

# Incidence of Acute Cardiorenal Syndrome Type 3 in India

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**Introduction.** The aim of this study was to determine the incidence of acute renocardiac syndrome (cardiorenal syndrome type 3) and its outcome in a suburban population in India.

**Materials and Methods.** In an observational study, 100 patients admitted with acute kidney injury were evaluated.

**Results.** Acute renocardiac syndrome was documented in 29%. Acute gastroenteritis (46%) was the leading cause of acute kidney injury. Cardiogenic pulmonary edema (56%) was the most common cause of acute cardiac dysfunction. Only 42% of the patients with acute renocardiac syndrome had complete recovery of kidney function. Requirement of renal replacement therapy was found to be significantly high in patients with acute renocardiac syndrome (43% versus 9% in those with AKI and no cardiorenal syndrome) and was associated with high rate of mortality (17%).

**Conclusions.** This study shows that the incidence of acute renocardiac syndrome is high and is associated with increased morbidity and mortality. Hence, there is a need for primordial prevention and early intervention on large scale.

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## INTRODUCTION

Over recent years, the field of medicine has been challenged by the twin epidemic of heart failure and renal insufficiency. Moreover, the coexistence of the two problems in the same patient, referred to as *cardiorenal syndrome* (CRS), has an extremely poor prognosis.<sup>1,2</sup> A description of the epidemiology of heart-kidney interactions is critical to understanding not only the overall burden of disease for each of the proposed CRS subtypes, but also their natural history, risk factors, associated morbidity and mortality, and potential health resource implications. Cardiorenal syndrome is classified into 5 subtypes: type I, acute CRS; type II, chronic CRS; type III, acute renocardiac syndrome; type IV, chronic renocardiac syndrome; and type V, secondary CRS, meaning systemic diseases such as diabetes mellitus, sepsis, and amyloidosis causing simultaneous cardiac and renal dysfunction.<sup>3,4</sup>

The acute renocardiac syndrome (CRS type 3) is

characterized by acute worsening of kidney function that leads to acute cardiac injury and dysfunction, such as acute myocardial infarction, congestive heart failure, pulmonary edema, and arrhythmia.<sup>5</sup> The pathophysiologic mechanisms underlying the interplay between kidney injury and heart dysfunction are still not completely understood. It is well known that a decline in cardiac function causes a decrease in tissue perfusion, and thus adversely affects renal perfusion leading to renal injury. On the other hand, acute kidney injury (AKI) can affect the heart through several pathways and can be separated into two categories of the direct effect of AKI on the heart and the effects of AKI on the remote organ function with indirect effects on the heart.<sup>6</sup> In the present study, we evaluated the incidence and associated outcomes of acute renocardiac syndrome (Type 3 CRS). The aim of this study was to evaluate patients admitted with AKI in a referral hospital for acute cardiac dysfunction, including acute decompensated heart

failure, acute myocardial infarction, cardiogenic pulmonary edema, and cardiac arrhythmias, and to assess the outcome with respect to complications and survival.

## MATERIALS AND METHODS

This observational study was conducted from November 2011 to May 2012. A total of 100 patients admitted with AKI were studied. Acute kidney injury was defined as an abrupt (within 48 hours) reduction in kidney function defined as an absolute increase in serum creatinine of either 0.3 mg/dl and greater or an increase of serum creatinine of 1.5-fold from baseline. This was in accordance with Acute Kidney Injury Network diagnostic criteria for AKI.<sup>7</sup> Patients with pre-existing diabetes mellitus, hypertension, heart diseases, chronic kidney disease, and other chronic systemic illness were excluded from the study. Diseases known to affect renal and cardiac systems simultaneously such as sepsis, malaria, leptospirosis, and vasculitis were also excluded from the study. The frequency of acute cardiac dysfunction, including acute decompensated heart failure, acute myocardial infarction, cardiogenic pulmonary edema, and cardiac arrhythmias were noted.

Statistical analysis was performed using the SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc, Chicago, Ill, USA). The mean and standard deviation were reported for continuous variables and absolute count and percentage were reported for categorical variables. The chi-square test was used to compare variables and *P* values less than .05 were considered significant.

## RESULTS

One hundred patients admitted with AKI were included in this study. The majority of the patients were men (62%) and in the age group of 50 to 60 years (Table 1). Acute gastroenteritis, drugs (nonsteroid anti-inflammatory drugs, aminoglycosides, and contrast media), and obstetric complications (postpartum hemorrhage, abruptio placenta) were the most common causes of AKI (Table 1). The stage of AKI was determined using the RIFLE criteria. Forty-six percent were found to be in the failure stage of AKI, 41% in the injury stage, 10% in the risk stage, and 3% in the loss stage.

The overall incidence of acute renocardiac

**Table 1.** Characteristics of 100 Patients with Acute Kidney Injury (AKI)

Characteristic	Number of Patients
Age, y	
< 30	0
30 to 40	2
40 to 50	14
50 to 60	39
60 to 70	50
> 70	20
Sex	
Male	62
Female	38
Cause of AKI	
Acute gastroenteritis	46
Drugs	23
Obstetric complications	18
Acute glomerulonephritis	6
Others*	7

\*Others included persistent vomiting and obstructive nephropathy.

**Table 2.** Outcome of Acute Renocardiac Syndrome

Outcome	% Patients
Cardiac sequelae	
Pulmonary edema	56
Arrhythmias	33
Acute decompensated heart failure	7
Acute myocardial infarction	4
Treatment outcome	
Complete recovery	42
Partial recovery	25
No recovery	16
Death	17

syndrome was 29%. The incidence was higher in females (n= 9; 19%) as compared to males (n = 10; 10%). Pulmonary edema and cardiac arrhythmias were the most common cardiac sequelae, following development of acute renocardiac syndrome (Table 2). Only 42% of patients with acute renocardiac syndrome had complete recovery of kidney function, and the remaining had either partial recovery (25%) or no recovery of kidney function (16%) or death (17%). Hemodialysis was required in 43% of the patients with acute renocardiac syndrome as compared to 9% of AKI patients without renocardiac syndrome (*P* < .001).

## DISCUSSION

Cardiorenal syndrome type 3 is characterized by acute worsening of kidney function that leads to acute cardiac injury and dysfunction. Defining the epidemiology of CRS type 3 is challenging

for several reasons. First, there is considerable heterogeneity in predisposing conditions causing AKI. Second, AKI has been variably defined across studies. Third, there is likely variable baseline risk for acute cardiac dysfunction across populations, such as increased susceptibility in selected individuals with subclinical cardiovascular disease. Finally, few clinical studies focused on AKI have reported on the event rates of acute cardiac dysfunction. Therefore, estimates of incidence and associated outcomes of acute cardiac dysfunction associated with AKI are largely context- and disease-specific.<sup>8</sup>

In children, isolated volume overload has been shown to induce myocardial dysfunction and CRS type 3.<sup>9</sup> The picture is not so clear in adults, when acute on chronic disease is a frequent paradigm. It is conceivable that CRS type 3 could precipitate acute coronary syndrome, stroke, or other acute cardiac event; however, the epidemiological evidence and pathophysiological basis are yet to be described.

A prospective multicenter study published in 1998 reported the association between acute kidney failure and multiorgan failure and showed the increase in mortality rate according to the number of organ failures both in intensive care unit (ICU) and non-ICU patients.<sup>10</sup> The mortality rate of patients with isolated acute renal failure in the ICU was reported to be 30%. In a recent retrospective study of AKI after trauma, including 129 patients with a 40.3% occurrence of AKI, the mortality rate was 100% among patients with AKI.<sup>11</sup> None of the abovementioned studies looked into the true incidence of CRS type 3. In our study, we tried to find out the true incidence of CRS type 3 in patients who got admitted with AKI. The incidence of CRS type 3 was 29% in our study.

In CRS type 3, acute kidney injury occurs as a primary event (eg, acute glomerulonephritis) or secondary event (eg, radiocontrast, exogenous or endogenous nephrotoxins, postsurgical, etc), and cardiac dysfunction is a common and often times fatal sequela.<sup>12</sup> In our study, acute gastroenteritis (46%) was the leading primary event for acute kidney injury and pulmonary edema was the most common (56%) sequela.

The most common causes of AKI in ICU are sepsis (50%), major surgery, low cardiac output, hypovolemia, and medications.<sup>12</sup> In the critical care setting, AKI affects up to 70% of patients,

with 5% to 25% developing severe AKI, with a reported overall mortality rate of 50% to 80%. The overall ICU period prevalence of AKI requiring renal replacement therapy was found in one large multinational study to be 6%, with a hospital mortality rate of 60%.<sup>13</sup> In the present study, we excluded sepsis as the cause of CRS type 3 as it is known to affect both the organs (renal and cardiac) and may confound the true diagnosis of CRS type 3. Hemodialysis was used as a modality of renal replacement therapy in our study and 43% with CRS type 3 required renal replacement therapy. Cardiorenal syndrome type 3 patients had a mortality rate of 17% in our study.

The present study has several limitations. First, the number of study group was small. Second, this is an observational study; large high-quality trials are urgently needed to provide results, which could support effective treatment strategies.

## CONCLUSIONS

A description of possible heart-kidney interactions is critical to our understanding and will guide future investigations into pathophysiology, screening, diagnosis, prognosis, and management of CRS type 3. Very little data have been reported on the incidence and outcomes of CRS type 3. This paper has summarized the incidence and outcomes of acute renocardiac syndrome. No standard evidence-based guidelines for management of this syndrome exist. Because of the high mortality and currently no pharmacologic agent is proven effective in the treatment of AKI, the best approach is prevention.

## CONFLICT OF INTEREST

None declared.

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