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# Frequency of Cardiorenal Syndrome Type-I in Hospitalized Children with Acute Heart Failure in a Tertiary-Care Hospital

Mehjabeen Zaidi, Arshalooz Jamila Rahman, Anwarul Haque, Saleem Sadqani and Prem Kumar Maheshwari

## ABSTRACT

**Objective:** To determine the frequency of cardiorenal syndrome in hospitalized children with acute heart failure.

**Study Design:** Descriptive study.

**Place and Duration of Study:** Paediatric Intensive Care Unit, The Aga Khan University Hospital, Karachi, from December 2010 to December 2011.

**Methodology:** Sixty eight (68) children with acute heart failure fulfilling the selection criteria were evaluated for worsening of renal function (WRF). Serum creatinine was done at baseline and repeated at 72 hours to see the worsening of renal function. Estimated serum creatinine clearance was calculated by Schwartz formula.

**Results:** Mean age of patients was  $43.6 \pm 55.2$  months. There were 43 (63%) males, 70% were under 57 months of age. Mean weight on admission was  $14.7 \pm 19.13$  kg and mean height was 83 cm ( $\pm 31.08$  SD). Mean serum creatinine on admission was 0.77 mg/dl ( $\pm 1.18$  SD). Worsening renal function was noted in 55 (81%) of children, out of those, majority 36 (70.5%) were under 5 years of age.

**Conclusion:** Worsening renal function was found in 81% of children admitted with the diagnosis of acute heart failure. Majority (70.5%) were under 5 years of age indicating a closer observation of renal status in younger age group to reduce, morbidity and mortality.

**Key Words:** Renal failure. Heart failure. Cardiorenal syndrome. Acute kidney injury. Children.

## INTRODUCTION

Worsening of renal function in patients with heart failure is common and has been reported in various studies of adult population. It is recognized as an independent risk factor for morbidity and mortality.<sup>1,2</sup> When both problems exists in the same patient, it is referred to as the cardiorenal syndrome (CRS).<sup>3</sup>

This emerging clinical syndrome was first defined in the World Congress of Nephrology, 2007.<sup>4</sup> Price *et al.* in their study reported 48% of children with acute heart failure had worsening of renal function during the hospitalization.<sup>5</sup> Local data regarding worsening of renal function in children suffering from heart failure has not been looked and reported.

This syndrome has been divided in five subtypes.<sup>6,7</sup> Type-I or acute CRS is characterized by an acute heart disorder leading to acute kidney injury.<sup>8</sup>

The pathophysiologic mechanism involved in type-I CRS, starts with systolic dysfunction resulting in decreased cardiac output, which sets up the activation of the renin-angiotensin-aldosterone system, the sympathetic

nervous and the natriuretic peptide systems via diminished renal blood flow, structural renal changes occurs which impair renal function and, with neuro-hormonal activation, causes increased water and sodium retention, vasoconstriction and diminished cardiac performance.<sup>9,10</sup> These adaptive mechanisms fails to normalize cardiac output, further amplifies the downward spiral of heart failure. Diuretic resistance ensues and the cardiorenal syndrome is "born".<sup>11</sup>

The rationale for prevention of CRS is predicated that once the syndrome begins it is difficult to interrupt, is not completely reversible in all cases, and is associated with serious adverse outcomes.

The aim of this study was to determine the frequency of cardiorenal syndrome in hospitalized children with acute heart failure.

## METHODOLOGY

The study was carried out from December 2010 to December 2011. Patients who presented with signs and symptoms of acute heart failure in paediatric ICU, requiring treatment were included in this study; heart failure was defined as a new onset or acute exacerbation of signs and symptoms of ventricular dysfunction requiring hospitalization and inpatient treatment. Symptoms and signs included tachycardia, tachypnea, hepatomegaly, gallop rhythm, dyspnea, peripheral edema, third heart sound, jugular venous distention, pulmonary rales with or without radiological findings (i.e cephalization of pulmonary vessels, bilateral

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pulmonary infiltrates, pleural effusion and cardiomegaly). Patients with known congenital renal disease or chronic kidney disease and acute kidney injury due to other systemic illness were excluded. Study was approved by Ethical Review Committee of the Aga Khan University and Hospital.

Relevant data was collected by using proforma, which include characteristics, admission diagnosis, comorbidities, signs and symptoms of heart failure, serum creatinine on admission, serum creatinine was repeated on third day of admission to see worsening of renal function.<sup>12</sup> Estimated serum creatinine clearance was calculated by Schwartz formula on day one and day three (estimated creatinine clearance =  $KL/P.Cr$  where  $K \rightarrow$  age specific constant,  $L \rightarrow$  length/height,  $P.Cr \rightarrow$  plasma creatinine). As the study was not based on hypothesis so the confounder were not checked. There was no issue of selection bias, (as all recruited patients follow the same selection criteria), recall bias (as none of our information was based on recall information). All the information retrieved was kept confidential.

Data was analyzed on SPSS (Statistical Package for Social Sciences) version 16. Mean and standard deviation were utilized for numerical variables while frequency and percentages were computed for categorical variables.

## RESULTS

The sample consisted of 68 children admitted with acute heart failure. Mean age of patients was  $43.6 \pm 55.2$  months, out of whom 43 (63%) were males, whereas 25 (36.8%) were females; 70.5% were under 57 months (4.7 years) of age.

Mean weight on admission was  $14.7 \pm 19.13$  kg and mean height was  $83 \pm 31.08$  cm. Mean serum creatinine on admission was  $0.77 \pm 1.18$  mg/dl.

Worsening renal function was noted in 55 (81%) of patients. Most of the patients (70.5%) who developed worsening renal functions were under 5 years of age (Table I). Left ventricular ejection fraction was low in 43 (63.2%) patients who developed CRS. Mean length of stay was 9.7 hours ( $\pm 7.22$  SD). Most of the patients 41 (60.3%) were discharged home after recovery, whereas 27 (39.7%) patients expired.

Those who expired were diagnosed with myocarditis in 10 patients, congenital heart disease in 13 patients,

**Table I:** Distribution of age (months) by worsening renal function.

Age in months	Worsening renal function		
	No	Yes	Total
1 - 57	12 (25.0%)	36 (75.0%)	48 (100.0%)
58 - 114	1 (11.1%)	8 (88.9%)	9 (100.0%)
115 - 171	0 (0.0%)	10 (100.0%)	10 (100.0%)
172+	0 (0.0%)	1 (100.0%)	1 (100.0%)
Total	13 (19.1%)	55 (80.9%)	68 (100%)

primary pulmonary hypertension in 2 patients and rheumatic heart disease and cardiac tamponade in one patient each.

## DISCUSSION

Cardiorenal syndrome is a well-established entity. Initially not much was understood about the pathophysiology of the cardiorenal syndrome but with increasing awareness and understanding mechanism of cardiorenal syndrome is now well understood.<sup>13,14</sup>

Out of various types of cardiorenal syndrome, Type-I CRS, characterized by worsening renal function (WRF) associated with acute heart failure is the most commonly encountered clinical scenario seen in clinical practice.<sup>15</sup> Its prognostic implication and morbidity associated with worsening renal function is well established.<sup>12,16</sup>

This data suggest an important pathophysiological interaction between heart and kidney in children who were hospitalized with acute heart failure. We also observed that preserving adequate renal function would help in delaying progression of acute heart failure.<sup>17,18</sup> The cardiorenal syndrome has been described previously in adult patients with heart failure.

Price *et al.* conducted a study looking at worsening renal functions in children admitted with acute heart failure.<sup>5</sup> Acute decompensated heart failure was defined as new-onset or acute exacerbation of heart failure signs or symptoms requiring hospitalization and inpatient treatment. Worsening renal function was defined as an increase in serum creatinine by  $> \text{ or } = 0.3$  mg/dL during hospitalization. Sixty-three patients (35 males, 28 females) comprised 73 patients hospitalizations. Median age at admission was 10 years. (range 0.1 - 20.3 years). Median serum creatinine at admission was 0.6 mg/dL (range 0.2 - 3.5 mg/dL), and median creatinine clearance was 103 mL/min/1.73 m<sup>2</sup> (range 22 - 431 mL/min/1.73 m<sup>2</sup>). Serum creatinine increased during 60 of 73 (82%) patient hospitalizations (median increase 0.2 mg/dL, range 0.1 - 2.7 mg/dL), and worsening renal function occurred in 35 of 73 (48%) patient hospitalizations. Clinical variables associated with worsening renal function included admission serum creatinine ( $p = 0.009$ ) and blood urea nitrogen ( $p = 0.04$ ) and, during hospitalization, continuous infusions of dopamine ( $p = 0.028$ ) or nesiritide ( $p = 0.007$ ). Worsening renal function was independently associated with the combined end point of in-hospital death or need for mechanical circulatory support (adjusted odds ratio 10.2; 95% confidence interval 1.7 - 61.2,  $p = 0.011$ ). Worsening renal function was also associated with longer observed length of stay ( $33 \pm 30$  days vs.  $18 \pm 25$  days,  $p < 0.03$ ). They concluded that cardiorenal interaction occurs in children hospitalized for acute decompensated heart failure.<sup>5</sup> Renal function commonly worsens in such patients and is associated with

prolonged hospitalization and in-hospital death or the need for mechanical circulatory assistance.

The results of this study were also consistent with reports in adult patients with congestive heart failure. Gottlieb and colleagues also used rise in serum creatinine > 0.3 mg/dL as a marker for WRF and reported WRF in 39% patients hospitalized with acute heart failure, for predicting in-hospital mortality.<sup>19</sup> Clinical characteristics available at hospital admission can be used to identify patients at increased risk for developing WRF.

Our sample was of 68 children who were admitted with acute heart failure, our results showed WRF in 55 (81%) of patients, we also found that 36 (70.5%) patients were under 5 years of age, which suggest that younger the age group, more the chances of developing WRF.

Cardiorenal syndrome is a well-established entity, over the last decade with increasing awareness and knowledge, mechanism of CRS is now well understood. An imbalance in interaction between the failing heart, neurohormonal systems and host inflammatory responses has been acknowledged, this interaction leading to structural and functional damage to the heart and kidney together has been confirmed recently.<sup>20</sup>

Out of various types of cardiorenal syndrome, Type-I CRS is the most commonly encountered clinical scenario in clinical practice, its prognostic implication and morbidity is well established.

This study acknowledges a subset of paediatric patients with acute heart failure showing cardiorenal interaction, as even a modest increase in serum creatinine could be an indicator of poor outcome.<sup>21</sup> In children with acute heart failure a small decrement in renal function predicts increased risk stratification for advanced heart failure.<sup>10</sup>

This study has several limitations. First, there were only a small number of patients with acute heart failure. Despite a small sample size, it is the first of its kind to determine frequency of CRS in our population. Second, there was no standardized definition of worsening of renal function in paediatrics. Third, patients who were not admitted in intensive care unit because of relatively less sick condition, having CRS, may have been missed and not included in the study. Fourth, the data has been collected at a single center where evaluation and management differs from other institutions, which make these results somewhat limited in their usefulness for generalization to all children hospitalized with heart failure. Fifth, neither this study was designed to determine therapeutic agents causing WRF, nor looked into causes of acute heart failure.

### CONCLUSION

These results showed that worsening renal function was present in a majority 81% of children admitted with the

diagnosis of acute heart failure. Most of them (70.5%) were under 5 years of age. The authors, therefore, recommend further studies with large sample and multiple settings to reach the firm conclusion.

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