

## ORIGINAL ARTICLE

## Perioperative Anemia, Gender, Blood Transfusion and Urine Output during Cardiopulmonary Bypass: Risk Factors for Acute Kidney Injury

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## ABSTRACT

**Objective:** The aim of current study was to find out the factors causing Acute Kidney Injury (AKI) in the postoperative period of cardiac surgery. This prospective study, Peri-operative Anemia, Urine Output, Gender, need for Intra-operative blood transfusion were analyzed for association of AKI.**Material and Method:** The study was conducted at Cardiac Center, QAMC Bahawalpur from January, 2019 to June, 2021. A total of 180 patients who underwent cardiopulmonary bypass for IHD and Valve surgery were studied. CPB hemoglobin levels, Blood Transfusion in OR, Gender specificity, Peri-operative urine output (Group 1 UO <4ml/kg/hr; Group 2 UO > 4ml/kg/hr) were correlated to establish their relationship in causing post-operative Acute Kidney Injury. The patients were divided into two groups one who had Acute Kidney Injury other who don't.**Results:** Acute kidney injury developed in 20 out of 180 patients, current study showed insignificant relation between CPB time, X clamp time, Gender, Surgery type, MAP and Postoperative Acute Kidney Injury. Acute Kidney Injury was more associated with diabetes, need of blood transfusion, perioperative hemofiltration and reduced urine output.**Conclusion:** Current study showed that Acute Kidney injury is an avoidable complication if hemoglobin levels are kept above 8-9 gm/dl to ensure proper oxygen supply and need of Intraoperative hemofiltration and BT is reduced by reducing circuit length thus hemodilution and found a urine output less than 4 ml/kg/hr during cardiopulmonary bypass carries major risk for AKI.**Keywords:** AKI Acute Kidney injury CPB Cardiopulmonary bypass UO urine output MAP Mean Arterial Pressure

## INTRODUCTION

Acute kidney injury in the postoperative period is a major causative of increase in morbidity and mortality among cardiac surgery patients. AKI in the post on pump cardiac surgery varies from 3% - 48%. The prevalence varies with the type of cardiac correction such as 2.5% in CABG, 2.8% in valvular, 1.0% in ASD and VSD, and 4.6% in CABG + valvular surgery. The mortality rate of patients with acute renal failure is up to 60% in the post-operative period.

Acute kidney injury is an abrupt loss of kidney function to maintain intracellular and extracellular volume and electrolytes. Determining the risk factors associated with acute kidney injury can boost postoperative recovery and perioperative surgery outcomes. So, identification of those risk factors and initiating timely interventions is crucial in reducing AKI incidence.

Hypoxia because of low hemoglobin, low perfusion pressures and insufficient pump flows can make kidneys more susceptible to acute kidney injury. As each kidney receives 20% of cardiac output with each heart beat so reduction in oxygen carrying capacity of blood and low renal perfusion pressure will ultimately results in renal hypoxia leading to tubular necrosis and renal infarction.

A blood flow of maintaining cardiac index 2.0 – 2.4 l/min/m<sup>2</sup> or 2.5 – 3 l/min/m<sup>2</sup> with perfusion mean pressure > 50 mmHg provide adequate kidney perfusion. Mean pressure is associated with postoperative AKI, increase creatinine levels and reduced GFR. Renal Blood flow is positively correlated to mean arterial pressure during hypothermia and non-pulsatile cardiopulmonary bypass. Patients risk for Aki increases with each 10mmHg reduction in mean pressure<sup>(1)</sup>

Perioperative Red Blood cell transfusion proposes a proportional relation with acute kidney injury in cardiac surgery. It accounts for 1.6% AKI incidents in patients with no preoperative anemia and 4.0% in preoperative anemic patients. Red blood cells are estimated to undergo irreversible biochemical and structural abnormalities which can reduce tissue oxygen delivery capacity, induce a pro-inflammatory condition and worsen tissue oxidative stress. With increase in pints of RBC transfusion the incidence of

AKI also increases proportionally. In patients with blood transfusion in patients with no preoperative anemia Aki was 3.2% as compared to those who were not transfused 1.7%. In Patients with preoperative anemia, in non-transfused Aki was 1.8% as compared to transfused patients 6.6%.<sup>(2)</sup>

Women are considered more prone to acute kidney injury because of their probation to anemia and needs of blood transfusion in the perioperative period. But very few studies have been done to confirm this relation. Few studies have demonstrated greater tolerance in women to hemodilution than men and greater incidence of AKI 9.2% in males as compared to 7.8% in females.<sup>(3)</sup>

Low Urine output volume is often considered to be associated with acute kidney injury. It is also considered to indicate AKI more prior than serum creatinine. But there are few researches advocating this consideration. Renal tubular reabsorption dysfunction and nephron function heterogeneity can paradoxically improve urine output. Moreover tubular damage due to inflammatory and thrombotic response during cardiopulmonary bypass can also increase urine output.

In order to access these factors relation with acute kidney injury in the Pakistani population we decided to conduct a randomized prospective study.

## MATERIAL AND METHOD

This randomized prospective study was conducted at the department of cardiac surgery of Cardiac Center, QAMC, Bahawalpur from January 2019 to June 2021. Written Informed consent of the patients enrolled in the study was taken in the Preop Room. Approval was obtained from the ethical committee. Out of total 200 patients only 180 patients undergoing cardiopulmonary bypass for cardiac surgery of both genders between ages 18-70 years were selected using non-probability purposive sampling technique. Patients with chronic kidney disorder n= 0, LVEF < 30% n=8, off pump cabg n = 4, Reopening within 72 hours n = 3, Patient expired within 48 hours n=3, and below and above the age n = 2 and were excluded.

Patients Demographic data (Age, Gender), Cardiovascular related risk factors (Hypertension, Diabetes, Smoking, Hepatitis),

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LVEF, Surgery type, Preoperative Urea, Creatinine, Creatinine clearance and Glomerular filtration rate, Hemoglobin levels, urine output were recorded. Intraoperative Blood Pressures, Hemoglobin levels, CPB time, X clamp time, Urine output, Hemofiltration and RBC transfusion was recorded. Post-operative Urea, Creatinine, Glomerular filtration rate and Creatinine clearance was also recorded.

Patients who had >1.5 % increase in urea and creatinine value in the early post-operative days were considered to have Acute Kidney Injury. Rife criteria was used to classify the patient extent of renal injury and factors were studied for 4 consecutive days.

**Management of Anesthesia and Cardiopulmonary bypass:** All patients were given 0.25 mg alprazolam before surgery day. Standardized general anesthesia based on hospital protocols was provided to all patients. Acuron and Nalbin boluses were given during surgery for muscle relaxation and general anesthesia. On re-warming, Isoket infusion was started for effective heat distribution and maintaining pressure, ECG changes in the ischemic-reperfusion period. A calculated dose of heparin 300 iu/kg was given before initiation of CPB. CPB was started when ACT crossed threshold value of 480 sec. Non pulsatile flow utilizing roller pump was used to conduct CPB. The circuit was primed with 1100 ml normal saline, 100 ml mannitol, 40 mEq bicarb and 5000 iu heparin was added. Pump flows were calculated by multiplying Bsa with CI 2.4l/min/m<sup>2</sup>. Mean pressure were kept between 60-80 mmHg. Heparin was reversed by titrating it with protamine. After surgery patients were shifted to ICU and standard postoperative care was provided.

## RESULTS

Only elective surgeries were performed, among 180 patients 20 patients had elevated urea and creatinine values on 3<sup>rd</sup> and 4<sup>th</sup> day. Thus, these patients were considered to have Acute Kidney Injury. Preop Urea values between both groups were statistically similar (P=0.06). Postoperative values of urea on day 3 and day were statistically more in AKI group (P=0.03) and (P=0.02) respectively. Preop serum creatine values between both groups were statistically insignificant. (P=0.377). Postoperative values of Serum creatinine from day 1 were statistically more in AKI group than Non AKI group Day1 (P=0.000), Day 2 (P=0.001), Day 3 (P=0.003) and Day 4 (P=0.02). There was no significant relation was found between preoperative GFR and AKI. (P=0.667). Preop creatinine clearance was statistically insignificant related to AKI. (P=0.663).

Table 1: The Demographic Variables

		AKI (-)	AKI (+)	P-value
Age		47± 14	57± 7	0.425
Gender	Male	101	16	0.213
	Female	59	4	
Hypertension	Yes	34	6	0.212
	No	126	14	
Smoker	Yes	12	3	0.316
	No	148	17	
Diabetes	Yes	37	13	0.001
	No	123	7	
Hepatitis	No	149	17	0.056
	HCV	0	2	
	HBV	11	1	
EF	30-45%	23	7	0.061
	46-60%	76	8	
	61-75%	61	5	

CPB time was 107±37 min in Group 1 and 131± 29 in Group 2 patients (P= 0.65). Cross clamp time 69± 26min in Group 1 and 80 ± 20 min group 2, Mean Arterial Pressure, Body temperature during CPB were similar between both groups. MAPs kept during CPB were 64.9±5.9 mmHg in group 1 and 66.4 ± 6.6 mmHg in group 2 (P=0.62) proved to be renal protective Hemoglobin value among both AKI and Non AKI groups were also same in preop and

intraoperative period. Periop Hb 9.4 ± 1.8 gm/dl and 8.9 ± 2.1 gm/dl (P= 0.09) was not in correlation with AKI. Need of blood transfusion and Hemofiltration was statistically higher in AKI group as compared to other group.

Urine output during cardiopulmonary bypass was similar in both groups but those patients having urine output less than 4ml/kg/hr (P=0.026) had more AKI complication in the post-operative period as compared to those who had greater than 4ml/kg/hr urine output

Table 2: Comparison of urea, creatinine, GFR and creatinine clearance

	AKI (-)	AKI (+)	P-value
Preop Urea	32± 8.7	46±14	0.06
Day1	48± 15	70 ± 17	0.069
Day 2	52± 14	61 ± 9	0.089
Day 3	54±20	70 ± 11	0.03
Day 4	44± 17	71 ± 13	0.02
Preop S.Creatinine	0.85 ± 0.38	1.2 ± 3.8	0.377
Day 1	0.86 ± 0.26	1.25 ± 0.33	0.000
Day 2	1.0 ± 0.31	1.7 ± 0.36	0.001
Day 3	1.2 ± 0.55	2.0 ± 0.55	0.003
Day 4	1.2 ± 0.76	2.0 ± 0.60	0.02
Preop GFR	90 ± 0.27	66 ± 28	0.667
Postp GFR	65 ± 22	33 ± 11	0.113
Prep Cr. Clearance	91 ± 29	74±/-26	0.663
Postop Cr. Clearance	69 ± 24	38±/-12	0.215

Table 3: Correlation of intraoperative factors with AKI

	AKI (-)	AKI (+)	P-value
CBP Time	107 ± 37 min	131 ± 29 min	0.963
X.C Time	69 ± 26 min	80 ± 20 min	0.613
B.T	Yes	18	0.01
	No	142	
Hemofiltration	Yes	59	0.017
	No	101	
MAP	64 ± 5 mmHg	66 ± 6 mmHg	0.768

Table 4: Correlation of Urine Output with AKI.

	AKI (-)	AKI (+)	P-value
Periop U.O	818 ± 414	633± 413	0.06
4ml/kg/hr	26	14	0.026
4ml/kg/hr	134	6	0.563

Table 5: Correlation Between Surgery Type And AKI

	AKI (-)	AKI (+)	P-value
CABG	104	16	0.200
MVR	36	2	
AVR	5	2	
Septal Defect	9	0	
DVR	5	0	
CABG+AVR	1	0	

## DISCUSSION

Postoperative acute kidney injury is associated with prolong hospital stay of patients. Low hemoglobin levels achieved during CPB due to prime volumes and CPG crystalloid volume affects oxygen supply to kidneys as well causing renal hypoxia, our intra-operative Hb values of 8.9, 2.1 showed renal protective properties which were not in line with the research of Ranucci et al (5) who showed mini mulhematocrit value <25 % were associated multiple organ dysfunctions, including cerebral, renal dysfunction. Karkouti k and coworkers (6) demonstrated an increased risk of abrupt kidney dysfunction when the values of the minimum hematocrit on CPB were either <21% or >25, in their research threshold lowest hematocrit level was 21%, our research showed opposite results with a reduce incidence rate when hemoglobin levels kept around 8.9 ± 2.1. Hemofiltration is associated with reduction in incidence of AKI but our study showed quite opposite results with more early postoperative AKI incidence in patients who require hemofiltration which was not in accordance to the research performed by Martin Friedrich et al who showed hemofiltration was associated with reduction in hemodilution, Blood transfusion need and thus

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reducing intravascular hemolysis. Blood transfusion is associated with increased risk of acute kidney injury as stored erythrocytes undergo various biochemical and morphological changes and can impair tissue oxygen delivery, promote inflammatory state and worsens tissue oxidative stress and our research is in accordance with the research performed by K. Karkouti et al<sup>(5)</sup> who also proved similar results. Both men and women are prone to deleterious effect of CPB showed no significance difference as it was shown in the research of Rajendra H Mehta et al<sup>(6)</sup> who showed a lower incidence of Aki in females.

Low urine output during cardiopulmonary bypass is an indicator of reduced renal perfusion and postoperative acute kidney injury as founded by Mehmet Yilmaz et al,<sup>(12)</sup> current research showed increase incidence of AKI in patients with urine output < 4ml /kg/hr. Young Song et al<sup>(13)</sup> also found relation between low urine output and Aki.

### CONCLUSION

Acute kidney injury is an avoidable illness after cardiopulmonary bypass if the preventive conditions are followed strictly. Reduction in the need of blood transfusion and keeping hemoglobin values above 8-9gm/dl, MAP above 65 mmHg are associated with the reduction in AKI incidence. Adequate urine output is proven to be renal protective in our study. As our study was consistent on patients operated in a single center and a sample population, it was limited by such factors.

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