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CONTRAST-INDUCED NEPHROPATHY;
INCIDENCES & RISK FACTORS AFTER CORONARY ANGIOGRAM.

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ABSTRACT… Introduction: Contrast induced nephropathy (CIN) is a disorder characterized by the onset of acute renal failure within 24 to 72 hours after the administration of iodinated contrast medium after coronary angiography. CIN is associated with prolonged hospitalization and adverse clinical outcomes. The objective of this study is to determine the frequency of contrast induced nephropathy in patients of coronary artery disease undergoing coronary angiography in local population. **Setting:** Department of Cardiology, Faisalabad Institute of Cardiology. **Period:** 16-04-2016 to 15-10-2016. **Subjects and Methods:** 200 patients of coronary artery disease booked for coronary angiogram. Study design was Cross-sectional. Baseline characteristic and history of risk factors of coronary artery disease were noted. Serum creatinine level was recorded at baseline and after 48 hours of angiography by sending blood sample to the hospital pathology department and were noted. Contrast induced nephropathy was assessed. **Results:** Mean age of the patients was 53.61±12.48 year. Patients with age between 30-50 years were 76(38%) and patients with age 51-70 years were 124 (62%). Out of 200 patients, 130 (65%) were males while remaining 70 (35%) were females. In the study population 14 (7%) developed contrast induced nephropathy (CIN). Mostly patients of 51-70 years of age group developed CIN. CIN was reported in 9(6.92%) male patients and 5(7.1%) female patients. Among diabetic 4 (3.57%) patient developed CIN. Among hypertensive patients 2 (2.77%) patient developed CIN. Similarly in patients presented with acute coronary syndrome 8 (7.61%) patient developed CIN. **Conclusion:** In conclusion, contrast induced nephropathy in patients with coronary artery disease undergoing coronary angiogram was found in 7%. CIN is a relative common finding following coronary angiography in patients especially in elderly and male patients. More incidences of CIN were noted in patients presented with acute coronary syndrome and in diabetic patients.

key words: Contrast induced nephropathy, Coronary angiography.

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INTRODUCTION

The iatrogenic acute renal injury after intravascular radio-opaque contrast media is known as Contrast-induced nephropathy (CIN). Contrast-induced nephropathy was first detected in 1950s during intravenous pyelography.[1,2] CIN is the third most common hospital acquired cause of renal impairment inspite all technological advances.[3] The development of new imaging methods and interventional procedures in both cardiac and non-cardiac modalities involves administration of intravascular contrast. Similarly widespead use of primary PCI and emerging cardiac modalities exposes patients to higher volume of contrast media, leading to increased risk renal injury.[4] Despite risk assessment and prophylactic measures, the prevention of renal injury after coronary angiogram remains a significant clinical challenge.[5]

Atherosclerotic coronary heart disease (CHD) is a worldwide health epidemic. CHD contributes to more than 1.2 million myocardial infarctions (MI) and nearly 500,000 deaths in the United States each year.[6] The development of atherosclerotic CHD is a complex, multifactorial process in which genetics, gender, risk factors, and aging play varying roles in predisposing susceptible patients. Accurate risk assessment is the cornerstone of cost-effective individual based

preventive care. Coronary angiogram is usually required in patients with high risk clinical features or noninvasive test findings. However these procedures are associated with complications. One of serious complication is Contrast-induced nephropathy (CIN), that is associated with intravascular injection of radiographic contrast media.[7,8] It has become one of common causes of hospital acquired acute renal impairment and has significant morbidity and mortality despite the use of less nephrotoxic contrast agent.[9]

The CIN is documented in 1%-6% in different studies.[10] The clinical and periprocedural factors helps in estimation of risk assessment of CIN. Although chronic kidney disease, is the identified risk factor for CIN however, cases are reported without pre-existing renal impairement.[3] Similarly higher risk of CIN are documented in patients planned for percutaneous coronary intervention (PCI) and patients with diabetes, hypertension, anemia, heart failure or acute coronary syndrome.[9,11] Risk scoring systems for CIN developed from cohort studies and helps in prevention.[12,13]

Contrast-induced nephropathy is well-suited area for ongoing cardiovascular and nephrology research. However scarce data is available on contrast induced nephropathy in patients who underwent angiogram in our community. The objective of this study is to know the burden of CIN in patients of coronary artery disease so that early preventive management will be applied to the patients to reduce the rate of this complication after coronary angiogram.

Material and method

After taking approval from hospital ethical committee, patients coming through the Emergency department of Faisalabad institute of cardiology were enrolled for six months starting from 16-04-2016. Informed consent was taken from them. Both males and females with age between 30-70 years presented with clinical features of coronary artery disease booked for coronary angiogram were included in the study. Following cases were excluded from the study:

- Patients treated with hemodialysis.
- Patients with renal transplantation.
- Patients received administration of metformin, nonsteroidal anti-inflammatory drugs, aminoglycosides before or after angiography.
- Patients with infection and a history of collagen vascular disease.
- Patients with abnormal renal function tests before angiography.

History of Diabetes Mellitus, Hypertension and Acute coronary syndrome were noted. Coronary angiography was performed from femoral route by the researcher. Low osmolar nonionic contrast media was used in angiography. Serum creatinine level was recorded at baseline and after 48 hours of angiography by sending blood sample to the hospital pathology department and noted. Contrast induced nephropathy was diagnosed as elevation of at least 0.5mg/dl in the serum creatinine concentration from base line up to 48 hours after administration of contrast agent. Patient was remain admitted in the hospital for follow-up. All the information was collected on proforma.

The Study design was Cross-sectional. Non-probability consecutive sampling Technique was used.

All the data was entered in SPSS version 16. Mean and standard deviation was calculated for all quantitative variables like age, serum creatinine level at baseline, after 48 hours and difference. Frequency and percentage was calculated for all qualitative variables like gender, diabetes mellitus, hypertension and acute coronary syndrome. Post-stratification Chi-square test was applied. P-value 0.05 was taken as significant.

RESULTS

Mean age of the patients was 53.61±12.48 year. Patients with age between 30-50 years were 76 (38%) and patients with age 51-70 years were 124 (62%). Out of 200 patients, 130 (65%) were males while remaining 70 (35%) were females (Table-I). In the study population 14 (7%) developed contrast induced nephropathy (CIN) (Figure-1). Mostly patients of 51-70 years of age group developed CIN. CIN was reported in 9(6.92%)

male patients and 5(7.1%) female patients. Among diabetic 4 (3.57%) patient developed CIN. Among hypertensive patients 2 (2.77%) patient developed CIN. Similarly in patients presented with acute coronary syndrome 8 (7.61%) patient developed CIN (Figure-2).

Parameter	Number (n=200)	%
AGE		
Mean±SD	53.61±12.48	
Age 30-50 years	76	38%
Age 51-70 years	124	62%
Gender		
Male	130	65%
Female	70	35%
Risk Factors		
Diabetes Mellitus	112	56%
Hypertension	72	36%
ACS	105	52.5%

Table-I. Baseline characteristics.

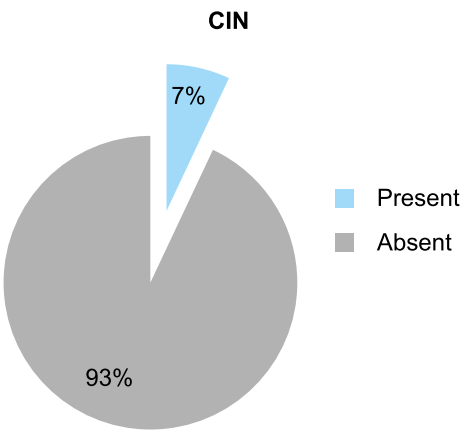

Figure-1. Incidences of contrast induced nephropathy (CIN).

DISCUSSION

Cardiovascular mortality and morbidity is decreased with the remarkable evolution in interventional therapies to treat coronary artery disease (CAD).[14] Coronary arteriography establishes the severity of CAD, defines therapeutic options, and determines the prognosis of patients. In the United States, approximately 2 million coronary angiograms are performed each year.

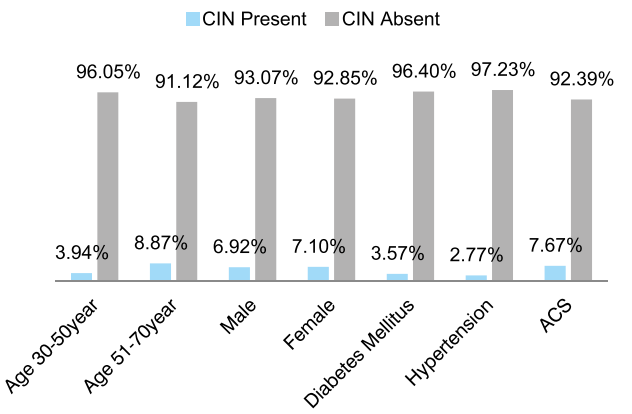

Figure-2. Incidences of contrast induced nephropathy (CIN) in different sub-group.

Although there are no absolute contraindications to coronary arteriography but certain disease states that are relative contraindications including renal impairment. Coronary angiogram is associated with complications, one of these is worsening of renal function after contrast agent administration. In the last few decades, invasive management strategies have established themselves as preferred way of revascularization in patients with CAD, this strategy exposes the patient to the risk of high contrast volume and Contrast induced nephropathy.

Contrast induced nephropathy (CIN) is a significant health problem. Although often a transient injury, CIN may cause persistent renal impairment and lead to prolonged hospital stay and adverse cardiovascular outcomes. The current definition of the CIN is based on the absolute or relative increase in the serum creatinine.[15] The creatinine may not actually reflect the underlying kidney function and give an accurate prediction of the glomerular filtration rate (GFR). Cystatin C is considered as a more robust marker for the estimation of GFR and may be useful in monitoring for the CIN.[16] CIN usually develops within 24–48 hours of exposure to the contrast medium.[17] The mechanisms of development of CIN are not completely understood yet.[18,19] Different incidences of CIN are reported in studies.[20-22] Mehran et al studied 8600 cases and found that 13% patients of coronary artery disease developed CIN.[13] Weisbord et

al, also studied development of CIN and found 13.7% cases with CIN which is close to our findings.[23] Rihal et al found an overall incidence of 3.3% in their series of 7586 patients who underwent cardiac catheterization and the risk of CIN in patients with normal renal function was 2.4%[24]. Few authors have shown a significantly higher incidence of CIN in patients undergoing contrast-related procedures ranging from 5% to 15%.[25] Our study also reported incidences of 5% in patients undergoing CAG, similar incidences are reported in previous studies.[26-28]The stringent exclusion criteria employed in our study could have contributed to the low incidence of CIN in comparison to other studies.[29] We excluded patients with preexisting CKD and a baseline creatinine more than 1.5 mg/dL, whereas other authors have included these patients in their study.[30] Moreover, the mean volume of contrast used in our study (<160 mL) was significantly lower than that in the studies mentioned above (240–290 mL) because we enrolled only patients of coronary angiogram who require less amount of contrast media as compare to patients of PCI[15]. Another important observation of our study is the self-limiting course of the CIN in all patients without the requirement of renal replacement therapy. A similar observation was noted by Lautin et al, but this is in contrast to many previous studies of CIN.[31,32] Multiple factors could explain this observation including careful patient selection, minimal use of CM, avoidance of nephrotoxic drugs, and ensuring proper hydration in the post procedure period.

Several risk factors of CIN are documented in studies. High risk patients for CIN are elderly, patients with prior renal insufficiency, diabetes mellitus, congestive heart failure, contrast material volume, recent exposure to contrast material and acute coronary syndrome.[15] Similarly Nikolsky et al documented anemia as an independent factor of CIN [101]. In our study, in addition to incidence of CIN, we studied the relationship of age, diabetes mellitus, hypertension and acute coronary syndrome with CIN. We reported higher incidence of CIN in the elderly than younger individuals. Previous studies did not show ethnicity as risk factor for CIN.[25,26] Another advantage of our study is that our population consists of Pakistani only, and the data may be applicable to other South Asians for the genetic and metabolic similarities between them.[27]

Our study is also consistent with that of many studies, who found the presence of hypertension to be a significant risk factor for the occurrence of CIN.[28,29] The role of hypertension in predisposing to CIN is related with advanced atherosclerosis of the aorta and athero-embolization to the kidney during coronary angiogram and hypertension-induced endothelial injury.[30]

In this study, apart from hypertension and advanced age, another risk factors such as diabetes mellitus was found to have a significant association with incidence of CIN. The reported incidences of CIN in diabetics ranges 5.2% to 35.7% in different studies.[31,32] Pre-existing renal disease also effect the incidence of CIN. In diabetics with normal renal functions CIN was reported between 9–40% while with pre-existing renal disease there is a higher incidence of 50–90% are reported.[33-36] However Parfrey et al documented comparable incidences of CIN to healthy population in diabetics with preserved renal function.[37] In our study the reported frequency of CIN among diabetics was 3.57%. We included patients with good glycemic control and ensured adequate hydration which are the best measures for prevention of CIN associated with diabetes.

CIN is more frequent in acute coronary syndrome patients as compared to stable angina.[38] In our study, incidences of CIN were reported in acute coronary syndrome. Dangas et al found that STEMI patients were more prone to develop CIN than patients with stable angina.[39] Mega et al studied CIN in over 8000 patients reported similar results.[40] In acute coronary syndrome, ischemia and hypoperfusion causes hypoxia which in turn causes direct toxicity to the renal tubules via reactive oxygen species leading to increase incidence of CIN.

The strengths of our study include careful selection of patients, judicious use of CM, documented

follow-up in a tertiary level multidisciplinary care setup, and highlighting the simple measures such as adequate hydration and withdrawal of nephrotoxic agents. The limitations of our study include small sample size, data derived from a single hospital may not be applicable to other centers, and a small number of CIN patients in the sample. Our data being derived from Pakistani patients may not be applicable to patients of other race and ethnicity.

In conclusion, CIN was found in 7% in cases of coronary angiogram. Old age, diabetics and acute coronary syndrome are high risk for CIN.

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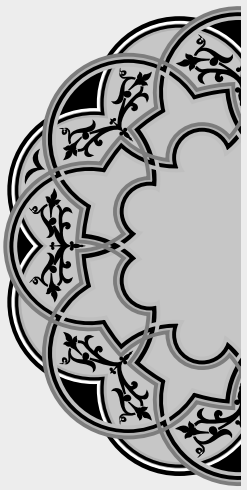

"Mistakes are proof that you're trying."

Unknown

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2	Liaqat Ali	Analysis	
3	Wasiq Anees	Data collection	