

Profile of Acute Kidney Injury in Patients Undergoing Cardiac Surgery with Use of Cardiopulmonary Bypass Machine



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ABSTRACT

Introduction: Acute kidney injury (AKI) is a well-known serious complication of cardiopulmonary bypass (CPB) surgery and one of the significant risk factors for mortality, prolonged hospital stay, and additional cost. Patients having preexisting kidney dysfunction are more likely to develop AKI in the perioperative period. The complexity of CPB surgery often leads to AKI. Mechanisms of AKI include kidney hypoperfusion due to low-pressure blood flow. The nonpulsatile perfusion of the kidney, hypothermia, and inflammatory milieu, which causes afferent arteriolar constriction, contribute to AKI. The early postoperative period is characterized by a low cardiac output state, which gradually surpasses kidney compensatory mechanisms and filtration reserve. Various indigenous and infused vasopressors cause markedly elevated afferent arteriolar resistance, leading to a drop in glomerular filtration rate (GFR). Several studies have assessed the value of risk factors and their association with AKI after cardiac surgery. The evidence was mixed, with some showing a positive association. With an aim to clarify this relationship further, especially in the Indian population, we tried to study the incidence and clinical profile of AKI and its correlation with functional and clinical outcomes. We also tried to look for any diagnostic markers of AKI in the setting of cardiac surgery.

Methodology: The study was conducted among patients attending the Department of General Medicine and Cardiology at a tertiary care hospital in Delhi. It was a prospective longitudinal observational study conducted between March 2022 and February 2024.

Around 200 patients underwent cardiac surgery using a cardiopulmonary bypass machine at the study center during the study period. History, including comorbidities such as transient ischemic attacks, previous stroke, coronary artery disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and complete physical examination, were recorded. Patients were followed up preoperatively and postoperatively up to day 28. Preoperative details such as hemoglobin, serum creatinine, blood transfusion, and urine output were recorded. Intraoperative details such as duration of surgery, ACC (aortic cross-clamp) duration, hypotension, vasopressor use, and re-exploration were recorded. Postoperative findings such as urine output and serial kidney function tests on day 3, day 7, and day 28 were documented.

Results: Among 200 subjects, 99 patients had hypertension, and 70 patients developed AKI. Older age (>60 years) was significantly associated with AKI (*p*-value 0.04367). Comorbid conditions such as T2DM, hypertension, dyslipidemia, and COPD were significantly associated with AKI as compared to those without comorbidities (Chi-squared test, *p*-value < 0.0001). In the study, there was no association between the type of surgery and the development of AKI (Chi-squared test, *p*-value 0.07). There was no relationship between AKI severity and cardiopulmonary bypass (CPB) duration. Similarly, there was no association between the severity of AKI and ACC duration. Intraoperative hypotension was significantly associated with AKI. About 53% of hypotensive patients developed AKI during surgery as compared to 19.44% of normotensive patients (*p*-value < 0.0001, Chi-squared test). AKI was linked with a significantly prolonged hospital stay. A prolonged stay of >3 weeks was seen in 8.5% (6 out of 70) of patients who developed AKI as compared to 2.3% (3 out of 130) of patients without AKI. Most patients with AKI (57%) recovered within 1 week, and 24.28% recovered between 1 and 4 weeks. In the study, 8 patients (11.2%) developed acute kidney disease (AKD), and 5 patients (7%) died.

Conclusion: This prospective study concluded that AKI is a common complication in the perioperative period of cardiopulmonary bypass surgery. Older age, comorbid conditions, and intraoperative hypotension were significantly associated with AKI. AKI was linked with extended hospital stay and longer recovery times. Severe grades of AKI were associated with progression to AKD, need for dialysis, and higher mortality. It is imperative to focus on interventions to minimize and address the risk factors to reduce morbidity and mortality associated with AKI in CPB surgery.

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INTRODUCTION

Acute kidney injury (AKI) is regarded as a very important complication of cardiac surgery and one of the important predictors

of mortality. In cardiopulmonary bypass (CPB) surgery, it is a frequently seen complication, and severe AKI increases mortality 3–8-fold, leading to increased hospital stay and

costs of care.^{1,2} Perioperative AKI is the most significant factor for immediate and delayed mortality after CPB surgery.^{3,4} Preexisting renal dysfunction predisposes patients to AKI and poor outcomes.^{5,6} A rise in serum creatinine by 50% in 7 days, >0.3 mg/dL in 48 hours, or oliguria qualifies as AKI as per KDIGO (Kidney Disease Improving Global Outcome). Depending upon the definition of AKI used, the incidence of cardiac surgery-associated AKI (CSA-AKI) varies. The CSA-AKI may be asymptomatic or severe enough to require renal replacement therapy (RRT), which increases operative mortality and length of stay in the intensive care unit and hospital. In cardiac surgery, approximately 20% of patients develop AKI, 1% require RRT, and 8% die within 90 days. The complexity of CPB surgery often leads to AKI. AKI is characterized by low-pressure blood flow leading to renal hypoperfusion. The nonpulsatile perfusion of the kidney, hypothermia, and inflammatory milieu cause afferent arteriolar constriction

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and contribute to AKI. The early postoperative period is also characterized by a low cardiac output state.⁷ When hypotension persists, it gradually surpasses kidney compensatory mechanisms and glomerular filtration reserve. Various endogenous and infused vasopressors cause markedly elevated afferent arteriolar resistance, leading to a drop in glomerular filtration rate (GFR). This may lead to prerenal azotemia with or without oliguria, but tubular function may still be preserved. Persistent ischemia results in structural tubular alterations, causing tubular cell disruption and obstruction of the tubular lumen with back leakage. This is accompanied by oxidative and inflammatory injury, causing worsening of hypoperfusion and further damage to tubular cells. Certain factors may predispose patients to AKI, including age, sex, preexisting cardiac or renal dysfunction, past cardiac surgery, or comorbidities such as obstructive pulmonary disease or poorly controlled diabetes mellitus.⁸ Nephrotoxic drugs may further contribute to AKI. Of particular interest are commonly used medications, for example, painkillers; drugs acting on the renin-angiotensin-aldosterone system; and diuretics, which may impair glomerular afferent and efferent arteriolar autoregulation.⁹ In the setting of normal baseline renal function and uneventful CPB surgery with stable perioperative hemodynamics, the risk of AKI is minimal (<2%). However, the risk of postoperative AKI and overall mortality rises significantly with preexisting renal dysfunction.

A rise in serum creatinine >1.5 mg/dL qualifies as AKI. However, serum creatinine presents several limitations when used as a marker of kidney function. Serum creatinine-based equations are inaccurate at GFR values above 60 mL/minute. In other words, serum creatinine does not rise until >50% of GFR is lost. A better measure of renal function is creatinine clearance, which more accurately predicts glomerular function.¹⁰ A GFR <60 mL/minute/1.73 m² is a better marker of renal dysfunction, and the risk of worsening AKI increases significantly below this level.⁴

The chronic kidney disease epidemiology collaboration (CKD-EPI) equation for estimation of GFR is more accurate at near-normal GFR. It provides better risk stratification of AKI for patients with near-normal renal function undergoing high-risk surgery than the MDRD equation. Even mild renal dysfunction is often linked with adverse renal outcomes and mortality. The risk of AKI increases 4.8 times with each 1 mg/dL increase in serum creatinine. Although severe AKI requiring RRT is infrequent (1–4%), it results in a significant

increase in operative mortality, ranging from 40 to 80%.

RATIONALE OF THE STUDY

It is important to implement all preventive strategies possible to preserve kidney function in the setting of CSA-AKI. Any preexisting renal impairment should therefore alert the physician to look for reversible factors to prevent AKI. Identification and correction of potential risk factors in the perioperative period will optimize renal perfusion and can prevent the complications and mortality associated with AKI following cardiac surgery.

In spite of many previously done studies, there still remains doubt about the predictors of AKI in post-CPB surgery patients. Recent studies showed promising, though not conclusive, evidence of risk factors for AKI as outcome-predictive markers. Several studies have assessed the value of risk factors and their association in the early phases of AKI after cardiac surgery, but not many evaluated the relationship between prognostic markers and functional outcomes.

The findings of most studies were inconclusive, with some showing a positive association. To clarify this issue, especially in the Indian population, we conducted this study to find the incidence and clinical profile of AKI, determine its association and correlation with functional and clinical outcomes, and also look for any prognostic marker.

METHODOLOGY

This study aimed to describe the incidence and clinical profile of AKI in post-CPB surgery with the use of a cardiopulmonary bypass machine and its association with clinical outcomes. Secondary objectives also included the study of risk factors for AKI after cardiac surgery. The study was conducted among patients attending the Departments of General Medicine and Cardiology at a tertiary care hospital in Delhi. It was a prospective longitudinal observational study conducted between March 2022 and February 2024. The study was approved by the institutional ethics committee, IEC registration number 38/1022, dated 22nd July 2022. Informed written consent was obtained from all subjects. Patients older than 12 years of age who underwent cardiac surgery using a cardiopulmonary bypass machine were included in the study. Kidney transplant recipients, donors, patients with end-stage kidney disease requiring maintenance hemodialysis or chronic peritoneal dialysis support, post-CPR patients without immediate return to a communicative state, HIV infection,

body weight <35 kg, nephrotic syndrome with anasarca, long-term corticosteroid therapy, and decompensated liver disease were excluded from the study.

Sample Size

Sample size was calculated for determining the proportion of patients who develop AKI after cardiac surgery by use of cardiopulmonary bypass with a 95% confidence level and 10% precision. Assuming 30% of patients develop AKI after cardiac surgery and a 15% lost-to-follow-up rate, the sample size required for the study was calculated at 96 patients.

Around 200 patients underwent surgery using a cardiopulmonary bypass machine at this study center during the study period. The subjects meeting the study criteria were explained the nature and purpose of the study, and informed consent was obtained. History, including comorbidities such as transient ischemic attack, previous stroke, coronary artery disease, diabetes mellitus, hypertension, and complete physical examination, was recorded. Patients were followed up preoperatively and postoperatively up to day 28. Preoperative details such as hemoglobin, serum creatinine, blood transfusion, and urine output were recorded. Intraoperative details such as duration of surgery, aortic cross-clamp (ACC) duration, hypotension, vasopressor use, and re-exploration were recorded. Postoperative findings such as urine output and serial kidney function tests on day 3, day 7, and day 28 were documented.

Statistical Analysis

Data was analyzed using SPSS version 26. Data was expressed as percentages for categorical variables. The Chi-square test, independent *t*-test, and paired *t*-test were used for analysis. A *p*-value of 0.05 was considered statistically significant for all statistical tests performed.

RESULTS

In this study, 200 subjects underwent cardiac surgery. Baseline characteristics of subjects are shown in Table 1. 70 subjects (35%) developed AKI. The mean age of the study population was 55.2 years, and in those with AKI it was 57 years. Table 2 describes various factors associated with AKI. About 42% of 200 subjects were above 60 years of age. Older age was significantly associated with AKI (*p*-value 0.043). About 48.5% of patients with AKI were older than 60 years, 37.1% of patients were in the 45–59 year age-group, and 11.4% were in the <44 year age-group. About 74.5% of subjects in the study population were males and 25.5% were

females. Among patients who developed AKI, 78.5% were males and 21.4% were females. There was no significant difference in the incidence of AKI between males and females (p -value 0.332).

Comorbid conditions such as T2DM, hypertension, dyslipidemia, and COPD were significantly associated with AKI as compared to those without comorbidities, as shown

in Table 2 (p -value < 0.0001, Chi-squared test). Out of 200 patients, 99 (49.5%) had hypertension, 83 (41.5%) had dyslipidemia, 59 (29.5%) had diabetes mellitus, 13 (6.5%) had chronic obstructive pulmonary disease (COPD), and 47 (23.5%) did not have any underlying comorbidity (Fig. 1). In the AKI group, these figures were 74.2, 65.7, 65.7, 5.7, and 5.7%, respectively.

In the study, there was no association between the type of surgery and the development of AKI (p -value 0.07, Chi-squared

test). There was no relationship between hemoglobin level and the incidence of AKI (p -value 0.49, Chi-squared test for linear trend) when AKI incidence was analyzed in 3 hemoglobin categories: <11 gm/dL, 11–14.9 gm/dL, and >15 gm/dL.

Intraoperative hypotension was significantly associated with AKI. About 70% of patients who developed AKI had a history of hypotension during surgery as compared to 30% of AKI patients who were normotensive (Chi-squared test, p -value < 0.0001). CSA-AKI was linked with a significantly increased hospital stay, as shown in Table 2. The duration of hospitalization among all patients was between 1 and 7 days in 94 (72.3%), 8–14 days in 29 (22.3%), 15–21 days in 4 (3%), and 21–28 days in 3 (2.3%) patients, as compared to 18 (25.7%), 37 (52.8%), 9 (12.8%), and 6 (8%) patients, respectively, in the AKI group. Prolonged stays of 8–14 days, 15–21 days, and 21–28 days were seen in 52.8, 12.8, and 8% of the AKI group as compared to 22.3, 3, and 2.3% in the non-AKI group, respectively (p -value 0.00001).

There was no relationship between CPB duration and the severity of AKI. The mean duration of CPB surgery was 190.6 minutes in those who developed stage 1 AKI as compared to 233 minutes in those who developed stage 2 and stage 3 AKI, but this difference was not significant (Table 3, p -value 0.117, Chi-squared test). Similarly, there was no relationship between the severity of AKI and aortic cross-clamp duration. The mean ACC duration was 118.7 minutes in those who developed stage 1 AKI and 157.8 minutes in those who developed stage 2 and stage 3 AKI (Table 3, Chi-squared test, p -value 0.067).

The recovery time among the AKI patients is shown in Table 4. The duration of recovery in the majority of the 70 AKI patients was between 4 and 28 days. In the study, 8 patients developed acute kidney disease (AKD). The overall mortality rate was 6%. The mortality rate was 7.1% among AKI patients and 5.6% among non-AKI patients. Most patients with CSA-AKI (57%) recovered within 1 week. A total of 17 patients (24.28%) recovered between 1 and 4 weeks. In the study, 8 patients (11.2%) developed AKD, and 5 patients (7%) died.

In the study, 70 subjects with AKI were classified according to KDIGO staging. 60 patients developed stage 1, 6 developed stage 2, and 4 developed stage 3 AKI, as shown in Table 5. AKI resolved in most patients with stage 1 AKI (91.6%, 55 out of 60) as compared to stage 2 AKI (33.3%, 2 out of 6). None of the patients with stage 3 AKI recovered

Table 1: Preop baseline characteristics

	Mean	SD
Age (Yr)	55.5	12.5
Weight (kg)	65.29	11.55
Hb (gm/dL)	13.20	1.55
Platelet (1000/mm ³)	222.79	76.21
Urine output (mL/min)	73.77	11.65
Serum creatinine (mg/dL)	0.84	0.24
Blood urea nitrogen (mg/dL)	14.36	6.23

Table 2: Distribution of AKI according to type of surgery

Type of surgery	Frequency (n = 200)	AKI (n = 70)
CABG	114 (57%)	48 (42.10%)
CABG + valve surgery	13 (6.6)	5 (38.46%)
Valve surgery	44 (22%)	10 (22.72%)
Others	29 (14.5%)	7 (24.13%)
Total	200	70

Table 3: Duration of hospitalization

Duration (days)	AKI (n = 70)	Non-AKI (n = 130)
1–7 days	18	94
8–14 days	37	29
15–21 days	9	4
21–28 days	6	3
Total	70	130

Table 4: Recovery time among the AKI patients (n = 70)

Recovery time (days)	Frequency
1–3 days	6 (8.5%)
4–7 days	34 (48.57%)
8–28 days	17 (24.28%)
AKD	8 (11.42%)
Died	5 (7%)

Table 5: Staging of AKI according to KDIGO among the AKI patients (n = 70)

KDIGO staging of AKI	Outcome at 28 days				
	AKI (n = 70)	AKI resolved (n = 57)	AKI to AKD (n = 8)	Renal replacement therapy requirement (n = 2)	Mortality (n = 5)
Stage 1	60	55	2	0	2
Stage 2	6	2	5	0	1
Stage 3	4	0	1	2	2
Total	70	57	8	2	5

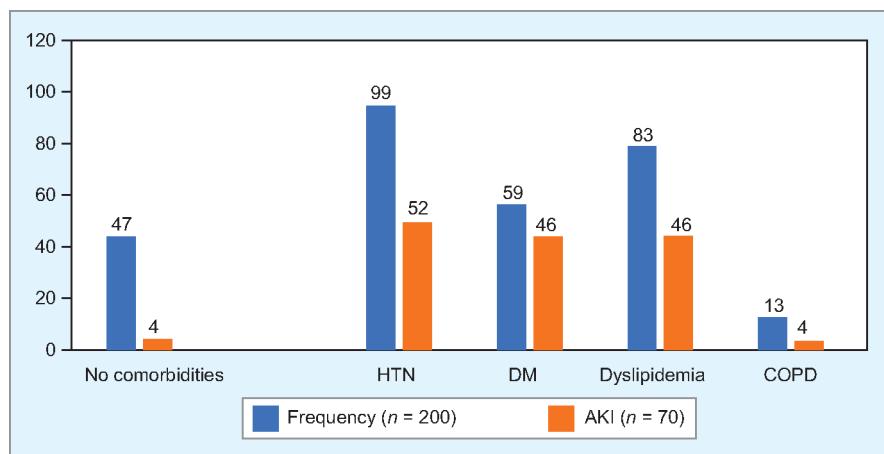


Fig. 1: Column chart showing comorbidity among the AKI patients

renal function (2 died, and 2 required renal replacement therapy).

DISCUSSION

This study describes the incidence and clinical profile of AKI in cardiac surgery from an Indian perspective. CSA-AKI is a common complication following cardiac surgery, including CABG and valve replacement. Previous studies have documented the incidence of AKI in the CABG setting in the range of 7.6–48.5%.¹¹ However, most of these studies were retrospective and used only a rise in serum creatinine rather than a fall in urine output.¹² Prospective data are scarce, particularly from the Indian setting. In this study, 70 subjects (35%) were diagnosed with AKI. The mean age of the study population was 55.2 years, and in those with AKI it was 57 years. Age >60 years was significantly associated with AKI. However, male or female gender was not associated with AKI. In a study by Wittlinger et al.,¹³ the median age in the AKI group was 68 years, 71% were males, and 29% were females. In another study by Karim et al.,¹⁴ the mean age of subjects was 37.01 ± 12.28 years, and female preponderance (57%) was noted. In another study by Hung et al.,¹⁵ 66.2% were males, 33.8% were females, and the mean age of study subjects was 68.6 ± 9.2 years.

The various comorbidities in the study subjects were hypertension, diabetes, dyslipidemia, and COPD. The most common comorbidities associated with AKI in our study were hypertension, diabetes mellitus, and dyslipidemia. The present study findings have similarity with the study by Clough et al.,¹⁶ in which the most common comorbidities among patients undergoing cardiopulmonary bypass were diabetes, hypertension, obesity, COPD, vascular disease, and liver disease. In a study by Patra et al.,¹⁷ common comorbidities were diabetes, hypertension, asthma, and COPD. Oliveira et al.¹⁸ also found that the majority of patients had at least 2 comorbidities, that is, diabetes and hypertension.

In our study, the incidence of AKI was not related to the type of surgery, that is, CABG with or without valve surgery. In a study by Priyanka et al.,¹⁹ 16% of patients with AKI had undergone CABG plus valvular surgery as compared to 1.8% of all patients with or without AKI. This study showed that CABG plus valvular surgery resulted in more AKI as compared to CABG alone. In a study by Gangadharan et al.,²⁰ CABG with valve repair was the most common procedure, followed by valve replacement and repair, in both AKI and non-AKI patients.

In our study, the severity of AKI was not dependent on the duration of CPB or ACC. In a study by Karim et al.,¹⁴ cross-clamp

time among non-AKI patients was 81.44 ± 30.99 minutes and among AKI patients was 64.49 ± 40.24 minutes. However, in a study by Zeng et al.,²¹ the type of cardiac surgery, CPB duration, and ACC duration were all significantly associated with AKI. In a study by Pontillo et al.,²² compared to patients with CPB duration above the median, patients with CPB duration below the median had a significantly lower incidence of AKI.

Intraoperative hypotension was the most important factor associated with the development of AKI in our study. 53% of patients having intraoperative hypotension developed AKI. Intraoperative hypotension is common in cardiac surgery and is a main contributor to the development of AKI. In a study by Patra et al.,¹⁷ 29.8% had intraoperative hypotension. In a study by Jung et al.,²³ the cumulative duration of intraoperative hypotension had a significant influence on the incidence of AKI (OR 1.004; 95% confidence interval (CI) 1.003–1.005; *p*-value < 0.001).

AKI was linked with extended hospital stay. A prolonged hospital stay of >3 weeks was seen in 8.5% (6 out of 70) of patients who developed AKI as compared to 2.3% (3 out of 130) of patients without AKI. In a study by Cheruku et al.,²⁴ AKI was also associated with a significantly higher length of stay in the intensive care unit (5.4 vs 2.2 days) and hospital (15.0 vs 10.5 days).

The mild form of AKI (grade I) recovered in the majority of patients. Severe AKI (grade II and grade III) was associated with progression to AKD, need for dialysis, and increased mortality. Most patients with CSA-AKI (57%) recovered within 1 week. About 24.28% recovered between 1 and 4 weeks. In the study, 8 patients (11.2%) developed acute kidney disease (AKD), and 5 patients (7%) died. A study by Jung et al.²³ showed that the incidence of AKI was 22.3% and the mortality rate was 10.7%. The mean duration of hospital stay was 15 days. Another study by Wittlinger et al.¹³ showed that the incidence of AKI among cardiopulmonary bypass patients was 7% and the mortality rate was 6%. In a study by Thakar et al.,²⁵ postoperative mortality was 5.9% among patients who developed AKI. Mortality across various studies, including our study, was significant and comparable.

CONCLUSION

This prospective study concluded that AKI is common during CPB surgery with a cardiopulmonary bypass machine. Older age, comorbid conditions, and intraoperative hypotension were significantly associated with AKI. AKI was linked with extended hospital stay and longer recovery times. Severe grades of AKI

were associated with progression to AKD, need for dialysis, and higher mortality. It is imperative to focus on interventions to reduce risk factors to minimize morbidity and mortality linked with AKI in cardiac surgery.

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