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RESEARCH ARTICLE

Association between blood transfusion and serum creatinine as a major risk factor in patients undergoing cardiac surgeries: An observational study

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ABSTRACT

Background: Blood transfusion is associated with altered serum creatinine levels. However, there are not many studies available to substantiate the cause of acute kidney injury (AKI) in patients undergoing cardiac surgeries. **Aims and Objectives:** The present study was aimed to assess and analyze serum creatinine levels, after blood transfusion (post-operative) in patients undergoing cardiac surgery and to assess its significance as a potential diagnostic and prognostic serum biomarker in predicting renal dysfunction. **Materials and Methods:** An observational study was performed after obtaining the Institution's Ethical Committee approval. Patients (n = 162) who underwent cardiac surgeries were considered for the study and were evaluated for alterations in serum creatinine levels and creatinine clearance rate, before (pre-operative) and after blood transfusion (post-operative). Analysis of variance, paired t-test, Chi-square test, and logistic regression test were used. **Results:** Statistically significant difference ($P < 0.0001$) in mean creatinine levels as well as creatinine clearance rate was observed in 70 patients who were at a greater risk of developing AKI (post-operative). Post-operative median creatinine level as well as creatinine clearance rate were also significantly different ($P < 0.001$) in AKI group, compared to non-AKI group. Mean difference between pre- and post-operative serum creatinine, for congenital procedure, was statistically significant ($P < 0.001$). **Conclusion:** Blood transfusion is often associated with altered serum creatinine levels, leading to unfortunate adverse effects of potentially renal dysfunction. Therefore, better blood conservation and anesthetic techniques should be studied upon to prevent excessive bleeding and avoid unnecessary blood transfusion.

KEY WORDS: Blood Transfusion; Creatinine; Acute Kidney Injury; Cardiovascular Risk; Blood Conservation; Anesthetic Techniques

INTRODUCTION

Cardiac surgery is associated with one of the highest rates of blood transfusion and has become one of the leading contributors to acute kidney injury (AKI) which is defined as an increase in serum creatinine ≥50% or >26.5 mmol[1] in patients admitted to intensive care. Acute blood loss or drop in hematocrit, due to hemodilution, is common in cardiac surgery necessitating blood transfusion to improve oxygen delivery to kidneys as well as to other vital organs, with the assumption that it would prevent ischemic injury.[2] However, it is believed that blood transfusion is no longer a benign procedural protocol and has its own clinical implications such as multiorgan failure including AKI in patients undergoing cardiopulmonary bypass. Blood transfusion brings a series of biochemical variations, leading to significant mortality as

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reported in literature – AKI occurs in up to 40% of patients undergoing cardiac surgery.[3]

The incidence of mortality among patients with AKI, after cardiac surgery, was rare (1–5%) in the past, but of late, has known to increase to 8%,[4] and is most often associated with an increase in serum creatinine levels, after blood transfusion; blood transfusion being an underlying pathophysiological factor. Since blood transfusion is a potentially modifiable factor in cardiac surgery-associated AKI, the association between blood transfusion and outcomes in cardiac surgery has been widely investigated.[5]

To date, however, most studies investigating the relationship between blood transfusion and AKI have used creatinine or dialysis as measures of AKI.[6] Serum creatinine is not considered a concrete marker yet for timely diagnosis in AKI due to the effect of several non-renal factors such as fluids, drugs, and muscle metabolism, on serum creatinine levels.[7] Therefore, the primary objective of the present study was to assess and analyze serum creatinine levels, after blood transfusion (post-operative) in patients undergoing cardiac surgery and to assess its significance as a potential diagnostic and prognostic serum biomarker in predicting renal dysfunction.

MATERIALS AND METHODS

Study Design and Setting

An observational study was conducted for a year, from February 2018 to January 2019, in the department of physiology of a tertiary care hospital, to assess the renal functional changes, postoperatively. A total of 162 patients, ranging from 15 to 60 years, following blood transfusion in coronary artery bypass graft (CABG), congenital, and valve surgeries were considered. The study was approved by Institution's Ethical Committee and patients who were willing to participate in the study and had a medical history of valvular diseases, congenital defects, and coronary artery diseases, requiring surgery, were included in the study. Whereas, geriatric patients, neonatal, and infants, as well as those who were reluctant to participate in the study, and were diagnosed with pre-operative renal failure, pre-operative anemia, renal artery stenosis, and allergic to blood transfusion, were excluded from the study.

Data Collection

A predesigned pro forma was used to record data of different parameters, and the intraoperative data were collected by the attending anesthesiologists, perfusionists, and surgeons. After eliciting a demographic and detailed medical history of the patients undergoing various cardiac surgical procedures, the subjects were weighed in standardized machine with minimum of their clothing nearest to 0.1 kg. Height was measured using stadiometer and the body mass index (BMI) was measured using quiet let index.[8] Depending on the various surgical procedures, the blood transfusion data were recorded, and accordingly, the pre-operative data, before blood transfusion, and post-operative data, after blood transfusion, were evaluated and various parameters such serum creatinine levels and creatinine clearance rate were assessed. The creatinine clearance rate was evaluated using the Cockcroft-Gault formula.[9]

Statistical Analysis

Data analysis was done by R i386.3.5.1 statistical software. Data were summarized as mean ± standard deviation for continuous variables and categorical variables were represented using percentages. Comparison of creatinine was done using analysis of variance. Comparison of continuous data was done using paired *t*-test, Mann–Whitney *U*-test and Chi-square test, whereas correlation between age, BMI, and serum creatinine was done using logistic regression. $P < 0.05$ was considered as statistically significant.

RESULTS

The mean age of patients was 41.34 ± 14.74 years. Male predominance was observed with 102 male patients among the total of 162 [Table 1].

From Table 1, a significant association between AKI status and BMI category and AKI and different surgical procedures was observed. The post-operative blood transfusion values showing statistical significance ($P < 0.0001$) in the rise of mean creatinine values and reduction in mean creatinine clearance rate were observed for overall, AKI, and no AKI categories of patients. The analysis also revealed a statistically significant difference ($P < 0.001$) between pre-operative and post-operative blood transfusion values of serum creatinine levels and creatinine clearance rate, in AKI group, compared to no AKI group.

Table 2 suggests that among pre-operative low serum creatinine level patients, 22.73% have high values, postoperatively. Almost 58.97% of pre-operative cases with normal serum creatinine level revealed higher values, postoperatively [Table 2].

An association between pre-operative and post-operative creatinine clearance rate is represented in Table 3. Almost 95.24% of the patients with normal pre-operative creatinine clearance levels were observed to have low rates after surgery. Interestingly, three patients with high pre-operative creatinine clearance rate were observed to have low creatinine clearance rate, postoperatively.

A statistically significant difference for post-operative serum creatinine levels over various groups of pre-operative serum creatinine levels was observed, with the mean difference between pre- and post-operative serum creatinine for low

Table 1: Association between age, height, BMI, and AKI

Factor	Overall *n* (%)	AKI *n* (%)	No AKI *n* (%)	*P*
Gender				
Male	102 (62.96)	44 (43.14)	58 (56.86)	1
Female	60 (37.04)	26 (43.33)	34 (56.67)	
Age (years)	41.39±14.80	44.24±14.62	39.22±14.66	-
Height (cm)	166.06±9.10	164.46±8.78	167.27±9.21	-
Weight (kg)	50.85±11.74	52.04±11.57	49.95±11.85	-
BMI (kg/m^2)				
Underweight	85 (52.47)	37 (52.86)	48 (52.17)	[a]0.0326*
Normal	60 (37.04)	21 (30)	39 (42.39)	
Overweight	17 (10.49)	12 (17.14)	5 (5.43)	
Procedures				
Valve	89 (54.94)	42 (60)	47 (51.09)	[a]0.0369*
Congenital	21 (12.96)	3 (4.29)	18 (19.57)	
CABG	33 (20.37)	15 (21.43)	18 (19.57)	
Others	19 (11.73)	10 (14.29)	9 (9.78)	
Pre-creatinine (mg/dl)	0.96±0.27	0.92±0.29	1.00±0.26	0.1374[b]
Post-creatinine (mg/dl)	1.42±0.45	1.73±0.40	1.18±0.33	0.0001*[b]
Pre-creatinine clearance rate (mL/min)	71.65±24.68	76.17±30.04	68.22±19.12	0.2946[b]
Post-creatinine clearance rate (mL/min)	50.60±20.93	38.84±11.14	59.56±22.21	<0.0001*[b]

*Indicates significance, [a]Chi-square test, [b]Mann–Whitney *U*-test. BMI: Body mass index, AKI: Acute kidney injury, CABG: Coronary artery bypass graft

Table 2: Association between pre- and post-creatinine level

Serum creatinine level*	Post-operative			
	Low (%)	Normal (%)	High (%)	Total
Pre-operative				
Low	0	17 (77.27)	5 (22.73)	22
Normal	4 (3.42)	44 (37.61)	69 (58.97)	117
High	0	3 (13.04)	20 (86.96)	23
Total	4	64	94	162

*Normal serum creatinine range in men and women is 0.7–1.3 mg/dL and 0.6–1.1 mg/dL, respectively

Table 3: Association between pre- and post-creatinine clearance level

Creatinine clearance rate*	Post-operative			
	Low (%)	Normal (%)	High (%)	Total
Pre-operative				
Low	136 (98.55)	1 (0.72)	1 (0.73)	138
Normal	20 (95.24)	1 (4.76)	0	21
High	3	0	0	3
Total	159	2	1	162

*Normal serum creatinine clearance range in men and women is 97–137 mL/min and 88–128 mL/min, respectively

level as well as normal level creatinine significantly more than high-level pre-operative serum creatinine (*P*adj = 0.0015 and *P*adj = 0.0029), respectively.

Furthermore, the mean difference in pre- and post-operative serum creatinine, between different categories of BMI, was statistically insignificant. However, the mean difference between pre- and post-operative serum creatinine [Table 4] for congenital procedure was statistically significant than CABG and valve procedures (*P*adj = 0.0367 and *P*adj = 0.0369), respectively.

From Table 5, using logistic regression, we infer that factors such as age, BMI category, and decrease in creatinine clearance significantly affect AKI status. For 1 unit increase in age, odds of having AKI increase by 1.1141. For underweight patients, odds of having AKI increase by 4.1701 times, as compared to normal subjects, whereas for overweight patients, odds of having AKI increase by 10.7797, as compared to normal subjects. For 1 unit increases in difference between creatinine clearance rates, odds of having AKI are increased by 1.433 times.

DISCUSSION

Variations in the serum creatinine levels after blood transfusion are the most important predictor to identify the presence of AKI in patients undergoing cardiac surgeries. Hence, the present study was conducted to evaluate the effects of blood transfusion on serum creatinine levels and serum creatinine clearance rate and to identify and establish serum creatinine levels as a diagnostic marker for predicting AKI as one of the most serious complications of blood transfusion in patients undergoing various cardiac surgeries.

Table 4: Comparison of difference in pre- and post-operative creatinine over BMI category and different intervention procedures

Pre-creatinine categories	Low	Normal	High	*P*
Post-creatinine	1.13±0.36	1.37±0.37	1.95±0.50	<0.0001
Difference[ǂ]	−0.57±0.42	−0.42±0.36	−0.51±0.49	0.2093
BMI category	Underweight	Normal	Overweight	*P*-value
Difference in creatinine[ǂ]	−0.45±0.40	−0.42±0.37	−0.59±0.39	0.2882
Difference in creatinine clearance rate[ǂ]	22.97±29.27	17.55±19.54	23.77±14.30	0.3863
Different procedures[#]	Valve	Congenital	CABG	*P*-value
Difference in creatinine[ǂ]	−0.47±0.40	−0.24±0.22	−0.51±0.39	0.0007
Difference in creatinine clearance rate[ǂ]	23.24±29.17	18.44±22.25	18.45±14.77	0.5562

[ǂ]Difference: Pre-post, [#]This calculation is done only for 143 patients. Underweight: BMI is <18.5 kg/m^2. Normal weight: BMI is 18.5–24.9 kg/m^2. Overweight: BMI is 25–29.9 kg/m^2. BMI: Body mass index, CABG: Coronary artery bypass graft

Table 5: Factors affecting AKI status

Parameters	Estimate	Odds ratio (confidence interval)	*P*-value
Age (years)	0.1081	1.1141 (1.0571–1.1889)	0.0003*
Sex male	0.6660	1.9464 (0.5601–7.2980)	0.3030
BMI underweight	1.4279	4.1701 (1.1046–18.6067)	0.0444*
BMI overweight	2.3777	10.7797 (1.4218–123.1322)	0.0329*
Difference in creatinine clearance	+0.3600	1.4333 (1.2749–1.6910)	<0.0001*

*Difference is pre-post, BMI-basal metabolic rate. BMI: Body mass index, AKI: Acute kidney injury

According to our study, it was revealed that patients with low and normal serum creatinine levels, before blood transfusion, showed a significant rise in mean of creatinine levels and reduction in mean serum creatinine clearance rate, postoperatively after blood transfusion. This indicated that 70 of 162 patients were at higher risk of developing AKI post blood transfusion, in concordance with the study by Karrowni *et al*.[10] and Khan *et al*.[11] According to their reports, all patients undergoing cardiac surgery and receiving blood transfusion demonstrated a rise in serum creatinine postoperatively, leading to AKI.[10,11] The current study also extends its findings to establish an association between serum creatinine clearance rate and blood transfusion. It was observed that patients with normal serum creatinine clearance levels had low levels of post-operative serum creatinine clearance rate, unlike three patients who had high values of serum creatinine clearance rate, preoperatively and low serum creatinine clearance rate, postoperatively. Similarly, a study by Shlipak *et al*.[12] suggested that for patients undergoing percutaneous coronary intervention, chronic kidney disease is an independent risk factor, with the risk for adverse events increasing with decreasing serum creatinine clearance rate.[13] Our study demonstrated that mean difference between pre- and post-operative serum creatinine, for congenital procedure, was significantly more than CABG and valve procedures, further supported by Oka *et al*.[13] who had evaluated renal dysfunction detection at an early age using Urine albumin-to-creatinine ratio method[13] unlike the Cockcroft-Gault formula used in our study, to arrive at similar observation. The present study also emphasized on the incidence of risk factor, leading to AKI, rising with increasing age, which is in line with the study by Funk *et al*.[14] stating that age affects the prognosis as older patients may be particularly vulnerable to circulatory or ischemic insults of the kidneys.[14] With the decrease in BMI, the creatinine clearance rate decreases, thus, putting the patient at greater risk of renal dysfunction post blood transfusion, in accordance with a study by Ju *et al*.[15] who established that BMI may be one of the predictors for AKI, thus affecting treatment outcome.[16]

Therefore, the novelty of the current study is established through extensive investigation stating that blood transfusion, although a pivotal part of any surgery, causes serious health complications due to alterations in serum creatinine levels, further substantiating the fact that serum creatinine is a useful biomarker which can serve as predictor tests for assessing kidney functions.[17] To further consolidate the current study, further research on alterations in serum creatinine levels and creatinine clearance rate is warranted in post blood transfusion in patients with cardiac disease not undergoing surgery and compared with cardiac patients undergoing surgery, post blood transfusion. This would further establish blood transfusion as the major factor for renal dysfunction ruling out acute trauma as the cause of fluctuations in serum creatinine levels during surgery. Furthermore, a larger sample for a multicentric study can also be undertaken in subjects that are suffering from the same cardiac ailments (such as congenital heart disease patients undergoing valve replacement) to maintain uniformity and better result

outcomes.[16,18] The limitations of this observational study were that the data collected were influenced by unknown confounders such as hemoglobin level and acute trauma during surgery. The study does not mention the association between the volume of blood transfusion and AKI.[19,20]

CONCLUSION

Blood transfusion during cardiac surgery causes an inevitable rise in serum creatinine levels, postoperatively, leading to significant renal dysfunction with AKI being a potentially fatal complication. Thus, blood transfusion during various surgical procedures often presents with unavoidable complications with significant morbidity and mortality and, therefore, should be judiciously used with meticulous anesthetic techniques.

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