Assessment of Acute Kidney Injury in Patients Undergoing Elective Coronary Angiography and Percutaneous Coronary Intervention

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Abstract:

Background: *CIN has gained increased attention in the clinical setting, particularly during cardiac intervention but also in many other radiological procedures in which iodinated contrast media are used. There is at present good clinical evidence from well-controlled randomized studies that CIN is a common cause of acute renal dysfunction.*

Methodology: *This was a prospective study conducted among the patients who underwent coronary angiography and percutaneous coronary intervention in the Department of Cardiology, Dhaka Medical College Hospital during January 2010 to December 2010. A total of 111 patients age range from 25 to 75 years were included in the study. Serum creatinine level at baseline and at the end of 48 hours was done in all these patients. Study population was divided into two groups according to development of acute kidney injury (AKI). Group-I = AKI, Group II = Not developed AKI.*

Results: *AKI developed 11.7% of the study patient. DM and Preexisting renal insufficiency were significantly higher in group I patients. HTN was (61.5% Vs 44.9%) higher in group I but not significantly. History of ACE inhibitor/ARB, NSAID intake and LVEF <40% were significantly higher in group I patients. The mean±SD volume of CM (Contrast Media) were 156.9±44.8 ml and 115.4±30.0 ml in group I and group II respectively, which was significant. The mean±SD of serum creatinine after 48-72 hours of CAG/PCI was 1.4±0.37 mg/dl and 1.1±0.2 mg/dl in group I and group II respectively. The serum creatinine level increased significantly (p<0.05) after 48-72 hours of CAG/PCI in group I. In group II, S. creatinine level increased but not significant (p>0.05). Impaired renal function was found 76.9% and 2.0% in group I and group II respectively. DM, HTN, preexisting renal insufficiency, ACE inhibitor/ARB, NSAIDs, contrast volume (>150 ml), eGFR (<60 ml/min/ 1.73m2) and LVEF (<40%) are significantly (p0.05) associated for CIN development,*

Conclusion: *CIN is an iatrogenic but preventable disorder results from the administration of contract media. Although rare in the general population, CIN occurs frequently in patients with underlying renal dysfunction and diabetes. In patients with pre angiographic normal renal function, the prevalence is low but in pre-existing renal impairment it may pose a serious threat. Thus risk factors are synergistic in their ability to predispose to the development of CIN. A careful risk-benefit analysis must always be performed prior to the administration of contrast media to patients at risk for CIN.*

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Introduction:

CIN has gained increased attention in the clinical setting, particularly during cardiac intervention but also in many other radiological procedures in which iodinated contrast media are used. There is at present good clinical evidence from well-controlled randomized studies that CIN is a common cause of acute renal dysfunction[1]

CIN is the acute deterioration of renal function after parenteral administration of radiocontrast media in the absence of other causes. CIN is generally defined as an increase in serum

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creatinine concentration of >0.5 mg/dL (>44 μmol/L) or 25% above baseline within 48 hours after contrast administration.[2]

In a study by Nash contrast-medium–induced nephropathy was reported to be the third most common cause of acute renal failure in hospitalized patients.[3] In the study, the contrast medium was assumed to be the cause of the renal fail-ure if it was administered in the 24 hours before renal failure and no other major kidney insult was identified. However, exposure to contrast medium may be a con-tributory rather than a sole cause of acute renal failure; concomitant insults may include low blood volume, surgery, atheroembolic disease, and the presence of other nephrotoxins.

Diabetes and renal impairment is a risk factor for deterioration in renal function after angiography.[4] Other factors vari-ably associated with increased rates of acute re-nal failure after the administration of contrast medium include age over 75 years, periprocedural volume depletion, heart failure, cirrhosis or ne-phrosis, hypertension, proteinuria, concomitant use of nonsteroidal antiinflammatory drugs, and intraarterial injection. In the setting of acute myocardial infarction or percutaneous coronary intervention, hypotension or use of an aortic bal-loon pump has been associated with a higher rate of acute renal failure after exposure to a con-trast medium.[5] However, it is uncertain to what extent these factors independently worsen renal function, as opposed to serving as markers for coexisting conditions. High doses of contrast medium also increase the likelihood of renal dys-function. The tolerable dose of contrast medium depends on kidney function.[6]

The risk of a decline in kidney function after the administration of contrast medium rises ex-ponentially with the number of risk factors pres-ent.[7]

The pathogenesis of CIN is poorly understood. It is believed that four dominant injury pathways exist and it is likely that these factors function together in concert to induce CIN in a given patient.

First, intra renal vasoconstriction causes renal medullary hypoxia that culminates in cell detachment, apoptosis and necrosis.[8] Second, radio contrast medium may precipitate in the distal tubule lumen along with glycoprotein and forming casts Third, radio contrast medium may directly damage tubular cells via the difference in osmolality or direct cytotoxicity. Finally, reperfusion injury may occur after initial tissue ischaemia via reactive oxygen species production.[8]

Contrast induced nephropathy most commonly clinically manifests either as a non oliguric or an oliguric nephropathy. In the non oliguric variety there is a transient decline in renal function .Serum creatinine levels begin to rise within 24 hours of contrast administration peaking at 3-5 days and then returning to baseline in 10-15 days. In the oliguric variety, which is a more severe form, there is a drop in urine output to less than 400 ml in 24 hours, serum creatinine levels peak in 5-10 days returning to normal in 14-21 days. In a small percentage the serum creatinine continues to rise, urine output drops, these individuals need then to be put on dialysis. Mortality from contrast induced nephropathy is also well documented.[9]

A decline in kidney function after the admin-istration of a contrast medium is associated with a prolonged hospital stay, adverse cardiac events, and high mortality both in the hospital and in the long term.[10] However, the association between these outcomes and the decline in func-tion may be explained at least in part by coexist-ing conditions, acuteness of illness, or other causes of acute kidney failure, such as atheroem-bolism.

During last few decades with the rapid development of interventional cardiology, coronary angiography and coronary angioplasty have gradually become part of the diagnostic therapeutic strategy for patients with ischaemic heart disease. In the last few years, the number of coronary angiography performed has grown enormously in Bangladesh. But there is little data of contrast induced nephropathy after such procedure. Contrast nephropathy is a serious complication of coronary angiography that is associated with considerably increased morbidity including the need for short term haemodialysis, extended hospitalization and permanent impairment of renal function. The purpose of this study is to assess the acute kidney injury in patients undergoing elective coronary angiogram (CAG) and percutaneous coronary intervention (PCI) as well as to determine the

possible risk factors which enhance the actue kidney injury. From this study we can identify the preventable risk factors of contrast induced nephropathy in our population, which will help clinicians to take appropriate preventive measures.

Materials and Methods:

This prospective observational study was conducted in the Department of Nephrology and Department of Cardiology of Dhaka Medical College Hospital from January 2010 to December 2010. Patients undergoing coronary angiography and percutaneous coronary intervention were enrolled in the study. However patients with pre-existing end stage renal disease requiring dialysis and patients treated with percutaneous coronary intervention for acute myocardial infarction were excluded from the study.

Detailed history, clinical examination and relevant investigations reports of all patients were recorded in pre designed data collection sheet at the beginning of the study. Low osmolar, non ionic radio contrast agent iopamidol was used for all patients. The anti ischemic, anti hypertensive, lipid lowering, platelet inhibitors and oral glycemic agents (except Metformin) if taking were continued.

Serum creatinine level was estimated before the procedure (coronary angiogram or percutaneous coronary intervention). This preprocedural serum creatinine was considered as basal serum creatinine. Serum creatinine level was again estimated at the end of 48 hours of contrast exposure. The rise of serum creatinine by e" 0.5 mg/ dl or >25% of baseline occuring within 48 hours of contrast administration was defined as contrast induced nephropathy. S. creatinine was again calculated after 30 days from the patients who developed contrast induced acute kidney injury.

Estimated GFR (eGFR) was calculated from MDRD formula both pre and 48 hours post procedure. Estimated GFR (eGFR) was again calculated from MDRD formula after 30 days from the patients who developed CIN after 48 hours.

Study population were divided in to two groups according to development of AKI.

Group-I = AKI, Group II = Not developed AKI.

We tried to analyze whether there is relation between the incidence of CIN with renal impairment, diabetes mellitus. Contrast volume, hypertension, left ventricular ejection fraction <40%, ACE inhibitor/ARB and NSAID.

All data was analyzed by using computer based SPSS (Statistical Program for Social Science) program. Continuous variables was expressed as mean ± standard deviation and categorical variables as frequencies. Continuous variables was assessed using students t-test and categorical variables was compared with chi-square test. A P value < 0.5 was considered significant.

For estimation of serum creatinine, blood surgar, venous blood samples were collected by sterile disposable syring with strict asceptic precaution. For estimation of blood sugar 2 cc of blood was poured to blood sugar bottle. 3 cc blood was kept in syringe for estimation of serum creatinine. All samples sent immediately to clinical pathology, DMCH. Serum creatinine was estimated using kinetic model; blood sugar was estimated by Glucose oxidase method. Echocardiography was done by colour Doppler Echocardiographic Equipment model GE system five by GE Vingmed ultrasound, Norway. Coronary angiogram was carried out by single plan angiogram machine model: Innova 2100-1Q, cardiovascular imaging system, 2007. General Electric Co. France.

Observations and Results:

A total of one hundred eleven patients fulfilled the inclusion criteria, were studied during the period. Patients were divided into two groups. Group I (n=13), those who developed AKI. Group II (n=98) those who did not develop AKI.

Table-I

Prevalence of AKI among study population (n=111)

AKI	Number of patients (n=111)	Percentage
AKI	13	11.7
Normal	98	88.3
Total	111	100.0

Table I showing development of AKI among study population 13(11.7%) developed

Table-II

Comparison of pre and post procedure serum creatinine concentration and estimated GFR (n=111)

S. creatinine (mg/dl)	Group I(n=13) Mean±SD	Group II(n=98) Mean±SD	P Value
Pre procedure	1.1±0.3	0.95±0.3	0.011[s]
Range (min – max)	(0.6- 1.9)	(0.6- 1.6)	
Post procedure at 48 hours	1.4±0.37	1.1±0.2	0.001[s]
Range (min – max)	(1- 2.2)	(0.7- 1.4)	
Mean difference pre and post procedure	0.3±0.2	0.15±0.2	
[a]P value	0.001[s]	0.123[ns]	
eGFR (ml/min/1.73 m^2)			
Preprocedure	66.7±10.6	89.1±10.7	
Range (min – max)	(50-80)	(80-100)	
Post procedure at 48 hours	56.6±15.6	83.2±3.2	
Range (min – max)	(30-83)	(80-90)	
Mean difference pre and post procedure	10.1±16.4	5.9±0.7	
[a]P value	0.001[s]	0.123[ns]	

Table-III

Risk factors for CIN and development of AKI among study populations (n=111)

Risk factors	Total(n=111)		Baseline rise in serum creatinine			
			>0.5mg/dl		>25%	
	n	%	n	%	n	%
DM	26	23.4	4	15.4	7	26.9
Pre-existing renal insufficiencye GFR < 60 ml/min/1.73m^2	9	8.1	3	33.3	4	44.4
HTN	52	46.8	3	5.8	5	9.6
ACE/ARB	39	35.1	3	7.7	6	15.4
NSAIDS	10	9.0	2	20.0	4	40
LVEF <40%	9	8.1	3	33.3	6	66.7
Dose of contrast £150ml	80	72.1	1	1.25	2	2.5
Dose of contrast >150ml	31	27.9	4	12.9	6	19.4

Table-IV

Logistic regression analysis of risk factors for CIN (n=111)

	OR	95% CI for OR		P
		Lower	Upper	Value
DM	4.15	1.21	14.24	0.024[s]
Preexisting renal insufficiency(e GFR < 60 ml/min/1.73m^2)	2.10	1.60	10.48	0.003[s]
ACE inhibitor/ARB	1.67	1.28	17.04	0.020[s]
NSAID	1.05	1.06	8.81	0.039[s]
Contrast volume (>150 ml)	3.63	3.05	31.37	0.027[s]
LVEF (<40%)	3.39	2.56	27.51	0.001[s]
Constant	0.16			0.001[s]

S=Significant

S. creatinine (mg/dl) was observed pre and post procedure. The mean±SD pre-procedure was 1.1±0.3 mg/dl with ranged from 0.6 to 1.9 mg/dl in group I patients. In Group II the mean±SD pre-procedure was 0.95±0.3 mg/dl with ranged from of 0.6 to 1.6 mg/dl. The mean S. creatinine difference pre-procedure was statistically significant ($p<0.05$) between two groups in unpaired t-test.

A total of 46.8% found HTN, out of which 5.8% had >0.5mg/dl rise serum creatinine and 9.6% patients had >25.0% rise serum creatinine. ACE/ARB found 35.1%, among them 7.7% had >0.5mg/dl rise serum creatinine and 15.4% patients had 25.0% rise serum creatinine. DM found 23.4% among them 15.4% had >0.5mg/dl rise serum creatinine and 26.9% patients had> 25.0% rise serum creatinine. Pre-existing renal insufficiency found 8.1%, among them 33.3% had >0.5mg/dl rise serum creatinine and 44.4% patients had >25.0% rise serum creatinine. NSAIDS found 9.0%, among them 20.0% had >0.5mg/dl rise serum creatinine and 40.0% patients had> 25.0% rise serum creatinine. LVEF <40% found 8.1%, among them 33.3% had >0.5mg/dl rise serum creatinine and 66.7% patients had >25.0% rise serum creatinine. Dose of contrast £150ml found 72.1%, among them 1.25% had >0.5mg/dl rise serum creatinine and 2.5% patients had >25.0% rise serum creatinine. Dose of contrast >150ml found 27.9%, among them 12.9% had >0.5mg/dl rise serum creatinine and 19.4% patients had> 25.0% rise serum creatinine.

For DM, the reference group is non DM. A patient who had DM compared to a non diabetic is 4.15 times more likely to develop CIN.

Preexisting renal insufficiency had a 2.10 times increased risk to developed CIN.

For patients getting ACE inhibitor/ARB, the reference group is those getting not ACE inhibitor/ARB. ACE inhibitor/ARB users compared to non users are 1.67 times more likely to develop CIN.

For NSAID user the reference group is non user of NSAID. NSAID users compared to non NSAID users are 1.05 times more likely to develop CIN.

Contrast volume level is a quantitative numerical variable, an abnormal contrast volume (>150 ml) had a 3.63 times increase in odds of more likely to developed CIN.

LVEF is a quantitative numerical variable, patients with low LVEF (<40%) had a 3.39 times increased risk to develop CIN.

Discussion:

A recent epidemiological study reported a CIN rate of 14.5% in series of approximately 1800 consecutive patients undergoing cardiac procedure.[9] Once contrast induced nephropathy occurs, it is associated with a markedly higher in hospital and long term mortality following PCI. This was also supported by Rihal et al from the Mayo clinic data base, reviewing predictors of death after PCI.

In this study it was observed that most (35.1%) of the patients was 50-59 years age group and mean age of the patients was 51.9±9.6 years with ranged from 25 to 75 years. Increased life expectancy, geographical and racial influences may have significant impacts on higher age ranges. Among the sex distribution male were predominant and male female ratio was 1.7:1

In the present study it was observed that 11.7% developed AKI and 88.3% did not develop AKI. It was also observed that 84.6% and 15.3% had diabetes mellitus (DM) in group I and group II respectively ($p=0.001^s$). Similarly, 53.8% in group I and only 2.0% in group II patients had preexisting renal insufficiency ($p=0.001$). Diabetes mellitus (DM) and preexisting renal insufficiency were significantly ($p<0.05$) higher in group I patients. As regards to the incidence of DM and preexisting renal insufficiency, a number of investigators studied and found similar findings in their study

In group I 61.5% patients had HTN and in group II 44.9% patients had HTN respectively, which was almost similar between two groups. No statistical significant ($p>0.05$) was found regarding HTN in this study.

More than two third (69.2%) of the patients in group I received angiotensin converting enzyme (ACE) inhibitor/ARB and 30.6% in group II patients. Similarly, NSAIDs found 46.2% in group I and only 4.1% in group II patients. ACE inhibitor/ARB and NSAID were significantly ($p<0.05$) higher in patients with CIN in the present study.

In group I more than two third (69.2%) had LVEF < 40 % however none had LVEF £ 40% in group II ($p=0.001$).

Regarding the contrast volume, it was found that the amount of contrast is positively correlated with the incidence of CIN. Our study revealed that 76.9% and 21.4% patients had volume of contrast media (CM) >150 ml in group I and group II had remarkable impact on the development of CIN. On the other hand mean volume of CM was significantly ($p<0.05$) higher in group I patients, which was 156.9±44.8ml and 115.4±30.0 ml in group II, which is almost similar with Soofi study, where the authors found contrast volume 62.31% and 37.68% in dose <150 ml and >150ml respectively.

In this study S. creatinine (mg/dl) was observed before and 48 hours after CAG/PCI and found that the mean±SD before CAG/PCI was 1.1±0.3 mg/dl with ranged from of 0.6 to 1.9 mg/dl and 0.95±0.3 mg/dl with ranged from of 0.6 to 1.6 mg/dl in group I and group II respectively. The mean S. creatinine level before CAG/PCI was significantly ($p<0.05$) higher in group I patients. On the other hand the mean±SD after 48 hours of CAG/PCI was 1.4±0.37 mg/dl with ranged from of 1 to 2.2 mg/dl in group I and 1.1±0.2 mg/dl with ranged from of 0.7 to 1.4 mg/dl in group II. The mean S. creatinine level after 48 hours of CAG/PCI was also significantly ($p<0.05$) higher in group I patients. The mean±SD difference of S. creatinine level before & after 48 hours of CAG/PCI was 0.3±0.2 in group I, which indicates that S. creatinine level was significantly ($p<0.05$) increased after 48 hours of CAG/PCI. However the mean±SD difference of S. creatinine level before & after 48 hours of CAG/PCI was 0.15±0.2 in group II which also increased after 48 hours of CAG/PCI but not significant ($p>0.05$). In this study it was observed that the mean serum creatinine was 1.10±0.3 mg/dl ranged from 0.6-1.9 mg/dl and 1.13±0.5 mg/dl ranged from 0.5 -1.9 mg/dl during baseline and after 30 days respectively in CIN patients. The mean difference was 0.12±0.3 mg/dl, which was not statistically significant ($p>0.05$). Similarly the mean eGFR was 66.7±10.6 ml/min/1.73 m^2 ranged from 50-80 ml/min/1.73 m^2 during base line and 65.2±8.9 ml/min/1.73 m^2 ranged from 50-80 ml/min/1.73 m^2 after 30 days. The mean eGFR difference was 1.5±4.9, which was not significant ($p>0.05$).

This indicates that even after development of CIN conservative treatment with appropriate medication and dietary restriction successfully prevents progression of AKI due to CIN to progressive renal failure.

Various international studies have identified risk factors for contrast nephropathy, which include pre existing renal impairment, diabetes mellitus, ionic contrast, high dose of contrast, concurrent use of nephrotoxic medication, non steroidal anti inflammatory drugs and angiotensin converting enzyme inhibitors. Presence of two or more risk factors was associated with high frequency of contrast nephropathy which again emphasises the fact that addition of another risk factor in presence of one risk factor greatly enhance the risk of CN.

In this study it was observed that DM, preexisting renal insufficiency, ACE inhibitor/ARB, NSAIDs, contrast volume (>150 ml), LVEF (<40%) are significantly ($p<0.05$) associated for CIN development. A patient who had DM compared to a non diabetic is 4.15 times more likely to develop CIN. Preexisting renal insufficiency had a 2.10 times increased risk to developed CIN. ACE inhibitor/ARB users compared to non users are 1.67 times more likely to develop CIN. NSAIDs users compared to non NSAIDs users are 1.05 times more likely to develop CIN. An high contrast volume (>150 ml) use had a 3.63 times increase in odds to develop CIN. Patients with low LVEF (<40%) had a 3.39 times increased risk to develop CIN.

Conclusion:

CIN is an iatrogenic but preventable disorder results from the administration of contract media. Although rare in the general population, CIN occurs frequently in patients with underlying renal dysfunction and diabetes. In patients with pre angiographic normal renal function, the prevalence is low but in pre-existing renal impairment it may pose a serious threat. Risk factors are synergistic in their ability to predispose to the development of CIN. A careful risk-benefit analysis must always be performed prior to the administration of contrast media to patients at risk for CIN.

Study Limitations:

This study included a small population, admitted to a single center and other cause of nephropathy could not be excluded. The definition of CIN is based on the absolute or relative increase in Cr

level, compared with baseline value, after a patient has been exposed to a contrast agent, when alternative explanations for renal impairment have been excluded. Although all the patients effectively underwent contrast media exposure, and 11.7% developed acute renal failure within 48 hours after it, this cannot exclude the possibility that other factors, such as hemodynamic instability, might have contributed, at least in part, to renal impairment, and influenced the clinical outcome of this patients.

Recommendations

To know the correct incidence of CIN and risk factors in Bangladeshi population, a large scale, multicenter study is likely to be needed.

Even small changes in renal function carry significant risk for the affected patients, making the prevention of CIN of paramount importance. Adequate risk assessment before exposure to contrast media is desirable. If possible, the risk factors should be corrected before contrast administration.

Patients with, non modifiable risk factors should received the minimal necessary dose of contrast, preferably below 100 ml and should have their renal function checked by serum creatinine before and at 48 to 72 hours after administration and estimated GFR should be calculated. Routine prophylaxis like periprocedural saline hydration is recommended because of high incidence of CIN. Alternative imaging in high risk patients should be considered.

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