Saudi J Kidney Dis Transpl 2015;26(3):489-496

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Cardiac Surgery-Associated Acute Kidney Injury in a Developing Country: Prevalence, Risk Factors and Outcome

Ekanem Nsikak Ekure[1], Christopher Imokhuede Esezobor[1], Anuradha Sridhar[2], Jyothi Vasudevan[2], Rajhavan Subramanyan[2], Kotturathu Mammen Cherian[2]

[1]Department of Pediatrics, College of Medicine, University of Lagos, Lagos, Nigeria, [2]Frontier Lifeline Hospital, Chennai, India

ABSTRACT. Little is known about cardiac surgery-associated acute kidney injury (CS-AKI) in children in developing regions of the world. The study aimed to determine the prevalence of CS-AKI, associated factors and its impact on mortality and utilization of hospital services. The hospital records of children aged 0–17 years who underwent CS at an Indian hospital were reviewed. CS-AKI was defined as a rise in serum creatinine of ≥0.3 mg/dL in any 48 h and or by urine output <0.5 mL/kg/h for an 8-h period in the first five days after CS. The study included 323 children with a median age of one year (0.04–17), of whom 22 (6.8%) were neonates and 18.3% had a single ventricle. About 60% of the children had Risk Adjusted Congenital Heart Surgery–I category 1 or 2 interventions. CS-AKI occurred in 39 children (12.1%). Factors associated with CS-AKI were sepsis and intra- and post-operative hypotension. In-hospital mortality was six-fold higher in children who developed CS-AKI. CS-AKI was associated with two to three days more of mechanical ventilation and Intensive care unit stay. CS-AKI occurs in children in developing countries, but at a lower frequency mainly due to the predominance of post-neonatal children undergoing less-complex CSs. CS-AKI was associated with higher in-hospital mortality and increased utilization of hospital services. Factors associated with CS-AKI included intra- and post-operative hypotension and sepsis.

Introduction

Acute kidney injury (AKI) is a recognized complication of cardiac surgery (CS) in children. It has a reported incidence of 5–68% in persons undergoing CS.[1-3] The underlying risk for AKI following CS includes demographic characteristics such as age, prolonged mechanical ventilation, cardiopulmonary bypass (CPB) time and peri-operative medications.[4,5] CS-associated AKI (CS-AKI) is reported to have a high mortality.[1,6] In addition, it is associated with a high utilization of hospital services such as intensive care unit (ICU), mechanical ventilation and renal replacement therapy, and, therefore, significantly increases the cost of hospitalization.[1,6,7]

Correspondence to:

Dr. Ekanem Nsikak Ekure
Department of Pediatrics,
College of Medicine, University of Lagos,
P.M.B. 12003, Lagos, Nigeria
E-mail: ekaekure@yahoo.com

In the currently available literature, there is paucity of information about CS–AKI in children in developing regions of the world. These regions of the world generally tend to have a lower level of sophistication of hospital services required for care of children with structural heart diseases and interventions such as CS may incur frequent and more severe complications. Also, the pediatric population included in the published studies was mostly neonates and infants.[1,4,6] This may limit generalization of the results of these studies to developing countries where children with congenital heart disease experience significant delays before CS due to financial reasons and lack of manpower availability, resulting in mostly older children undergoing CS. Therefore, the current study was conceived to determine the prevalence of CS-AKI in an Indian hospital and to identify demographics and the pre-, peri- and post-operative factors associated with the development of CS-AKI. A secondary objective was to determine the association between CS-AKI, in-hospital mortality and utilization of hospital resources.

Methods

This was a retrospective study of children from birth to 17 years who underwent CS between 1st July 2011 and 31st June 2012 (both months inclusive) in The International Centre for Cardiothoracic and Vascular Diseases (A Unit of Frontier Lifeline and Dr. K. M. Cherian Heart Foundation), Chennai. Approval for the study was obtained from the Ethics Committee of the hospital. Children who underwent procedures such as device closure procedures, patent ductus arteriosus closure and pacemaker insertion were excluded from the study. Children with prior renal transplant or dialysis requirement were also excluded from the study.

From the hospital record of each child, demographic, pre-, intra- and post-operative variables were extracted. The demographic variables obtained were age at surgery, sex, weight and height at surgery, cardiac diagnosis and history of previous CS. Pre-operative variables extracted included history of pre-operative shock, inotropic support within one week of CS and cardiac catheterization within 72 h prior to the index CS. Others were single ventricle status, exposure to aminoglycosides or non-steroidal anti-inflammatory drugs (NSAIDs) and pre-operative serum creatinine. Intra-operative information obtained included Risk Adjusted Congenital Heart Surgery (RACHS-I) category, cardiopulmonary bypass (CPB), cross-clamped time and intra-operative hypotension. Post-operatively, data on duration of mechanical ventilation, exposure to aminoglycosides or NSAIDs, incidence of hypotension and use of inotropic medications were also extracted. Other information obtained were peak serum creatinine during hospital stay and before discharge, hourly urinary output while in the ICU, use of peritoneal dialysis (PD) and AKI resolution before discharge from the hospital.

Definition of terms

CS-AKI was defined as a rise of ≥0.3 mg/dL in the serum creatinine level in any 48 h and/or by urine output <0.5 mL/kg/h for an 8-h period in the first five days after CS. The severity of CS-AKI was classified as stage I–III using the Acute Kidney Injury Network definition as modified for children by Blinder.[4] Resolution of AKI was defined as return of serum creatinine to below 1.5-times the pre-operative serum creatinine. Pre-operative period refers to the period within one week prior to the index CS, except for pre-operative serum creatinine that referred to the latest serum creatinine before CS. The post-operative period referred to the period not longer than 72 h after the index CS. Hypotension (pre-, intra- and post-operation) was defined using the description by Li et al.[8]

Data management

The data were analyzed using IBM SPSS Statistics version 20. Categorical variables were summarized as percentages while continuous variables were tested for normality and represented as either mean ± standard deviation or median (range), as appropriate. Univariate analysis was performed using demographic and

Table 1. Types of cardiac lesion and RACHS-I scores of children.

Descriptors	N = 323 (%)
Types of cardiac lesion	
TAPVC, d-TGA or truncus arteriosus	33 (10.2)
Left heart obstructive lesions	17 (5.3)
Pulmonary atresia ± VSD	26 (8.0)
Shunt lesions	105 (32.5)
Single ventricular physiology	60 (18.6)
Tetralogy of Fallot	82 (25.4)
RACHS-1 category	
1 and 2	198 (61.3)
3	108 (33.4)
4	15 (4.6)
5 and 6	2 (0.6)

pre-, intra- and post-operative characteristics to identify factors associated with developing CS-AKI (Student's *t*-test or Mann–Whitney U test as appropriate for continuous variables and Chi square test for categorical variables). Factors found to be significantly associated with CS-AKI on univariate analysis were included in a multivariate analysis model to identify independent predictors of CS-AKI. Similarly, all the factors identified on univariate analysis to be associated with in-hospital mortality were combined in a multivariate model to predict in-hospital mortality. In all the analyses, the significant statistical level was set at *P*-value <0.05.

Results

Three hundred and twenty-three children met the study eligibility criteria and were included in the analysis. Children with shunt lesions, Tetralogy of Fallot and single ventricular physiology made up 32.5%, 25.4% and 18.6% of the studied population, respectively. About 61% of the children had RACHS-I category 1 or 2 cardiac interventions and 33.4% had RACHS-I category 3 (Table 1).

The age range was 0.04–17 years with a median of one year; 6.8% were younger than one month. Females made up 39.9%, and 73 children (22.6%) had at least one previous CS.

AKI occurred in 39 children (12.1%) following CS. All children with CS-AKI met the serum creatinine criteria but only 27 (69.2%) met the urine component of the AKIN criteria for AKI. In the majority of the children with CS-AKI, it developed within 48 h of CS. In 14 (35.9%) children with AKI, the maximum category of AKI was either stage II or III. Resolution of CS-AKI before discharge from the hospital was achieved in 22 (56.4%) children (Table 2).

Factors associated with CS-AKI

Table 3 depicts the association of various demographic and pre-, intra- and post-operative variables with CS-AKI. Children who developed CS-AKI were similar in age, gender and anthropometric variables, such as weight and height at surgery. Although RACHS-I category ≥3, single ventricular physiology and undergoing cardiac catheterization within 72 h of CS were associated with a higher frequency of CS-AKI, the associations did not reach a significant level.

Of the pre-operative factors, only aminoglycoside administration was associated with developing CS-AKI ($P = 0.01$).

Children who developed CS-AKI were more likely to have developed hypotension during CS (17.9% versus 0.7%; $P = 0.00$). Although the proportion of children who underwent CPB or aortic cross-clamping was similar in children with or without CS-AKI, among the children who underwent CPB, the CPB duration was

Table 2. Nature of cardiac-surgery associated acute kidney injury (AKI).

Descriptors	n = 39 (%)
Post-operative oligoanuria	
Yes	27 (69.2)
No	12 (30.8)
Severity of AKI	
Stage I	25 (64.1)
Stage II	9 (23.1)
Stage III	5 (12.8)
Time to AKI	
0–24 h	15 (38.5)
25–48 h	19 (48.7)
>48 h	5 (12.9)
Resolution of AKI before discharge	
Yes	22 (56.4)
No	17 (43.6)

Table 3. Prevalence of cardiac surgery-associated acute kidney injury (AKI) and related factors.

Descriptors	All, n = 323	CS-AKI[a]		*P*-value
		No n = 284 (87.9%)	Yes n = 39 (12.1%)	
Age at surgery, years	1.0 (0.04–17.0)	2.0 (0.04–17.0)	0.9 (0.04–15.0)	0.17
Age at surgery ≤1 month, n (%)	22 (6.8)	18 (6.3)	4 (10.3)	0.32
Female, n (%)	129 (39.9)	112 (39.4)	17 (43.6)	0.62
Weight at surgery, kg	9.0 (2.3–77.0)	9.5 (2.3–77.0)	6.6 (2.5–52.0)	0.12
Height/length at surgery, m	0.80 (0.44–1.69)	0.80 (0.44–1.69)	0.72 (0.47–1.63)	0.13
Body mass index at surgery, kg/m^2	13.7 (6.8–28.3)	13.8 (6.8–28.3)	13.0 (9.0–20.4)	0.46
Had previous cardiac surgery, n (%)	73 (22.6)	63 (22.2)	10 (25.6)	0.63
Single ventricle, n (%)	60 (18.9)	50 (17.6)	10 (25.6)	0.23
Cath[b] within 72 h prior to surgery, n (%)	42 (13.0)	33 (11.6)	9 (23.1)	0.05
Pre-operative NSAIDs, n (%)	28 (8.7)	22 (7.7)	6 (15.4)	0.11
Pre-operative aminoglycoside, n (%)	1 (0.3)	0 (0.0)	1 (2.6)	0.01*
Pre-operative serum creatinine, mg/dL	0.6 (0.5–1.2)	0.6 (0.5–1.0)	0.6 (0.5–1.2)	0.49
Pre-operative inotrope, n (%)	7 (2.2)	5 (1.8)	2 (5.1)	0.18
RACHS-1[c] score ≥3, n (%)	125 (38.7)	105 (37.0)	20 (51.3)	0.09
Intra-operative hypotension, n (%)	9 (2.8)	2 (0.7)	7 (17.9)	0.00*
Cardiopulmonary bypass, n (%)	299 (92.6)	261 (91.9)	38 (97.4)	0.22
Cardiopulmonary bypass time, min[d]	114 (31–396)	107 (31–378)	138 (53–396)	0.00*
Cross clamp, n (%)	250 (77.4)	219 (77.1)	31 (79.5)	0.74
Cross clamp time, min[e]	51 (5–226)	48 (5–226)	66 (15–172)	0.02*
Post-operative NSAIDs, n (%)	88 (27.2)	74 (26.1)	14 (35.9)	0.20
Post-operative aminoglycoside, n (%)	51 (15.8)	41 (14.4)	10 (25.6)	0.07
Post-operative hypotension, n (%)	33 (10.2)	10 (3.5)	23 (59.0)	0.00*
Post-operative sepsis, n (%)	29 (9.0)	19 (6.7)	10 (25.6)	0.00*

All continuous data are median (minimum–maximum).
[a]CS-AKI: Cardiac surgery-associated acute kidney injury, [b]Cath: Cardiac catheterization, RACHS-1: Risk Adjusted Congenital Heart Surgery-1; [d]only those who underwent cardiopulmonary bypass; [e]only those who underwent cross-clamp.

longer in the group of children with CS-AKI (138 min versus 107 min; $P = 0.00$). Similarly, among all children who underwent cross-clamping, children who developed CS-AKI had a longer cross-clamping time (66 min versus 48 min; $P = 0.02$).

About 25% of the children, who developed sepsis post CS, developed CS-AKI compared with 6.7% of those who did not develop sepsis after CS. Similarly, post-operative hypotension was significantly associated with CS-AKI (59% versus 3.5%; $P = 0.00$). In contrast, post-operative administration of aminoglycoside or NSAIDs was not significantly associated with the development of CS-AKI.

In multivariate analysis, developing post-operative hypotension was associated with a 26.95-fold (95% CI: 10.3–70.42) increase in the risk of CS-AKI; sepsis, intra-operative hypotension and receiving aminoglycoside before CS no longer predicted the development of CS-AKI.

Impact of CS-AKI on utilization of hospital resources and in-hospital mortality

Developing CS-AKI was associated with increased use of hospital services. Children who developed CS-AKI required a longer duration of inotropic support and mechanical ventilation and longer ICU stay. Fourteen children of the 39 who developed CS-AKI required PD compared with five children without CS-AKI who received PD prophylactically post-operatively (Table 5). The PD was performed for a median duration of four (1–17) days.

Table 4. Multivariate analysis of factors associated with cardiac surgery-associated acute kidney injury.

Independent variables	Adjusted odds ratio (95% confidence interval)	*P*-value
Post-operative sepsis	2.57 (0.80–8.29)	0.11
Pre-operative aminoglycoside	0 (0)	1.00
Intra-operative hypotension	8.01 (0.96–66.84)	0.05
Post-operative hypotension	26.95 (10.31–70.42)	0.00

Table 5. Association between cardiac surgery-associated acute kidney injury, mortality and utilization of hospital services.

Descriptors, post-operation	All, n = 323	Post-cardiac surgery AKI		*P*-value
		No, n (%)	Yes, n (%)	
Duration of inotropic support (days)	2 (0–31)	2 (0–14)	5 (1–31)	0.00
Duration of ICU stay (days)	2 (1–50)	2 (1–23)	5 (1–50)	0.00
Duration of mechanical ventilation (days)	1 (1–22)	1 (1–14)	3 (1–22)	0.00
Length of hospital stay (days)	10 (2–73)	10 (2–32)	11 (3–73)	0.17
Post-operative peritoneal dialysis, n (%)	19 (5.9)	5 (1.8)	14 (35.9)	0.00
In-hospital mortality, n (%)	25 (7.7)	7 (2.5)	18 (46.2)	0.00

Among the 39 children who developed CS-AKI, 46.2% died compared with a 2.5% mortality in the group who did not have CS-AKI. In the multivariate analysis, only CS-AKI, intra-operation hypotension and post-operation hypotension remained significant predictors of in-hospital mortality. There was a six-fold increase in the risk of in-hospital mortality with CS-AKI [5.93 (95% CI: 1.41–24.85)] (Table 6).

Discussion

The present study documented the prevalence of CS-AKI, risk factors and its implications for utilization of hospital services in a developing country, India. The study documented a CS-AKI prevalence of 12.1%, a strong association with intra- and post-operation hypotension and an increased need for hospital services such as longer ICU stay, longer duration of mechanical ventilation and inotrope use and increased mortality in children who develop AKI after CS.

Similar to previous studies, the prevalence of CS-AKI in the present study is high and supports the uniformly frequent occurrence of AKI following CS in children and adults.[4,5,8-10] However, the 12.1% prevalence of CS-AKI in our study contrasts significantly with the higher prevalence of AKI reported in most other reports. In several series, AKI occurred in 30–50% of children who underwent CS, with a relatively lower prevalence reported in adult series.[4,7,8,11] For instance, four studies involving children who underwent CS for structural heart diseases published in the year 2013 documented CS-AKI prevalence or incidence between 52% and 68%.[1,4,6,12] The lower CS-AKI prevalence in the present study compared with published reports may be explained by the differences in characteristics of the children. The relatively older age of the children in the present study may have contributed to the lower frequency of CS-AKI. This observation was buttressed by Taylor[13] and Sethi,[14] who documented a CS-AKI prevalence of 15% and

Table 6. Multivariate analysis of factors associated with in-hospital mortality in children undergoing cardiac surgery.

Independent variables	Adjusted odds ratio (95% confidence interval)	*P*-value
Pre-operation ionotrope use	0.21 (0.01–36.86)	0.56
Intra-operation hypotension	46.92 (3.00–733.03)	0.01
Post-operation hypotension	26.58 (5.59–126.38	0.00
CS-AKI	5.93 (1.41–24.85)	0.02

11%, respectively, in a study of relatively older children. In both studies, the children had a median age of 11.6 months and a mean age of 120 months. CS in younger children tends to be more technically demanding, resulting in longer cardiopulmonary and cross-clamp time, both of which are uniformly strong predictors of CS-AKI.[1,3,6] On the other hand, a higher incidence of CS-AKI in younger children may underline an increased risk to both reperfusion ischemic and inflammatory renal insults in a setting of immature kidneys.[8]

The relatively older age group in the current study, similar to the report by Sethi and colleagues[14] in India, also reflects the delay children with congenital heart disease in developing countries experience before being taken up for CS, mostly as a result of delay in diagnosis and inability to pay the high financial cost of such services. For instance, only 6.8% of the 323 children with congenital heart disease in the present study were neonates. Hence, it is conceivable that during this waiting period, the more ill children with complex heart diseases are likely to die before cardiac intervention and hence will not be included in the series of CS from developing countries. For instance, while about two-thirds of the population in the present study had RACHS-I category 1 or 2 cardiac interventions, in most studies from developed countries such as USA and Canada, the proportions of children with RACHS-I category 3 or more cardiac interventions were between 47% and 92%. With a higher RACHS-I score associated with a higher frequency of CS-AKI, the relatively lower prevalence of CS-AKI in the present study is not unusual.[4,12,13] It is conceivable that with early and universal access to CS for children with congenital heart disease in developing countries like India, the prevalence of CS-AKI also may rise.

Although there was no significant difference in the prevalence of CS-AKI in children who underwent CPB and those who did not in the present study, when analysis was limited to only the group of children that had CPB, the duration of CPB was significantly longer in the cohort that developed CS-AKI compared with the group that did not develop CS-AKI. A similar observation was made for aortic cross-clamping. These findings are consistent with the reports of most investigators.[4,8,13] Although the exact mechanisms of CS-AKI from CPB and aortic cross-clamping are not known, ischemia–reperfusion, neuro-hormonal activation, oxidative and pro-inflammatory processes may be responsible.[15]

Most children with AKI after CS develop this within 48 h of surgery, underling the intra-operative period and the first few hours after surgery as the most critical period for kidney insult.[5,8] The present study supports this observation; demographic and pre-operative variables were not associated with a higher risk of developing CS-AKI. In contrast, the factors associated with CS-AKI were intra- and post-operative factors such as intra-operative hypotension, post-operative hypotension and sepsis. Even after multi-variate regression, post–operative hypotension remained a strong predictor of CS-AKI. Hypotension results in significant fluid shifts with blood relatively shunted away from the kidneys. With re-establishment of effective perfusion, pro-inflammatory cytokines and processes are triggered, resulting in reperfusion injury that may manifest as AKI.[15]

As highlighted in most studies of AKI in the general population and in those undergoing CS, AKI is not a benign condition.[1,4,16] In the present study, children who developed CS-AKI were about six-times more likely to die during hospitalization than children who did not develop CS-AKI, even after accounting for differences in inotropic use and intra- and post-operative hypotension. Similar association of CS-AKI with in-hospital mortality has been commonly reported by other investigators.[1,5] Studies involving adults undergoing CS have also reported a higher mortality in the cohort who developed CS-AKI than in the group that did not develop CS-AKI.[10,17] The mechanisms by which CS-AKI contribute to in-hospital mortality are not well known but may be related to worsening fluid overload, especially in the lungs, which requires prolonged mechanical ventilation and its attendant complications. In addition, failure of one organ

of the body increases the likelihood of multi-organ failure, which is uniformly associated with higher mortality, the so-called "organ cross talk," one of which is the cardiorenal syndrome.[18]

Apart from increased mortality, CS-AKI is associated with increased utilization of hospital resources. In the present study, as in most published studies,[4,8] children who had CS-AKI required mechanical ventilation and ICU stay for two to three days longer than those who did not develop CS-AKI. With retention of fluid in most cases of AKI, children with CS-AKI are thought to have stiffer wet lungs, which dramatically increase the need for mechanical ventilation and simultaneously prolong the duration of ICU admission. Although the duration of ICU stay was longer in the children who developed CS-AKI, the overall length of hospital stay was similar. This observation has also been made by some other investigators, suggesting that predictors of ICU and hospital stay may not be similar.[4,19] With intra- and post-operative hypotension associated with development of CS-AKI, it was explicable that CS-AKI will be associated with longer inotropic support. As part of the treatment of CS-AKI, the majority of children who received dialysis after CS had CS-AKI. Together, the increased use of hospital services in children who developed AKI after CS dramatically increases the overall cost of hospitalization, underlining another reason to identify modifiable predictors of CS-AKI.[7]

A limitation of this study was its retrospective nature, which limits the spectrum and quality of data available for collection and the degree to which causality can be ascertained. We were not able to test the association between packed red cell transfusion and CS-AKI; however, in the published literature, the association has not been consistent.[10,13] Also, because the study was carried out in a single center, it limits the generalization of the findings to other centers in developing regions of the world. Nonetheless, the findings of this report broaden what is known about CS-AKI in children by describing CS-AKI in children in a developing country, which has not been frequently described previously.

In conclusion, AKI occurs in children undergoing CS in developing countries, but at a lower frequency, probably due to the predominance of post-neonatal children undergoing less-complex CS. CS-AKI was associated with higher in-hospital mortality and increased utilization of hospital services such as ICU, mechanical ventilation, cardiac inotropic support and dialysis. Factors associated with CS-AKI included intra- and post-operative hypotension and sepsis.

Conflict of interest: None declared.

References

1. Morgan CJ, Zappitelli M, Robertson CM, et al. Risk factors for and outcomes of acute kidney injury in neonates undergoing complex cardiac surgery. J Pediatr 2013;162:120-7.
2. Thakar CV, Worley S, Arrigain S, Yared JP, Paganini EP. Improved survival in acute kidney injury after cardiac surgery. Am J Kidney Dis 2007;50:703-11.
3. Seitz S, Rauh M, Gloeckler M, Cesnjevar R, Dittrich S, Koch AM. Cystatin C and neutrophil gelatinase-associated lipocalin: biomarkers for acute kidney injury after congenital heart surgery. Swiss Med Wkly 2013;143:w13744.
4. Blinder JJ, Goldstein SL, Lee VV, et al. Congenital heart surgery in infants: Effects of acute kidney injury on outcomes. J Thorac Cardiovasc Surg 2012;143:368-74.
5. Aydin SI, Seiden HS, Blaufox AD, et al. Acute kidney injury after surgery for congenital heart disease. Ann Thorac Surg 2012;94:1589-95.
6. Ricci Z, Di Nardo M, Iacoella C, Netto R, Picca S, Cogo P. Pediatric RIFLE for Acute Kidney Injury Diagnosis and Prognosis for Children Undergoing Cardiac Surgery: A Single-Center Prospective Observational Study. Pediatr Cardiol 2013;34:1404-8.
7. Dasta JF, Kane-Gill SL, Durtschi AJ, Pathak DS, Kellum JA. Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. Nephrol Dial Transplant 2008;23:1970-4.
8. Li S, Krawczeski CD, Zappitelli M, et al. Incidence, risk factors, and outcomes of acute kidney injury after pediatric cardiac surgery: A prospective multicenter study. Crit Care Med 2011;39:1493-9.

9. D'Onofrio A, Cruz D, Bolgan I, et al. RIFLE criteria for cardiac surgery-associated acute kidney injury: Risk factors and outcomes. Congest Heart Fail 2010;16 Suppl 1:S32-6.
10. Karkouti K, Wijeysundera DN, Yau TM, et al. Acute kidney injury after cardiac surgery: Focus on modifiable risk factors. Circulation 2009;119:495-502.
11. Parolari A, Pesce LL, Pacini D, et al. Risk factors for perioperative acute kidney injury after adult cardiac surgery: Role of peri-operative management. Ann Thorac Surg 2012;93:584-91.
12. Morgan CJ, Gill PJ, Lam S, Joffe AR. Peri-operative interventions, but not inflammatory mediators, increase risk of acute kidney injury after cardiac surgery: A prospective cohort study. Intensive Care Med 2013;39(5):934-41.
13. Taylor ML, Carmona F, Thiagarajan RR, et al. Mild postoperative acute kidney injury and outcomes after surgery for congenital heart disease. J Thorac Cardiovasc Surg 2013;146: 146-52.
14. Sethi SK, Goyal D, Yadav DK, et al. Predictors of acute kidney injury post-cardio-pulmonary bypass in children. Clin Exp Nephrol 2011; 15:529-34.
15. Bellomo R, Auriemma S, Fabbri A, et al. The pathophysiology of cardiac surgery-associated acute kidney injury (CSA-AKI). Int J Artif Organs 2008;31:166-78.
16. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int 2007;71:1028-35.
17. Che M, Li Y, Liang X, et al. Prevalence of acute kidney injury following cardiac surgery and related risk factors in Chinese patients. Nephron Clin Pract 2011;117:c305-11.
18. Kociol R, Rogers J, Shaw A. Organ cross talk in the critically ill: The heart and kidney. Blood Purif 2009;27:311-20.
19. Zappitelli M, Bernier PL, Saczkowski RS, et al. A small post-operative rise in serum creatinine predicts acute kidney injury in children undergoing cardiac surgery. Kidney Int 2009; 76:885-92.