

# Contrast Induced Nephropathy and its predictors after Primary Percutaneous Intervention

Krishna Chandra Adhikari<sup>1</sup>, Rabi Malla<sup>2</sup>, Arun Maskey<sup>2</sup>, Sujeeb Rajbhandari<sup>2</sup>, Bishow Raj Baral<sup>1</sup>, Arjun Budhathoki<sup>1</sup>, Shreya Bhandari<sup>2</sup>, Shipra Shrestha<sup>2</sup>, Rabindra Simkhada<sup>2</sup>, Parag Karki<sup>3</sup>

<sup>1</sup>Department of Cardiology, National Academy Of Medical Sciences, Bir hospital, Kathmandu, Nepal.

<sup>2</sup>Department of Cardiology, Shahid Gangalal National Heart center, Kathmandu, Nepal.

<sup>3</sup>Department of Medicine, Army Institute of Health Sciences, Shree Birendra Hospital, Nepal.

**Corresponding Author:** Krishna Chandra Adhikari  
Department of Cardiology, National Academy of Medical Sciences  
Bir hospital, Kathmandu, Nepal  
**Email:** drkrishnacadhikari@gmail.com  
**ORCID ID NO:** 0000-0001-9781-1405

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## Abstract

**Background and Aims:** Worldwide many patients are receiving intravascular contrast media (CM) during interventional procedures. Contrast media are used to enhance visualization and guide percutaneous coronary interventions (PCI). However, the use of CM also carries the risk of complications and it is important to be aware of these complications. Complications with CM range from mild symptoms to life-threatening conditions like anaphylaxis, hypotension and renal dysfunction and contrast-induced nephropathy (CIN) is one of them which can have both short and long term consequences. This study aimed to know the incidence of CIN in our center and possible predictors associated with it.

**Methods:** This is the single hospital based cross sectional observational study. Patients undergoing primary PCI were enrolled in the study. All the patients underwent thorough history taking and physical examination. Baseline required laboratory investigations were sent. Electrocardiogram and echocardiography screening was done before taking patient to primary PCI as per the protocol of the hospital.

**Results:** The number of patients enrolled in the study was 83 out of which 65(78.2%) were males and mean age was 59.7±13.2. Mean Arterial Pressure (MAP) among the patients was 103.8±21.3. Almost 2/3rd of the population received intravenous fluids. Minimum contrast volume used was 50ml and maximum was 270. When absolute rise in creatinine was considered 12 (14.5%) had CIN and when percent rise was also considered total 28 (33.7%) had CIN. While evaluating the predictors of CIN, higher mean age (p=0.01), hypotension with mean MAP <60 mmhg (p=0.04) and higher contrast volume >100ml (p=0.04) was found to be significant.

**Conclusion:** The incidence of CIN in patients undergoing PPCI was similar to the studies done in other parts of the world. Evaluating the predictors of CIN, higher mean age, hypotension and higher contrast volume was the significant predictor.

**Keywords:** Contrast Media, Contrast Induced Nephropathy, Primary Percutaneous Coronary Intervention

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## Introduction

Worldwide many patients are receiving intravascular contrast media (CM) during interventional procedures. Contrast media are used to enhance visualization and guide percutaneous coronary interventions (PCI)<sup>1</sup>. Improvements and effectiveness of PCI procedures have increased the number of patients receiving CM. However, complications with CM range from mild symptoms to life-threatening conditions<sup>2</sup>.

CIN refers to potentially reversible acute kidney injury following iodinated contrast medium<sup>3,4</sup>. The mechanism of CIN is medullary hypoxia and acute tubular necrosis caused by increased adenosine, endothelin, free radical-induced vasoconstriction and a direct toxic effect of the contrast agent<sup>5</sup>.

CIN is characterized as either an absolute increase in serum

creatinine (SCr) concentration of 0.5 mg/dL (44.2 mmol/L) or a relative increase of >25% from baseline<sup>6</sup>. CIN typically manifests clinically within 3 days of CM administration, peaks within 3 to 5 days, and returns to baseline within 10 to 21 days<sup>7</sup>. To monitor for CIN, it is recommended that SCr measurements be continued for >48 hr after exposure to CM<sup>8</sup>. CIN is responsible for an increased mortality rate of 14%.<sup>9</sup> Clinical and metabolic disorders requiring renal replacement therapy occur in approximately 3% of patients<sup>10</sup>.

Predictors for the development of CIN include diabetes mellitus, urgent versus planned PCI, congestive heart failure, older age, hypertension, hypotension, and, most importantly, Chronic Kidney Disease (CKD)<sup>11</sup>. CM are categorized according to their osmolality as so-called high-osmolar (osmolality 1000 mosm/kg), low-osmolar (600 to 1000 mosm/kg), and iso-osmolar (280 to 290 mosm/kg)

contrast media<sup>12</sup>. Nowadays, high-osmolar contrast media have been replaced by low-osmolar and iso-osmolar contrast media<sup>13</sup>.

Primary PCI (PPCI) is defined as emergency PCI with balloon, stent or other approved device performed on the infarct-related artery without previous fibrinolytic therapy and PPCI results in fewer ischemic complications, preserved ventricular function<sup>14, 15</sup>.

The single observational study done showed the incidence of CIN in our center after PCI was 13.2 %<sup>16</sup>. Similar study done other center showed the incidence of CIN after diagnostic and interventional angiography to be 15.48%<sup>17</sup>. The number of patients undergoing PPCI is increasing day by day, the total number being 265 in the year of 2018<sup>18</sup>.

## Methods

This study is the single hospital based cross sectional observational study done at Shahid Gangalal National Heart Centre, Basbari, Kathmandu during the time period of 6 months with including all the patients who had undergone primary percutaneous intervention and fulfilling the inclusion criteria. Informed written consent was taken from each of the selected patient prior to enrollment in study. The sample size was calculated according to the total number of PCI done in SGNHC and the incidence of CIN in the previous studies.

All the patients underwent thorough history taking and physical examination. Baseline required laboratory investigations were sent. Electrocardiogram and echocardiography screening was done before taking patient to primary PCI as per the protocol of the hospital. The entire patient undergoing PPCI were included on this study. Renal function tests and other required investigations was done as per the requirement of our study. Patient was followed till the discharge. Data was collected as per the pre-designed proforma according to the need of our study. All the personal details, required history, physical findings, laboratory reports, ECG details, echocardiography details, procedural details of cath including volume of contrast used were recorded in proforma.

## Statistical Analysis

All data was entered and the statistical analysis was done using the IBM SPSS version 20 software. Qualitative variables were summarized as absolute frequencies and percentages. The quantitative data was expressed as means  $\pm$  standard deviation or medians and interquartile ranges (25th percentile–75th percentile) according to distribution for each variable. Diagnostic groups were compared with independent-samples, using t-tests and chi-square tests as appropriate. A p value of <0.05 was taken to indicate significance.

## Results

In our study, 83 participants were enrolled out of whom males were 65(78.3%) more common than females. Mean age was 59.7 $\pm$ 13.2. Over a quarter of study population 22(26.5%) were diabetics. The mean arterial pressure (MAP) among the patients was 103.8 $\pm$ 21.3. The number of patients with hypertension was 44 (53.0%) and maximum-recorded BP was 213/134 mmHg. 2 patients presented with hypotension with MAP less than 60. The mean age of LVEF among patient was 41.8 $\pm$ 6.1. 42 (50.6%) of the patient had EF $\leq$  40% at presentation. At presentation range of creatinine was 41 to 203  $\mu$ mol/L with mean of 82.2 $\pm$ 28.2  $\mu$ mol/l and 6(7.2%) patients with preprocedural Kidney Injury. The range of creatinine post procedure was 52 to 713  $\mu$ mol/L. The post procedure change in creatinine ranged from 50  $\mu$ mol/L to 551  $\mu$ mol/L with mean of 109.6 $\pm$ 100.8. Almost 2/3rd (63.9%) of the population received intravenous fluids. Minimum contrast volume used was 50ml and maximum was 270 with mean volume of 117.9 $\pm$ 42.6. When absolute rise in creatinine was considered 12 (14.5%) had CIN and when percent rise was also considered total 28 (33.7%) had CIN. (Table 1)

Those with CIN had higher mean age. Gender was not a significant risk factor for CIN. Both the patients who presented with MAP less than 60 developed CIN (p=0.04). There was no significant difference of Systolic, Diastolic or Mean Arterial Blood Pressure between those with or without CIN. Hypertension at presentation showed reduced risk of CIN by 33% however was not statistically significant. The patient who developed CIN has higher amount of contrast use (133.2  $\pm$  52.4 ml) in comparison to (110  $\pm$  34.5ml) in patients who didn't develop CIN. There was no difference in mean Ejection Fraction between the groups. In our study those who had EF less than or equal to 40% had lower CIN than those with preserved EF, however the finding was not statistically significant. There was no significant difference in mean pre-procedure creatinine or eGFR. Mean Post procedure creatinine was significantly higher in CIN group. Those who didn't receive IV fluids were at 22% higher risk of developing CIN, however this value was also not statistically significant. Also there was significant reduction in CIN in those who received IV contrast less than or equal to 100 ml by 63% compared to those who received more than 100 ml. (Table 2)

**Table 1:** Baseline Characteristics

Variables	83 (100%)
Age(years)	59.7 $\pm$ 13.2
Males n(%)	65(78.3%)
Females n(%)	18(21.7%)
Systolic BP (mmhg)	136.8 $\pm$ 30.3
Diastolic BP (mmhg)	87.3 $\pm$ 18.6
Mean Arterial Pressure (mmhg)	103.8 $\pm$ 21.3
Hypertension n(%)	44(53.0%)
LVEF (%)	41.8 $\pm$ 6.1
HFrEF n(%)	42(50.6%)
Diabetes n(%)	22(26.5%)
Creatinine at admission ( $\mu$ mol/L)	82.2 $\pm$ 28.2
Pre Procedure eGFR (ml/min/1.73m <sup>2</sup> )	88.3 $\pm$ 32.9
Post Procedure eGFR (ml/min/1.73m <sup>2</sup> )	109.6 $\pm$ 100.8
Change in creatinine ( $\mu$ mol/L)	87.5 $\pm$ 85.6
Patients receiving IV fluids n (%)	53(63.9%)
Contrast Volume (ml)	117.9 $\pm$ 42.6
CIN n(%)	28(33.7%)

**Table 2:** Risk factors for CIN

Variables		Total	CIN	NO CIN	T-Test	OR (95% CI)	P
		83 (100%)	28 (33.7%)	55 (66.3%)	Mean Difference ± σ $\bar{x}$ , t (df) = t stats		
Age							
(Years)		59.7 ± 13.2	64.7 ± 12.6	57 ± 12.9	7.4 ± 2.9, t (55.6) = 2.521	NA	0.01
Males							
n(%)		65 (78.3%)	23 (35.4%)	42 (64.6%)	NA	1.4 (0.4-4.49)	0.54
Females							
n(%)		18 (21.7%)	5 (27.8%)	13(72.2)	NA	0.7 (0.22-2.21)	0.54
Systolic BP							
(mm of Hg)		136.8 ± 30.3	135.6 ± 36.7	137.4 ± 26.8	-1.8 ± 7.8, t (42.1) = -0.233	NA	0.81
Diastolic BP							
(mm of Hg)		87.3 ± 18.6	84.2 ± 20.7	88.9 ± 17.4	-4.7 ± 4.3, t(46.9) = -1.038	NA	0.30
MAP							
(mm of Hg)		103.8±21.3	101.3±25.4	105.1±19.2	-3.7±5.4, t(43.0)=-0.692	NA	0.49
Hypertension							
n(%)		44 (53.0%)	13(29.5%)	31(70.5%)	NA	0.67(0.26-1.64)	0.39
LVEF							
(%)		41.8±6.1	42.5±4.8	41.5±6.7	0.95±1.42, t(71.8)=0.743	NA	0.46
HF <sub>r</sub> EF	Yes	42 (50.6%)	10(23.8%)	32(76.2%)	NA	0.63 (0.13-2.91)	0.06
	n(%) NO	41(49.4%)	18(43.9%)	23(56.1%)			
Creatinine at Admission (μmol/L)		82.2±28.2	79.54±33.8	83.6±25.1	-4.0±7.2, t(42.6)=-0.564	NA	0.57
Pre Procedure eGFR (ml/min/1.73m <sup>2</sup> )		88.3±32.9	99.2±45.9	82.7±22.41	16.5±9.1, t(33.7)=1.802	NA	0.08
Post Procedure Creatinine (μmol/L)		109.6±100.8	152.6±164.2	87.78±22.4	64.8±31.1, t(27.5)=2.079	NA	0.04
Change In Creatinine (μmol/L)		27.5±85.6	73.0±137.0	4.1±10.4	68.9±25.9, t(27.1)=2.657	NA	0.01
IV Fluids n(%)	No	30 (26.1%)	11 (36.7%)	19 (63.3%)	NA	1.22(0.47-3.13)	0.81
	Yes	53 (63.9%)	17(32.1%)	36 (67.9%)			
Contrast Vol (ml)		117.9±42.6	133.2±52.4	110.0±34.5	23.2±10.9,t(39.4)=2.117	NA	0.04
Contrast							
≤ 100ml		43(51.8%)	10 (23.3%)	33(76.7%)	NA	0.37 (0.14-0.95)	0.04
>100ml		40 (48.2%)	18(45.0%)	22(55.0%)			

## Discussion

This study shows that overall incidence of CIN in STEMI patients undergoing primary PCI was 14.5% when absolute rise in creatinine was considered, and when percent rise was also considered total 33.7% developed CIN. The incidence was similar to the studies done abroad<sup>15,16</sup>. The elderly patients have a higher risk as expected and our study also showed the similar results where mean age for development of CIN was higher. In our study, we found that patients developing CIN were relatively of higher age  $64.7 \pm 12.6$  vs  $57 \pm 12.9$  in patients not developing CIN. Basal renal function doesn't predict the development of CIN as most of the patients in our study have normal baseline creatinine level.

Our study was unable to identify the variables that traditionally increase the risk of CIN. The variables that were different in the comparison of patients with and without CIN were not statistically significant. The traditional risk factors were: LVEF  $\leq 40\%$ , Killip  $\geq 2$ , however, in our study we didn't find the significant difference of LVEF between the patients developing CIN and patient without developing CIN. The patient who developed CIN has higher amount of contrast use ( $133.2 \pm 52.4$  ml) in comparison to ( $110 \pm 34.5$  ml) in patients who did not develop CIN. Those who didn't receive IV fluids were at 22% higher risk of developing CIN. Also there was significant reduction in CIN in those who received IV contrast less than or equal to 100 ml by 63% compared to those who received more than 100 ml. In general, lower contrast volume was used in our study (average infused volume was  $<150$  ml), below the cutoff points in other literature  $>200$  ml and  $>300$  ml<sup>19,20</sup>

## Limitation

Number of sample size is small. This study is retrospective and non-randomized exposed to the usual bias of retrospective study.

Because all patients in the present study underwent emergency PCI, no protocol-defined pre- or post-procedural hydration could be given. All the other etiologies of in-hospital development of AKI sometimes is difficult to rule out

## Conclusion

The incidence of CIN in patients undergoing PPCI was similar to the studies done in other parts of the world. Evaluating the predictors of CIN, higher mean age, hypotension and higher contrast volume was the significant predictor.

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## Conflict of interest

None

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