96 patients fulfilling the inclusion criteria, i.e., clinical history and examination suggestive of both cardiac and renal dysfunction, were included in the study to prevent selection bias.

Patients' demographic details were recorded. A pilot-tested questionnaire was used to collect information regarding patient's sociodemographic profile, history of cardiovascular disease risk factors such as systemic hypertension, diabetes, dyslipidemia, history of cerebrovascular episode, hypothyroidism, and addictions in the form of alcohol and smoking. Clinical examination included anthropometric measurements, recording of blood pressure and respiratory rate, assessing mental status, detailed cardiovascular, respiratory and per abdomen examination. The quick Sepsis Related Organ Failure Assessment (qSOFA) score was used to identify patients with sepsis as it facilitates simple and approximate earliest identification of sepsis outside hospitals and wards.

All patients were subjected for laboratory investigations which included CBC (complete blood count), KFT (kidney function test), FBS (fasting blood sugar), PMBS (post meal blood sugar), fasting lipid profile (including Total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein).

**Assessment of Cardiac Function:** Cardiac dysfunction was identified as patients having HF as per the Framingham criteria, or with a history of ongoing treatment for HF. 2D echocardiography (ECHO) was done to estimate left ventricular ejection fraction which was calculated by using the SIMPSON'S formula.

**Assessment of Renal Function:** Renal function was studied using the levels of serum creatinine and estimated glomerular filtration rate (eGFR); the latter was calculated using MDRD equation and was used in staging of CKD. Ultrasonography of kidney, ureter, and bladder was done in all patients to differentiate AKI from that of CKD. The echogenicity of renal cortex and differentiation of the cortex and medulla were assessed. The echogenicity of renal cortex was compared and graded with that of spleen and renal medulla and, thus, renal parenchymal disease was graded.

**Definitions**

Definition and classification of CRS: We adopted the definition suggested by Ronco et al. in 2008 at a consensus conference under...
the patronage of the Acute Dialysis Quality Initiative (ADQI). Cardio renal syndrome is defined as “Disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other.” CRS is classified into five types depending on whether kidney or heart was the initial organ of insult. Accordingly, in type 1 and 2 CRS, worsening of acute HF (type 1) or chronic HF (type 2) leads to kidney dysfunction. In types 3 and 4 (termed acute and chronic renocardiac syndromes, respectively), consisting of AKI or CKD causes worsening of HF. In type 5 CRS, various systemic conditions cause simultaneous worsening of the heart and kidney.

Diabetes mellitus was defined as patients already on oral hypoglycemic agents, insulin, or newly diagnosed as per the 2017 guidelines of American Diabetic Association. Patients who were on antihypertensive medications or diagnosed as per JNC7 criteria (Joint National Committee's seventh report) were defined as hypertensives. Patients who had had past documented or present history of myocardial infarction, unstable angina, percutaneous coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) were classified as having CAD.

Statistical analysis

Data was presented as either mean (SD) or proportion. To study the association of risk factors with CRS, t-test or chi-square test of significance was used. Multiple regression analysis was used to study the independent association of risk factors with outcome of cardio renal syndrome. All the analysis was done by STATA version 14.

Results

Table 1 shows the baseline characteristics of our CRS patients in which majority belonged to the age above 60 years i.e., 51 (53.13%). The minimum age of our patients was 20 years and maximum was 81 years. In our study, males were more in number, i.e., 60% which may be due to the increase in the prevalence of CAD and cardiovascular risk factors such as HTN, diabetes and dyslipidemia. The lowest eGFR was 4 ml/min and highest was 47 ml/min, lowest LVEf was 15% and highest was 65%, and the minimum length of hospital stay was zero and maximum was 47 days.

The maximum number of patients of CRS, i.e., 46 (48.42%) had grade 1 RPD. More CRS patients were of stage 4 of CKD, i.e., 38 (39.58%) followed by stages 3B and 5. Type 1 CRS is the most common type followed by type 2 and 4 [Figure 1].

The most common risk factor found to be associated with patients of CRS in our study was HTN which is found in 46 (47.92%) of patients [Figure 2].

The most common risk factors were CAD in type 1 and 2 CRS, HTN and sepsis in type 3 CRS, and CKD in type 4 CRS, and sepsis in type 5 CRS [Table 2].

It was found that in type 1 and 2 CRS, the maximum number of patients were managed conservatively without dialysis. While in type 3 CRS, all patients were managed conservatively. In types 4 and 5, more number of patients were subjected to dialysis [Table 3].

| Variables                        | Mean    | Std. Dev. |
|----------------------------------|---------|-----------|
| Age (years)                      | 56.46   | 14.4      |
| Male No. (%)                     | 58 (60.42%) |
| Female No. (%)                   | 38 (39.58%) |
| Body Mass Index (BMI) (kg/m²)    | 23.22   | 3.66      |
| Waist circumference (cm)         | 83.19   | 4.89      |
| Hip circumference (cm)           | 95.98   | 4.31      |
| Waist Hip Ratio (WHR)            | 0.86    | 0.03      |
| Estimated Glomerular Filtration Rate (eGFR) (ml/min) | 21.50   | 12.18     |
| Left ventricular ejection fraction (LVEf) (%) | 39.63   | 13.23     |
| Smoking; No. (%)                 | 23 (23.96%) |
| Alcohol; No. (%)                 | 20 (20.83%) |
| Length of stay at hospital in days | 9.45   | 9.41      |

Figure 1: Prevalence of various types of CRS

Figure 2: Prevalence of risk factors among patients of CRS
The outcome of the patients of CRS was studied in which 52 (54.16%) patients survived and were discharged from hospital in a stable condition. However, 44 (45.83%) of the study participants died which shows that mortality was significantly high in the patients of CRS in our study [Table 4].

In our study, the risk factors associated with mortality were age being more than 60 years, smoking, HTN, CAD, DM, and laboratory parameters such as blood urea, serum creatinine, eGFR, and LVEF [Table 5].

### Discussion

CRS has emerged as an important health issue due to the increase in various lifestyle disorders such as HTN, CAD, and DM. CRS

| Table 2: Types of CRS with risk factors |
|----------------------------------------|
| TYPE 1 (n=47) | TYPE 2 (n=22) | TYPE 3 (n=3) | TYPE 4 (n=19) | TYPE 5 (n=5) | P |
| HTN (n=46) | 16 (34.04%) | 13 (59.09%) | 1 (33.33%) | 13 (68.42%) | 3 (60%) | \(\chi^2=8.474\) P=0.076 |
| CAD (n=45) | 28 (59.57%) | 10 (45.45%) | 0 | 6 (31.58%) | 1 (20%) | \(\chi^2=8.944\) P=0.063 |
| Hb <10 gm/dl (n=44) | 16 (36.04%) | 10 (45.45%) | 0 | 16 (84.21%) | 2 (40%) | \(\chi^2=16.109\) P=0.003 |
| DM (n=33) | 16 (51.50%) | 10 (50%) | 0 | 5 (26.31%) | 1 (20%) | \(\chi^2=4.959\) P=0.291 |
| CKD (n=19) | 0 | 0 | 0 | 19 (100%) | 0 | \(\chi^2=56.000\) P=0.000 |
| Sepsis (n=19) | 8 (17.02%) | 1 (4.55%) | 1 (33.33%) | 4 (21.05%) | 5 (100%) | \(\chi^2=24.077\) P=0.000 |
| Dyslipidemia (n=14) | 7 (14.89%) | 3 (13.65%) | 0 (0%) | 3 (15.79%) | 1 (20%) | \(\chi^2=6.71\) P=0.055 |
| Hypothyroidism (n=13) | 6 (17.77%) | 4 (18.18%) | 0 | 3 (15.79%) | 0 | \(\chi^2=1.6737\) P=0.779 |
| CVE (n=12) | 6 (17.77%) | 4 (18.18%) | 0 | 1 (5.26%) | 1 (20%) | \(\chi^2(4)=2.2249\) P=0.690 |

| Table 3: Modality of treatment among various types of CRS |
|----------------------------------------|
| Type 1 (n=47) | Type 2 (n=22) | Type 3 (n=3) | Type 4 (n=19) | Type 5 (n=5) | P |
| Haemodialysis (n=19) | 3 (6.38%) | 4 (18.18%) | 0 | 9 (47.36%) | 3 (60%) | \(\chi^2=20.293\) P=0.000 |
| Conservative management (n=58) | 44 (93.61%) | 18 (81.81%) | 3 (100%) | 10 (52.36%) | 2 (40%) | \(\chi^2=20.293\) P=0.000 |

| Table 4: Comparison of outcomes among various types of CRS |
|----------------------------------------|
| Type 1 (n=47) | Type 2 (n=22) | Type 3 (n=3) | Type 4 (n=19) | Type 5 (n=5) | P |
| Death (n=44) | 20 (42.55%) | 9 (40.93%) | 3 (100%) | 8 (42.10%) | 4 (80%) | \(\chi^2=6.4214\) P=0.170 |
| Survived (n=52) | 27 (57.44%) | 13 (59.09%) | 0 | 11 (57.89%) | 1 (20%) | \(\chi^2=6.4214\) P=0.170 |
| Length of stay (mean+sd) | 7.25 (7.06) | 10.81 (10.69) | 11.66 (3.21) | 10.89 (10.95) | 17.2 (18.30) |

| Table 5: Risk factors associated with mortality |
|----------------------------------------|
| Mortality (n=44) | Survived (n=52) | P |
| Age >60years (n=51) | 29 (65.90%) | 22 (42.31%) | \(\chi^2=5.331\) P=0.021 (s) |
| Female (n=38) | 17 (38.64%) | 21 (40.38%) | \(\chi^2=0.030\) P=0.861 (ns) |
| Male (n=50) | 27 (56.10%) | 31 (59.62%) | 0.849 (ns) |
| BMI; ( Mean±sd) | 23.30±0.60 | 23.16±0.46 | 0.072 (ns) |
| WHR (Mean±sd) | 0.86±0.03 | 0.87±0.03 | |
| Smoking (n=23) | 15 (34.04%) | 8 (15.38%) | \(\chi^2=4.577\) P=0.032 (s) |
| Alcohol (n=20) | 9 (20.45%) | 11 (21.51%) | \(\chi^2=0.007\) P=0.933 (ns) |
| Hypertension (n=46) | 16 (36.36%) | 30 (57.69%) | \(\chi^2=4.344\) P=0.037 (s) |
| Coronary artery disease (n=45) | 15 (34.09%) | 30 (57.69%) | \(\chi^2=5.431\) P=0.021 (s) |
| Anaemia (n=44) | 19 (43.18%) | 25 (48.07%) | \(\chi^2=1.405\) P=0.000 (s) |
| Diabetes Mellitus (n=33) | 10 (27.22%) | 23 (44.23%) | \(\chi^2=4.885\) P=0.037 (s) |
| Sepsis (n=19) | 16 (36.36%) | 3 (5.76%) | \(\chi^2=0.0585\) P=0.809 (ns) |
| Chronic kidney disease (n=19) | 8 (18.18%) | 11 (21.51%) | \(\chi^2=0.1326\) P=0.716 (ns) |
| Dyslipidemia (n=14) | 6 (13.63%) | 8 (15.38%) | \(\chi^2=0.0585\) P=0.809 (ns) |
| Cerebro-vascular episode (n=12) | 7 (15.9%) | 5 (9.61%) | \(\chi^2=0.863\) P=0.355 (ns) |
has an extremely poor prognosis[17,22] with associated significant morbidity and mortality. Cardiac and renal dysfunctions often occur simultaneously because they share the common pathogenetic mechanisms.[4] The pathophysiology of CRS is attributed to various hemodynamic and nonhemodynamic mechanisms some of which are decreased renal perfusion, increase in congestion of pulmonary and/or systemic circulation which in turn affects the perfusion of kidneys and/or sympathetic nervous system (SNS) activation, activation of RAAS, chronic inflammation and disproportionate production of nitric oxide (NO) and reactive oxygen species (ROS).[4] The high prevalence of anemia in CRS may be caused by the increase in oxidative stress and reduction in the supply of oxygen to heart which causes a compensatory increase in heart rate and the stroke volume which then causes the activation of RAAS and SNS leading to vasoconstriction of renal vessels and retention of salt and water.[23] Renal dysfunction may also be an adverse effect due to the management of HF with ACE-inhibitors, angiotensin receptor blockers (ARBs), and mineralocorticoid receptor antagonists (MRAs), thiazides, and loop diuretics.[24] The present HF management is more targeted on improving the myocardial performance and hemodynamic balance, but they may have the potential consequences for causing renal dysfunction. Thus, it shows that the guidelines about optimal management of patients with CRS are still deficient.[25] There is often a dilemma in treating CRS as various life-saving medications such as ACE-inhibitors, ARBs, and MRAs are withheld in patients of CRS. At times, renal dysfunction also leads to diuretic resistance, thus complicating the management of CRS.[26] Till date there is limited data available regarding clinical profile, associated risk factors, and outcomes of CRS in rural Indian population. Thus, our present study on the clinical profile of CRS was done which targeted to determine the prevalence of five types of CRS and the risk factors associated with their morbidity and mortality.

In our study, of the 96 patients with CRS, about half of the patients were of type 1 followed by types 2 and type 4. The most common risk factors associated with CRS were HTN, CAD, and anemia which were found in almost half of them. Regarding treatment modality, around one-fifth of patients were dialysed and four-fifth were given optimal medical management. Mortality was seen in almost half of the CRS patients which was significantly high. The high mortality was common in

| Table 6: Results of odds ratio univariate and multivariate analysis for predictors of mortality |
|---------------------------------------------------------------|
| **Univariate OR (95% CI)** | **P** | **Multivariate OR (95% CI)** | **P** |
|----------------------------|-------|-----------------------------|-------|
| cGFR 0.97 (0.96-0.98)      | 0.002 | 0.96 (0.95-0.97)            | 0.01  |
| LVef 1.03 (0.99-1.06)      | 0.05  | 1.02 (0.98-1.06)            | 0.154 |
| Smoking 0.35 (0.13-0.93)  | 0.036 | 0.43 (0.13-1.42)            | 0.169 |
| Blood urea 0.99 (0.98-0.99)| 0.007 | 0.98 (0.97-0.99)            | 0.010 |
| Sr. Creatinine 0.97 (0.85-1.11) | 0.003 | 0.95 (0.84-0.90)            | 0.01  |
| Coronary artery disease 2.63 (1.14-6.05) | 0.022 | 1.27 (0.42-3.78)            | 0.665 |
| Diabetes mellitus 2.69 (1.10-6.58) | 0.029 | 2.42 (0.79-7.43)            | 0.121 |
| Sepsis 0.10 (0.02-0.40)   | 0.001 | 0.10 (0.02-0.41)            | 0.002 |
| Age 1.00 (0.98-1.03)      | 0.547 |                            |       |
| BMI 0.98 (0.88-1.10)      | 0.848 |                            |       |
| Female 1.07 (0.47-2.44)   | 0.861 |                            |       |
| FBS 1.00 (0.99-1.01)      | 0.312 |                            |       |
| PMBS 1.00 (0.99-1.00)     | 0.531 |                            |       |
| HB 1.03 (0.86-1.24)       | 0.697 |                            |       |
| WHR 1.57 (0.67-3.63)      | 0.291 |                            |       |
| Alcohol 1.04 (0.38-2.80)  | 0.933 |                            |       |
| Dyslipidemia 1.15 (0.36-3.61) | 0.809 |                            |       |
| CVE 0.56 (0.16-1.91)      | 0.357 |                            |       |

| Table 7: Comparison of characteristics of CRS patients with other studies |
|---------------------------------------------------------------|
| **Baseline characteristics** | **H R Shah et al.[6]** | De Silva et al.[7] | **Present study** |
| Mean age (in years)       | 64.18±12.9 | 71±10.8 | 56.46±20.1 |
| % males                   | 66%        | 69 %   | 60.42%    |
| cGFR 29.0±11.7            | 32.70±12.8 | 34.2±10.2 | 39.63±13.23 |
| Sr. creatinine 3.38±2.18  | 9.0±5.5   | 4.23±3.01 | 4.23±3.01 |
| Haemoglobin 9.88±2.33     | 13.11±6   | 10.00±2.23 | 10.00±2.23 |

| Table 8: Comparison of Risk factors associated with CRS and its types with other studies |
|---------------------------------------------------------------|
| **Risk factors** | **H R Shah et al.[6]** | Mavrakanas et al.[8] | **Present study** |
| Hypertension 78% | 59 % | 47.92% |
| Coronary Artery Disease 48% | 60 % | 46.88% |
| Anaemia 3.38±2.18 | 9.0±5.5 | 4.23±3.01 |
| Diabetes mellitus 64% | 21.1 % | 34.38% |
| Chronic Kidney Disease 50% | - | 19.79% |
| Sepsis 0.10 (0.02-0.40) | 0.001 | 0.10 (0.02-0.41) |
| Dyslipidemia 44% | - | 14.58% |
| Hypothyroidism 16% | - | 13.54% |

The present HF management is more targeted on improving the myocardial performance and hemodynamic balance, but they may have the potential consequences for causing renal dysfunction. Thus, it shows that the guidelines about optimal management of patients with CRS are still deficient.[25] There is often a dilemma in treating CRS as various life-saving medications such as ACE-inhibitors, ARBs, and MRAs are withheld in patients of CRS. At times, renal dysfunction also leads to diuretic resistance, thus complicating the management of CRS.[26]
The mean eGFR in the study done by De Silva et al. was higher as compared to our study indicating that renal involvement was more severe in our patients with CRS.

The mean hemoglobin levels in our study were lower compared to the study done by De Silva et al., where the mean Hb was 13 gm/dl. This high prevalence of anemia can be attributed to severe renal involvement in our CRS patients. Moreover, 60% of the study population were females, in whom anemia is more common. However, the mean haemoglobin levels were comparable to the study done in India by HR Shah et al., which shows that the prevalence of anemia is more in Indian population as compared to the western population. This may even state that Indians are lacking behind in the prevention and optimal management of anemia. In a study done by RP Silva et al., the prevalence of anemia in CRS patients was studied and they concluded that although anemia was more prevalent in CRS it was not associated with increase in mortality. This was similar to our study as although anemia was a common risk factor found, it was not associated with mortality.

Table 8 shows the comparison of risk factors in our study with the studies done by HR Shah et al., and Mavrakanas et al. It is found that in the study done by HR Shah et al., HTN was present in 78% patients which was higher than our study and in the study by Mavrakanas et al., CAD was found to be higher, i.e., 60% which may be due to the fact that our study was done in rural population where the prevalence of CAD is lesser than the urban population.

In our study, the risk factors associated with mortality were age more than 60 years, smoking, HTN, CAD, DM, sepsis, and laboratory parameters such as blood urea, serum creatinine, eGFR, and LVEF. This was similar to the studies done by HR Shah et al., where serum creatinine, eGFR and HTN, DM, and CAD, respectively, were identified as the risk factors found to be significantly associated with mortality. So to summarize the findings of the present CRS study among the rural population of central India, CRS is more common among people aged more than 60 years. The prevalence of type 1 CRS was the highest followed by the type 2 and type 4 CRS. The most common risk factor found in our study was HTN followed by CAD, DM, and anemia. One fifth of the patients of CRS in our study were dialysed. Mortality was very high (about half of the patients succumbed). Of the five types of CRS, types 3 and 5 were associated with higher mortality than the others. The risk factors like HTN, CAD, smoking, reduced eGFR, low ejection fraction and sepsis were significantly associated with worse outcomes across all types of CRS. We highlight that early detection and optimal management of HTN, CAD, and sepsis is required to decrease mortality. This can be prevented by the early identification and appropriate management of CRS patients.

There is need for more population as well as hospital-based studies for confirming our study findings.

**Limitations and Recommendations**

Our study was single-centeric with a small sample size. Cystatin C was not estimated due to the lack of facility at our institute. There may be selection bias and detailed treatment history was not recorded. So also, due to time constraints, follow-up of the patients after discharge was not done. Thus, more of follow-up studies evaluating the long-term outcome are recommended.

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**Conflicts of interest**

There are no conflicts of interest.

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