Section: Radiodiagnosis

Original Research Article

INCIDENCE OF CONTRAST INDUCED NEPHROPATHY FOLLOWING CONTRAST ENHANCED COMPUTED TOMOGRAPHY

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Abstract

Background: Contrast-induced nephropathy is a significant adverse event that can occur after using non-ionic iodinated contrast agents. The occurrence of CIN in rural populations is currently unknown. It is essential to determine the frequency of CIN and identify common risk factors that may contribute to its development. **Materials and Methods:** This observational study took place over a 22-month period from March 2021 to December 2022, involving 310 patients who underwent contrast-enhanced computed tomography with non-ionic contrast agents. **Results:** The average age of the patients in our study was 52.6 years ± 16.4 years (mean ± standard deviation), ranging from 23 to 90 years. There was a slightly higher number of male patients (n = 174; 56.1%). Out of the 310 patients, 12 (3.87%) developed CIN, all of whom had at least one risk factor. However, all cases of CIN resolved within seven days without any complications. The most common contrast examination performed was a CECT abdomen for 111 patients (35.8%), followed by CECT neck for 80 patients (25.8%). The initial serum creatinine level averaged at 1.135 ± 0.163 mg/dL (mean ± SD), ranging from 0.8 to 1.5 mg/dL. The risk factors evaluated in our study included elderly age (n = 67; 21.6%), hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%), NSAID use (n = 10; 3.2%), and renal insufficiency (n = 3; 1.3%). Risk factors were present in 102 patients (32.9%), with 72 patients (23.2%) having one risk factor, 25 patients (16.13%) having two risk factors, and five patients (4.84%) having three risk factors, totaling 137 risk factors. Among the risk factors, hypertension was observed in five patients (1.61%), diabetes mellitus and elderly age group in four patients each (1.29%), and renal insufficiency in two patients (0.65%). None of the patients who had a history of NSAID use developed CIN. **Conclusion:** Our study found a relatively low risk of contrast-induced nephropathy following CECT examinations. The identified risk factors for developing CIN were diabetes mellitus, elderly age (>65 years), hypertension, and renal insufficiency. Serum creatinine levels returned to baseline within a week for all patients who developed CIN. In conclusion, the use of non-ionic iodinated contrast media is associated with a low risk of CIN, and CECT studies do not cause a significant increase in its occurrence.

INTRODUCTION

Contrast media are increasingly used in computed tomographic (CT) studies, particularly in contrast-enhanced CT (CECT) studies. However, the rise in contrast media usage has led to an increase in adverse events associated with its use. Contrast-induced nephropathy (CIN) is a significant adverse event that occurs following the administration of intravenous iodinated contrast. CIN is defined as an absolute (≥ 0.5 mg/dL) or relative (≥ 25%) increase in serum creatinine levels from baseline within 48 to 72 hours. It is considered the third most common cause of hospital-acquired renal failure, with an incidence as high as 11% in cases involving impaired renal perfusion and nephrotoxic medications, highlighting its severity.[1,2]

CIN is also associated with higher morbidity and mortality rates. It has been shown to prolong hospital stays and increase the risk of cardiovascular diseases, including coronary disease and stroke. The overall incidence of CIN in the general population remains uncertain and has been reported to range from 0.6% to 4.96% in various studies. Existing data on CIN primarily come from intra-arterial cardiac interventions, which involve the use of high volumes and sometimes high-osmolar contrast media. This differs from patients undergoing CECT studies, as they receive lower amounts of contrast and non-ionic contrast media, which may play a role in the development of CIN.[3,4]

There is a gap between evidence-based guidelines and the daily practice of radiologists regarding CIN prevention. Therefore, it is crucial to determine the prevalence of CIN in patients undergoing CECT studies and identify individuals at risk of developing CIN. Known risk factors for CIN include comorbidities such as diabetes mellitus, advanced age, hypertension, the use of non-steroidal anti-inflammatory drugs (NSAIDs), and renal insufficiency.[5]

There is a lack of data on the risk of CIN in patients undergoing CECT studies in our population, as well as a need to identify the specific risk factors for CIN in our rural population. Hence, this study aims to determine the incidence of CIN in patients undergoing CECT and identify the risk factors that predispose individuals to CIN in rural areas.

Objectives

The objectives of this study were to assess the incidence of contrast-induced nephropathy following the use of non-ionic contrast agents in tomographic imaging and to evaluate the risk factors that may predispose individuals to developing CIN.

MATERIALS AND METHODS

This observational study was conducted at the Department of Radiodiagnosis in Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj, Bihar. The study included individuals who underwent contrast-enhanced CT (CECT) studies and met the specified inclusion and exclusion criteria. The study took place over a period of 22 months, from March 2021 to December 2022. Prior to undergoing CECT, all patients underwent a baseline renal function test.

A hospital-based prospective observational study was conducted, and informed consent was obtained from each participant. The study was approved by the Institutional Ethics Committee of M.G.M. Medical College & L.S.K. Hospital, Kishanganj, Bihar, prior to its commencement.

Inclusion Criteria

Normal renal function, defined as a serum creatinine level of ≤1.4 mg/dL, which is the standard of care at our hospital. Patients who provided consent to undergo the procedure involving contrast media administration. Patients who had both pre-procedure and post-procedure serum creatinine level analyses performed at the same reference laboratory to eliminate inter-laboratory variability.

Exclusion Criteria

Age younger than 18 years. Pregnancy. Allergy to contrast media. Patients with acute kidney injury (AKI) due to other clear causes. Patients who requested withdrawal from the study. Patients who did not undergo timely re-examination of renal function indicators after surgery. Patients who underwent hemodialysis within 48 hours after surgery.

Data Collection Method: The study received approval from the institutional ethical committee and review board. Informed consent was obtained from all patients who agreed to participate. Prior to their inclusion in the study, individuals scheduled for CECT studies underwent a baseline recording of renal function by measuring serum creatinine levels. The CECT studies performed included CECT abdomen, CECT thorax, CECT neck, CECT kidney-ureter-bladder (KUB), CT pulmonary angiography, and CECT brain. Baseline demographic data was collected, and the patients' medical history of CIN risk factors was recorded, including hypertension, renal insufficiency, age (with age over 65 years considered as high risk), chronic use of NSAIDs, and diabetes mellitus.

Assessment of CIN

After the CECT study, a follow-up renal function test measuring serum creatinine levels was conducted between 48 to 72 hours later. Patients with an absolute (≥ 0.5 mg/dL) or relative (≥ 25%) increase in serum creatinine from baseline were classified as positive for CIN. These patients were then monitored for a period of up to 11 days to evaluate the short-term outcome, which was the return to baseline serum creatinine values (Figure 9). Individuals who were lost to follow-up were excluded from the final analysis.

Statistical Analysis

Data was recorded into Microsoft® Excel® and was analyzed using Open Epi ® software. All the data were presented as mean ± SD. For radiation dose

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and mean as delivered, a paired t-test was performed to compare both the groups. Since each patient served as his/her own control, the results obtained in the standard-dose group was considered as standard and findings from low-dose group were compared with standard-dose group. Sensitivity and specificity for low-dose group was compared with results obtained from standard-dose group. A P value of <.05 was considered as statistically significant.

RESULTS

Table 1: Gender-wise Distribution of Patients

Gender	Numberof patients	%
Male	174	56.1
Female	136	43.9
Total	310	100

Therewereatotalof310patientsinourstudy.Themeanageofpatientsinourstudywas52.6years±16.4years(mean±SD)(range23to90years).Therewasa slight male preponderance in our study (n = 174; 56.1%). The mean age of males was 51.09 ± 17.34 years (mean ± SD) and the mean age of females was 54.52 ± 14.9 years (mean ± SD), the difference of which was not statistically different(P=.06).

Table 2: Various CECT Examination Performed

Type of study	No of patients	%
CECT abdomen	111	35.81
CECT neck	80	25.81
CECT thorax	56	18.06
CECTKUB/C Turography	31	10.00
CECT Brain	29	9.35
CEPA	3	0.97
Total	310	100
CECT=contrast enhanced computed tomography; KUB=kidney ureter bladder; PA=pulmonary angiography		

In our study, the most frequently performed contrast examination was CECT abdomen, which was conducted on 111 patients, accounting for 35.8% of the total. This was followed by CECT neck with 80 patients (25.8%), CECT thorax with 56 patients (18.06%), CECT KUB/CT urography with 31 patients (10%), CECT brain with 29 patients (9.35%), and finally, CT pulmonary angiogram with 3 patients (0.97%).

Table 3: Risk Factors for CIN

Riskfactor*	Noofpatients	%
Elderly†	**67**	**21.6**
Hypertension	**30**	**9.7**
Diabetes	**26**	**8.4**
NSAIDuse	**10**	**3.2**
Renalinsufficiency	**4**	**1.3**
Total	**137**	**44.19355**
CIN=contrast induced nephropathy; NSAID= non-steroid a lanti-inflammatory drug; †elderly age was definedasage>65years *There were72 patients with one risk factor, 25 patients with two risk factors and five patients with three risk factors		

The mean serum initial serum creatinine level was1.135 ± 0.163mg/dL (mean ±SD) (range0.8to1.5mg/dL). The risk factors evaluated in our study were elderly (n = 67; 21.6%), hypertension (n = 30; 9.7%), diabetes mellitus (n = 26; 8.4%),NSAID use (n = 10; 3.2%) and renal insufficiency (n = 3; 1.3%). Risk factors were seen in total of 102 patients (32.9%). Among them, 72 patients (23.2%) had one risk factor followed by two risk factors in 25 patients (16.13%) and lastly five patients(4.84%)had three risk factors with totalof137risk factors.

Table 4: Initial vs Post CECT Serum Creatinine Levels

	Serumcreatininelevel (mg/dL)				
	Initial		Post CECT		P
	Mean	SD	Mean	SD	
Elderly(n =67)	**1.149**	**0.479**	**1.267**	**0.526**	**P=.17**
Hypertension(n =30)	**1.167**	**0.348**	**1.337**	**0.399**	**P=.08**
Diabetes(n=26)	**1.135**	**0.318**	**1.306**	**0.365**	**P=.07**
NSAIDuse(n =10)	**1.16**	**0.208**	**1.18**	**0.210**	**P=.8**
Renalinsufficiency(n= 4)	**1.15**	**0.130**	**1.45**	**0.166**	**P=.026**
Overall	**1.13**	**0.163**	**1.25**	**0.170**	

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CECT = contrast enhanced computed tomography; NSAID = no steroidal anti-inflammatory drug ; SD = standard deviation. P<.05 considered significant

The mean initial serum creatinine levels in the study were 1.13 ± 0.163 mg/dL (mean ± SD), and the mean post-CECT serum creatinine levels were 1.25 ± 0.17 mg/dL (mean ± SD). When considering patients with specific risk factors, the mean initial serum creatinine levels in elderly individuals were 1.149 ± 0.479 mg/dL (mean ± SD), and the mean post-CECT serum creatinine levels were 1.267 ± 0.526 mg/dL (mean ± SD). However, the increase in serum creatinine levels was not statistically significant (P = 0.17). Similarly, in patients with hypertension, the mean initial serum creatinine levels were 1.167 ± 0.348 mg/dL (mean ± SD), and the mean post-CECT serum creatinine levels were 1.337 ± 0.399 mg/dL (mean ± SD), which also did not show statistical significance (P = 0.08).

For diabetic patients, the initial mean serum creatinine levels were 1.136 ± 0.318 mg/dL (mean ± SD), and the post-CECT serum creatinine levels were 1.306 ± 0.365 mg/dL (mean ± SD). This difference was not statistically significant (P = 0.07). Among patients with NSAID use, the mean initial serum creatinine levels were 1.16 ± 0.208 mg/dL (mean ± SD), and the mean post-CECT serum creatinine levels were 1.18 ± 0.21 mg/dL (mean ± SD) (P = 0.8), indicating no significant change. However, there was a statistically significant increase (P = 0.026) in post-CECT serum creatinine levels in patients with renal insufficiency (initial mean serum creatinine level 1.15 ± 0.13 mg/dL, and post-CECT mean serum creatinine level 1.45 ± 0.166 mg/dL). It is important to note that this difference could be attributed to the limited sample size, which may have influenced the results.

Table 5: Risk Factors in Patients with CIN

RiskFactorsinCIN*	Noofpatients	%
Hypertension	5	1.61
Diabetes	4	1.29
Elderly†	4	1.29
Renalinsufficiency	2	0.65
NSAIDuse	0	0.00
Total	15	4.84

CIN=contrast induced nephropathy ;NSAID=non-steroid alanti-inflammatory drug;
†Elderly age was defined a sage>65 years
***10 patients had one risk factor and one patient each had two and three risk factors.**

In our study, contrast-induced nephropathy (CIN) was observed in 12 patients, accounting for 3.87% of the total participants. All of these patients had at least one risk factor. Fortunately, CIN resolved in all patients within seven days of follow-up, and no complications were reported. Among the identified risk factors, hypertension was present in five patients (1.61%), while diabetes mellitus and elderly age group were each found in four patients (1.29%). Renal insufficiency was observed in two patients (0.65%). Interestingly, none of the patients with a history of NSAID use developed CIN in our study. Out of the total participants, 10 individuals had a single risk factor (3.2%), one patient had two risk factors (diabetes mellitus and hypertension), and one person had three risk factors (diabetes mellitus, elderly age, and hypertension), each accounting for 0.3%. Patients who developed CIN were treated with hydration and N-acetyl cysteine.

Table 6: Proportion of Patients with Risk Factors Developing CIN

RiskFactor	CINpresent	CINabsent	%	P
Renalinsufficiency	2	2	50	<0.001
Hypertension	5	25	16.67	<0.001
Diabetes	4	22	15.38	<0.001
Elderly*	4	63	5.97	0.001
NSAIDuse	0	10	0	NA

CIN=contrast induced nephropathy ;NA=not applicable ;NSAID=non-steroid alanti-inflammatory drug;
P =probability ;Mid -P exactest
***Elderly age was defined as age>65 years**

We conducted a further analysis to determine the proportion of patients with risk factors who developed CIN. Our findings revealed that patients with renal insufficiency had the highest risk, with a 50% incidence of developing CIN (P<.001). Hypertension was the second-highest risk factor, with five out of 30 patients (16.67%) developing CIN (P<.001), followed by diabetes mellitus with a 15.38% incidence (four out of 26 patients; P<.001). Among the risk factors, the elderly age group had the lowest risk, with four out of 63 patients (5.97%) developing CIN (P = .001). Notably, none of the

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patients who reported NSAID use developed CIN. Comparing these results with the overall general population, there was no statistically significant increased risk of developing CIN.

DISCUSSION

Our study focused on the rural population who underwent CECT studies. We found a slightly higher proportion of males in our study, accounting for 56.1% of the participants. The average age of the patients was 52.6±16.4 years, ranging from 23 to 90 years.

Our study population is comparable to a study conducted by Bhatt et al., where they also reported a higher percentage of males (58.8% males vs. 41.2% females). Other studies have also shown a higher male preponderance, although some studies have reported a higher percentage of females, but these studies had specific patient populations, such as patients with underlying carcinoma or azotemia.[6]

In terms of age, our study's age group aligns with a study by Lee et al., who reported a similar mean age of 57.9±15.5 years in their study involving 140,838 CT examinations. However, Bhatt et al.[6] reported a lower mean age of 41.41±16.63 years in their study, which could be attributed to the rural setup in our patients compared to an urban setup in their study.

The most commonly performed contrast studies in our study were CECT abdomen (35.81%), followed by CECT neck (25.81%) and CECT thorax (18.06%). This pattern reflects the common indications seen in the rural setting, such as bowel obstruction, trauma, gastrointestinal and hepatobiliary malignancies for CECT abdomen, head and neck cancers for CECT neck, and lung infections and carcinoma for CECT thorax. CT urography is also becoming more prevalent compared to intravenous urography.[7,8]

These findings are consistent with studies by Baird et al. and Mitchell et al., where they reported a similar distribution of contrast studies in their patient groups.[7]

In our study, the risk of contrast-induced nephropathy (CIN) was low, with only 12 cases out of the total population of 310 (3.87%). All patients who developed CIN had at least one risk factor. The incidence of CIN varies in the literature, but our study utilized widely accepted criteria for defining CIN, which is an absolute (≥ 0.5 mg/dL) or relative (≥ 25%) rise in serum creatinine from baseline at 48 to 72 hours.

The incidence of risk factors in our study population was as follows: elderly (21.6%), hypertension (9.7%), diabetes mellitus (8.4%), NSAID use (3.2%), and renal insufficiency (1.3%). A total of 102 patients (32.9%) had at least one risk factor, with most patients having one risk factor (23.2%), followed by two risk factors (16.13%), and a few having three risk factors (4.84%).[8,9]

Our findings align with previous studies that have shown an increased risk of CIN in patients with risk factors such as diabetes, advanced age, renal insufficiency, and NSAID use. However, the risk of developing CIN in our study population compared to the general population was not statistically significant.

The increase in serum creatinine levels after CECT was not statistically significant in most cases, except for patients with renal insufficiency, where a significant increase was observed. This difference could be attributed to the association between renal insufficiency and the development of CIN, along with the limited sample size in our study.

The risk factor profile and incidence of risk factors in our study align with previous literature, although some variations exist. Diabetes mellitus, advanced age, and renal insufficiency have consistently been associated with an increased risk of CIN in most studies, while the association with hypertension and NSA.[10,11]

Due to this reason, patients with renal insufficiency are at an increased risk of developing CIN. Additionally, it is suggested that diabetes mellitus disrupts renal autoregulation, making diabetics more susceptible to CIN. Diabetic patients may experience significant variations in serum creatinine levels after contrast administration, which could be a result of the higher incidence of CIN. These findings might reflect the serum creatinine variation rather than indicating CIN or renal damage.[12,13]

Some argue that the increased risk of CIN could be attributed to the use of high osmolar contrast agents primarily utilized in cardiac catheterizations, and may not be applicable to the currently used low- or iso-osmolar contrast media used in CECT studies. Furthermore, there is a contention that the current observational and retrospective studies examining the risk of CIN and renal injury may not be sufficient to fully understand the true impact of CIN on mortality and morbidity. Comparative studies with a control group are needed to obtain more comprehensive data.[13-15]

It can also be argued that in general practice, patients are typically monitored after CECT, which may influence the true incidence of CIN. Moreover, hospitalized patients often have one or more risk factors for CIN, leading to biased data on the risk of CIN. These patients are also at a higher risk of mortality and morbidity due to underlying health conditions, making it challenging, if not impossible, to establish a causal relationship with CIN. Further research is necessary to evaluate the genuine risk of CIN associated with iodinated contrast media.

Until the exact relationship between the use of contrast media and the development of CIN is determined, the current data strongly supports the observation that iodinated contrast media increases the risk of CIN. The identified risk factors for CIN include diabetes mellitus, hypertension, advancing age (over 65 years), and renal insufficiency.

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CONCLUSION

Our study found that there is a slight risk of CIN after CECT studies. The risk factors identified for developing CIN were diabetes mellitus, being elderly (over 65 years of age), hypertension, and renal insufficiency. In all the patients who developed CIN, their serum creatinine levels returned to baseline within a week. Based on these findings, we concluded that the use of non-ionized iodinated contrast media is associated with a low risk of CIN, and CECT studies themselves do not significantly increase the likelihood of developing CIN. However, further studies incorporating a control group may be necessary to accurately quantify the exact risk posed by iodinated contrast media in relation to CIN.

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