STUDY OF RISK FACTORS FOR CONTRAST-INDUCED NEPHROPATHY IN PATIENTS WITH CORONARY ARTERY DISEASE

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ABSTRACT

BACKGROUND
Contrast-Induced Nephropathy (CIN), a disorder of renal function is next only to surgery and hypotension in causing acute renal failure (Acute kidney injury) in hospitalised patients. CIN is one of the main reasons for morbidity and mortality in these patients as iodinated contrast media is being used increasingly in diagnostic imaging and interventional procedures coronary angiography.

MATERIALS AND METHODS
100 patients with ischemic heart disease who underwent coronary interventional procedures in KIMS, Hubli from 1st January 2016 to 30th June 2016 were included in the study. Clinical evaluation with progress of acute kidney injury and recovery was studied.

RESULTS
Incidence of CIN in this study was 9%. Patients with age more than 50 years had comparatively higher incidence of CIN (12.1%) compared to a 4.8% in age less than 50 years group. Male patients had higher incidence of CIN (10.6%) as compared to females (5.9%). In the study group of 100 patients, 21% of total diabetic patients developed CIN (p=0.041). 23.5% of total hypertensive patients developed CIN (p=0.000). 23.5% of the total anaemic patients developed CIN (p<0.05). Among ACS (acute coronary syndrome) patients, STEMI (ST ELEVATION MI) patients had higher incidence of CIN (21.74%) compared to 5.19% in NSTEMI/UA (UNSTABLE ANGINA) patients (p<0.05). Mean ejection fraction (EF) was comparatively lower in CIN group than in non-CIN patients though statistically not significant with p>0.05. Among the patients who developed CIN, regional wall motion abnormality (RWMA) was frequently noted in the LAD (left anterior descending) territory. Most common culprit vessel involved in CIN patients was LAD followed by LCA (left circumflex artery) and RCA (right circumflex artery). Out of 9 CIN patients, 5 patients had double vessel disease and one patient had triple vessel disease. CIN patients were followed up for 7 days. Serum creatinine levels returned to normal values in all the patients. None of the patients required dialysis.

CONCLUSION
The incidence of CIN is 9%. Age more than 50 years (12.1%), hypertension (23.5%), diabetes (21.1%) and anaemia (23.5%) are major risk factors in contributing to the development of CIN. Patients with multivessel involvement and proximal LAD disease along with above-mentioned risk factors are at greater risk for CIN.

KEYWORDS
Contrast-Induced Nephropathy, Coronary Artery Disease, Serum Creatinine.


BACKGROUND
Contrast-Induced Nephropathy (CIN), a disorder of renal function is next only to surgery and hypotension in causing acute renal failure in hospitalised patients. CIN is one of the main reasons for morbidity and mortality of patients as iodinated contrast media is being used increasingly in diagnostic imaging and interventional procedures like high-risk coronary angiography.1

Despite technological advances, CIN remains responsible for a third of all Hospital-Acquired Acute Kidney Injury (HAKI)2,3 and affects between 1% and 2% of the general population and up to 50% of high-risk subgroups following Coronary Angiography (CA) or Percutaneous Coronary Intervention (PCI).4

The widespread adoption of primary PCI for the treatment of Acute Myocardial Infarction (AMI) despite significantly improving cardiovascular outcomes has increased the incidence of CIN due to the inherent difficulties in rapidly assessing CIN risk, instigating prophylactic measures, attendant haemodynamic compromise and higher contrast volumes, all known risk factors for the development of CIN.5

CIN is defined as 25% relative increase or a 0.5 mg/dL (44 mmol/L) absolute increase in serum creatinine (Scr)
Clinical examination was done within 48-72 hrs of contrast exposure in the absence of an alternative explanation.6

OBJECTIVES
1. To know incidence of CIN in patients undergoing coronary angiography and angioplasty.
2. To identify the risk factors for CIN.

MATERIALS AND METHODS
Hundred patients with ischaemic heart disease patients who were admitted to the ICCU (Intensive Cardiac Care Unit) of Karnataka Institute of Medical Sciences Hospital, Hubli from 1st January 2016 to 30th June 2016 and underwent coronary angiography (CAG) or angioplasty were enrolled for the study after explaining the objectives of the study. It is a cross-sectional observational study. Informed written consent was taken. The study was conducted after obtaining the ethical clearance.

Inclusion Criteria
Patients with ischaemic heart disease undergoing interventional studies.

Exclusion Criteria
Patients with pre-existing renal disorder were excluded from the study.

Methods
Protocol
The history was obtained from the patients with special reference to risk factors for developing CIN and co-morbid conditions. Basic clinical examination was done on all patients. Each patient was also subjected to the following investigations on admission and subsequently 24 hrs and 48 hrs post intervention as described. Renal function tests, liver function tests, serum electrolytes, fasting plasma glucose, postprandial plasma glucose, complete blood count, Chest X-Ray (CXR), Electrocardiography (ECG), echocardiography and coronary angiography/angioplasty.

RESULTS
General Characteristics
Mean age of the study population was 47.50±14.53 years (mean±S.D). Majority were of the age group of 40 years to 60 years (68%), which represents the high risk age group for CAD (Table 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age (years) Mean±SD</td>
<td>47.50±14.53</td>
</tr>
<tr>
<td>Range</td>
<td>30-60</td>
</tr>
<tr>
<td>2. Sex ratio (M:F)</td>
<td>2.1:1</td>
</tr>
<tr>
<td>3. Hypertension</td>
<td>34 (34%)</td>
</tr>
<tr>
<td>4. Diabetes mellitus</td>
<td>19 (19%)</td>
</tr>
<tr>
<td>5. Anaemia</td>
<td>34 (34%)</td>
</tr>
</tbody>
</table>

Table 1. General Characteristics of the Patients Studied

Incidence of CIN
Incidence of CIN in the present study is 9%.

Risk Factors for CIN
Risk factors for CIN in this study were age >50 years, diabetes mellitus, hypertension and anaemia.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>CIN</th>
<th>Non-CIN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percentage</td>
<td>Frequency</td>
</tr>
<tr>
<td>Age &lt;50yrs</td>
<td>2</td>
<td>4.8</td>
<td>40</td>
</tr>
<tr>
<td>Age&gt;50yrs</td>
<td>7</td>
<td>12.1</td>
<td>51</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8</td>
<td>23.53</td>
<td>26</td>
</tr>
<tr>
<td>Anaemia</td>
<td>8</td>
<td>23.53</td>
<td>26</td>
</tr>
</tbody>
</table>

Table 2. Risk Factors for CIN

Angiographic Data
In patients who developed CIN, the most common culprit vessel involved was LAD followed by LCA and RCA (Table 3).

<table>
<thead>
<tr>
<th></th>
<th>CIN</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main coronary artery</td>
<td>0</td>
<td>0.00%</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>7</td>
<td>10.77%</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>3</td>
<td>11.54%</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>2</td>
<td>5.56%</td>
</tr>
</tbody>
</table>

Table 3. Culprit Vessels Involved in CIN Patients
Follow Up
All CIN patients were followed up for 7 days. Serum creatinine levels returned to baseline values in all patients. None of the patients required dialysis.

DISCUSSION
An increasing incidence of chronic kidney diseases, especially in elderly people and more people opting for radiography has lead to an escalated radiographic contrast media use in clinical practices, which has further intensified the prevalence of contrast-induced nephropathy in hospitalised patients. CIN has been identified as an important source of mortality and morbidity. Utilisation of contrast media leads to severe toxic effects on cells of renal tubules leading to Contrast-Induced Nephropathy (CIN).1 CIN is usually related to increased length of hospital stay, necessity for dialysis, high costs and increase in mortality.8,9

Pathogenesis of CIN
Renal vasoconstriction, which is a commonly occurring phenomenon in contrast nephropathy is partly mediated by contrast agent’s high osmolality and partly by contrast-induced release of adenosine and endothelin.10 Another primary event in the pathogenesis of CIN is the tubular injury, which occur either in alliance with generation of oxygen free radicals or due to direct cytotoxic effects.11 It is observed that tubular injury might act in concert with renal vasoconstriction.12

Risk Factors for CIN
Diabetes mellitus, hypertension and anaemia have been identified as well recognised risk factors for development of CIN.13

Diabetes Mellitus
In the present study, it is observed that Type 2 Diabetes mellitus could be an independent risk factor for the development of CIN. There is a significant difference in the rate of incidence of CIN in diabetic patients compared to non-diabetic patients (21% and 6%, respectively). Lautin et al13 also found similar results in their study as the incidence of CIN was found to be low (2%) in patients without diabetes, but visibly higher (16%) in patients with diabetes.

Diabetes is an important predisposing factor for CIN particularly in patients with renal function impairment. Renal hypoxia combined with the generation of reactive free oxygen radicals plays a central role in the pathogenesis of CIN and the diabetic kidney is particularly susceptible to intensified hypoxic and oxidative stress following the administration of contrast media.14

The pathophysiology of this vulnerability is a complex one and involves various mechanisms including enhanced tubular transport activity, oxygen consumption and the generation of reactive oxygen species. Redistribution of renal blood flow from medulla to cortex causing medullary ischaemia is also cited as one of the contributing factors.15

The regulation of vascular tone and peritubular blood flow may also be altered, particularly due to defective microvasodilatation, enhanced endothelin production and a particularly increased responsiveness to adenosine-related vasoconstriction.16

Hypertension
In this study it was found that there is a significant increase in rate of incidence of CIN in hypertensives compared to non-hypertensives (23.53% and 1.52%, respectively). Similar findings were also observed in the study conducted by Yuniadi and Ningrum17 involving 312 patients who underwent coronary intervention. Hypertension was found in 27.6% of CIN patients in that study.

The modifications of intrarenal vasoactive mediators like nitric oxide or renin-angiotensin system in hypertensive patients might contribute to the increased occurrence of CIN in these patients. Another factor which may predispose hypertensive patients to CIN could be the reduced number of nephrons in hypertensives.16

Sine atherosclerosis is one of the important complications of long standing hypertension, athereomobilization of the kidney during per cutaneous coronary intervention (PCI) may also be an important cause of acute renal failure.18

Anaemia
Association of anaemia as a risk factor in the development of CIN is known. Similar to hypertension as a risk factor, it was also noted in this study that a significantly increased proportion of patients with anaemia had developed CIN compared to those who didn’t had anaemia. (23.53% and 1.52% respectively). This is in accordance with the results of Kim et al who found that the contrast media is capable of increasing the haemoglobin’s oxygen affinity, so that the oxygen delivery to the peripheral tissues gets affected. This could lead to decreased oxygen delivery causing renal medullary hypoxia, thus increasing the overall risk of developing CIN.

ACS - UA/NSTEMI
In our study, it is found that the incidence of CIN is more in patients with STEMI (21.74%) as compared to NSTEMI/UA (5.19%). This being statistically significant (p<0.05). This is similar to the observation of Channappagoudra et al19 who observed increased incidence of CIN in patients undergoing interventions for STEMI.
Coronary vessels
In this study, it is found that among patients who developed CIN, the most common culprit vessel involved was LAD followed by LCA and RCA. LAD involvement causes large area of myocardial infarction leading to systolic dysfunction and hypotension. This may predispose to higher risk of development of CIN. These findings are similar to the results obtained study by Marenziet al in 208 patients with Acute Myocardial Infarction (AMI). They found that in 77% of the patients with CIN, the artery related to culprit lesion was Left Anterior Descending (LAD) artery; in 20% of the patients who developed CIN, the artery related to culprit lesion was right Coronary Artery (RCA) and in 5% of patients with CIN, the culprit lesion artery was Left Circumflex Artery (LCA).

All the 9 patients with CIN were followed up for 7 days. All CIN patients had a fall in the serum creatinine levels to return to baseline levels within 7 days. None of these patients required dialysis.

CONCLUSION
The overall incidence of CIN after contrast media exposure is 9%. Patients with age >50 years, pre-existing hypertension, anaemia and diabetes mellitus are at increased risk of acquiring CIN. Patients with multivessel involvement and proximal LAD disease also predisposes to development of CIN post contrast media exposure. Presence of these risk factors should alert the treating physician to take preventive measures to prevent CIN like maintaining hydration, good intravascular volume and maintaining mean arterial pressure (MAP).

Limitations of the Study
Our study included a small population of patients who were admitted to one health center. Therefore the findings of the study may not be generalised.

REFERENCES