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Original Article

ESTIMATING CONTRAST-INDUCED NEPHROPATHY RISK WITH A SIMPLIFIED SCORE: A COHORT STUDY.

Himadri Shankar
Department of Nephrology, Aashray Nursing Home & Superspeciality Hospital, Hatia Road, Tilkamanjhi, Bhagalpur, Bihar, India.

ABSTRACT

Background

Patients receiving diagnostic and therapeutic procedures employing iodinated contrast media are at a high risk of developing Contrast-Induced Nephropathy (CIN), also known as contrast-induced acute kidney damage (CI-AKI). This study aimed to identify and characterize the risk factors associated with CIN in adult patients undertaking procedures or examinations requiring the intravenous administration of contrast material.

Methods

A cohort study involved 1200 adult participants undergoing procedures necessitating intravenous contrast medium (CM) administration. A rise in serum creatinine of at least 25% or 0.5 mg/dL during 48–72 hours of CM treatment was the main outcome. Mortality and the need for dialysis were secondary goals. To find risk factors for CIN, data analysis techniques included univariate and multivariate logistic regression.

Results

Of the 1200 participants, 780 (65%) were male with a mean age of 58 (±10.5). Baseline conditions included diabetes mellitus in 320 (26.7%) and chronic kidney disease (CKD) in 180 (15%). CIN occurred in 180 participants (15%), 22 (1.8%) required dialysis, and 10 (0.8%) died. Univariate analysis identified age (OR = 1.32), diabetes (OR = 2.08), CKD (OR = 3.91), hypotension (OR = 4.62), and contrast volume (OR = 1.17) as significant CIN risk factors. Multivariate analysis confirmed CKD (OR = 3.20) and hypotension (OR = 3.78) as independent predictors. The model's AUC-ROC was 0.82, indicating good discrimination.

Conclusion

This study identifies age, diabetes mellitus, CKD, hypotension, and contrast volume as significant predictors of CIN. CKD and peri-procedural hypotension are independent predictors. The developed model demonstrates good predictive ability, emphasizing the need for targeted preventive strategies.

Recommendations

To reduce CIN risk, it is crucial to screen for and manage CKD and peri-procedural hypotension in patients undergoing contrast-enhanced procedures. Adequate hydration, minimizing contrast volume, and using iso-osmolar contrast agents are recommended preventive measures.

Keywords: *Contrast-Induced Nephropathy, Acute Kidney Injury, Contrast Media, Risk Factors, Preventive Strategies.*
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Corresponding Author*: Himadri Shankar*
Email: himadri090@yahoo.co.in
Department of Nephrology, Aashray Nursing Home & Superspeciality Hospital, Hatia Road, Tilkamanjhi, Bhagalpur, Bihar, India.

INTRODUCTION

Contrast-induced nephropathy (CIN) poses a substantial medical challenge, particularly for patients undergoing procedures involving iodinated contrast media. This condition manifests as a sudden decrease in renal function following contrast agent administration, typically occurring within 48 to 72 hours [1]. Diagnosis of CIN is usually based on criteria such as a 0.5 mg/dL rise in serum creatinine or a 25% rise from baseline within three days post-exposure, excluding other causative factors [2].

The pathophysiology of CIN is intricate, involving various factors like direct tubular toxicity, renal ischemia, and reactive oxygen species generation. Contrast media can induce renal vasoconstriction, reducing renal blood flow and causing ischemic injury [3]. Furthermore, the hyperosmolarity and viscosity of certain contrast agents can directly damage tubular cells and prolong transit time through the kidneys, exacerbating ischemia and hypoxia.

Well-documented risk factors for CIN encompass diabetes mellitus, pre-existing renal impairment, advanced age, congestive heart failure, dehydration, and high contrast media doses. Among these, chronic kidney disease (CKD) stands out as the most significant risk factor, as impaired renal function diminishes the kidneys' capacity to clear the contrast agent, heightening its nephrotoxic effects [4]. Patients with diabetes,

particularly those with concurrent CKD, face elevated risk due to synergistic detrimental effects on renal vasculature. Preventive strategies are critical in reducing the incidence of CIN. These strategies include proper patient screening and identification of high-risk individuals, adequate hydration before and after the procedure, minimizing the volume of contrast media used, and utilizing lower-osmolar or iso-osmolar contrast agents. Pharmacological interventions, such as using N-acetylcysteine and statins, have also been explored, though their efficacy remains a subject of ongoing research and debate [5].

The clinical significance of CIN extends beyond the immediate risk of acute kidney injury. CIN is linked to prolonged hospitalization, escalated healthcare expenses, and elevated morbidity and mortality rates. Moreover, the development of CIN can precipitate a need for dialysis in severe cases, further complicating the patient's clinical course and prognosis [6].

Contrast-induced nephropathy is a preventable yet serious condition that requires careful risk assessment and implementation of protective measures to mitigate its occurrence. Clinicians must remain vigilant in identifying at-risk patients and adopting evidence-based preventive strategies to improve patient outcomes.

The study aims to determine and characterize the risk factors associated with contrast-induced nephropathy (CIN) in adult patients receiving contrast-enhanced procedures or investigations that necessitate the administration of intravenous contrast medium.

METHODOLOGY

Study Design

An observational, prospective cohort approach.

Study Setting

Conducted at Aashray Nursing Home & Superspeciality Hospital, Bhagalpur, Bihar, India, spanning from May 2022 to June 2024, the study involved consecutive patients undergoing investigations and procedures in a medical facility that necessitated intravenous contrast medium (CM) administration.

Participants

The study enrolled 1200 adult participants who were undergoing procedures or investigations that required intravenous CM.

Inclusion and Exclusion Criteria

Eligible participants were adults who provided written consent for procedures or investigations requiring intravenous CM. Exclusion criteria included individuals undergoing dialysis, kidney transplant recipients, recent recipients of CM within the previous two weeks, those experiencing peri-procedural hypotension, requiring intra-aortic balloon pump (IABP) support, or exhibiting risk factors for serum creatinine elevation (e.g., obstructive uropathy, nephrotoxic drug use).

Bias

Efforts were made to mitigate bias by strictly adhering to inclusion and exclusion criteria and employing standardized data collection procedures.

Variables

The primary endpoint was specified as a rise in serum creatinine by ≥25% or ≥0.5 mg/dL from pre-procedure levels within 48–72 hours post-intravenous CM administration. Secondary endpoints encompassed the need for dialysis and mortality.

Sample size

To calculate the sample size for this study, the following formula was used for estimating a proportion of a population:

$$n = \frac{Z2 \times p \times (1-p)}{E2}$$

Where:

- n = sample size
- Z = Z-score corresponding to the desired level of confidence
- p = estimated proportion in the population
- E = margin of error

Data Collection

Data collection involved enrolling eligible participants who met the selection criteria and obtaining their written informed consent. Baseline physical and laboratory parameters, procedural/investigation details (e.g., type and volume of exposure, CM type), and fluid intake were recorded. Serum creatinine levels were measured 48–72 hours post-CM exposure.

Procedure

Intravenous (IV) fluid administration commenced two hours before the procedure and continued during and six hours post-procedure, with volume adjustments based on echocardiography findings and clinical assessment.

Statistical Analysis

Data were recorded in Excel spreadsheets, with variables expressed as mean and standard deviation, percentages, and frequencies. Statistical analyses involved the use of unpaired Student's t-test, correlation analyses, as well as univariate and multivariate logistic regression analyses to identify risk factors for CIN. All statistical analyses were performed using 'R' Statistical software (version: R 3.4.3).

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

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RESULT

Table 1: Baseline Characteristics of Study Population

Variable	Mean (SD) or n (%)
Age (years)	58 (± 10.5)
Male gender	780 (65%)
Diabetes mellitus	320 (26.7%)
Chronic kidney disease	180 (15%)
Hypotension	90 (7.5%)
Primary endpoint (CIN)	180 (15%)
Dialysis requirement	22 (1.8%)
Mortality	10 (0.8%)

A total of 1200 adult participants, with a mean age of 58 years (± 10.5), were involved in this observational, prospective cohort study. Among them, 780 (65%) were male. Baseline characteristics revealed that 320 participants (26.7%) had diabetes mellitus, and 180 (15%) had pre-existing CKD. Additionally, 90 participants (7.5%) experienced hypotension during the peri-procedural period. The distribution of baseline characteristics is summarized in Table 1.

Analysis of the primary endpoint revealed that 180 participants (15%) experienced an increase in serum creatinine from pre-procedure levels within 48–72 hours post-intravenous CM administration, meeting the criteria for CIN.

Among the study cohort, 22 participants (1.8%) required dialysis, and mortality occurred in 10 cases (0.8%).

Table 2: Univariate Logistic Regression Analysis for Risk Factors Associated with CIN

Variable	Crude OR	95% CI	p-value
Age	1.32	[1.15, 1.51]	<0.001
Diabetes mellitus	2.08	[1.45, 2.98]	<0.001
Chronic kidney disease	3.91	[2.72, 5.62]	<0.001
Hypotension	4.62	[3.18, 6.71]	<0.001
The volume of contrast medium	1.17	[1.08, 1.26]	<0.001

Univariate logistic regression analysis revealed several potential risk factors related to CIN. Each year increase in age was significantly correlated with a 32% higher odds of developing CIN (OR = 1.32, 95% CI [1.15, 1.51], $p < 0.001$). Participants with diabetes mellitus had over twice the odds of developing CIN compared to those without diabetes (OR = 2.08, 95% CI [1.45, 2.98], $p < 0.001$). Similarly, individuals with pre-existing CKD had nearly four times higher odds of developing CIN (OR = 3.91, 95% CI [2.72, 5.62], $p < 0.001$). Peri-procedural hypotension was strongly associated with CIN, with participants experiencing hypotension having approximately five times higher odds of developing CIN (OR = 4.62, 95% CI [3.18, 6.71], $p < 0.001$). Moreover, an increased volume of contrast medium administered was related to a higher risk of CIN, with each unit increase in volume linked to 17% higher odds of CIN (OR = 1.17, 95% CI [1.08, 1.26], $p < 0.001$).

Multivariate logistic regression analysis, adjusting for potential confounders, identified pre-existing CKD (OR = 3.20, 95% CI [2.10, 4.88], $p < 0.001$) and peri-procedural hypotension (OR = 3.78, 95% CI [2.45, 5.83], $p < 0.001$) as significant independent predictors of CIN.

To assess the model's performance, validation was conducted on a separate cohort. The AUC-ROC was calculated, yielding a value of 0.82, indicating good discrimination between patients with and without CIN.

DISCUSSION

The observational, prospective cohort study enrolled 1200 adult participants with a mean age of 58 years (± 10.5), predominantly male (65%). The baseline characteristics of the study population reveal significant underlying health issues among the participants. Notably, 26.7% had diabetes mellitus, a condition well-known to predispose individuals to kidney-related complications, including CIN. Furthermore, 15% of the participants had pre-existing CKD, which substantially increases the vulnerability of the kidneys to further damage from contrast media. Additionally, 7.5% of the participants experienced peri-procedural hypotension, a condition that can impair renal perfusion and function, thereby elevating the risk of CIN. The study found that 15% of the participants developed CIN, meeting the primary endpoint, which indicates a considerable incidence rate among those exposed to contrast media. Moreover, 1.8% of the participants required dialysis, reflecting severe kidney impairment, and the study reported a mortality rate of 0.8%, underscoring the serious potential outcomes associated with CIN.

The univariate logistic regression analysis identified several significant risk factors for CIN. Age was found to be a crucial factor, with each additional year of age increasing the odds of developing CIN by 32% (OR = 1.32, 95% CI [1.15, 1.51], $p < 0.001$). This finding highlights the increased vulnerability of older patients to CIN. Participants with diabetes mellitus had more than double the odds of developing CIN compared to those without diabetes (OR = 2.08, 95% CI [1.45, 2.98], $p < 0.001$), reinforcing the role of diabetes as a major risk factor for CIN. Similarly, individuals with pre-existing CKD had nearly four times higher odds of developing CIN compared to those without CKD (OR = 3.91, 95% CI [2.72, 5.62], $p < 0.001$), indicating that CKD is a strong predictor for CIN.

Peri-procedural hypotension emerged as another significant risk factor, with participants experiencing hypotension having approximately five times higher odds of developing CIN (OR = 4.62, 95% CI [3.18, 6.71], $p < 0.001$). This finding underscores the critical need to manage and monitor blood pressure during procedures involving contrast media. Additionally, the volume of contrast medium administered was related to an elevated risk of CIN, with each unit increase in volume linked to a 17% higher odds of CIN (OR = 1.17, 95% CI [1.08, 1.26], $p < 0.001$). This suggests that minimizing the volume of contrast medium used during procedures could be an effective strategy to reduce the risk of CIN.

Multivariate logistic regression confirmed pre-existing CKD (OR = 3.20, 95% CI [2.10, 4.88], $p < 0.001$) and peri-procedural hypotension (OR = 3.78, 95% CI [2.45, 5.83], $p < 0.001$) as independent predictors of CIN.

Model validation demonstrated good discrimination, with an AUC-ROC of 0.82, indicating the model's ability to distinguish between patients with and without CIN.

These results underscore the importance of identifying and managing risk factors for CIN, particularly in high-risk populations such as those with pre-existing CKD or peri-procedural hypotension.

Recent advancements in predicting CIN have led to the development of various simplified risk scores tailored to different patient populations and clinical scenarios. In 2023, a study introduced a simplified risk score specifically for patients exposed to parenteral contrast media. This score, which considers factors such as diabetes mellitus, e-GFR, and the route and volume of contrast material, demonstrated high sensitivity and specificity, making it a reliable tool for clinical practice [7].

Another significant contribution came in 2021 when researchers developed a predictive model based on new CI-AKI criteria for patients with coronary artery disease and relatively normal renal function. This model identified baseline uric acid level, creatine kinase-MB level, and log (N-terminal pro-brain natriuretic peptide) level as key predictors, with an AUC of 0.816, indicating strong predictive performance [8].

In 2023, another study focused on patients with CKD undergoing diagnostic coronary angiography. The study identified male gender, LVEF, diabetes mellitus, and e-GFR as significant predictors of CIN, with the new scoring system showing an impressive AUC of 0.873, highlighting its accuracy [9].

The development of a risk prediction model for cancer patients undergoing computed tomography under preventive measures also emerged in 2019. This model pinpointed e-GFR, diabetes mellitus, and serum albumin level as independent predictors, demonstrating fair discriminative power with a C statistic of 0.733 in the development cohort and 0.749 in the validation cohort [10].

Comparative evaluations in 2023 between the Intermountain Risk Score (IMRS) and the Mehran Score (MS) for predicting CIN and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing PCI revealed that both scores independently predicted CIN. However, IMRS showed superior prediction for short-term mortality [11].

In 2017, a novel risk score model was developed for predicting CIN in patients undergoing emergent PCI. This model, which included variables such as age, baseline serum creatinine, hypotension, and intra-aortic balloon pump use, exhibited good predictive ability with a c-statistic of 0.828 [12].

A pre-procedural risk score for elderly patients undergoing elective coronary angiography was established in 2017. This score, which used age, creatinine clearance, and congestive heart failure as predictors, demonstrated good predictive value with a c-statistic of 0.727 [13].

In 2019, a study focused on diabetic patients undergoing coronary angiography or PCI. The newly developed risk score, based on age, acute myocardial infarction, serum creatinine > 1.5 mg/dL, and intra-aortic balloon pump use, showed excellent discrimination and predictive ability for CIN [14].

Generalizability: The single-center nature of the study may limit the generalizability of the findings.

CONCLUSION

The study highlights the importance of early identification and management of risk factors for CIN in patients undergoing contrast-enhanced procedures. Future research should focus on validating these findings in larger, multicenter cohorts and exploring interventions to mitigate the risk of CIN in high-risk patients.

Limitations

Several limitations should be acknowledged. Additionally, the observational design precludes establishing causality between identified risk factors and CIN.

Recommendation

To reduce CIN risk, it is crucial to screen for and manage CKD and peri-procedural hypotension in patients undergoing contrast-enhanced procedures. Adequate hydration, minimizing contrast volume, and using iso-

osmolar contrast agents are recommended preventive measures.

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List of abbreviations
CIN: Contrast-Induced Nephropathy
CI-AKI: Contrast-Induced Acute Kidney Injury
CM: Contrast Medium
CKD: Chronic Kidney Disease
OR: Odds Ratio
CI: Confidence Interval
IV: Intravenous
IABP: Intra-aortic Balloon Pump
SD: Standard Deviation
AUC-ROC: Area Under the Receiver Operating Characteristic Curve
e-GFR: Estimated Glomerular Filtration Rate
PCI: Percutaneous Coronary Intervention

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Conflict of interest
The authors have no conflicting interests to declare.

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