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Impact of Diabetes on the Incidence of Contrast-Induced Nephropathy

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Abstract:

Background: **Serum creatinine elevated by more than 25% or ≥0.5 mg/dl absolute from baseline within 48 hours of contrast administration is known as contrast-induced nephropathy (CIN). It is the third most common cause of iatrogenic acute kidney insult in hospitals and raises the risk of subsequent renal injury, length of hospitalization, and mortality rate, particularly in cardiac patients with multiple comorbidities [(1)]. Many factors related to both the patient and the contrast affect the incidence of CIN; one of the independent risk factors is diabetes mellitus DM)[(2)]. *Aim:* to evaluate the impact of diabetes mellitus on the incidence of CIN in cardiac patients to improve the patients' outcomes. *Subjects and Methods:* pre-post study that included 62 patients recruited from the cardiac catheterization unit of Suez Canal University Hospital, Ismailia City, to assess the risk of CIN among diabetic and non-diabetic patients following coronary interventions. *Results:* The incidence of CIN in the study was 9.7%. There was no statistically significant difference in DM or its duration between the CIN and non-CIN groups. Glycemic control is crucial, as found by the statistically significant differences in HbA1C levels between CIN and non-CIN groups. The study found that the most significant risk factors for CIN were low EF%, anemia, high serum cholesterol, advanced age, and chronic kidney disease. *Conclusions:* Glycemic control is one of the most important risk factors for the development of CIN as opposed to DM and its duration; strict glycemic control may improve patient outcomes.**

Keywords: CIN, diabetes mellitus, coronary interventions.

Introduction:

CIN has been identified as the third most frequent cause of hospital-acquired acute kidney insult and linked to significant morbidity and mortality [(3)].

The incidence of CIN ranges from 1.3% to 33.3%. Such differences may be caused by many risk factors related to patients, such as having chronic kidney disease and diabetes [(4)].

Some studies show that glycemic control on admission is a useful marker of CIN in diabetic patients [(5)], while others demonstrate that the length of DM plays a significant role [(6)].

Furthermore, anemia, advanced age, hydration status, and the type and

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quantity of contrast media are additional risk factors in many studies [7].

Mehran 2004) reported a risk score for the prediction of CIN following percutaneous coronary intervention PCI), the most commonly used method for predicting acute kidney injury caused by contrast [8].

Because no definite treatment to ameliorate CIN has been established, the importance of preventive measures has been highlighted, and identifying patients at high risk for CIN is the first step in prevention [9].

Subjects and Methods:

A pre-post intervention study was conducted on 62 patients at the cardiac catheterization unit, Suez Canal University Hospital, in Ismailia City, scheduled for coronary angiography 25 patients) or PCI 37 patients).

Half of the patients were known to be diabetic (31/62 patients). The included patients (42/20 males and females) were admitted between December 2021 and January 2022; those who refused to participate were ruled out.

We excluded patients who had undergone emergency coronary angiography, patients who had undergone radiographic studies with contrast media within one week before the study, patients with acute heart failure or shock, patients on dialysis, and patients who received nephrotoxic drugs, such as non-steroidal anti-inflammatory drugs.

Date collected from each patient included:

- Interview: to obtain the following:

- Personal data: name, age, telephone number.

- Medical history of chronic illnesses such as DM, hypertension, chronic kidney disease, and ischemic heart disease.

- Clinical Examination: - Systolic / diastolic BP – temperature.
- Laboratory Investigations:

Blood Sampling: About 5 ml of venous blood sample was collected from each patient as follows: 3 ml of blood sample was collected in a sterile plain tube to measure: i) Lipid profile: serum total cholesterol, triglycerides TG), high density lipoprotein HDL), and low density lipoprotein LDL). ii) Serum Creatinine before receiving contrast, and also another sample after receiving contrast, 48 hours later.

- Estimated glomerular filtration rate calculated through the CKD-EPI equation. e-GFRcr = 142 x minScr/κ, 1)α x maxScr/κ, 1)-1.200 x 0.9938Age x 1.012 (if female) Where: Scr = standardized serum creatinine in mg/dL κ = 0.7 females) or 0.9 males) α = -0.241 female) or -0.302 male) Age years).

iii) 2 ml of the blood sample was collected in an EDTA tube for: i) Measurement of glycosylated haemoglobin HbA1C). ii) Measurement of hemoglobin levels.

Patients received I.V. contrast Ultravist iopromide) or Omnipaque iohexol); both are low-osmolar contrast media.

Oral hydration was encouraged after the procedure unless the patient was impaired in kidney function; preventive therapies such as hydration with 500 cc of saline at least) and acetyl cysteine were done.

Patients were monitored for clinical signs of heart disease, UOP, and serum creatinine after 48 hours. Follow up with the patient who was diagnosed to have CIN until recovery is obtained.

The obtained data were entered and analyzed using the Statistical Package of

Social Sciences (SPSS) version 22. Comparisons were performed using a t-test for quantitative data and a chi-squared test for qualitative data. Significance is considered at a p-value of ≤ 0.05.

The study was approved by the local Medical Ethics Committees of the Faculty of Medicine, Suez Canal University, Ismailia, Egypt Approval number: 4670). Written informed consents were obtained from all study participants. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Results:

The baseline demographics of the patients who were included are displayed in table (1). The patients' ages ranged from 36 to 76 years old, with a mean age of 59. Nearly 68% of them were men, and while one-third were current smokers, nearly half were not.

Table (1): Demographic data of patients included in the study (n=62).

Age (year)	Range	36 - 76
	Mean ± SD	58.77 ± 9.74
Gender	Male N (%)	42 (67.7 %)
	Female N (%)	20 (32.3 %)
Smoking	No smoking N (%)	28 (45.2 %)
	X-smoker N (%)	14 (22.6 %)
	Current smoker N (%)	20 (32.3 %)

The included patients' baseline clinical characteristics are displayed in table (2). Nearly 85.5% of our patients had documented ischemic heart disease. Regarding presentation, 89% of patients complained of chest pain, while the remaining patients presented with dyspnea. About 70% of included patients had hypertension, 16% had chronic kidney disease, and 50% had diabetes mellitus. Two-thirds of diabetics were on oral hypoglycemic drugs, and the remaining one-third were on insulin.

Table (2): Clinical data of chronic illness of the studied populations (n=62).

Hypertension	N (%)	43 (69.4 %)
	Systolic BP Mean ± SD	133.87 ± 12.97
	Diastolic BP Mean ± SD	78.55 ± 8.267
	Mean of BP : Mean ± SD	96.98 ± 8.57
Diabetes Mellitus	N (%)	31 (50 %)
	Duration of DM (year): Mean ± SD	5.60 ± 8.046
	On insulin N (% in diabetic pt.)	9 (29 %)
	On OHD N (% in diabetic pt.)	22 (71 %)
Ischemic heart disease	N (%)	53 (85.5 %)
	Presentation: *Chest pain N (%)*	55 (88.7 %)
	Dyspnea N (%)	7 (11.3 %)
Chronic kidney disease	N (%)	10 (16.1 %)

As shown in table (3) forty percent of the patients were scheduled for diagnostic coronary angiography, and sixty percent were scheduled for percutaneous coronary intervention. Low-osmolar contrast media were used, and 40% of patients received doses of 50 ml or less, 44% received doses of 100–150 ml, and 16% received doses of 200 ml.

Table (3): Coronary interventions in the study (n=62).	
Percutaneous coronary intervention N (%)	37 (59.7 %)
Coronary angiography N (%)	25 (40.3 %)
Dose of IV contrast	
(50 or less) N (%)	25 (40.3 %)
(100) N (%)	13 (21.0 %)
(150) N (%)	14 (22.6 %)
(200) N (%)	10 (16.1 %)

CIN and Mehran score assessment in the study individuals:

Approximately 75% of our patients were at low risk for CIN by using the Mehran score, 23% were at moderate risk, and 3% were at high risk. In our study, the incidence of CIN was 9.7%. (Table 4)

Table (4): Mehran score assessment in the study individuals (n=62).	
Low risk (≤5) N (%)	46 (74.2 %)
Moderate risk (6 to 10) N (%)	14 (22.6 %)
High risk (11 to 15) N (%)	2 (3.2 %)
Very high risk (≥15) N (%)	0 (0 %)
CIN in the study (n=62).	
CIN N (%)	6 (9.7 %)

Baseline characteristics of patients who developed CI-AKI and those who did not (Table 5)

Six patients from 62 patients developed CIN (9.7%), with a mean age of 67.5 ± 9.7 years, significantly older than non-CIN patients. Neither hypertension nor IHD shows any statistical difference between the two groups.

Regarding the impact of Diabetes, DM and its duration showed no statistically significant difference between the CIN and non-CIN groups.

While HbA1C levels in diabetic patients show a statistically significant difference between both groups **(p-value 0.000),** which highlight the importance of glycemic control.

Anemia, hypercholesterolemia, and low EF% were additional factors that were statistically significant. Chronic kidney disease is another important risk factor for CIN, with a p-value of 0.048.

Mehran score is a good predictor tool for assessing the incidence of CIN, with statistically significant results in our study (p-value 0.000).

The dose of contrast in our study fails to show any statistical difference between the two groups, although it's higher in the CIN group

Table (5) Baseline characteristics of patients who developed CI-AKI and those who did not			
Variable	CIN (6 patients)	Non-CIN (56 patients)	Significance p value
Age (years) Mean ± SD	67.5 ± 9.7	57.84 ± 9.3	0.020*
Hypertension (n, %)	6 (13.9%)	37 (86.1%)	0.099
DM (n, %)	4 (13.3%)	26 (86.7%)	0.238
Duration of DM (years) Mean ± SD	3.83± 4.8	5.79 ± 8.3	0.57
IHD (n, %)	6 (11.3%)	47 (88.7%)	0.373
CKD (n, %)	3 (30%)	7 (70%)	0.048*
Hypercholesterolemia (n, %)	3 (37.5%)	5 (62.5%)	0.024*
HB A1C Mean ± SD	8.4 ± 1.2	6.9 ± .45	0.000*
Anemia (n, %)	5 (38.5%)	8 (61.5%)	0.001*
Ejection Fraction % Mean ± SD	43.7 ± 12	55.3 ± 9.5	0.007*
Mehran Score Mean ± SD	3.32 ± 2.62	9 ± 3.52	0.000*
Contrast volume (ml) Mean ± SD	125 ± 68.9	104.6 ± 55	0.405

Discussion:

Our study's 9.7% incidence of CIN was consistent with a meta-analysis of 120 studies involving 974,898 participants worldwide; the pooled incidence proportion of CIN was 9.06% [10].

In numerous studies, DM is a significant risk factor for CIN. Diabetes prevalence is considerably higher in the CIN group, according to the Abdel-Ghany et al. study [11]. DM has also been identified as one of the risk factors for CIN in high-risk patients in the Shams and Mayrovitz study [9].

The length of DM was the most important factor that led to the development of CIN in Özkan et al. study [6].

However, neither DM nor its duration showed any statistically significant differences in our study.

In an agreement of a study involving 347 patients, the prevalence of diabetes was comparable in those with and without CIN [12].

Our study highlights the importance of controlling glucose. HbA1c was statistically significantly higher in CIN diabetic patients.

These results matched the results of the meta-analysis study conducted by Kewcharoen et al., which included eight studies that demonstrate that procedural hyperglycemia was associated with an increased risk of CIN even in non-diabetic patients [13].

Li et al, in another study, focused on evaluating and controlling the lipid and glucose profiles while administering contrast. The results indicate a significant correlation between the triglyceride-glucose TyG) index and an increased risk of CIN. In our study, this correlation was seen for both total cholesterol levels and HbA1c [14].

The results of the study also revealed that there was a statistically significant difference between the CIN and non-CIN groups regarding age, CKD, anemia, hypercholesterolemia, and low EF%. While traditional comorbidities such as

hypertension and IHD failed to show any statistical significance.

Age, heart failure, and chronic kidney disease were the predictors of CIN, according to a 2019 meta-analysis study that included twelve publications with a total of 6342 patients. These findings were consistent with our findings. Contrary to what our results showed, DM, HTN, and IHD were also risk factors for CIN [15].

Regarding dose of contrast, Yildiz et al. and Şimsek et al. presented evidence showing that CM volume was found to be an independent predictor of CIN [16], [17].

Another study of Saylık et al. presented the ratio of contrast volume/e-GFR, and found that the contrast media volume was found to be an independent predictor of CIN [18].

However, our findings concurred with those of Özdemir et al., who found that the CIN group received a higher dose of CM without a statistically significant difference between the two groups [19].

Mehran score is a good predictor tool for assessment of the incidence of CIN, with a statistically significant difference in our study p-value 0.000).

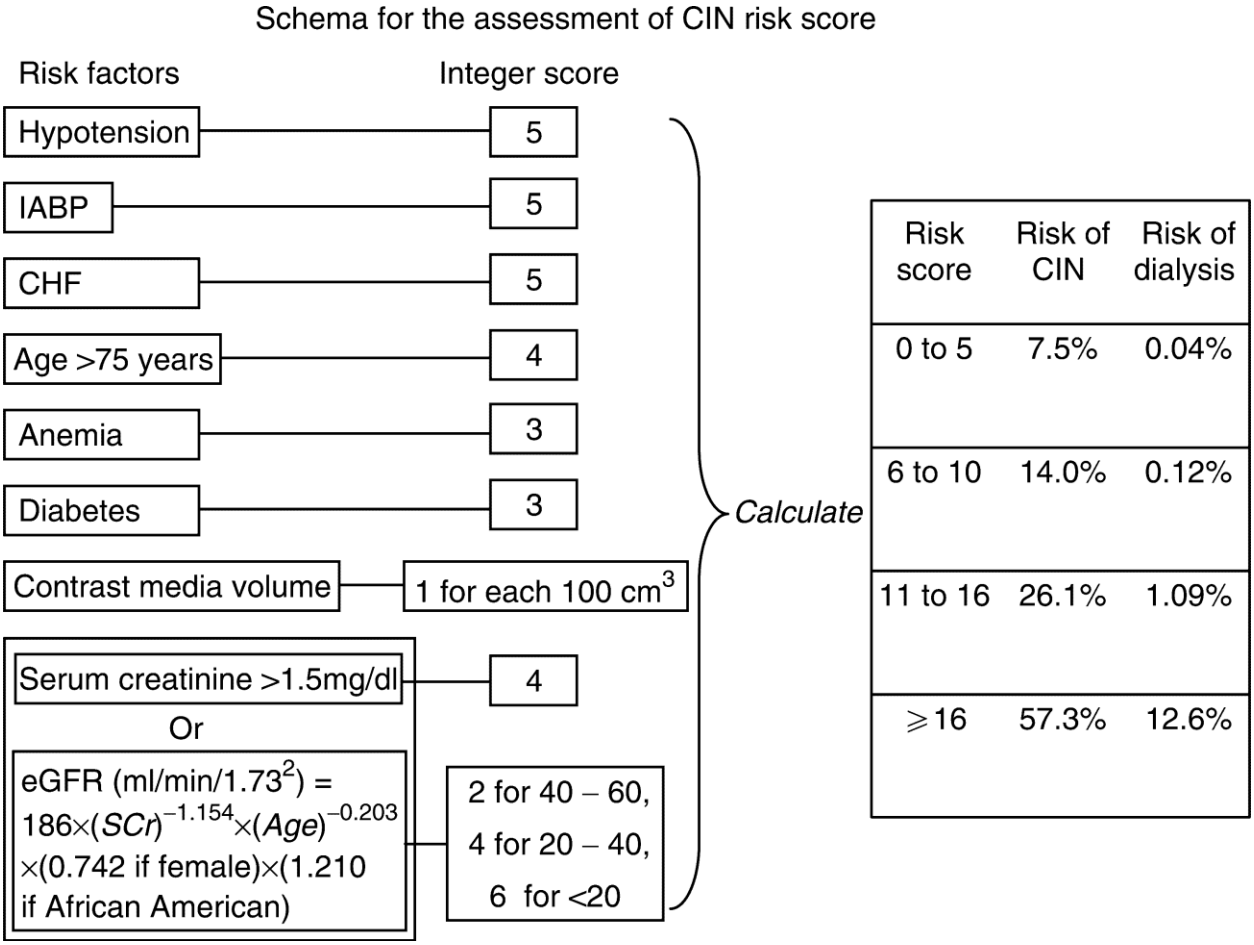
These results matched the results obtained by Kumar et al., which show the validity of the Mehran Risk Score for the risk stratification of CIN in patients who underwent PCI [20].

Limitation:

- Sample Size: The study included only 62 patients, which may not be a large enough sample size to draw definitive conclusions and could affect the generalizability of the results. Larger studies with more diverse populations should be conducted to validate the findings.
- Single-center study: The study was conducted at a single center, which may limit the generalizability of the results to other hospitals and populations. Multicenter studies are needed to validate the findings.
- Confounding Factors: Other factors not accounted for in the study might have influenced the results. These could include differences in patients' comorbidities, medications, baseline kidney function, and procedural variables, which could impact the risk of CI-AKI.

Conclusion:

One of the most significant risk factors for the onset of CIN as opposed to DM and its duration is glycemic control, which tight glycemic control adds on improving the patients' outcomes.



Appendix:

Scheme to define Mehran score [8].

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