

Incidence of Contrast Induced Acute Kidney Injury, Its Risk Factors and In-Hospital Outcomes in Patients Undergoing Coronary Angiography and Angioplasty

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ABSTRACT

Introduction

Contrast-induced acute kidney injury (CI-AKI) is a serious complication of angiographic procedures with significant morbidity and mortality. We aimed to find the incidence, risk factors and outcomes of CI-AKI in patients who have undergone coronary angiography/angioplasty in a referral hospital in Nepal.

Methods

It was a descriptive observational study of consenting consecutive patients above 18 years undergoing coronary angiography/angioplasty at Manmohan Cardiothoracic Vascular and Transplant Centre, Nepal from July 2015 to September 2017. CI-AKI was defined as an elevation of serum creatinine of >25% or ≥ 0.5 mg/dl ($44 \mu\text{mol/L}$) from baseline within 48 hour of exposure to contrast. Statistical analysis was performed using SPSS 18 software. Statistical analysis was completed using Student's t-test, chi-square test and multivariable logistic regression analysis.

Results

Out of 240 patients, 156 (65%) were male, mean age was 60.36 ± 11.29 years. Eighteen patients (7.5%) developed CI-AKI. Incidence of CI-AKI was 20% in patients with chronic kidney disease (CKD), 5.4% in diabetics, 13.6% in patients >70 years, 12.79 % in patients with anaemia and 12.3% in patients with prior contrast exposure. Multivariate logistic regression analysis found smoking and history of prior contrast exposure to be independent predictors for development of CI-AKI. Among patients with CI-AKI, one (5.88%) required dialysis and one (5.88%) died.

Conclusion

Incidence of CI-AKI after coronary angiography/angioplasty was 7.5%. Patients with prior contrast exposure and smoking were at significantly increased risk of CI-AKI; higher trend of CI-AKI was seen in patients with CKD, diabetes, elderly and anaemia.

Keywords: *Angiography, angioplasty, contrast induce acute kidney injury, contrast media,, contrast nephropathy*

INTRODUCTION

Nephropathy induced by exposure to contrast agents is associated with significant in-hospital and long-term morbidity and mortality.¹ Patients with pre-existing renal failure are at particularly high risk.^{2,3}

The reported incidence of CI-AKI varies widely. It is low (1–2%) in patients with normal kidney function⁴ and may be as high as 25% in patients with pre-existing renal impairment or in presence of certain risk factors, such as chronic kidney disease (CKD), diabetes, congestive heart failure (CHF), advanced age, and concurrent administration of nephrotoxic drugs.⁵

The most likely cause of CI-AKI is acute tubular necrosis (ATN) secondary to medullary hypoxia.^{6,7} Medullary hypoxia may result from increased viscosity, disturbed balance between nitric oxide, endothelin, and/or adenosine and direct result of the cytotoxic effects of the contrast agents on tubular cells.^{6,9} In patients who develop CI-AKI, greater the increase in serum creatinine, greater is the risk of adverse outcome.¹⁰

Increasing cardiovascular disease burden leads to increase in use of diagnostic and therapeutic cardiac interventions exposing patients to contrast media and the subsequent risk. This study was undertaken to study the incidence of CI-AKI and to identify risk factors (predictors) for its development in patients undergoing coronary angiography / angioplasty and to document the in-hospital outcomes of the same.

Having such data in Nepalese population help in stratifying risks and undertake preventive measures for CI-AKI.

METHODS

It was a cross-sectional descriptive observational study conducted in the Department of Cardiology, Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC), Institute of Medicine (IOM), Nepal. The study was conducted from July 2015 to September 2017 after obtaining ethical approval from the Institutional Review Committee (IRC) of IOM. The sample size was calculated using STATA S.E version 13 with power of 80%. The required sample size was 239. We included 240 patients in the study. Adult patients undergoing angiography and angioplasty and who signed informed consent were eligible for the study.

CI-AKI was defined as a rise in serum creatinine of ≥ 0.5 mg/dl (≥ 44 mmol/l) or a 25% increase from base-line value, assessed at 48 hours after a radiological procedure.¹¹ Anaemia was defined as haemoglobin (Hb) levels < 12.0 g/dL in women and < 13.0 g/dL in men according to World Health Organization (WHO) criteria.¹² Hypertension was diagnosed as blood pressure of $\geq 140/90$ mm Hg

or in a person who was under antihypertensive medications regardless of the observed blood pressure based on the definition by the seventh report of the Joint National Committee diagnosis.¹³ Diabetes was diagnosed as per American Diabetes Association (ADA) criteria¹⁴ if any of the following criteria were met: Fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/L) or Two-hour plasma glucose ≥ 200 mg/dl (11.1 mmol/L) during an oral glucose tolerance test or a random plasma glucose ≥ 200 mg/dl (11.1 mmol/L) in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis or $HbA_1C \geq 6.5$. Smoker was described as a person who had smoked at least 100 cigarettes in lifetime but had quit at the time of interview.¹⁵

All patients undergoing angiography or angioplasty at the treating cardiologist's discretion at MCVTC were enrolled in the study. The relevant baseline clinical and laboratory parameters were recorded. Serum creatinine level was documented at baseline and 48 hours after the procedure. Record was also kept about the volume of contrast used, type of angiographic procedure (i.e. diagnostic or interventional), its findings, post-procedural complications, duration of hospital stay, requirement of dialysis and death due to CI-AKI. Estimated Glomerular filtration rate was calculated using the Modification of Diet in Renal disease (MDRD) equation.¹⁶

Patients who were considered at risk of developing CI-AKI⁵, received hydration in the form of I.V normal saline and oral Acetylcysteine at a dose of 600 mg twice daily prior to the procedure to reduce the subsequent risk of developing CI-AKI.

Continuous variables were presented as mean \pm SD and compared using Student's t test. Categorical variables were presented as counts and percentages and compared with χ^2 -test. A multivariable logistic regression analysis was used to identify independent characteristics associated with CI-AKI. A p value of ≤ 0.05 was considered statistically significant. All data were processed using SPSS version 18.

RESULTS

Out of total of 240 studied patient, 156 (65%) were male and 84 (35%) were female. The mean age of patients included in the study was 60.3 ± 11.2 years. Eighteen (7.5%) patients developed CI-AKI (figure 1). The baseline characteristics of the patients with CI-AKI are shown in the table 1.

The baseline mean serum creatinine of patients without CI-AKI and with CI-AKI was similar (0.981 ± 0.062 mg/dl and 0.993 ± 0.119 mg/dl $p=0.62$). Though CI-AKI group received higher volume of contrast than non-CI-AKI group, the difference was not statistically significant (153.8 ± 5.7 vs $86.9 \pm$

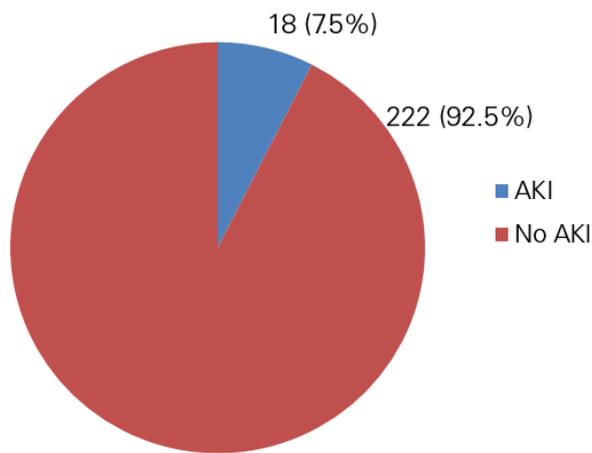


Fig 1. Incidence of contrast induced AKI

Table 1. Baseline characteristics of the study population

Variables	Values
Age (years)	60.3±11.2
Male sex - no. (%)	156 (65)
Systolic BP (mmHg)	134.9±24.4
Diastolic BP (mmHg)	76.9±12.9
Estimated GFR (ml/min/1.73m ²)	90.0±26.7
Hemoglobin (mg/dl)	12.9±2.2
Contrast volume (ml)	156.3±86.3
Hypertension - no. (%)	121 (50.4)
Diabetes Mellitus - no. (%)	74 (30.8)
Chronic Kidney disease - no. (%)	5 (2.1)
Smoking - no. (%)	105 (43.8)
History of contrast exposure - no. (%)	65 (27.1)
Hydration - no. (%)	141 (58.7)
N-acetyl cysteine - no. (%)	43 (17.9)

20.0; p=0.91).

Multivariate Logistic Regression Analysis revealed that the relative risk (RR) for the CI-AKI after exposure to contrast agent was significant for smoking (RR 7.6, 95%, CI 1.06 to 54.9) (p=0.047) and history of prior contrast exposure (RR 7.8, 95%CI 1.6 to 37.7) (p=0.01).

The incidence of CI-AKI was similar for the percutaneous coronary intervention (PCI) and non-PCI group (8.77%vs 4.3% p=0.23).Other risk factors such as age >70years, anemia, diabetes, hypertension, CKD, heart failure were not significantly associated with development of CI-AKI. Similarly, use of hydration and N-Acetyl cysteine (NAC), Left ventricular (LV) function did not significantly impact development of CI-AKI (Table 2).

Of the total patients who developed CI-AKI (18

Table 2. Overall incidence of CI-AKI after coronary angiography/angioplasty

Risk factors	Incidence of AKI		p value
	No.	%	
Age>70 years	7/52	13.6%	0.06
Age<70 years	11/188	5.8%	
Hypertension	9/121	7.4%	0.97
Non-hypertensive	9/119	7.5%	
Diabetes	4/74	5.4%	0.40
Non diabetics	14/166	8.5%	
CKD	1/5	20%	0.28
Without CKD	18/235	7.8%	
Smoker	11/105	11.1%	0.02
Non-smoker	4/135	2.8%	
History of previous contrast exposure	8/65	12.3%	0.047
No previous contrast exposure	10/175	5.7%	
N-acetyl cysteine used	3/43	6.1%	0.07
N-acetyl cysteine not used	27/197	13.9%	
Hydration	12/141	8.51%	0.47
No hydration	6/99	6.1%	
Anaemia	12/97	12.8%	0.06
Non anaemic	7/143	4.89%	
Left ventricular systolic function			0.15
Normal	5/112	4.5%	
Mild LVSD	5/50	8%	
Moderate LVSD	9/69	13.0%	
Severe LVSD	0/9	0	

patients), dialysis support was required in one patient (5.88%) and death occurred in the same patient. In the rest of the patients including the patient with CKD, serum creatinine returned to the baseline value within a week.

DISCUSSION

The risk of CI-AKI may be very high in patients undergoing percutaneous coronary angiography due to presence of multiple risk factors.^{2,3} CI-AKI is the third most common cause of acute renal failure and is responsible for 11% cases of hospital acquired renal insufficiency.¹ The mean age of patients in the present study was 60.36 ± 11.29 years, 65% were male which is similar to a study by Bradley et al.¹⁷

The overall incidence of CI-AKI in our study is 7.5% which is similar to a study by Nough et al.¹⁸ Pre-existing renal functional impairment is the most important risk factor for developing CI-AKI.¹⁹ We observed CI-AKI in 20% of patients with CKD and the

overall mortality rate of 0.41% which is consistent with the finding of the Visipaque Angiography/Interventions with Laboratory Outcomes in Renal Insufficiency (VALOR) Trial²⁰ and study by Weisbord et al.¹⁰ Our study had only five patients with CKD and none of them required dialysis. A study by Freeman et al. showed dialysis requirement in almost 4% of patients with underlying renal impairment.²¹ This difference could be due to small number of patients with CKD in our study who were exposed to contrast agent.

In this study, the incidence of CI-AKI in patients >70 years was 13.46% compared with 5.8% in patients <70 years of age ($p=0.06$). This result is consistent with the study by McCullough et al where age above 70 appeared to be an independent predictor of CI-AKI.² Similarly, in a study by Rich et al the incidence of CI-AKI among the patients 70 years or older was 11%.²² The reasons for this higher risk of CI-AKI are probably multifactorial, including age-related changes in renal function, the presence of multi-vessel disease, and more difficult vascular access requiring relatively large amounts of contrast.

Multivariate logistic regression analysis showed that history of smoking and prior history of contrast administration were independent risk factors for CI-AKI in the study population. Published literature quote smoking as a minor risk factor for CI-AKI.²³ In a human clinical controlled study, smoking and nicotine were accompanied by significant acute changes in renal hemodynamic and albuminuria.²⁴ This could be the possible reason for the increase risk of CI-AKI in patients who smoke.²⁴ The risk of CI-AKI after repeated contrast exposure was evaluated by Trivedi et al²⁵ where significant increase in mean serum creatinine and decline in eGFR after a second exposure was observed with the incidence of CI-AKI of 14.3%. In our study this incidence was 12.3% as compared to 5.74% in patients without prior exposure to the contrast agent. This difference was statistically significant with $p=0.047$. This highlights the importance of minimising repeat exposure to contrast agent. The minimum interval after which patients in our study underwent repeat exposure to contrast was three days.

Anaemia is an established risk factor for the development of CI-AKI. A study by Nikolsky et al.²⁶ found that lower baseline haematocrit was an independent predictor of contrast-induced nephropathy. A study by Dargas and colleagues²⁷ showed lower baseline haematocrit were most significant independent predictors of CI-AKI. In our study the incidence of CI-AKI in patients with anaemia was 12.79% and without anaemia was 4.89% ($p=0.06$). Even though the difference was not statistically significant there is trend towards higher incidence of CI-AKI in patients with anemia at baseline. The combination of contrast-induced

vasoconstriction and anaemia may decrease oxygen delivery sufficiently to cause renal medullary hypoxia and subsequently acute medullary necrosis. Thus Anaemia-induced deterioration of renal ischemia and hypoxia may be one reason for the higher incidence of CI-AKI in anaemic patients.⁷

The beneficial effect of the use of N-acetyl cysteine (NAC) for the prevention of CI-AKI is uncertain.²⁸ In the present study, the incidence of CI-AKI who did and did not receive NAC were 6.09% and 13.95% respectively ($P=0.07$). Based on this finding, the potential benefit of NAC to prevent CI-AKI needs to be further explored in larger randomized well controlled clinical trials.

All patients received low molecular weight contrast media, Iohexol. The volume of contrast agent administered for the CI-AKI group and non-CI-AKI group were similar (153.8 ± 5.7 and 86.9 ± 20.09 ; $P=0.91$). No correlation was observed between the amount of contrast agent administered and the change in serum creatinine. There is a debate whether the quantity of contrast agent predicts the degree of renal dysfunction.^{29,30} However, there is a general consensus on the use of small dose of contrast agent and hence the avoidance of repeated, closely spaced studies (within 48 to 72 hours) represents one of the most important recommendations to prevent CI-AKI.³¹ These preventive measures become even more important when dealing with patients with impaired renal function.

We do acknowledge some of the limitations of this study. Because of its observational design, definite causal relationship could not be established between development of CI-AKI and other variables. The sample size was relatively small. Less number of patients with impaired baseline renal function were exposed to contrast agent in our study. In a few patients, rise in serum creatinine could have occurred after 48 hours¹¹, which might have resulted in underestimation of CI-AKI in our study. Another limitation was the use of MDRD equation for estimating eGFR as its performance is not known in Nepalese population.

CONCLUSION

The incidence of contrast induced acute kidney injury was 7.5% in our study. Smoking and history of prior contrast exposure were independently associated with a higher risk of development of CI-AKI. Age more than 70 years and anaemia appeared to pose higher risk of development of CI-AKI. Use of N-acetyl cysteine could have a role for prevention of CI-AKI.

CONFLICT OF INTEREST

None declared.

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