

# Contrast Induced Nephropathy and its Predictors after Primary Percutaneous Intervention

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## ABSTRACT

**Background:** contrast-induced nephropathy (CIN) is the most common complications associated with contrast media after angiographic procedures. The therapeutic intervention for CIN after the procedure, to date, is not yet conclusive. Therefore, the main reliance for the management of CIN is considered to be adequate assessment of risk-benefit and the preventive strategies. A little research has been done to identify the predictors of CIN in Pakistan.

**Objective:** To assess the incidence and the predictors of CIN in our setting.

**Methodology:** A total of 120 patients of Punjab Institute of Cardiology, Lahore who underwent primary PCI during January to July 2022, were observed to CIN through cross-sectional observational study. The baseline and some postprocedural laboratory findings, angiographic and interventional characteristics were observed on a pre-formed Performa and the data was analyzed using SPSS. Logistic regression analysis was implied to assess the independent predictors of CIN.

**Results and conclusion:** CIN developed in 15% of the patients. LVEF, admission blood glucose, haemoglobin, eGFR, and contrast volume greater than 100 ml were all shown to be linked with CIN in univariate analysis. Age, eGFR, admission serum glucose, diabetes mellitus, and contrast volume more than 100 ml were shown to be independent predictors of CIN in the study participants.

## INTRODUCTION

Intravascular contrast media (CM) is being received by numerous patients during procedures for intervention around the globe. CM are utilised for the enhancement of visualisation and guidance of percutaneous coronary intervention (PCI).<sup>1</sup> The PCI procedures is improved and its effectiveness has increased in patients who receive CM. Nevertheless, there is a range of CM complications from mild symptoms to conditions which are life-threatening.<sup>2</sup> Amongst the complications associated with contrast media after angiographic procedures, one of the most common is contrast-induced nephropathy (CIN) which refers to acute kidney injury that is potentially reversible following iodinated CM.<sup>3</sup> Several studies report CIN incidence between 5 to 25 percent after cardiovascular interventions.<sup>4,5</sup>

CIN is described as either an absolute increase of 0.5mg/dL (44.2 mmol/L) in the concentration of serum creatinine (SCr) or a relative >25% increase from the baseline.<sup>6</sup> Typically, CIN appears clinically in the duration of 3 days of administration of CM, peaks during 3-5 days, and returns to baseline during 10-21 days.<sup>7</sup> Following factors are associated with CIN; longer hospital stay, increased renal replacement therapy risk, recurrent procedures for revascularization and higher mortality.<sup>8,9</sup> CIN can be reversible, however, almost 15 percent of the patients may require temporary dialysis.<sup>10</sup> Patient who need dialysis and develop renal failure after PCI have a in-hospital and 2-yrs mortality rate of 40% and 80%, respectively.<sup>11</sup>

The particular therapeutic intervention for CIN after the procedure, to date, is not conclusive yet. Therefore, the main reliance for the management of CIN, apart from supportive therapy, is considered to be adequate assessment of risk-benefit and the preventive strategies. A number of risk factors have been shown to be associated with CIN which include the dosage and type of CM, inflammation, concomitant nephrotoxic medication, diabetes mellitus, congestive heart failure (CHF), renal insufficiency, low haemoglobin and WBCs count, increasing age and female gender.<sup>12-14</sup> For minimising the risk of CIN development, a crucial step is the identification of the patients who are at risk by the estimation of CIN predictors and subsequently initiating relevant prophylactic measures.<sup>15</sup> A little research has been done to identify the predictors of CIN in Pakistan. Therefore, this study aims to assess the incidence and the predictors of CIN in our setting.

## MATERIAL AND METHODS

The current single-centre cross sectional observational study was conducted in Punjab Institute of Cardiology, Lahore during January-July 2022 including 120 patients who had CAD and underwent primary PCI within the span of 12 hours after symptoms onset. The exclusion criteria for patients included severe infection, pregnancy or breastfeeding, cardiogenic shock, allergy to CM, undergoing treatment for chronic haemodialysis peritoneal dialysis and exposure to CM and nephrotoxic medications during the past 7 days.

All the patients included in the study underwent thorough physical examination and history taking after informed consent. The blood samples were collected at the time of admission to emergency department and tested for WBC count, platelet count, hemoglobin levels, C-reactive protein (CRP), estimated glomerular filtration rate (eGFR), peak and baseline creatinine by the use of standard techniques for biochemical analysis. Lipid profile measurements were taken during initial 24 hours after the fast of ≥ 8 hours. Additionally, levels of cardiac biomarker including creatine kinase-myocardial band (CK-MB) and troponin I were measured at the time of admission and for analysis their peak values were noted. As per the hospital protocols, screening of electrocardiogram and echocardiography was performed before the patient was taken to primary PCI. On all the patients, PCI was performed via femoral artery by the use of iodixanol (320 mg iodine/mL, 290 mOsm/kg water; Vispaque, GE Healthcare Inc., USA) which is an iso-osmolarity, non-ionic contrast medium. The measurement of level of serum creatinine in all patients, was repeated at 48-72 hrs after the exposure of contrast medium. Modified Simpson method was used for the calculation of Left ventricular ejection fraction (LVEF) by echocardiography during 24 hrs after the time of admission. Following details were recorded on pre-designed Performa; personal details, physical findings, required history, laboratory reports, ECG and echocardiography details, procedural details that included used volume of contrast.

All the collected data was statistically analysed after entry by the use of the software IBM SPSS version 20. The qualitative and quantitative variables were represented as absolute frequencies and percentages and as means ± standard deviation, respectively. For categorical variables and continuous variables, chi-square and independent-samples t test were used, respectively to perform comparisons in between groups. Univariate and multivariate logistic regression analysis were performed for the determination of predictors that are independently associated with CIN.

Univariate analysis was used to assess the potential candidate predictor. The variables in univariate analysis found to be associated with CIN were included in a multivariate logistic regression model as covariates. The p-value of <0.05 was considered significant for all results.

**RESULTS**

There were 102 (85%) patients without CIN and 18 (15%) patients with CIN out of a total of 120 patients that were enrolled in the trial. Table 1 summarises the baseline clinical features of study participants with and without CIN. The difference in mean age between the groups (65.9 ± 9.7 vs. 57.8 ± 11.8) was statistically significant (p = 0.006). The group with CIN had a higher mean age. Blood pressure and gender did not statistically differ between the with-CIN group and the without-CIN group. Patients in the CIN group were considerably more likely to have diabetes, hypertension, prior MI and had lower LVEF than without CIN.

Table 1: Baseline characteristics of the patients

Variables	With CIN n = 18	Without CIN n = 102	p-value
Male gender, n (%)	12 (66.6 %)	74 (72.5 %)	0.61
Age (years)	65.9 ± 9.7	57.8 ± 11.8	0.006*
Systolic blood pressure, mmHg	124.8 ± 32.2	128.3 ± 24.4	0.59
Diastolic blood pressure, mmHg	83.1 ± 18.2	77.3 ± 13.4	0.11
Comorbidities, n (%)			
Diabetes mellitus	10 (55.6 %)	21 (21.6 %)	0.002*
Hypertension	13 (72.2 %)	21 (20.6 %)	<0.001*
Smoking	9 (50 %)	40 (39.2 %)	0.39
Hyperlipidaemia	5 (27.7 %)	34 (33.3 %)	0.64
Previous MI	3 (16.7 %)	4 (3.9 %)	0.03*
LVEF, %	36.1 ± 14.1	45.1 ± 19.1	0.05*

\*Statistically significant

Table 2 displays the laboratory, angiographic, and interventional results of study participants in the CIN group and the without CIN group. Basal creatinine and serum glucose levels were greater in the with-CIN group, whilst eGFR, LVEF, and hemoglobin levels were lower. Patients with CIN had substantially higher post-procedural creatinine levels at 48–72 hours than patients without CIN (2.71 ± 1.31 vs. 1.09 ± 0.76, P < 0.001).

Furthermore, between the groups with and without CIN, there was no distinction in terms of ACS type or responsible

Table 3: Univariate and multivariate logistic regression analysis predictors of the postprocedural CIN

Variables	Univariate analysis Odds ratio (95% CI)	p-value	Multivariate analysis Odds ratio (95% CI)	p-value
Age (years)	1.071 (1.036–1.085)	0.007	1.031 (0.95–1.061)	0.05*
Diabetes mellitus	0.57 (0.17 – 0.195)	0.003	0.065 (0.007 – 0.566)	0.42
Hypertension	0.100 (0.032 – 0.311)	<0.001	8.816 (0.60 – 129.4)	0.112
Previous MI	0.204 (0.042 – 1.003)	0.05	0.834 (0.112 – 6.217)	0.859
LVEF	0.979 (0.971 – 0.989)	0.02	0.989 (0.975–1.011)	0.41
eGFR	0.965 (0.959–0.977)	<0.001	0.976 (0.963 – 0.986)	<0.001*
Hemoglobin	0.762 (0.654 – 0.832)	<0.001	0.920 (0.804 – 1.049)	0.32
Glucose on admission	1.006 (1.002 – 1.009)	<0.001	1.005 (1.001–1.009)	0.02*
Contrast vol.>100ml	0.037 (0.010 – 0.143)	<0.001	0.035 (0.004 – 0.338)	0.004*

\*Statistically significant

**DISCUSSION**

Cardiovascular catheterizations frequently employ contrast media for therapeutic and diagnostic objectives. When contrast media are administered, a disease known as contrast-induced nephropathy develops, which has a poor prognosis.<sup>16</sup> CIN usually appears 48–72 hours after being exposed to intravascular iodinated contrast medium.<sup>17</sup> The incidence of CIN is rising as a result of an increase in coronary angiography or PCI procedures. A greater prevalence of CIN is also linked to primary PCI as compared to elective operations. According to the defining criteria that were applied, the incidence of CIN ranged from around 10.6% to as high as

vessel. In contrast to individuals who did not develop CIN, the patient who did had higher contrast usage (135.7 ± 53.7 ml) than those who did (114.2 ± 36.7 ml). Additionally, there was a significant decrease in CIN in patients who got less than or equal to 100 ml of IV contrast compared to those who received more than 100 ml.

Table 2: Laboratory, angiographic and interventional characteristics of the patients of both the groups

Variables	With CIN n = 18	Without CIN n = 102	p-value
Laboratory parameters			
Basal creatinine (mg/dL)	1.45 ± 0.98	1.03 ± 0.82	0.05*
Postprocedural creatinine (mg/dL)	2.71 ± 1.31	1.09 ± 0.76	<0.0001*
eGFR, mL/min/1.73 m <sup>2</sup>	56.4 ± 26.9	82.1 ± 26.5	0.0002*
Hemoglobin, g/dL	12.55 ± 2.23	13.65 ± 1.76	0.02*
Glucose on admission, mg/dL	164.2 ± 96.8	128.6 ± 68.7	0.02*
Angiographic parameters			
Type of ACS, n (%)			0.64
STEMI	9 (50 %)	57 (55.8 %)	
NSTEMI	9 (50 %)	45 (44.2 %)	
Culprit vessel, n (%)			0.89
LM	1 (5.5 %)	3 (2.94 %)	
LAD	7 (38.8 %)	44 (43.1 %)	
LCX	5 (27.7 %)	23 (22.5 %)	
RCA	5 (27.7 %)	32 (31.4 %)	
Multivessel disease, n (%)	7 (38.8 %)	42 (41.1 %)	0.85
Contrast volume (ml)	135.7 ± 53.7	114.2 ± 36.7	0.03*
Contrast volume categories			<0.001*
>100 ml	15 (83.3 %)	16 (15.7 %)	
≤ 100 ml	3 (16.7 %)	86 (84.3 %)	

\*Statistically significant

Table 4 lists the factors for the postprocedural CIN in the study population using a univariate and multivariate logistic regression analysis. Age, prior MI, hypertension, diabetes mellitus, LVEF, admission blood glucose, haemoglobin, eGFR, and contrast volume greater than 100 ml were all shown to be linked with CIN in univariate analysis. Age, eGFR, admission serum glucose, diabetes mellitus, and contrast volume more than 100 ml were shown to be independent predictors of CIN in the study participants.

27.7%.<sup>18,19</sup> CIN occurred in 15% of the individuals in the current research.

The research has identified several factors that contribute to the onset of CIN.<sup>8,18</sup> However, because of the interindividual variation in the nephrotoxic effects of contrast medium, the prediction of CIN might occasionally be challenging in practical practise.<sup>20</sup> In the previous research, CIN develops at considerably higher rates in STEMI patients than in patients with a stable clinical presentation, owing to the primary PCI complexity, hemodynamic instability, greater use of contrast medium, and inadequate precautionary measures.<sup>21</sup> However, we did not observe any difference in frequency of CIN in STEMI and NSTEMI patients in

our study which can be attributed to the modest sample size of the study.

It is essential to identify people who are at high risk of developing CIN in order to improve poor clinical outcomes since preventative measures can slow the disease's onset and progression.<sup>22</sup> The predictor assessment of the present study revealed that The older patients had a higher risk, as expected, and our study found comparable results to those where the mean age for CIN occurrence was higher.<sup>23</sup> In our study, we discovered that patients developing CIN had a greater age  $65.9 \pm 9.7$  versus  $57.8 \pm 11.8$  in patients who did not develop CIN and it was also observed to be the independent predictor in the multivariate analysis.

With regard to laboratory parameters, given that the majority of the patients in our research had baseline creatinine levels that were normal, basal renal function did not predict the development of CIN. Additionally, we discovered that eGFR and glucose levels at admission were also independent predictors of CIN. Chronic kidney disease, as expected, is the most prominent intrinsic risk factor for CIN. Every decrease in GFR increases the risk, and in individuals with GFRs of 10-15 mL/min, the chance of developing CIN may surpass 50%.<sup>24</sup> Diabetes is another well-known major risk factor for developing CIN.<sup>25</sup> Diabetes mellitus was not a significant component in this trial, however glucose level at admission was observed to be an important independent predictor of CIN. In a trial that was conducted parallel with ours, Baydar et al.<sup>26</sup> found that patients with NSTEMI-ACS receiving primary PCI who had acute hyperglycaemia had a significantly higher incidence of CIN. It was also demonstrated by their study that hyperglycaemia was linked to higher CIN risk, in-hospital mortality, and morbidity.<sup>26</sup> Increased glucose levels at admission can be a sign of both worsening diabetes under control and an increased inflammatory stress response via non-insulin pathways. These might increase the value of admission glucose level over diabetes in the aspect of CIN in ACS patients. Moreover, we failed to independently associate LVEF with CIN which is normally considered as a traditional risk factor for CIN development.

The patient who developed CIN has higher amount of contrast use in comparison to in patients who did not develop CIN ( $135.7 \pm 53.7$  ml vs  $114.2 \pm 36.7$  ml,  $p = 0.03$ ). Also, there was significant reduction in CIN in those who received IV contrast less than or equal to 100 ml compared to those who received more than 100 ml. In general, observably less amount of contrast is used in our study compared to other studies.<sup>18,27</sup> However, we still observed contrast volume  $\leq 100$  ml as an independent predictor of CIN which is consistent with the findings of Adhikari et al.<sup>23</sup>

## CONCLUSION

The CIN incidence in patients undergoing primary percutaneous coronary intervention was similar with the studies conducted in different areas around the world. In the evaluation of CIN predictors, eGFR, higher mean age, glucose level at admission and higher level of contrast were found to be the significant predictors.

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