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Original Research Article

Study on Incidence and Risk Factors of ContrastInduced Nephropathy in Patients Undergoing Cardiac Catheterization Studies

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Abstract:

Aim of the Study: To assess the incidence of contrast induced nephropathy, defined as a raisein post-procedural creatinine by >25% over the baseline, in patients undergoing cardiac catheterization studies**.**

Material & Methods: Patients were identified as hypertensives if already diagnosed and on treatment or newly detected with a Blood pressure of 140/90 or more as defined by JNC. Patients with Diabetes mellitus were defined as known diabetics on treatment or patientswith a random blood sugar value of >200mg/dl as defined by ADA guidelines. Blood.

Results: Results are presented as mean ± SD or a percentage of the total. The significance of difference in means between two groups was calculated by means of Student's t test and the significance of difference in proportions were compared with Pearson's $\chi 2$ (chi-square) test. Statistical significance was taken to be significant at 1% level when P value was < 0.001, significant at 5% level when P value was between 0.011 to 0.05, and not significantat 5% level when P value was >0.05.

Conclusion: It was noted that among the 200 patients followed up in the Department of Cardiology 56 developed CIN (28%). Among the patients who developed CIN, it was noted that common risk factors were increased Age, elevated baseline serum creatinine,low baseline creatinine clearance, and multi-vessel coronary disease. Identification of these risk factors before subjecting the patient to angiogram studies gives us an opportunity to anticipate development of CIN and to use prophylactic measures to prevent CIN.

Keywords: Contrast Induced Nephropathy; Non-Steroidal Anti-Inflammatory Drugs.

Introduction

Nephropathy induced by contrast media is a significant yet underestimated problem in clinical practice. With the increasing use of contrast media in diagnostic and interventional procedures over the last 30 years, this form of nephropathy has become the third leading cause of hospital-acquired acute renal failure, accounting for 12% of all cases [1]. CIN is the third most usual cause of hospital-acquired acute renal failure after impaired renal perfusion and nephrotoxic treatments. The incidence of CIN has been calculated to be >2% in the general population but in high-risk patients, i.e., diabetic patients, subjects with history of congestive heart failure, chronic renal impairment, and older age, the incidencehas been considered to be >20% to 30% [2].

The risk of contrast-medium nephropathy continues to be considerable, despite the use of newer and less nephrotoxic contrast agents in high-risk patients in recent years [2]. Affected patients are at increased risk of morbidity and death. They may require short- term hemodialysis, which can extend their hospital stay and increase the risk of permanent impairment of the renal function [3]. The rate of contrast-medium nephropathy reported in studies that included patients with pre-existing renal dysfunction or diabetes mellitus in whom a standard hydration protocol was not administered [4] is between 12% and 26%. Lower rates (3.3%) have been reported among patients without these risk factors [5].

The reason a number of patients develop acute renal failure following a cardiac procedure is the necessity to perform theseprocedures in the presence of pre-existing, and often non-modifiable, risk factors for renal impairment. Previous retrospective work in outpatients who underwent CECT found the prevalence of CIN to be 5 to 13% and indicates that patients without baseline renal insufficiency or chronic kidney disease may still be at risk for CIN

in this population. Many individual risk factors have been reported for the development of CIN. The combination of two or more risk factors is rather common in daily practice; the cumulativerisk of several variables on renal function is recognized. A simple risk score has been developed by which the risk of contrast induced nephropathy after PCI can be simply assessed using readily available information [6]. Recently suggested definition by Harjai, et al. categorized, contrast nephropathy as grade 0 (serum creatinine increase <25% above baseline and <0.5 mg/dL above baseline), grade 1 (serum creatinine increase ≥25% above baseline and <0.5 mg/dL above baseline), or grade 2 (serum creatinine increase ≥0.5 mg/dL above baseline).

This study aims to assess the incidence of contrast induced nephropathy and identify the common risk factors of contrast induced nephropathy in patients undergoing percutaneous coronary intervention procedures.

Aims of the Study

1. To assess the incidence of contrast induced nephropathy, defined as a raise in post-procedural creatinine by >25% over the baseline, in patients undergoing cardiac catheterization studies.
2. To identify the common and important risk factors of contrast induced nephropathy in patients undergoing cardiac catheterization studies.

Material & Methods

The present study was undertaken in the Department of Internal medicine and cardiology Osmania Medical College / Hospital. All procedures were elective, no emergency procedure was included in the study, thereby ruling out patients with MI within the previous 72 hours from the study.

None of the patients included in the study had any prior angiographic study within the previous week. Hydration status was assessed clinically. No specific hydration protocol was followed in the patients.

Study Design

Contrast induced nephropathy was defined as an increase in post-procedural creatinine by more than 25% from the baseline. All patients who had an increase in post-procedural creatinine by more than 25% over baseline were diagnosed to have Contrast Induced Nephropathy. Serum creatinine was estimated by ERBA XL 300 automated analyzer using Alkaline picrate method in our Biochemistry department. Serum creatinine values were followed up in the patients before coronary angiogram was performed and at 24 and 48 hours after the procedure, and peak serum creatinine levels were considered for calculation of increase from baseline. Patients were identified as hypertensives if already diagnosed and on treatment or newly detected with a Blood pressure of 140/90 or more as defined by JNC 8.

"Anemia" was defined according to the World Health Organization (WHO), anemia is defined as hemoglobin (Hb) levels <12.0 g/dL in women and <13.0 g/dL in men.

Serum cholesterol was measured using enzymatic method, serum triglyceride using enzymatic colorimetric method and serum HDL-C using Polyethylene Glycol-CHOD-PAP method by the automated analyzer. Dyslipidemia was defined by ATP3 guidelines as Total cholesterol > 200mg/dl, LDL-C >130mg/dl, HDL-C < 40 in men and <50 in women,TGL > 150mg/dl. Lipoprotein analysis was performed on serum obtained after a 12 hour fast. Total cholesterol, HDL-C and TGL were measured, and LDL-C was calculated using the Friedewald's formula.

LDL-C = Total cholesterol - HDL-C – (TGL/5)

Height and weight of all patients was documented, and Body Mass Index calculated usingthe formula.

BMI = (weight in kg)/ (Height in metres2)

Urine output of the patient was monitored. Urine albumin, echocardiogram for quantification of Left Ventricular function and renal angiogram was also performed to rule out possibility of renal artery stenosis. All patients were screened with a urine examination for albuminuria and an ultrasound of the abdomen to rule out underlying primary renal disease.

None of the patients included in the study had underlying renal disease. The contrast media used were non-ionic monomer Iohexol (Low osmolar) and iso osmolar iodixanol. Use of high or iso osmolar contrast medium was subject to availability and presence of Left Ventricular dysfunction or renal failure in view of the high cost of iso- osmolar contrast medium.

All patients were observed for development of hypotension, anaphylactoid reactions to contrast medium, or any other procedural complication during and immediately after the angiogram. None of the patients in the study developed any significant hypotension during the procedure requiring inotropic support and no patient developed any serious reaction to the contrast medium.

No specific prophylactic measure was used towards prevention of contrast induced nephropathy.

Results

Table 1: Baseline Characteristics of Study Population

	Frequency	Percent
Age		
≤50	79	39.5
51 - 60	68	34.0
> 60	53	26.5
Gender		
Male	160	80.0
female	40	20.0
HTN	90	45.0
DM	78	39.0
BMI < 25	154	77.0
BMI ≥ 25	46	23.0

Table 2: Distribution based on gender

	CIN		No CIN	
Gender	**No.**	**%**	**No.**	**%**
Male	41	73.2	119	82.6
Female	15	26.8	25	17.4
Total	56	100.0	144	100.0
chi square	2.23		p value	0.135

Table 3: Distribution based on other baseline characteristics

	CIN		No CIN		Chi square	P value
	No.	**%**	**No.**	**%**		
HTN	25	44.6	65	45.1	0.004	0.95
DM	23	41.1	55	38.2	0.14	0.708

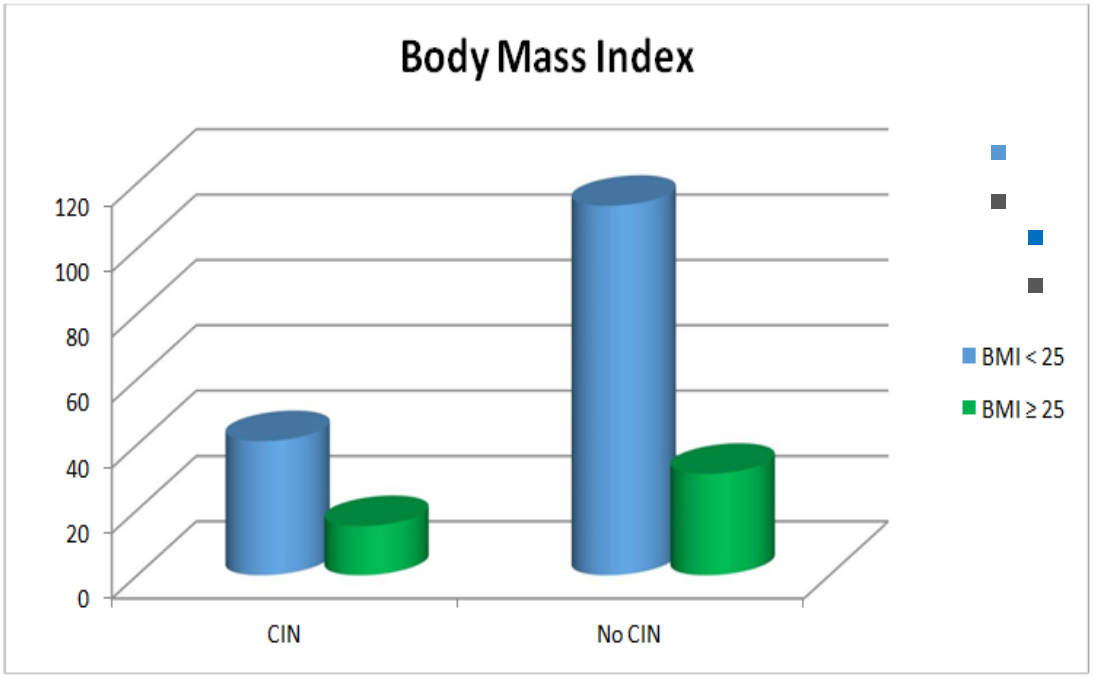

Figure 1: Body Mass Index

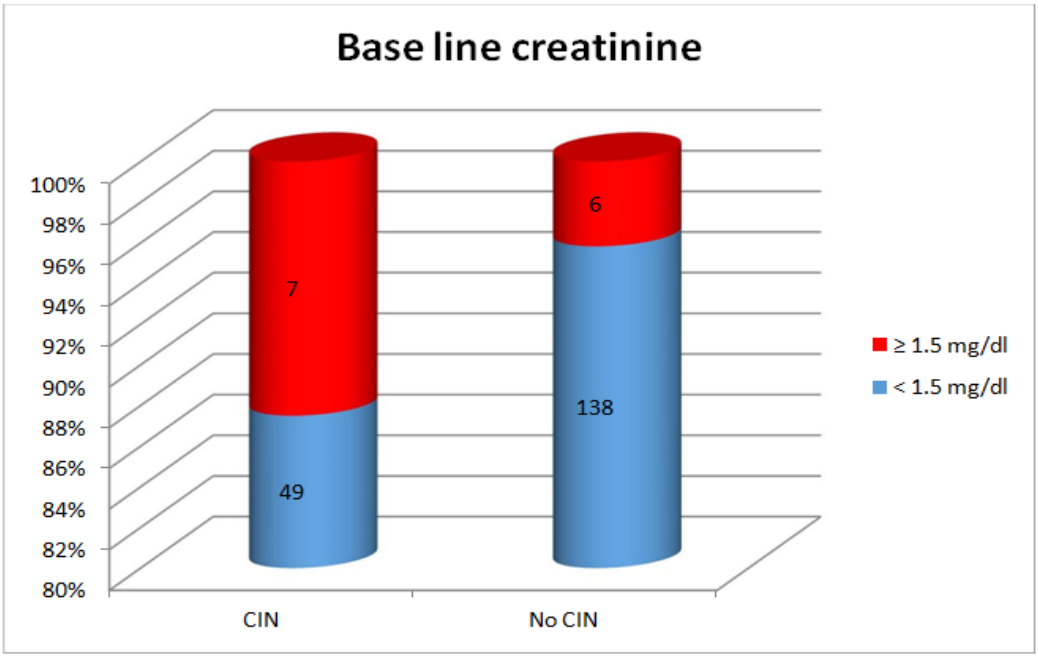

Figure 2: Baseline Creatinine

Table 4: comparison between Left ventricular Ejection Fraction and CIN

LVEF	CIN		No CIN	
	No.	%	No.	%
< 40 %	17	30.4	12	8.3
≥ 40 %	39	69.6	132	91.7
Total	56	100.0	144	100.0
chi square	15.7		p value	0.001

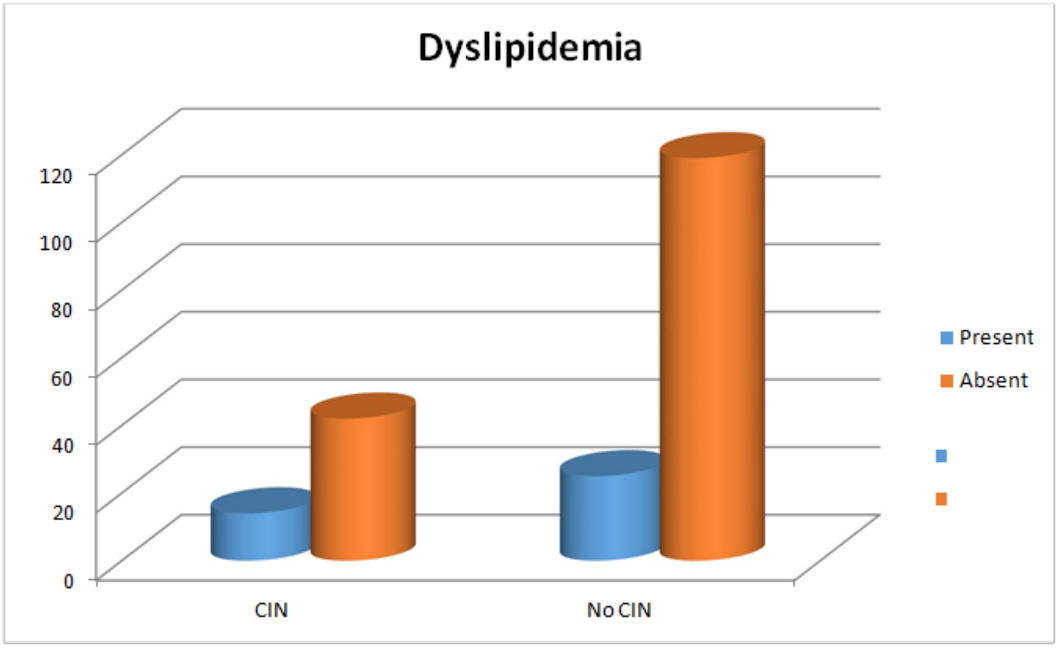

Figure 3: Dyslipidemia

Table 5: comparison between use of contrast media and CIN

Contrast	CIN		No CIN	
	No.	%	No.	%
IOCM	29	51.8	93	64.6

LOCM	27	48.2	51	35.4
Total	56	100.0	144	100.0
chi square	2.7		p value	0.096

Table 6: Comparison between No. of Vessels involved and CIN

No. of Vessels	CIN		No CIN	
	No.	%	No.	%
1	22	39.3	54	37.5
> 1	34	60.7	90	62.5
Total	56	100.0	144	100.0
chi square	0.192		p value	0.909

Table 7: Study parameter between groups

	CIN		No CIN		t value	p value
	Mean	SD	Mean	SD		
Age	57.9	6.7	51.4	9.8	4.574	.001
BMI	22.3	2.8	22.0	2.8	.452	.652
Hb	11.9	1.5	12.0	1.4	0.336	.737
Urea	30.7	6.3	31.2	5.9	0.556	.579
Creatinine	1.2	.2	1.1	0.2	2.732	.007
Cr. Clearance	77.8	17.7	85.3	22.9	2.19	0.029
PCV	32.7	1.8	32.6	1.6	.369	.713
LVEF	51.1	12.7	54.0	8.3	1.915	.057
Amount of contrast	34.64	8.5	36.5	8.15	1.44	0.149

Discussion

Our study has attempted to assess the incidence of contrast induced nephropathy in patients undergoing cardiac catheterization studies in our hospital and to identify the major risk factors for developing CIN in this population. The major findings of this study are that the incidence of contrast nephropathy is as high as 28% among the population undergoing cardiac catheterization studies at our Institute. The rates of contrast induced nephropathy reported in various studies that included patients with pre-existing renal dysfunction or diabetes mellitus in whom a standard hydration protocol was not administered is between 12% and 26 %. No patient in our study developed acute renal failure necessitating Haemodialysis [7]. The incidence of ARF requiring Haemodialysis has been reported in most studies as <1%.

Mc Cullough PA et al [8] also reported an increase in serum creatinine by 25% in 14.5% of patients who underwent coronary angiography (95 percent confidence interval, 12.9 to 16.1 percent). An incidence of 16.5% was reported by Iakovou I et al [9], who also reported an increased incidence of CIN among females. In our study females form only 15% of the study population but the incidence of CIN among them was 16.6%, higher than the incidence among males (14.4%), comparable with the incidence reported by Iakovou et al though not found to be statistically significant. Most studies performed internationally have found that the risk of CIN increases with increasing age and age >75 years was a significant risk factor for development of CIN. The study by Mehran et al [9] in 2004 puts the incidence at as high as 21.8% among those aged >75 years. The cause is probably multifactorial and related to alterations in renal glomerular and tubular functions and perhaps to renovascular disease. Our study shows that incidence of CIN does increase with increasing age, with the population between 51-60 years having an incidence as high as 58.9%. Age has also been found to be a statistically significant factor in development of CIN in our study.

That osmolality is an important factor in contrast-medium–induced nephropathy is supported by several studies. In a prospective, randomized study involving 1196 patients who underwent angiocardiography, Rudnick et al(10) found no differences in the incidence of nephropathy (defined as an increase of 0.5 mg per deciliter or more in the serum creatinine concentration within 72 hours after the administration of contrast medium) between patients receiving iohexol (low-osmolar; 780 mOsm per kilogram of water) and patients receiving diatrizoate (high-osmolar; 1870 mOsm per kilogram of water) among low-risk patients (patients without diabetes who had a base-line serum creatinine concentration of less than 1.5 mg per deciliter [133 μmol per liter]).

However, among patients without diabetes whose serum creatinine concentrations were higher than 1.5 mg per deciliter, the incidence of nephropathy was reduced from 27.0 to 12.2 percent by the use of Iohexol [10] Among patients with diabetes, the

incidence was reduced from 47.7 to 33.3 percent. Overall, patients receiving high-osmolar contrast medium were 3.3 times as likely to have nephropathy induced by contrast medium as that receiving low-osmolar contrast medium [10]. Barrett and Carlisle performed a metaanalysis to determine the relative nephrotoxicity of contrast mediums using the results of 14 trials and concluded that the use of low-osmolar contrast medium rather than high-osmolar contrast medium was beneficial to patients with preexisting renal failure [11]. A similar pattern was observed by Aspelin et al [12] in a study conducted in 2003. Our study revealed almost same incidence of CIN among patients in whom LOCM and IOCM was used. As our institution doesn't recommend the usage of HOCM we couldn't assess the effects of HOCM.

In most studies, the volume of contrast medium administered during coronary angiography correlates with the risk of CIN. A study of more than 7000 patients by Rihal CS et al [5] showed that each 100 mL of contrast medium administered correlates with a hazard ratio for CIN of 1.12(5). In our study, there was no significant difference among the incidence of CIN with regards to the amount of contrast used. Murphy SW et al [10] also noted that the individuals with chronic renal insufficiency (Serum creatinine >= 2.0mg/dl) were at a greater risk of contrast induced renal injury.

In many studies preexisting renal disease has been the greatest independent predictor of CIN, and its severity (as measured by serum creatinine concentration) directly correlating with the incidence of CIN. In a study by Gruberg et al that included 439 patients with serum creatinine levels of 1.8 mg/dL or higher before coronary angiography, the incidence of CN was 37%; 7.1% and 0.9% of the patients underwent short-term and long- term dialysis, respectively. Similar pattern was also noted in studies conducted by Mehran et al [12], Manske CL et al [13].

Our study also showed a similar pattern, with a baseline serum creatinine value of >1.5mg/dl being observed to be a statistically significant risk factor for the development of CIN. It was also noted in our study that the baseline creatinine clearance as calculated by the Cockroft and Gault formula was lower (67.89 ml/min) in the study population who developed CIN compared to those who did not (83.23ml/min). Creatinine clearance was also observed to be a statistically significant risk factor with a p-value of 0.001. It was also found to be a significant independent predictor of deterioration of renal function by logistic regression.

Hypertension was reported to be an independent predictor of CIN in the study conducted by Iakovou I et al. The study by Mehran R et al also finds hypertension to be a significant predictor of CIN with 15.9% among hypertensives developing CIN. The study by Gruberg L et al does not find a statistically significant association between hypertension and CIN. In our study the incidence of CIN in hypertensives was 44% but there was no statistically significant association between hypertension and CIN. However, it was found to be a significant risk factor in predicting development of CIN by logistic regression.

Body Mass Index was not found to be a statistically significant risk factor in our study. No study has been done to correlate BMI with CIN. There has been one study by Omer Toprak et al [14] published in March 2006 which showed an increased risk of CIN among patients with metabolic syndrome. In this group of patients, it was reported that impaired fasting glucose, high triglyceride levels were independent predictors of risk of CIN. In our study there was no statistically significant difference observed in patients based on BMI between CIN and No CIN p >0.05.

Dyslipidemia in our study defined as per ATP 3 guidelines was found to be statistically not significant as a risk factor for CIN. 25% of patients with dyslipidemia developed CIN in our study. Hypercholesterolemia has been shown to be a significant risk factor for the development of CIN in the study by Mehran R et al with an incidence of CIN being 13.2%. Hypertriglyceridemia has been shown to be a significant risk factor for CIN in the study by Omer Toprak et al [14]. There has also been an animal study by Andrade L et al which shows that hypercholesterolemia in rats aggravates radio contrast nephropathy.

Multiple coronary vessels being diseased as detected by coronary angiogram was not a significant risk factor statistically. Incidence of CIN in patients with more than one vessel disease was 60.7%. However, by logistic regression it was an independent predictor of CIN. It has also been documented as a significant risk factor for CIN in studies by Mehran R et al [12] and Omer Toprak et al [14].

Studies have shown that reduced left ventricular ejection fraction (≤49%), advanced congestive heart failure (New York Heart Association class III or IV), or any history of congestive heart failure are independent risk factors for CN and contribute even greater risk in patients with diabetes or renal disease. A recent study conducted by Marenzi.G et al has reported a Left ventricular ejection fraction of <40% as being a significant risk factor for development of CIN following primary angioplasty. The risk associated with congestive heart failure is likely due to derangements in renal blood flow due to low cardiac output. The risk is probably increased by this population's use of

specific medications such as angiotensin converting enzyme (ACE) inhibitors, diuretics, and aspirin [15]. Our study showed an incidence of CIN to be 30.4% among patients with an LVEF <40%, which was statistically significant.

This study has shown that risk factors for CIN are an elevated baseline creatinine, a low creatinine clearance, the type and amount of contrast medium used, LVEF and the presence of multivessel CAD. Identification of these risk factors before subjecting the patient to angiogram gives us an opportunity to use prophylactic measures to prevent CIN and also anticipate CIN in high-risk patients.

Conclusions

- There is a significant risk of contrast induced nephropathy in patients undergoing cardiac catheterization studies especially among the elderly, and among those with pre- existing renal failure.
- The risk of CIN is also increased by the presence of multivessel coronary disease by angiogram and by the presence of left ventricular dysfunction,
- There were no patients in this study who developed renal failure needing Haemodialysis. The type of contrast and amount used also determine development of CIN.
- Risk of CIN can be predicted before the procedure based on risk factors and suitable precautions can be taken including use of low or iso-osmolar contrast media, minimizing the amount of contrast medium used.

It was noted that among the 200 patients followed up in the Department of Cardiology 56 developed CIN (28%). Among the patients who developed CIN, it was noted that common risk factors were increased Age, elevated baseline serum creatinine, low baseline creatinine clearance, and multi-vessel coronary disease. It was also noted that incidence of CIN was higher among patients with hypertension, diabetes, poor LV function, and among the patients who underwent studies with higher amounts of contrast medium was used. Identification of these risk factors before subjecting the patient to angiogram studies gives us an opportunity to anticipate development of CIN and to use prophylactic measures to prevent CIN.

Scope for Future Studies

This study identifies only potential risk factors of Contrast Induced Nephropathy. Furtherstudies need to be done regarding possibility of preventing CIN, various prophylactic measures that might be useful in a Government Hospital setting. This study has not included patients undergoing emergency angiographic procedures like PTCA etc. In such conditions the risk factors are likely to be more and unique to the situation. A study in such a setting will help define the risks better. A long term follows up of patients who develop CIN could be done to determine the degree of residual renal damage and possibility of permanent renal dysfunction leading to Chronic Kidney Disease. A thorough study regarding the relationship between atheromatous disease load and CIN can also be done considering the fact that dyslipidemia, multivessel CAD have been known to predispose to CIN.

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