Acute Kidney Injury in Children After Cardiopulmonary Bypass: Risk Factors and Outcome

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Objective: To determine the incidence, risk factors and outcomes of acute kidney injury in children undergoing cardiac surgery for congenital heart disease. **Methods:** We enrolled 208 patients undergoing cardiac surgery for congenital heart disease during January 2012 to March 2013. Acute kidney injury was defined as per Acute Kidney Injury Network criteria. **Results:** Twenty patients had Acute kidney injury; 14 were infants. Age <1 yr, cardiopulmonary bypass time, prolonged ventilator requirement, pump failure, sepsis and hematological complications were identified as independent risk factors for any degree for acute kidney injury. All patients with acute kidney injury recovered the kidney function at the time of discharge. **Conclusions:** Acute kidney injury is common in children after cardiac surgery, especially in infants.

Keywords: *Cardiac surgery, Complications, Intensive care unit.*

Acute kidney injury (AKI) is a frequent complication of pediatric cardiac surgery and negatively effects short and long term outcomes. Studies report variable (3-42%) incidence of post- operative AKI with an associated mortality of 20% to 79% [1-5]. AKI requiring dialysis occurs in about 5% of these patients, in whom the mortality rate approaches 80% [6]. Even minor degrees of postoperative AKI may increase the risk of morbidity and mortality [6]. The aim of this study was to assess the incidence of AKI using the Acute Kidney Injury Network (AKIN) criteria in children undergoing surgery for congenital heart disease, and to find its risk factors and outcomes.

METHODS

The children (age <18 yrs) who were undergoing cardiac surgery with cardio-pulmonary bypass for congenital heart disease at the Pediatric Cardiothoracic unit of our hospital from January 2012 to March 2013 were eligible for inclusion. Exclusion criteria were: preoperative mechanical ventilation or extra corporeal life support, use of pre-operative inotropes, and pre-existing renal dysfunction [7].

Informed consent was taken from all parents prior to the inclusion in the study. This study was approved by the Research Ethics Board of the institution.

The demographic variables obtained were: age at surgery, weight at surgery, and cardiac diagnosis. Intra-operative information collected included cardio-pulmonary bypass (CPB) time, evidence of low output syndrome or pump failure. Post-operative variables included prolonged ventilator requirement, evidence of sepsis, hematological dysfunction or hepatic dysfunction and requirement of renal replacement therapy. Any inotropic or chronotropic medications (*e.g.*, epinephrine, dopamine, milrinone) were documented by utilizing the vasoactive inotropic score. Baseline Serum creatinine was obtained pre-operatively, either in the preoperative clinic (usually within 1 wk of surgery) or on the day of surgery. Post-operative serum creatinine was routinely done on arrival to the intensive care unit (day 1) and daily till discharge. Arterial blood gas was done 4-hourly for the first 48 hrs and then it was done 6-hrly for another 48 hrs. after which it was done 12-hrly till discharge from the ICU.

The definition and severity of AKI was based on the AKIN staging system [8]. As peritoneal dialysis is used routinely at our institution for perioperative fluid and electrolyte management, we did not use renal replacement therapy as a criterion for AKI. Instead, we defined the maximum AKI stage on the basis of serum creatinine criteria. Baseline renal function was defined according to Schwartz formula. We did not evaluate urine output as a determinant of AKI because 95% of the patients in our unit receive a diuretic within 12 hours of arriving to the intensive care unit (ICU), which may limit the reliability of urine output being a direct indication of innate renal function.

The diagnosis of pump failure or low output syndrome was made as per criteria laid by Hoffman [9,10]. Hematological dysfunction was defined as platelet count <80,000/mm^3 or a decline of 50% from the highest value recorded over the last 48 hours. Hepatic Dysfunction was defined as Alanine transaminase level more than twice upper limit of the normal. Prolonged ventilatory requirement was defined as need for invasive ventilation for more than 48 hours.

The results were analyzed using SPSS software. We performed Student's *t* test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables, and chi-square test for categorical variables. Statistical significance was defined as a probability value less 0.05. Univariate logistic analysis was then performed to examine the risk factors for AKI. Any variable with a probability value less than 0.1 was entered into a multivariate stepwise logistic regression analysis to analyze independent predictors for AKI. The following risk factors were included in the analysis: gender, age group (<1 year, >1 year), body weight (<10 kg, >10 kg), duration of cardiopulmonary bypass, pump failure, prolonged ionotrope requirement, hepatic dysfunction, hematological complications, ventilator requirement, and sepsis. Two children who required peritoneal dialysis for management of fluids post-operatively in view of complex prolonged surgery and pump failure, in the absence of creatinine or urine output criterion were excluded from the analysis.

RESULTS

We studied 208 patients (150 boys) who underwent cardiac surgery for congenital heart disease from January 2012 to March 2013. The mean (SD) age and weight of patients was 66.9 (95.6) months and 16.3 (16.5) kg, respectively. Mean (SD) CPB time was (38) minutes, and mean (SD) hospital stay was 11.5(3) days.

The spectrum of surgeries included ventricular septal defect closure (56), tetralogy of fallot correction (47), arterial switch operation (29), atrial septal defect closure (18), total anamolous pulmonary venous connection repair (8), fontan procedure (9), truncus repair (3), coarctation of aorta repair (3) and others (35). One patient had Risk Adjustment in Congenital Heart Surgery Surgical Severity Score (RACHS score) of 1, 148 patients had RACHS score of 2, 48 patients had RACHS score of 3, and 10 patients had RACHS score of 4.

Sepsis developed in 41 (19.7 %) patients. Prolonged ventilator support was required in 33 (15.9%) patients, and eight patients developed pump failure during the surgery. Hematological complications developed in 22 (10.6%) of patients and five (2.4%) patients died following the surgery.

The mean (SD) baseline renal function, as assessed by Schwartz formula, was 100.4 (12.3) mL/min/1.73 m^2, and mean (SD) urinary protein/creatinine ratio was 0.11 (0.06).

Twenty patients (9.6%) had AKI (AKI-I 15 patients; AKI-II 1 patient and AKI-III 4 patients). One patient with stage III AKI died. In most patients AKI occurred within the first five post-operative days. Ten patients required peritoneal dialysis. The duration of peritoneal dialysis ranged from 24 hours to 4 days. All patients with AKI recovered the kidney function at the time of discharge, with normal blood pressures.

The comparison of intra- and post- operative variables with the incidence of AKI is shown in ***Table* I**. CPB time, age <1yr, pump failure, prolonged ventilator requirement, sepsis, length of ICU stay, hematological complications and requirement of renal replacement therapy were more common in children with AKI. On multivariate logistic regression analysis, young age, CPB time, prolonged ventilator requirement, pump failure, sepsis and hematological complications were independently associated with higher odds of AKI **(*Table* II)**.

TABLE I COMPARISON OF INTRA- AND POST-OPERATIVE VARIABLES IN CHILDREN WITH OR WITHOUT AKI.

Parameters	*AKI (n=20) No. (%)*	*No AKI (n= 188) No (%)*
*Age <12 mo	17 (85)	30 (60)
*Requirement for prolonged ventilation	12 (60.0)	21 (11.2)
#Pump failure	3 (15.0)	5 (2.7)
*Sepsis	12 (60.0)	29 (15.4)
*Hematological complications	8 (40.0)	14 (7.5)
Hepatic dysfunction	2 (10.0)	14 (7.5)
*Renal replacement therapy	8 (40.0)	2 (1.1)
*CPB time (min)	97.0 (48.0)	69.0 (36.2)
*Maximum inotrope score	13.8 (5.6)	7.2 (4.5)
Weight (Kg)	13.0 (21.9)	16.7 (15.9)
Mortality	1 (5.0)	4 (2.1)
*ICU stay (d)	12.6(2.2)	9.8 (2.7)

*AKI = Acute kidney injury; *P<0.01; #P=0.01.*

TABLE II RISK FACTORS FOR AKI IN STUDY CHILDREN

Parameter	*OR (95% CI)*
Age (<12 mo)	3.7 (1.4-10.2)
Gender (males)	1.6 (0.5-5.0)
CPB time (minutes)	2.5 (0.9-6.9)
Prolonged ventilator requirement	11.9 (4.4-32.5)
Pump failure	6.4 (1.4-29.3)
Sepsis	8.2 (3.1-21.9)
Hematological complications	8.3 (2.9-23.6)
Hepatic dysfunction	1.4 (0.3-6.5)
Mortality	2.4 (0.2-22.7)

AKI – Acute kidney injury.

All ten patients in the study who required dialysis were less than 12 months. Age <12 mo. was a strong predictor of post-operative complications *viz*. prolonged ventilator requirement, pump failure, AKI, sepsis, hematological complications, RRT requirement, and prolonged hospital stay (P<0.001). The mean (SD) length of ICU stay in children <12 months was 12.6 (3.5) days in comparison to 10.8 (2.4) days in children >12 months (P<0.001).

DISCUSSION

We found the incidence of acute kidney injury in children, following a cardiopulmonary bypass to be 9.6%. Children who were young, had a prolonged CPB time, prolonged ventilator requirement, pump failure, sepsis and hematological complications were more likely to have acute kidney injury. Infancy was a strong predictor of post-operative complications, including a longer ICU stay and mortality.

The incidence observed in the present study is in broad agreement to the earlier studies [10,11]. Higher (52-68%) incidence of cardiac surgery associated AKI (CS-AKI) in the few other studies [4,12-15] could be due to inclusion of younger children in those studies. Associations of acute kidney injury with young age, prolonged bypass time, pump failure, sepsis has been reported previously [6,11-15]. The increased frequency of post-operative complications during infancy may be due to an increased risk to reperfusion, oxidative stress and systemic inflammatory response insults in the setting of immature kidneys, CPB induced hypothermia, and case complexity of the surgery.

There were several limitation in our study, being a small sized, single center study. We did not evaluate urine output as a determinant of AKI. We chose to do this because 95% of the patients in our unit receive a diuretic within 12 hours of arriving to the ICU, which may limit the reliability of urine output being a direct indication of innate renal function. We also did not look at proteinuria and hypertension on follow up in our patients. This shall be a part of future research in these patients.

We conclude that the risk of AKI is far greater in infants and young children. Infants with prolonged surgery, prolonged ventilator requirement, pump failure, sepsis and hematological complications post-operatively are at highest risk of developing AKI, and require a longer hospital stay. There is a need for more research on children post cardiac surgery, and looking at strategies to prevent complications.

Contributors: SKS: concept of study, data collection, analysis, drafting and revision of manuscript; MK: concept, design; collection of data; and drafting the manuscript; RS: supervision of the work; collection of data; and drafting and revision of manuscript; SB: supervision of the work; collection of data; and drafting and revision of manuscript;; VK: supervision of the work, data analysis and revision of manuscript. SKS will act as the guarantor.

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WHAT THIS STUDY ADDS?

- Children with prolonged cardiac surgery, prolonged ventilator requirement, pump failure, sepsis and hematological complications are at highest risk of developing acute kidney injury and adverse outcomes post-operatively.

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