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ORIGINAL ARTICLE

Incidence and risk factors for acute kidney injury in children with congenital heart disease undergoing cardiac surgery in a tertiary care center.

Rajab Ali Khokhar[1], Mujeeb Ur Rehman[2], Saad Bader Zakai[3], Aliya Kemal Ahsan[4], Veena Kumari[5], Ammad Hussain[6], Abdul Sattar Shaikh[7]

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ABSTRACT… Objective: To determine the incidence and risk factors associated with acute kidney injury (AKI) in children with congenital heart diseases (CHDs) who underwent cardiac surgery in a tertiary care center. **Study Design:** Cross-sectional study. **Setting:** Paediatric Cardiac Intensive Care Unit (PCICU) of National Institute of Cardiovascular diseases, Karachi, Pakistan. **Period:** November 2022 to May 2023. **Material & Methods:** We included patients of both genders and any age who underwent open or closed heart surgery for congenital heart defects. All patients undergoing CHD repairs were monitored for the total duration of PCICU stay. The development of AKI was labeled as per RIFLE criteria, and management thereafter was performed as per standard institutional protocols. **Results:** In a total of 93 patients with CHD, there were 50 (53.8%) males and 43 (46.2%) females. The mean age was 9.71±9.14 year ranging between 3 months to 60 years. There were 6 (6.5%) patients who developed AKI post-surgery. Overall, mortality was noted in 7 (7.5%) patients. Cardiopulmonary bypass (CPB) time and aortic cross-clamp (ACC) time were significantly higher among patients who developed post-surgery AKI (<0.001). Moreover, post-surgery AKI was significantly associated with intra-operative hypotension (p<0.001), post-operative hypotension (p<0.001), and post-operative sepsis (p<0.001). It was also found that AKI had significant association with higher post-operative inotropic scores (p<0.001), prolonged duration of mechanical ventilation (p<0.001), and length of PCICU stay (p<0.001). Mortality had significant association with AKI (33.3% vs. 5.7%, p=0.013). **Conclusion:** We noted the incidence of AKI among patient who underwent cardiac repairs to be 6.5%. CPB time and ACC time were significantly higher among patients who developed post-surgery AKI. Post-surgery AKI was significantly associated with intra-operative hypotension, post-operative hypotension, and post-operative sepsis. Mortality was significant high among cases that had AKI.

Key words: Acute Kidney Injury, Hypotension, Inotropic Score, Intensive Care Unit, Mechanical Ventilation.

INTRODUCTION

Acute kidney injury (AKI) is a prevalent and recurrent complication observed in children who have congenital heart diseases (CHDs) and are undergoing cardiac surgery. Moreover, Its occurrence varies from 9.6% to 64.6%, based on the criteria used to define AKI and the age group being studied.[1-3] AKI frequently leads to higher rates of morbidity and mortality, while also prolonging the need for mechanical ventilation and the overall stay in the pediatric cardiac intensive care unit (PCICU).[4] The outcomes of AKI generally correlate with the seriousness of the condition.[5]

There are studies which have shown that pediatric cardiac surgery associated AKI is often responsible for longer hospital stay and may cause chronic kidney disease (CKD) in these children.[6,7] Studies have shown that risk factors for AKI in children with CHD include younger age, preoperative elevated serum creatinine, high "cardiopulmonary bypass (CPB) time", "aortic cross clamp (ACC) time", cyanotic CHDs and low cardiac output syndrome post-surgery.[8-10]

1. FCPS (Pediatric Medicine), MRCPI (Pediatric Medicine), Assistant Professor Pediatric Cardiac Intensive Care Unit, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
2. FCPS (Pediatric Cardiology), Senior Registrar Paediatric Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
3. MRCS (General Surgery), FCPS (General Surgery), FCPS (Cardiac Surgery), Associate Professor Pediatric Cardiac Surgery, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
4. FCPS (Pediatric Cardiology), Assistant Professor Paediatric Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
5. FCPS (Pediatric Cardiology), Assistant Professor Paediatric Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
6. FCPS (General Surgery), FCPS (Cardiac Surgery), Senior Registrar Pediatric Cardiac Surgery, National Institute of Cardiovascular Diseases, Karachi, Pakistan.
7. FCPS (Pediatric Cardiology), Associate Professor Pediatric Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan.

Correspondence Address:
Dr. Mujeeb Ur Rehman
Department of Paediatric Cardiology,
National Institute of Cardiovascular Diseases,
Karachi, Pakistan.
mujeeburrehman113@gmail.com

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The wide variation in the incidence of AKI in children with CHD could mainly due to discrepancy in the definitions used for AKI. The most widely acceptable definitions include that used by the "Acute Kidney Injury Network (AKIN)", "Risk Injury Failure Loss End-stage renal disease (RIFLE)", and "pediatric modified Risk Injury Failure Loss End-stage renal disease (pRIFLE)", and also that definition used by "Kidney Disease: Improving Global Outcomes (KDIGO)" group.[11,12] Researchers have found recent important diagnostic marker for the early and effective diagnosis of AKI in children with CHDs like serum cystatin-C and urinary "Neutrophil gelatinase-associated lipocalin (NGAL)" which are more sensitive and specific then serum creatinine.[13]

Postoperative AKI is a frequent and serious complication among children with CHDs undergoing cardiac surgery and is a major threat to the patient's post-operative morbidity and mortality. It also indirectly has a strong impact on the resources utilized towards the patient along with the financial, emotional burden on the families. Local data not available. This study will help us to identify the correctable risk factors which will help in improving overall outcome of post-operative patients. In addition we will have our local data for future references. This study was performed to determine the incidence and risk factors associated with AKI in children with CHDs who underwent cardiac surgery in a tertiary care center.

MATERIAL & METHODS

This cross-sectional study was performed in the PCICU of "National Institute of Cardiovascular diseases (NICVD)", Karachi, Pakistan from November 2022 to May 2023. Approval from "Institutional Ethical Committee" (ERC-97/2021) was acquired. Written as well as informed consents were taken from patients or their parents/guardians. Sample size of 93 was calculated taking the incidence of post-surgery AKI among patients who underwent cardiac repair as 9.6%[3] with 95% confidence level and 6% margin of error.

Inclusion criteria were patients of both genders and any age who underwent open or closed heart surgery for congenital heart defects. We excluded patients with known pre-existing chronic kidney disease, pre-operative acute renal injury or patients who had genetic syndromes. All patients undergoing CHD repairs were monitored for the total duration of PCICU stay that was reviewed by consultant PCICU. The development of acute kidney injury was labeled as per RIFLE criteria[11], and management thereafter was performed as per standard institutional protocols.

Data was analyzed using "Statistical Package for Social Sciences (SPSS)" 26.0. Continuous data were expressed as mean ± standard deviation, while categorical variables were presented as frequencies (%). For the comparison of quantitative data, the independent sample t-test or analysis of variance (ANOVA) was employed when suitable. Categorical variables were evaluated using chi-square analysis. A significance level of p-value < 0.05 was considered statistically significant.

RESULTS

In a total of 93 patients with CHD, there were 50 (53.8%) males and 43 (46.2%) females. The mean age was 9.71±9.14 year ranging between 3 months to 60 years. The mean weight was 26.41±17.96 kg. The mean tricuspid annular plane systolic excursion (TAPSE) was 17.56±4.46 mm. Baseline urea, creatinine, hemoglobin, hematocrit, platelets, potassium, and bicarbonate levels were 24.33±6.97 mg/dl, 0.47±0.17 mg/dl, 13.46±2.50 g/dl, 40.02±7.93, 245±67, 4.35±3.96, and 50.86±75.03 respectively. Table-I is displaying characteristics of patients.

Baseline Characteristics		Frequency (%)
Gender	Male	50 (53.8%)
	Female	43 (46.2%)
Age (years)	<1	6 (6.5%)
	1-5	37 (39.8%)
	6-18	39 (41.9%)
	>18	11 (11.8%)
Cyanosis		35 (37.6%)
Left ventricular ejection fraction < 60%		11 (13.1%)
History of previous cardiac surgery		5 (5.4%)

Table-I. Characteristics of children undergoing cardiac surgery

The most common underlying cardiac diagnosis were tetralogy of fallot, and atrial septal defect noted in 24 (25.8%), and 16 (17.2%) patients respectively. Figure-1 is showing details about the distribution frequency of underlying congenital heart disease.

Types of surgery were open in 80 (86.0%) while closed in 13 (14.0%) patients. The mean CPB time and ACC time were 79±50 minutes and 45.±36 minutes. Intra-operative hypotension was noted among 4 (4.3%) patients. Table-II is showing comparison of mean urea and creatinine levels.

There were 6 (6.5%) patients who developed AKI post-surgery. Two (33.3%) patients underwent peritoneal dialysis while hemodialysis was performed in 1 (16.7%) patients. AKI improved in 4 (66.7%) patients while persisted in 1 (16.7%) patient. Overall, mortality was noted in 7 (7.5%) patients. CPB time and ACC time were significantly higher among patients who developed post-surgery AKI (<0.001). Moreover, post-surgery AKI was significantly associated with intra-operative hypotension (p<0.001), post-operative hypotension (p<0.001), and post-operative sepsis (p<0.001). It was also found that AKI had significant association with higher post-operative inotropic scores (p<0.001), prolonged duration of mechanical ventilation (p<0.001), and length of PCICU stay (p<0.001). Mortality had significant association with AKI (33.3% vs. 5.7%, p=0.013) as shown in Table-II.

Parameters	Post-operative			P-Value
	Day-1	Day-2	Day-3	
Urea	29.22±10.00	30.56±16.22	31.30±26.51	0.748
Creatinine	0.53±0.18	0.53±0.18	0.52±0.56	0.976

Table-II. Comparison of mean urea and creatinine levels (n=93)

Study Variables		AKI		P-Values
		Yes (n=6)	No (n=87)	
Gender	Male	1 (16.7%)	49 (56.3%)	0.060
	Female	5 (83.3%)	38 (43.7%)	
Age (years)	<1	-	6 (6.9%)	0.079
	1-5	4 (66.7%)	33 (37.9%)	
	6-18	-	39 (44.8%)	
	>18	2 (33.3%)	9 (10.3%)	
Cyanosis		4 (66.7%)	31 (35.6%)	0.129
Left ventricular ejection fraction < 60%		2 (33.3%)	9 (10.3%)	0.092
History of previous cardiac surgery		1 (16.7%)	4 (4.6%)	0.205
Pre-surgery Urea (mg/dl)		19.33±4.72	24.68±6.99	0.069
Pre-surgery creatinine (mg/dl)		0.48±.012	0.47±0.17	0.845
Pre-surgery hemoglobin (g/dl)		15.2±3.69	13.34±2.38	0.078
Types of Surgery	Open	6 (100%)	74 (85.1%)	0.307
	Closed	-	13 (14.9%)	
Cardiopulmonary bypass time in minutes		196±110	70±33	<0.001
Cross-clamp time in minutes		123±79	40±24	<0.001
Intra-operative hypotension		2 (33.3%)	2 (2.3%)	<0.001
Post-operative hypotension		5 (83.3%)	6 (6.9%)	<0.001
Post-operative sepsis		4 (66.7%)	-	<0.001
Post-operative inotropic score		25.4±4.2	10.87±6.81	<0.001
Post-operative mechanical ventilation (hours)		139±35	18±31	<0.001
Length of PCICU stay (days)		19±10	3±3	<0.001
Mortality		2 (33.3%)	5 (5.7%)	0.013

Table-III. Pre-operative, Intra-operative, and post-surgery variables with respect to AKI (n=93)

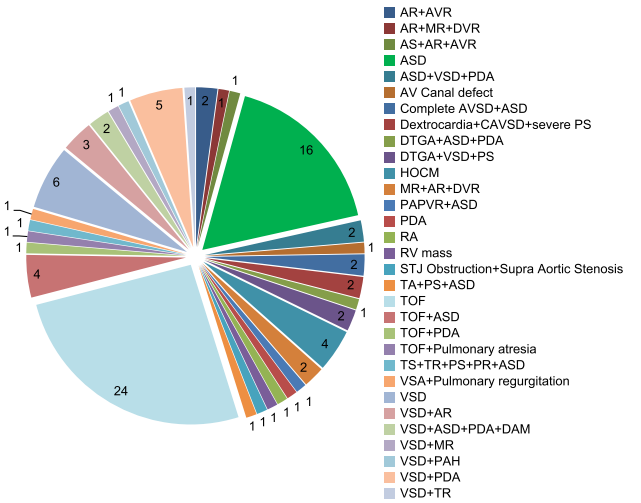

Figure-1. Frequency of underlying congenital cardiac disease (n=93)

DISCUSSION

In this study, we found a 6.5% incidence of AKI following cardiac repair surgery for CHD. Overall, mortality was reported in 7.5% patients while the in-hospital mortality among children who had AKI was 33.3% (p=0.013). The proportion of AKI found in this study is lower than what was reported by Kourelis et al from Greece.[14] Some researchers have shown that AKI incidence following cardiac repair can vary widely, spanning from 11.5% to 62%.[15-18] The documented in-hospital mortality related to AKI ranges from 1.1% to 79%.[15-18] This broad range in incidence can be attributed to the utilization of diverse definitions for AKI, variations in patient demographics or procedural attributes, and a gradual reduction in the risk of postoperative AKI over a period of time. Limitations also exist rendering to different AKI diagnostic criteria for early detection of AKI, especially in younger children. We had adopted RIFLE criteria fort eh diagnosis of AKI. Serum creatinine serves as an indicator of renal function rather than indicating damage, leading to a delay of more than 48 hours in its elevation following a renal injury, and a decrease of over 50% in glomerular filtration rate before serum creatinine levels increase.[19] Changes in renal function can be viewed as a sequence of progressive stages that arise due to a combination of factors that make the kidneys susceptible to damage. Various models have shown that when multiple insults are combined, which might not individually cause significant renal injury, the susceptibility of the renal medulla to damage becomes apparent. This susceptibility primarily arises from imbalances between the supply and demand of oxygen in the medulla, as well as issues like membrane damage and dysfunction of mitochondria.[20]

In the past, some researchers have shown that surgical age and weight are some of the risk factors for post-surgery AKI[20,21] but we were unable to observe associations in this study. In the past, there has been consistent evidence that a longer duration of cardiopulmonary bypass (CPB) time is significantly linked to the occurrence of postoperative acute kidney injury (AKI).[17,23] This correlation aligns with our current findings and various mechanisms have been proposed like the decline in the pulsatile flow, inflammation, mechanical damage to erythrocytes, hemoglobinuria, and an elevated development of reactive oxygen species.[17,23] In order to counteract the adverse impact of prolonged CPB time on renal function, strategies aimed at limiting the duration of cardiopulmonary bypass and further exploration of the use of vasodilator agents are necessary.[24]

We highlighted the considerable adverse influence of postoperative AKI on multiple factors, including the duration of mechanical ventilation and hospitalization length. Moreover, we observed an elevated probability of all-cause mortality, underscoring the unfavorable impact of AKI on the survival of patients who underwent cardiac surgery. Longer periods of mechanical ventilation could suggest a poorer clinical condition arising from factors such as heart failure, compromised respiration, hypoxia, and circulatory shock, that can impact renal functionality.[22] However, it's important not to overlook the negative effects of invasive ventilation on renal function as well. Our findings also demonstrated a significant correlation between prolonged mechanical ventilation and PCICU stay with the occurrence of AKI, aligning with previous research in this area.

Excessive fluid accumulation caused by the retention of water and salt, a known factor associated with AKI following cardiac surgeries,

can extend the recovery period through various mechanisms.[25] This includes the development of interstitial and alveolar lung edema, leading to decreased lung compliance and compromised gas exchange. Additionally, myocardial edema can impair both contractility and diastolic function of the heart. Gut congestion resulting from fluid overload might lead to reduced tolerance to feeding, resulting in decreased intake of calories and nutrients.[26] The impact of renal dysfunction might extend to drug elimination, leading to prolonged periods of sedation. Furthermore, tissue edema can impede proper wound healing.

It is an observational study so difficult to establishment any causality. We only noted in-hospital outcomes so further research is required to adopt prospective nature designs to further establish the burden of AKI and its related outcomes among similar set of patients.

CONCLUSION

We noted the incidence of AKI among patient who underwent cardiac repairs to be 6.5%. CPB time and ACC time were significantly higher among patients who developed post-surgery AKI. Post-surgery AKI was significantly associated with intra-operative hypotension, post-operative hypotension, and post-operative sepsis. It was also found that AKI had significant association with higher post-operative inotropic scores, prolonged duration of mechanical ventilation, and length of PCICU stay. Mortality was significant high among cases that had AKI.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Rajab Ali Khokhar	Data collection, Data analysis.	
2	Mujeeb Ur Rehman	Data collection, Drafting.	
3	Saad Bader Zakai	Concept and Designing.	
4	Aliya Kemal Ahsan	Data collection.	
5	Veena Kumari	Data collection.	
6	Ammad Hussain	Data collection.	
7	Abdul Sattar Shaikh	Supervision, Critical revisions.