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Prevalence of Acute Kidney Injury in Pediatric Patients with Congenital Heart Disease Following Open Heart Surgery

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ABSTRACT

Background: Acute kidney injury (AKI) occurs in approximately 40% of children undergoing cardiac surgery and is a risk factor for morbidity and mortality. Such injury leads to several complications, including fluid and electrolyte disturbances.

Objective: To determine prevalence of acute kidney injury in pediatric patients with congenital heart disease following open heart surgery.

Patients and Methods: We conducted a case control study on 20 patients with congenital heart disease (10 males and 10 females) with mean age of 3.39 ± 1.17 years old, and a range from 1 to 5 years old. They were recruited from Pediatric Cardiothoracic Unit, Zagazig University Hospital and 20 sex and age matched healthy children worked as control group.

Results: The mean age of our patients was 3.39 ± 1.17 years old with a range from 1 to 5 years. 50% were males and 50 % were females with no statistically significant difference between both groups regarding age and sex. about 1/3 of the studied group had ASD (30 %), while 1/4 of them had Fallot tetralogy (25 %), and only 15% of them had VSD, subaortic membrane and PM + VSD. The mean serum creatinine level was 0.8 ± 0.15mg/dl, with a range from 0.22 - 0.9 mg/dl. 70% of the patients had no acute kidney injury, 15% developed AKI stage 1 and 15% developed stage 2 AKI. In addition, all patients with AKI needed dialysis.

Conclusion: Present study identified that high percentage of pediatric patients with congenital heart disease following open-heart surgery developed acute kidney injury.

Keywords: Prevalence, AKI, Congenital heart disease, Cardiac surgery.

INTRODUCTION

Congenital heart malformations are one of the most prevalent birth defects that accounts for one third of children with birth defects. Its prevalence is about 8 – 10 cases per 1000 births. Ventral septal defect (VSD) is the most important defect with an estimated prevalence rate about 40 % of the congenital heart diseases (CHD). The majority of those defects are isolated cardiac anomalies while there is still 20 % who have more than one cardiac defect [(1)]. Surgical correction of these CHD is the GOLD STANDERED to avoid the serious unwanted implications of these lesions on patient-associated morbidity & mortality and thus improves quality of life and life expectancy to those patients [(2)].

Acute kidney injury is a common and serious complication of cardiothoracic surgery. In cardiac surgery patients, postoperative increases of serum creatinine of 20–25% from preoperative baselines are associated with increased morbidity and mortality [(3, 4)]. The development of acute kidney injury is one of the risk factors for negative hospital outcomes for patients who undergo cardiac surgery. Intense contemporary research has been directed toward validating other biomarkers to predict acute kidney injury earlier than is feasible with acute changes in serum creatinine. The best global index for renal function is GFR, which can be estimated using inulin clearance, (51Cr-EDTA), iohexol, serum creatinine value. However, there is a need to develop early biomarkers of acute kidney injury following cardiac surgery, where morbidity and mortality are increased by its presence [(5)].

The study aimed to determine prevalence of acute kidney injury in pediatric patients with congenital heart disease following open-heart surgery.

PATIENTS AND METHODS

A) Site of the study: This study was carried out in Pediatric Cardiothoracic Unit, Zagazig University Hospital.

B) Type of study: Cross sectional comparative study.

C) Sample size: Assuming that the total population size of children under open-heart surgery is 30 patients in the study period (6 months) and predictive value positive of Cystatin C in detection of AKI is 95 %, so the sample size is 20 patients and 20 healthy matched controls.

D) Target population: Patients diagnosed with congenital heart diseases (CH D) in Pediatric Department, Zagazig University Hospital (ZUH) who will undergo open heart for correction of the defect at cardiothoracic surgery department.

Inclusion Criteria:

- Age > 2 years and <18 years old

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- Children diagnosed with congenital heart diseases and undergoing cardiopulmonary bypass (CPB) at our center for surgical correction or palliation of congenital heart lesions.
- Approval to sign an informed written consent.

Exclusion criteria:

- Age < 2 years & >18 years old.
- pre-existing renal insufficiency (based on age-adjusted normal ranges for SCr),
- Diabetes mellitus
- Peripheral vascular disease
- Use of nephrotoxic agents up to 1 week before or during the study period
- Urgent cases
- Refusal of the parents to sign an informed written consent.

Ethical approval:

The study was approved from Institutional Review Board, Faculty of Medicine, Zagazig University. Approval of the study was obtained from Pediatrics Clinical Pathology and Cardiothoracic Surgery Departments of Zagazig University. An informed written consent was taken from patients and/or their guardians.

All patients were subjected to:

(1) Full history taking.
(2) Complete clinical examination.
(3) Routine laboratory investigations including liver functions tests, serum creatinine level preoperative and at 6 hours and 24 hours postoperative and echo (preoperative and postoperative).

Statistical analysis:

The collected data were analyzed by computer using Statistical Package of Social Services version 24 (SPSS). Data were represented in tables and graphs. Continuous quantitative variables e.g. age were expressed as mean ± SD & median (range). Categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). Independent student's T test was used to compare between two groups of normally distributed data. Paired t test was used to compare between two groups before and after therapy. Categorical data were compared using Chi square t tests. Suitable statistical tests of significance were used after checked for normality. The results were considered statistically significant when the significant probability was equal or less than 0.05 ($P \leq 0.05$). P-value < 0.001 was considered highly statistically significant (HS), and P-value > 0.05 was considered statistically insignificant (NS).

RESULTS

This table showed that the mean age of the studied cardiac group was 3.39 ± 1.17 years old, with a range from 1 to 5 years old. Half of the studied group were males, and 50 % were females. Age of control group ranged from 2- 6 years old, with no statistically significant difference between both groups regarding age and sex (Table 1).

Table (2) showed that the mean weight of the studied children was 14.04 ± 2.12 kg. About 1/3 of the studied group had atrial septal defect (ASD) (30 %), while 1/4 of them had Fallot tetralogy (25 %), and only 15% of them had VSD, subaortic membrane and PM + VSD.

Table (3) showed that the mean pre-operative creatinine value was 0.8 ± 0.15 mg/dl, with a range from 0.22 - 0.9 mg/dl. The mean pre-operative hemoglobin level among the studied patients was 12.33 ± 1.25 gm/dl, with a range from (11-16 gm/dl).

Table (4) showed that the mean 6 hrs postoperative creatinine was 0.85 ± 0.16 mg/dl, with a range from 0.24-1 mg/dl. The mean 6 hrs postoperative hemoglobin level among the studied patients was 10.95 ± 0.86 gm/dl, with a range from 10-13.5. In addition, the mean of 24 hrs postoperative creatinine level was 1.14 ± 0.27 mg/dl, with a range from 0.75-1.6 mg/dl. The 24 hrs postoperative mean value of hemoglobin level among the studied patients was 11.5 ± 1.57 gm/dl, with a range from (8-14 gm/dl).

Table (5) showed that the mean creatinine level was significantly increased by 6.25% and 42.5% after 6 hrs and 24 hours postoperative respectively.

Table (6) showed that cardiopulmonary bypass time ranged from (13-65 min) and its mean value was 31.10 ± 16.47 min. In addition, the mean of ischemic time was 17.55 ± 14.17 min, with a range from 7-55 min.

Table (7) and figure (1) show that about 1/3 of the studied patients (30 %) developed acute kidney injury and needed kidney dialysis. Figure (1) showed that 70% of the studied cardiac children had no acute kidney injury, 15% developed AKI stage 1 and 15% developed stage 2 AKI.

Table (1): Demographic data of the studied children (N=40)

Demographic data	Cases children (N=20)		Control (N=20)		est	-value
	No.	%	No.	%		
Age (years)						
Mean ± SD	3.39 ± 1.17		3.53 ± 1.06		193.00	0.858 (NS)
Median (Range)	3.65 (1.0-5)		3.5 (2-6)			
Sex						
Male	10	50.0	8	40.0	0.404	0.751 (NS)
Female	10	50.0	12	60.0		

Chi-square test Mann-Whitney test P value < 0.05 is significant NS: Non significant

Table (2): Present history and clinical picture of the studied children.

Item	Studied children (N=20)	
	No.	%
Weight (Kg)		
Mean ± SD	14.04 ± 2.12	
Median (Range)	13.5 (10-18)	
Cardiac defect		
ASD	6	30.0
VSD	3	15.0
Fallot tetralogy	5	25.0
PM + VSD	3	15.0
Subaortic membrane	3	15.0

Table (3): Preoperative characteristics among the studied cardiac children.

Item	Studied children (N=20)
enal function tests	
Creatinine (mg / dl)	
Mean ± SD	0.80±0.15
Urea (mg / dl)	
Mean ± SD	19.8 ± 1.47
iver function tests	
LT (IU / L)	
Mean ± SD	22.21±5.44
ST (IU / L)	
Mean ± SD	29.14±1.2
lbumin (gm/dl)	
Mean ± SD	4.11±0.44
emoglobin (gm/dl)	
Mean ± SD	12.33 ± 1.25
NR	
Mean ± SD	1.01 ± 0.11
level (mequ/litre)	
Mean ± SD	3.36 ± 0.94

Table (4): Post-operative characteristics after 6 and 24 hours among the studied cases

hrs. Postop. CCC		24 hrs. Postop. CCC	
ariable	**Studied children (N=20)**	**variable**	**Studied children (N=20)**
Renal function tests			
S. Creatinine (mg / dl)			
ean ± SD	0.85 ± 0.16	ean ± SD	1.14 ± 0.27
S. Urea (mg / dl)			
ean ± SD	22.7 ± 3.65	ean ± SD	31.9 ±1.12
Liver function tests			
LT (IU / L)			
ean ± SD	74.16 ± 4.64	ean ± SD	21.24 ±41.3
ST (IU / L)			
ean ± SD	119.59 ± 6.5	ean ± SD	95.39 ± 8.8
Albumin (gm / dl)			
ean ± SD	3.27 ± 0.1	ean ± SD	8.15 ± 1.45
Hemoglobin (gm/dl)			
ean ± SD	10.95 ± 0.86	ean ± SD	11.5 ± 1.57
INR			
ean ± SD	1.29 ± 0.22	ean ± SD	1.38 ± 0.09
K level (mequ/litre)			
ean ± SD	4.17 ± 1.41	ean ± SD	3.9 ± 1.32

Table (5): Percentage of change in renal function test among the studied cardiac patients

Renal function test	Preoperative	6 hours Postoperative	24 hours Postoperative	% of change Pre- post 1	% of change Pre-post 2
S. Creatinine					
Mean ± SD	0.80 ± 0.15	0.85 ± 0.16	1.14 ± 0.27	↑ 6.25%	↑ 42.5 %
Median (Range)	0.80(0.22-0.9)	0.87(0.24 -1)	1.0(0.75-1.6)		
‡p-value 1	0.000*				
#p-value 2	Ref	0.001*	0.001*		
	-------	Ref	0.003*		

‡ P1: p-value of Freidman # P2: p-value of Wilcoxon signed rank test Significant: P-value < 0.05

Table (6): Operative characteristic among the studied cardiac children

Item	Studied children (N=20)
Cardiopulmonary bypass time (min)	
Mean ± SD	31.10 ± 16.47
Ischemic time (min)	
Mean ± SD	17.55 ± 14.17

Table (7): Acute kidney injury among the studied cardiac children

Item	Studied children (N=20)	
	No.	**%**
Stage of acute kidney injury		
No	14	70.0
Stage 1	3	15.0
Stage 2	3	15.0
Dialysis		
No	14	70.0
yes	6	30.0

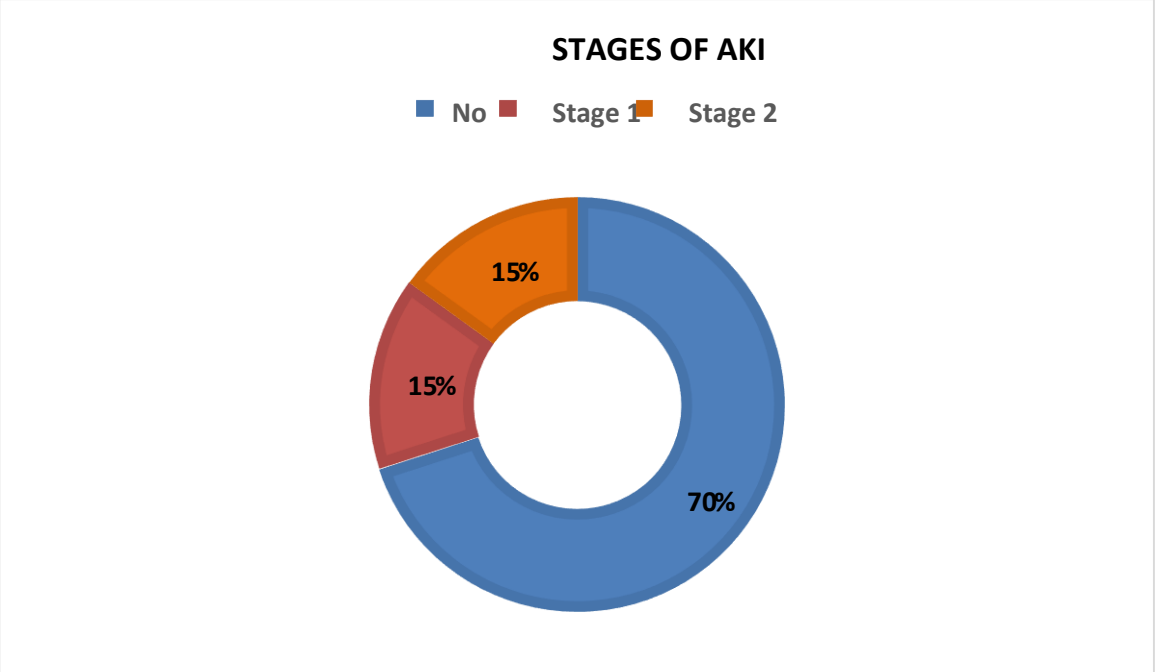

Figure (1): Stage of acute kidney injury among the studied cardiac children

DISCUSSION

The mean age of our patients was 3.39 ± 1.17 years with a range from 1 to 5 years. 50% were males and 50 % were females with no statistically significant difference between patients' group and control group regarding age and sex. about 1/3 of the studied group had ASD (30 %), while 1/4 of them had Fallot tetralogy (25 %), and only 15% of them had VSD, subaortic membrane and PM + VSD. Similarly, **Krawczeski *et al.*** [6] reported in their study on children with congenital heart disease, that the mean age was 1.5 ± 2.9 years in patients who developed AKI and 4.4 ± 5.4 years in patients without AKI with highly statistically significant difference ($p < 0.0001$). In addition, they reported that there was no statistically significant difference regarding sex distribution among their studied groups. In addition, **Zappitelli *et al.*** [5] reported in their study on pediatric population with cardiac surgery that the mean age of the patients was 3.8 ± 4.5 years and there was no significant difference regarding sex distribution (55% of study population were males).

The mean weight of the studied children was 14.04 ± 2.12 kg, which is below 50th centile. This underweight is probably attributed to chronicity of the disease, bad general condition and malnourishment of the children as a result from frequent hospital admission. In the contrary, **Zappitelli *et al.*** [5] reported that the mean weight of their study population was 16.4 ± 17.3 kg (above 50th centile), which is higher than our study and this could be explained by different race of study population and large sample size (228 child).

AKI was defined as the development of at least stage (1) AKI defined by AKI Network (AKIN) as at least a ≥ 50% rise or a ≥ 0.3 mg/dl rise from baseline serum creatinine during hospitalization after cardiac surgery. Stage (2) AKI was defined as a doubling in serum creatinine from baseline. Stage (3) AKI was defined as a tripling in serum creatinine from baseline or receiving acute dialysis during the hospital stay [7]. Stage (1) is at least a 50% SCr rise from baseline within 7 days or a 0.3-mg/dL rise within 48 hours, stage (2) is SCr doubling, and stage (3) is SCr tripling requiring dialysis or an eGFR of less than 35 mL/min/1.73 m^2 at any time.

The Cys C-AKI was defined by applying the Kidney Disease:

Improving Global Outcomes definition but using Cys C change instead of SCr changes similar to what has been done by others.

According to previous definition, serum creatinine rise ≥ 0.3 mg/dl from baseline at 24-hour postoperative denoted stage (1) AKI, while serum cystatin C increased by 80% at 6 hours post-operative. Regarding stages of acute kidney injury, our results revealed that 70% of the patients had no acute kidney injury, 15% developed AKI stage (1) and 15% developed stage (2) AKI. In addition, all patients with AKI needed dialysis. On the contrary, **Greenberg *et al.*** [8] reported that only 3 (11%) of patients with AKI in progression needed dialysis, versus 0% of patients

with no progressive AKI with significant difference (p= 0.001).

Regarding serum creatinine level in our study, at 6 and 24 hours postoperatively, our results revealed that the mean serum creatinine level was 0.85 ± 0.16 and 1.14 ± 0.27 mg/dl with percentage of increase 6.25% and 42.5 % from baseline preoperative level respectively with highly statistically significant difference (P=0.000). Similarly, **Zappitelli *et al.*** [5] reported that First postoperative percent SCr change was also independently associated with the development of stage (1) AKI, but not of stage (2) AKI. When percent SCr change was added to the clinical variable predictive model, AUC was increased by ~ 5% for predicting future stage (1) AKI (P < 0.01), but by only ~ 2% for predicting stage (2) AKI (P = 0.2). When time after surgery (hours) of first postoperative blood sample was controlled for in all analyses, ORs were nearly identical except confidence intervals (CIs) were wider.

Our results revealed that the mean Cardiopulmonary bypass time was 31.10 ± 16.47 min with a range from 13-65 min. The mean ischemic time was 17.55 ± 14.17 min, with a range from 7-55 min. In addition, the mean hospital stay was 2.60 ± 1.5 days ranged from 1-8 days.

CONCLUSION

Present study identified that high percentage of pediatric patients with congenital heart disease following open-heart surgery developed acute kidney injury.

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