

# CONTRAST INDUCED NEPHROPATHY IN PATIENTS OF ACUTE CORONARY SYNDROME WITH NORMAL RENAL FUNCTIONS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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## ABSTRACT:

### BACKGROUND:

Contrast induced nephropathy is a well-known entity but it is less known that whether cardiac disease is a risk factor for this complication. Contrast induced nephropathy (CIN) is related with increase mortality and morbidity and the chances of this complication rises in patients who have coronary artery disease (CAD).

### AIMS & OBJECTIVE:

The objective of the study is to identify the frequency of contrast induced nephropathy in patients undergoing percutaneous coronary intervention (PCI) who have normal baseline renal functions.

### MATERIAL & METHODS:

This cross sectional study conducted at angiography department of Punjab Institute of Cardiology, Lahore over a period of 2 years from January 2015 to January 2017. All the patients underwent coronary angioplasty. Renal function tests were checked 48 hours after procedure. The patients who had their creatinine level raised by 0.5mg/dl after 48hrs were labeled as sufferers of contrast induced nephropathy (CIN).

### RESULTS:

Out of 5400 patients who underwent coronary angioplasty, 2988 (55.4%) patients were males & 2412 (44.6%) were females. Out of 5400 patients, 936 (17.33 %) suffered from CIN after PCI. Patients suffered from CIN when following volume of contrast was used: <100ml, 36 (3.84%) patients, 100-200 ml, 288 (30.7%) patients and >200ml, 612 (65.3%) patients. According to the age group following patients suffered from CIN: 30-40 years, 72 (8.6%) patients, 41-55 years, 288 (11.2 %) patients and 56-65 years 576 (28.5%) patients. Out of 2988 male patients, 324 (10.8 %) patients suffered from CIN ( $p=0.06$ ). Similarly, out of 2412 females 612 (25.3 %) patients had CIN ( $p=0.05$ ). In 936 patients suffering from CIN, 684(73.1%) patients were diabetic and 252 (26.9%) were non-diabetic.

### CONCLUSION:

There is a high frequency of contrast induced nephropathy in elderly and ACS patients who undergo PCI even if they have normal preexisting renal functions, so this complication can be avoided by the minimum use of contrast during the procedure.

### KEY WORDS:

Contrast induced nephropathy, percutaneous coronary intervention, complications of PCI.

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## INTRODUCTION:

Globally, CAD is a major cause of death.<sup>1</sup> Contrast media is used in coronary angiography and PCI for the visualization of coronary arteries which can produce iatrogenic CIN.<sup>2</sup> Every year about tens of millions of radiologic procedures are carried-out using iodinated contrast media.<sup>3</sup>

PCI is a therapeutic procedure in which narrowed segments of coronary arteries are fixed with stents. Globally, more than two million patients underwent PCI procedure in 2006.<sup>4</sup> The number of cardiac angiographies and PCIs are increasing day by day.<sup>5</sup>

Excluding the other explanations for renal dysfunction, CIN is absolute ( $\geq -0.5\text{mg/dl}$ ) or relative ( $\geq 25\%$ ) increase in serum creatinine. As compared to baseline serum creatinine, it increases at 48 to 72 hours after contrast exposure.<sup>6</sup> The consequences of CIN are linked with economic, prolonged hospitalization, dialysis and increased risk of mortality.<sup>7</sup> It also increases cost in high risk patients who undergo PCI as well as it is a major cause of morbidity and mortality.<sup>8</sup> It is observed that CIN is low in general population but it rises up to 20% in patients with cardiac disease.<sup>9</sup>

Worldwide, CIN is third major cause of hospital acquired acute kidney injury.<sup>10</sup> There are multiple risk factors are included i.e age, female gender, diabetes, hypertension, anemia ( $\text{HB} < 11\text{g/dl}$ ), low LVEF ( $< 40\%$ ), contrast volume ( $> 200\text{ml}$ ) and low BMI ( $< 18$ ).<sup>11</sup>

Due to high mortality and morbidity in CIN after PCI, preventive measures should be taken in high risk patients who have CAD.<sup>12</sup>

## MATERIAL AND METHODS:

This cross sectional descriptive study conducted at Angiography department of Punjab Institute of Cardiology, Lahore over a period of 2 years from January 2015 to January 2017. The calculated sample size was 5400 cases with 3% margin of error 95% confidence level, taking expected percentage of contrast induced nephropathy (CIN is  $0.5\text{mg/dl}$  increase in serum creatinine at 48 hours after exposure to a contrast agent compared to baseline serum creatinine values) i.e, 20% in patients undergoing PCI. Patients of both genders, age above 30 and below 65 years, patients

undergoing PCI, patients who had normal serum creatinine before procedure ( $< 2\text{mg/dl}$ ), diabetic and non-diabetic patients (defined by fasting BSL more than  $126\text{mg/dl}$ ), patients having body mass index  $> 18$  were included in the study. Patients with chronic kidney disease who were on dialysis ( $\text{GFR} < 15\text{ml/min/1.73m}^2$ ), patients having severe anemia ( $\text{Hb} < 7\text{g/dl}$ ), patients having congestive cardiac failure defined by  $S_3$ , basal crepts in lungs raised JVP hepatomegaly or pedal edema, patients who undergo circulatory collapse requiring CPR or any major complication during angioplasty like cardiogenic shock, renal failure or unconsciousness, patients with ejection fraction  $< 30\%$  were excluded from the study.

## DATA COLLECTION PROCEDURE:

Total 5400 patients were enrolled who underwent angiography fulfilling the inclusion criteria. Study was reviewed and approved by IRB of Punjab Institute of Cardiology, Lahore. This study complied with the guidelines of by EMRO National Bioethics Committee Pakistan Medical Research Council. Demographic data, age, gender, and address was recorded. Effects modifiers such as history of diabetes and volume of contrast used were controlled through stratification. Patients were kept in hospital for 2 days after angioplasty and serum creatinine was measured once daily after procedure for two days with the gap of 24 hours. Any increase in serum creatinine  $\geq 0.5\text{mg/dl}$  from baseline was considered as cut off for diagnosis of contrast induced nephropathy.

## DATA ANALYSIS PROCEDURE:

Study data was analysed using SPSS 11. Numerical data like age and volume of contrast used were presented as mean and standard deviation. Qualitative data like gender and status of patients regarding presence or absence of diabetes were presented on frequency tables and percentages. Data was stratified for volume of contrast used ( $\leq 100\text{ml}$ ,  $101$  to  $200\text{ml}$  and  $> 200\text{ml}$ ) and diabetes mellitus. Chi-square test was applied after stratification. Less than 0.05 p-value was taken as significant.

## RESULTS:

Results were compiled after studying the specific variables. Total number of 5400 patients undergoing PCI were analyzed.

**Table:1 Baseline characteristics of study population. (n=5400)**

Baseline Characteristics		Frequency	Percent
Age group (Years)	30 to 40	828	15.3%
	41 to 55	2556	47.3%
	56 to 65	2016	37.3%
Gender	Male	2988	55.3%
	Female	2412	44.6%
Status of Diabetes	Present	2160	40%
	Not present	3240	60%

**Table No 2: Distribution of patients by frequency of CIN (n=5400)**

CIN	No.	Percentage
Present	936	17.3%
Absent	4464	82.6%
Total	5400	

**Table no 3: Frequency of CIN according to gender distribution (n=936).**

CIN	Gender	No.	Percentage
Yes	Male	324	34.6%
	Female	612	65.38%

**Table no 4: Distribution of patients according to the volume of contrast used (ml) (n=5400)**

Vol of contrast used (n=5400)	Number of Patients	Percentage
≤ 100ml	1440	24.66%
101 to 200 ml	2628	48.66%
>200 ml	1332	24.66%

**Table no 5: Frequency of CIN according to volume of contrast, age group and status of diabetes (n=936)**

		Number of patients	Percentage
VOL of Contrast Used(ml)	≤100	36	3.84%
	101-200	288	30.7%
	>200	612	65.3%
Age Groups (years)	30-40	72	7.69%
	41-55	288	30.7%
	56-65	576	61.5%
Status of diabetes	Diabetics	684	73.1%
	Non-Diabetics	252	26.9%

Out of 5400 patients 2988 (55.3 %) patients were males & 2412 (44.6%) were females. There were 828 (15.33 %) patients in the age range of 30 to 40 years, 2566 patients (47.33 %) were of 41 to 55 years of age, while 2016 (37.33 %) patients were of 56 to 65 years of age (Table 1). Total 936 patients (17.33 %) suffered from CIN after PCI, while 4464 patients (82.66%) did not have this grave complication (CI 95%,  $p=0.001$ ) (Table 2). The frequency of CIN according to gender distribution is given (Table 3).

Study participants were divided into three different groups according to volume of contrast used (Table 4). Out of 936 patients, when less than 100ml contrast was used, 36 (3.84%) patients suffered from contrast induced nephropathy. When contrast was used between 100 - 200ml, 288 (30.7%) patients suffered from CIN. When contrast was used more than 200ml, 612 (65.3%) patients had CIN. In age group of 30 to 40 years, 72 (8.6 %) patients suffered from CIN, 756 (91.3 %) did not suffer from CIN. Total 288 (11.2 %) patients in age group of 41 - 55 years had CIN while 2268 (88.7 %) patients escaped from this. 576 patients (28.5 %) in age group of 56 to 65 years had CIN while 1368 (67.8 %) did not. Out of 2988 male patients, 324 (10.8 %) patients suffered from CIN while it was absent in 2664 (89.1 %) patients ( $p=0.06$ ). Similarly, out of 2412 females 612 (25.3 %) patients had CIN while 1800 (74.7 %) patients escaped from this complication ( $p=0.05$ ). In patients with CIN, 684 (73.1%) patients were diabetic and 252 (26.9%) were non-diabetic. (Table 5)

#### DISCUSSION:

Post cardiac intervention, CIN is well known consequence. The third most common reason of acute renal failure is associated with acute radio-contrast nephropathy which results in temporary dialysis or progress to end-stage renal disease in up to 7% of these patients.<sup>10</sup>

In a research by Lasser EC et al. CIN was assessed 0.6 – 2.3% in the general population.<sup>13</sup> Prevalence of CIN is significantly higher in several patient subsets especially in patients suffering from cardiac diseases.<sup>13,14-17</sup>

In different studies, the incidence of CIN is varied because of presence of other potential causes of acute renal failure. McCullough PA et al. reported a rate of 14.5% where approximately 1800 patients underwent cardiac procedures.<sup>15</sup> There was incidence of acute renal impairment in 147/1000 patients and 7.7/1000 patients who required dialysis. Dialysis-dependent acute renal failure was not observed in patients who had received <100 ml radio-contrast and those who had a creatinine clearance >47 ml/min. Creatinine clearance, diabetes, and radio-

contrast dose were independent predictors. There was in-hospital mortality was 35.7% in patients with acute renal failure and 2 years survival was 18.8%.

Dangas et al.<sup>18</sup> studied CIN in 7230 patients with or without chronic kidney disease (CKD) who underwent first time PCI. In our study, CIN was labeled when increase noted in level of serum creatinine at 48hrs post procedure to values >25% or >0.5 mg/dl above as compared to pre-procedure value. CIN was assessed in 19.2% of the patients with chronic kidney disease while (13.1%) of patients without CKD. Regardless of the baseline renal function, there was increased duration of hospitalization and complications in patients with CIN as well as significant high rate of mortality at one year. One year mortality was predicted by lower eGFR and other known factors such as age, diabetes, LV dysfunction, and further indices of cardiac malfunction such as peri-procedural hypotension or selection of intra-aortic, balloon-assisted, percutaneous coronary intervention. CIN was the main powerful predictors in all of them at one-year mortality, irrespective of the presence (odds ratio 2.37; 95% confidence interval 1.63 to 3.44) or absence of CKD at baseline (odds ratio 1.78; 95% confidence interval 1.22 to 2.60). The frequency of CIN was less in patients without CKD at baseline, CIN was predicted by the same risk factors.<sup>18</sup>

In the present study, 600 patients with normal renal function before the procedure underwent PCI were assessed for CIN. There were 104 out of 600 patients who had increased creatinine level within 48 hours after the cardiac procedure i.e; 17.33 % patients had CIN. As compared to the international studies, this is a little bit higher percentage but higher incidence of CIN is reported in cardiovascular patients as high as 20%.<sup>9</sup>

In our research, male population was dominant i.e (55.3%). This is similar to other studies. Mehran R et al, studied risk score for CIN where 71.2% patients were male.<sup>19</sup>

In diabetic patients, frequency of CIN varies from 5.7% to 29.4%.<sup>13,20</sup> In a study by Berns AS, 27% diabetic patients developed CIN with baseline serum creatinine 2.0–4.0 mg/dl.<sup>21</sup> In another study by Nikolsky E et. al, 15.1% patients suffered from CIN after PCI without having CKD. 20 Pafrey PS, et al<sup>22</sup> studied CIN in patients having diabetes without renal dysfunction and found out that CIN was present

in 8.8% of patients having diabetes without renal dysfunction as compared to 1.6% in controls. In the present study, 60% of patients were diabetic. Out of total patients, CIN was present in 12.6% of diabetic patients which is concordant with other studies. and out of all the patients who have CIN 73.1% of patients were diabetic so diabetes is a major risk factor which should be controlled to reduce CIN.

This study also relates increase tendency of CIN with increase in use of contrast volume. Nicolisky et al(20) studies that in diabetic patients, CIN developed in every 5th, 4th and 2nd patients with 200 -400 ml. 400-600 ml and > 600 ml contrast used. In the same study, every 100 ml increase in volume of contrast used there was 30% increase in odds of CIN. Another study including 5571 patients, showed 14.6% increase risk( $p=0.045$ ) with increase in contrast volume. In the present

study, out of all patients presented with CIN ,3.84% fell in the group in which  $\leq 100$  ml contrast volume was used. In the second group in which 100 – 200 ml contrast volume was used 30.7% had CIN. The patients receiving contrast volume > 200 ml represented the largest number of patients having CIN i.e.; 65.3%. Low use of contrast volume, when possible, can lead a sufficient reduction in the patient's CIN risk.

#### CONCLUSION:

There is high frequency of CIN after PCI in our population and mostly sufferers of this complication are females, diabetics population and in the patients in whom larger volume of contrast is used. CIN if present after PCI; early detection and management can reduce the mortality of this complication. Low volume of contrast should be used with proper preventive measures to reduce the incidence of CIN.

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