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Original Article

Assessment of Effect of Radio Contrast Enhanced Computed Tomography on the Renal System in Diabetic Patients

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***ABSTRACT*:**

Background: Diabetes conceivably predisposes to contrast induced nephropathy (CIN) principally through the amplification of these changes and the disruption of protective mechanisms, designed to maintain medullary oxygenation and to ameliorate oxidative stress. Hence; we planned the present study to evaluate the effect of contrast agents on renal functions based on serum creatinine and creatinine clearance in patients with diabetes.**Materials & methods:** The present study included assessment of effect of radio contrast enhanced computed tomography on the renal system in diabetic patients. We included a total of 60 patients and divided them broadly into two study groups with 30 patients in each group as follows:Group 1: All patients without a pre-existing renal disease non diabetic non hypertensive, and Group 2: Diabetic patients on treatment and not known hypertensive. Relative risk was calculated based on exposed as patients with CIN and non-exposed as without CIN. All the results were analyzed by SPSS software. **Results:**CIN was present in 13.3 percent of the control group population and 36.7 percent of the diabetic group population. Significant results were obtained while comparing the preoperative and postoperative creatinine values in both the study groups.**Conclusion:** Risk of development of contrast nephropathy is increased in diabetic patients.

Key words: Diabetes, Radio contrast, Renal system

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INTRODUCTION

With the introduction of risk factors, like diabetes, the number rises to 9%, with incidences being as high as 90% in diabetics with CKD.[1, 2] Therefore, the number and the type of preexisting risk factors directly influence the incidence of renal insufficiency. It is also procedure dependant, with 14.5% overall in patients undergoing coronary interventions compared to 1.6-2.3% for diagnostic intervention, as reported in literature. Diabetes and the administration of iodinated radiocontrast agents are both associated with marked alterations of renal physiology, including changes in GFR and renal hemodynamics, enhanced tubular transport activity and oxygen expenditure and intensification of medullary hypoxia, and ROS generation.[3- 5]

Diabetes conceivably predisposes to CIN principally through the amplification of these changes and the disruption of protective mechanisms, designed to maintain medullary oxygenation and to ameliorate oxidative stress.Patients with CKD in the setting of diabetes mellitus have a 4-fold increase in the risk of CIN compared with patients without diabetes mellitus or preexisting CKD.[6- 8]

Hence; we planned the present study to evaluate the effect of contrast agents on renal functions based on serum creatinine and creatinine clearance in patients with diabetes who are well controlled on medications.

MATERIALS & METHODS

The present study was conducted in the department of radio-diagnosis of the medical institute and included assessment of effect of radio contrast enhanced computed tomography on the renal system in diabetic patients. Ethical approval was taken from instructional ethical committee and written consent was obtained after explaining in detail the entire research protocol. We included a total of 60 patients and divided them broadly into two study groups with 30 patients in each group as follows:

Group 1: All patients without a pre-existing renal disease non diabetic non hypertensive.

Group 2: Diabetic patients on treatment and not known hypertensive

Exclusion criteria:

- Patients who didn't gave written consent
- Patients with history of pre-existing renal disease
- Patients with history of allergy to any type of contrast media
- Patients with history of pregnancy
- Patients with presence of malignancy of any tissue
- Any other disease or drug treatment affecting renal function

Detailed demographic details and clinical history of all the patients was recorded. Investigations were performed to assess contrast induced nephropathy and before the procedure blood urea levels and serum creatinine levels were measured. Patient was injected with low osmolarnonionic contrast media intravenously in the dose of 1.5 ml/kg body weight. After the 48-72 hrs of procedure repeat creatinine and creatinine clearance was measured. CIN either 25% increase in serum creatinine or 0.5 mg% increases in absolute value were categorised for diagnosis. Incidence rate of CIN was calculated for each group. Risk difference was calculated after comparing the group 2 or group 3 incidences with control (group 1). All rates were expressed as proportions. Relative risk was calculated based on exposed as patients with CIN and non-exposed as without CIN. All the results were analyzed by SPSS software. One way ANOVA and chi-square test were used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

A total of 60 patients were included in the present study and were broadly divided into two study groups; group 1 and group 2. Mean age of the subjects of the control group and the diabetic group was 46.5 years and 48.7 years respectively. CIN was present in 13.3 percent of the control group population and 36.7 percent of the diabetic group population. Significant results were obtained while comparing the preoperative and postoperative creatinine values in both the study groups.

Table 1: CIN distribution in the study groups

	Group 1 (No comorbidity)	Group 2 (with Diabetes)
CIN (Number)	4	11
Proportion	13.3%	36.7%

Table 2: Comparison of mean plasma creatinine post-operative values in between various groups

Group comparison	Mean plasma creatinine post-operative values	p-value
Group 1	0.92	0.12
Group 2	1.07	

Table 3: Comparison of mean creatinine clearance value in the two study gorups

Group	Mean creatinine clearance value		P- value
	Pre-operative	Post-operative	
Group 1	107.57	94.85	0.00
Group 2	107.94	85.70	0.00

DISCUSSION

Contrast media induce various factors that may increase vasoconstriction and decrease vasodilatation in the renal medulla, leading to hypoxia and acute tubular necrosis known as contrast-induced nephropathy (CIN) that tends to occur in diabetics and patients with preexisting renal insufficiency. Contrast media inhibit mitochondrial enzyme activities and subsequently increase adenosine through hydrolysis of ATP. Both catabolism of adenosine and medullary hypoxia generate reactive oxygen species (ROS) that scavenge nitric oxide (NO). Released along with endothelin and prostaglandin from endothelial cells exposed to contrast media, adenosine activates the A1 receptor that mainly constricts afferent arteriole at the glomerulus but not the medullary vasculature. Adenosine also activates the A2 receptor that increases NO production, leading to medullary vasodilatation which is induced by activation of endothelin-B receptor and G-protein coupled E-prostanoid receptor 2, and 4 of prostaglandin PGE2 respectively as well. Conversely medullary vasoconstriction is mediated by activating endothelin-A receptor and G-protein coupled E-prostanoid receptor 1, and 3 of prostaglandin PGE2 respectively. The osmotic load of contrast media increases interstitial pressure and sodium transport and thus oxygen consumption. Risking hypoxia, increased medullary oxygen consumption may also result from stimulating Na(+)-K(+)-ATPase activity by endothelin-A receptor. N-acetylcysteine (NAC) scavenges ROS and therefore preserves NO that not only dilates medullary vasculature but also reduces sodium reabsorption and oxygen consumption, tipping the balance against medullary vasoconstriction, hypoxia, and thus CIN. While prostacyclin and its analog, iloprost, prevent CIN by inducing medullary vasodilatation, atrial natriuretic peptide (ANP) may do so by inhibiting renin secretion.[9-11]

The key findings included as risk ratio of 2.75for diabetes for CIN compared to the patients without history of diabetes. The risk of CIN was more than doubled in patients with diabetes. Moreover, the mean plasma creatinine and creatinine clearance were also elevated significantly ($p<0.05$) in all groups compared to the baseline levels. The clinical course of CIN is usually characterized by serum creatinine rise within 24 hours after administration of CM, typically peaking on the second or third day. Usually, serum creatinine returns to baseline value within 7–10 days. Although the clinical relevance of CIN may not be immediately evident given the subclinical course and the high frequency of recovery of renal function, some degree of residual renal impairment has been reported in as many as 30% of those affected and up to 7% of patients may require temporary

dialysis or progress to end-stage renal failure.[12] Serious clinical consequences, including death, may occur in patients developing CIN. Patients with CIN were observed to have several noncardiac in-hospital complications, including hematoma formation, pseudoaneurysms, stroke, coma, adult respiratory distress syndrome, pulmonary embolism, and gastrointestinal hemorrhage. Patients who develop CIN after PCI have a 15-fold higher rate of major adverse cardiac events during hospitalization than patients without this complication. They also have a 6-fold increase in myocardial infarction and an 11-fold increase in coronary vessel reocclusion. Although few patients with CIN require dialysis (<1%), the latter have a more complicated clinical outcome than those who do not require renal replacement therapy, including a significantly higher rate of non-Q-wave myocardial infarction (46% vs. 15%), pulmonary edema (65% vs. 3%), and gastro-intestinal bleeding (16% vs. 1%). Moreover, they have a 15-fold longer stay in the intensive care unit and a 5-fold longer in-hospital stay.[13, 14]

Rehman et al conducted astudy to assess the incidence of contrast-induced nephropathy (CIN) after coronary angiogram (CAG) and percutaneous transluminal coronary angioplasty (PTCA). Contrast induced nephropathy is the third leading cause of acute renal failure in hospitalized patients. Diabetes mellitus, volume depletion, baseline renal insufficiency, and high volume of contrast agent are a few risk factors. In 245 consecutive patients undergoing CAG or PTCA, we measured serum creatinine at baseline and after 24 and 48 hours of the procedure. CIN was defined as rise in serum creatinine >/=0.5mg/dL or 25% rise from baseline. Two hundred twenty three (91%) subjects were male and 22(9%) were female. Among the 245 subjects 155 (63.3%) were diabetic. Total 59(24.08%) patients developed contrast induced nephropathy. Among these patients, 57(36.8%) were diabetic whereas only 2(2.2%) were non-diabetic. In 59 CIN cases 57(96.6%) were diabetic (p</=0.0001). Among total 59 CIN cases, more than 100 ml of contrast agent used in 51(86.4%) patients (p</=0.0001). Diabetic patients are more prone to develop CIN than non-diabetic. Volume of contrast agent used during procedure is an important predictor for the development of CIN.[15]According to an extensive review by **Heyman et al**, diabetes plays role at various stages in predicposing the patients to CIN[6]. Plausible synergic adverse impact of radiocontrast agents and diabetes upon the kidney, leading to contrast-induced nephropathy (CIN) is described in the following figure. Both conditions, diabetes and the administration of iodinated radiocontrast agents, lead to altered renal physiologic processes (in yellow): there is an excess formation of reactive oxygen species (ROS) and altered renal oxygenation, related to disregulated renal microcirculation and enhanced tubular transport and oxygen consumption. Evolving renal parenchymal hypoxia and enhanced ROS formation lead to tubular and vascular endothelial injury, with subsequent reduction of glomerular filtration rate (GFR), the hallmark of CIN. Conceivable interactions between these processes are outlined by arrows and discussed in depth in the text. In brief, both diabetes and contrast agents enhance ROS formation. They also hamper renal oxygenation, either directly or through increased generation of ROS. Vascular endothelial cell injury may further amplify renal hypoxia via a feed-forward loop of altered microcirculation.[16]

CONCLUSION

From the above results, the authors concluded that risk of development of contrast nephropathy is increased in diabetic patients. However; future studies are recommended.

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