Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/q5h0t023

TO STUDY THE CORRELATION OF THE NEUTROPHIL TO LYMPHOCYTE RATIO AND C-REACTIVE PROTEIN TO ALBUMIN RATIO WITH CONTRAST INDUCED NEPHROPATHY IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTIONS

Dr. Neha Athale[1*], Dr. Amar Kulkarni[2], Dr. Avinash Chaudhari[3]

[1*]Resident, Department of Nephrology, DY Patil Medical College and Hospital, Navi Mumbai, Maharashtra, India.
[2]Associate Professor, Department of Nephrology, DY Patil Medical College and Hospital, Navi Mumbai, Maharashtra, India.
[3]Professor & HOD, Department of Nephrology, DY Patil Medical College and Hospital, Navi Mumbai, Maharashtra, India.

ABSTRACT

Background

CIN (Contrast-Induced Nephropathy) is a form of acute kidney injury that arises following exposure to iodinated contrast media, particularly during PCI (Percutaneous Coronary Interventions). CIN is associated with increased morbidity, prolonged hospitalization, and adverse cardiovascular outcomes. Inflammatory markers such as the NLR (Neutrophil-to-Lymphocyte Ratio) and CAR (C-Reactive Protein to Albumin Ratio) have recently been proposed as potential predictors of CIN.

Methods

This prospective observational study was conducted at Dr. D.Y. Patil Medical College Hospital, Mumbai, between 2023 and 2024, enrolling 100 patients undergoing PCI. Baseline demographics, comorbidities, and laboratory parameters including NLR and CAR were recorded. CIN was defined as a ≥0.5 mg/dL or ≥25% rise in serum creatinine within 48–72 hours post-contrast exposure. Data were analyzed using appropriate statistical methods including chi-square, t-tests, and multivariate regression.

Results

CIN occurred in 14% of patients. A statistically significant association was observed between CIN and hypertension ($p = 0.021$), elevated blood sugar levels ($p = 0.0378$), low hemoglobin ($p = 0.0041$), low lymphocyte count ($p = 0.0400$), high neutrophil count ($p = 0.0024$), and increased CRP levels ($p < 0.001$). Mean NLR was significantly higher in the CIN group (6.58 ± 4.69 vs. 4.27 ± 3.42, $p = 0.0289$), and CAR was also notably elevated (2.06 ± 2.13 vs. 0.53 ± 0.61, $p < 0.001$).

Conclusion

The findings suggest that elevated NLR and CAR values are significantly associated with the incidence of CIN in patients undergoing PCI. These inflammatory markers can serve as simple, cost-effective tools for early identification and risk stratification of patients at risk for CIN.

Keywords: Contrast-Induced Nephropathy, Percutaneous Coronary Intervention, Neutrophil-yo-Lymphocyte Ratio, C-Reactive Protein to Albumin Ratio, Inflammatory Markers, Acute Kidney Injury.

INTRODUCTION

CIN (Contrast-Induced Nephropathy) is defined as an acute deterioration in renal function, typically evidenced by an absolute increase in serum creatinine of ≥0.5 mg/dL or a relative increase of ≥25% from baseline within 48–72 hours of iodinated CM (Contrast Media) exposure, in the absence of other identifiable causes.[1] CIN is a known complication of PTCA (Percutaneous Transluminal Coronary Angioplasty), a procedure requiring CM to visualize coronary arteries.[2] The contrast agent may induce renal vasoconstriction and direct tubular toxicity, leading to inflammation and cellular injury. While often asymptomatic in early stages, CIN may later present with oliguria, edema, nausea, vomiting, fatigue, hypertension, and electrolyte disturbances.[3]

Risk factors for CIN include DM (Diabetes Mellitus), advanced age, CKD (Chronic Kidney Disease), and dehydration. Additionally, the type and volume of CM and the duration of the procedure influence CIN risk.[4] Global incidence following PCI or coronary angiography ranges from 3% to 19%, with studies showing a 13.3% incidence in PCI patients, particularly those with DM and CKD.[4,5] CIN is associated with serious outcomes, including acute kidney injury requiring dialysis, prolonged hospital stay, and increased cardiovascular risk, such as heart failure and myocardial infarction.[6]

Recent attention has focused on inflammatory markers like NLR (Neutrophil-to-Lymphocyte Ratio) and CAR (C-Reactive Protein to Albumin Ratio) as predictors of CIN. Elevated NLR reflects systemic inflammation, while high CAR indicates both inflammation and poor nutritional status, both potentially contributing to renal injury.[7]

This study aims to evaluate NLR and CAR as predictive markers for CIN in PCI patients, supporting early risk assessment and prevention strategies.

AIMS AND OBJECTIVES

The study aims to investigate the correlation between inflammatory markers-specifically the NLR and the CAR-and the development of CIN in patients undergoing PCI. The objectives include evaluating the association of these markers with the incidence of CIN and assessing their potential role as predictive risk factors, with the goal of enhancing early identification and prevention strategies for at-risk patients.

MATERIALS AND METHODS

This was a prospective observational study conducted at Dr. D.Y. Patil Medical College Hospital, Mumbai, over the duration of one year from 2023 to 2024. The study population included patients undergoing PCI, who were selected based on predefined inclusion and exclusion criteria to evaluate the association between inflammatory markers and the incidence of CIN.

Inclusion and Exclusion Criteria

The study included all patients undergoing PCI, regardless of their baseline renal function. Patients were excluded if they had prior exposure to contrast media within one month before presentation to the tertiary care center, were on nephrotoxic medications, or presented with clinical features of shock.

Data Collection Tools

Data were collected using a pre-designed template developed to systematically record demographic, clinical, and laboratory information. Laboratory assessments included serum creatinine, white blood cell count, differential leukocyte count, CRP, and serum albumin levels. A Cell-Dyn 37000

Hematology Analyzer (Abbott Diagnostic Division, Wiesbaden, Germany) was used to perform complete blood counts, including neutrophils and lymphocytes, from which the NLR was calculated. Serum creatinine was measured using the Architect Plusci 4100 analyzer (Abbott Laboratories, Abbott Park, Illinois). CRP was analyzed via the immunoturbidimetric method using the Toshiba 200FR Neo analyzer, and serum albumin was measured using a calorimetric assay. The CAR was then calculated.

Data Collection Procedure

Demographic details such as age, sex, and comorbidities were recorded at the time of hospital admission. Coronary angiography was performed within 1 to 72 hours of admission, following standard interventional protocols. Patients were confirmed to be euvolemic before PCI, and no changes were made to their ongoing medications. Blood samples were collected at admission for baseline laboratory investigations, including complete blood counts and inflammatory markers. Serum creatinine levels were measured before PCI, then daily for three days post-procedure, at discharge from the coronary care unit, and again at hospital discharge. White blood cell differential counts were taken at admission before catheterization. The NLR and CAR were calculated based on the laboratory values obtained. CIN was defined as either an increase in serum creatinine by ≥0.5 mg/dL or a 25% relative increase from baseline within 48–72 hours post-PCI.

Statistical Analysis

The compiled data were entered into an Excel spreadsheet and analyzed using GraphPad Prism (version 9.2.0). Descriptive statistics were used to summarize baseline characteristics, presented as means with standard deviations or medians for continuous variables and as frequencies or percentages for categorical variables. Comparisons between groups were made using the Student's t-test and one-way ANOVA for parametric data. Non-parametric data were also analyzed accordingly. The chi-square test or Fisher's exact test was employed for categorical variables. Variables found to be statistically significant in univariate analysis were further evaluated using multivariate analysis to identify independent predictors of CIN.

RESULTS

Gender	CIN (+) (N=14)	%	CIN (-) (N=86)	%	P-Value
Male	12	16.22%	62	83.78%	0.2812
Female	2	7.69%	24	92.31%	

Table 1: Distribution of Patients on the Basis of Gender

Table 1 observes the gender distribution among patients with and without CIN. Although more males developed CIN compared to females, the difference was not statistically significant (p = 0.2812).

Age Group	CIN (+) (N=14)	%	CIN (-) (N=86)	%	P-Value
<60 years	5	9.8%	46	90.1%	0.2196
≥60 years	9	18.37%	40	81.63%	
Mean age	60.3 ± 12.42		59.7 ± 12.5		0.8680

Table 2: Distribution of Patients on the Basis of age

Table 2 shows that CIN was slightly more common in patients aged ≥60 years. However, the age-related difference in CIN incidence was not statistically significant.

Coexisting Disease	CIN (+) (N=14)	%	CIN (-) (N=86)	%	P-Value
Hypertension	11	22%	39	78%	**0.021**
Diabetes Mellitus	7	20.59%	27	79.41%	0.175
None	3	7.3%	38	92.7%	0.1102

Table 3: Distribution Based on Co-Existing Diseases

Table 3 indicates a statistically significant association between hypertension and CIN (p = 0.021), while diabetes and absence of comorbidities were not significantly associated with CIN.

Procedure	CIN (+) (N=14)	%	CIN (-) (N=86)	%	P-Value
CAG	11	13.41%	71	86.59%	0.719
PTCA	3	16.67%	15	83.33%	
Table 4: Distribution Based on Procedure Performed					

Table 4 evaluates the procedure type, CAG or PTCA,-and its relation to CIN development. There was no significant difference observed between procedure type and CIN incidence.

Parameter	CIN (+) (N=14)	CIN (-) (N=86)	P-Value
Systolic BP (mmHg)	130.86 ± 6.78	126.72 ± 8.05	0.0718
Diastolic BP (mmHg)	77.43 ± 7.62	78.58 ± 7.49	0.5963
Blood Sugar (mg/dL)	137.07 ± 19.26	128.80 ± 16.69	**0.0378**
Hemoglobin (g/dL)	10.76 ± 1.95	12.49 ± 2.06	**0.0041**
WBC (*10⁹/L)	10.72 ± 4.07	9.37 ± 3.00	0.1418
Lymphocyte count (*10⁹/L)	1.57 ± 0.91	2.2 ± 1.07	**0.0400**
Neutrophil count (*10⁹/L)	7.97 ± 3.96	5.14 ± 3.01	**0.0024**
CRP (mg/L)	64.81 ± 6.41	20.55 ± 23.04	**<0.001**
Albumin (g/dL)	3.45 ± 0.79	3.99 ± 0.42	**0.002**
Table 5: Laboratory Measurements in Patients with and without CIN			

Table 5 shows several significant differences in lab values between CIN and non-CIN groups. Notably, higher blood sugar, neutrophil count, CRP, and lower hemoglobin, albumin, and lymphocytes were significantly associated with CIN.

Time Point	CIN (+) (N=14)	CIN (-) (N=86)	P-Value
Day 1	1.98 ± 1.11	1.06 ± 0.45	**<0.001**
Day 3	2.65 ± 1.17	1.17 ± 0.44	**<0.001**
Follow-up	2.26 ± 1.00	1.08 ± 0.40	**<0.001**
Table 6: Serum Creatinine at different time points			

Table 6 highlights that serum creatinine levels were consistently and significantly elevated at all time points in CIN patients, reinforcing the diagnosis and severity of renal impairment.

Ratio Type	CIN (+) (N=14)	CIN (-) (N=86)	P-Value
NLR	6.58 ± 4.69	4.27 ± 3.42	**0.0289**
CAR	2.06 ± 2.13	0.53 ± 0.61	**<0.001**
Table 7: NLR and CAR Ratios in CIN vs. Non-CIN Patients			

Table 7 demonstrates that both NLR and CAR were significantly higher in patients who developed CIN, highlighting their potential as predictive inflammatory biomarkers.

DISCUSSION

CIN remains a significant complication following invasive cardiovascular procedures such as PCI, often exacerbated by factors like procedural complexity, hemodynamic instability, and inadequate preventive strategies. CIN has been consistently linked to prolonged hospital stays, increased morbidity, and elevated mortality risk. Early identification of at-risk patients is therefore vital. Inflammatory processes have been shown to play a central role in the pathogenesis of CIN, and biomarkers such as NLR and CAR have emerged as potential predictive tools.

In our prospective observational study of 100 patients undergoing PCI, the incidence of CIN was found to be 14%, which aligns with prior research by Kaya et al. (13%),[8] ZenginTemel et al. (10.4%),[9] and Kurtul et al. (13.2%),[10] but lower than that reported by Karakurt et al. (42%).[11]

No statistically significant difference in CIN incidence was noted between genders (16.22% in males vs. 7.69% in females, p=0.2812), a trend similarly observed by Kaya et al.[8] and Karabag et al,[12] though some studies, such as Rasheed et al.[13] showed higher incidence in females.

Age appeared to be an influencing factor, as patients with CIN had a slightly higher mean age (60.3 ± 12.42 years) compared to those without (59.7 ± 12.5 years), a pattern also documented in studies by Kaya et al.[8] and Karabag et al.[12] While the difference was not statistically significant in our cohort, advanced age is known to correlate with reduced glomerular filtration rate and increased vulnerability to renal injury.

A significant association was observed between hypertension and CIN in our study (p = 0.021), consistent with Kaya et al.[8] However, Ishikawa et al. reported no such association.[14] Diabetes mellitus was not significantly associated with CIN (p = 0.175), though previous findings are mixed on this point.

Notably, blood sugar levels were significantly higher in the CIN group (137.07 ± 19.26 mg/dL vs. 128.80 ± 16.69 mg/dL, p = 0.0378), reflecting the role of hyperglycemia in oxidative stress and inflammation. Kaya et al. similarly reported significantly higher blood glucose levels among patients with CIN.[8]

Pathophysiologically, CIN develops through renal vasoconstriction, resulting in medullary hypoxia and direct tubular toxicity from contrast agents. The release of reactive oxygen species and cytokines, coupled with endothelial dysfunction and impaired vasodilation, leads to kidney injury. Inflammatory cell infiltration, especially by neutrophils, exacerbates this process.

In our study, patients with CIN had significantly higher neutrophil counts (7.97 ± 3.96 vs. 5.14 ± 3.01 $\times 10^9$/L, p = 0.0024) and lower lymphocyte counts (1.57 ± 0.91 vs. 2.2 ± 1.07 $\times 10^9$/L, p = 0.0400), resulting in a higher NLR (6.58 ± 4.69 vs. 4.27 ± 3.42, p = 0.0289). These findings are in line with those of Kurtul et al.[10] Kaya et al.[8] and Tanik et al.[15] who identified NLR as an independent predictor of CIN and a marker of systemic inflammation.

CRP and albumin, as individual markers, also revealed important insights. In our study, CRP levels were significantly higher in the CIN group (64.81 ± 6.41 mg/L vs. 20.55 ± 23.04 mg/L, p<0.001), while albumin levels were lower (3.45 ± 0.79 vs. 3.99 ± 0.42 g/dL, p = 0.002). These shifts translated into a significantly higher CAR in the CIN group (2.06 ± 2.13 vs. 0.53 ± 0.61, p<0.001), indicating a strong inflammatory burden and poorer nutritional status.

Our findings are supported by studies such as those by Kurtul et al.[10] who reported elevated CRP in CIN patients, and Ishikawa et al.[14] who found lower albumin levels in AKI patients. Kaya et al.[8] and Karabag et al.[12] also demonstrated that higher CRP and lower albumin levels were predictive of CIN.

CLINICAL IMPLICATIONS

The combined utility of NLR and CAR offers a convenient, cost-effective method for identifying patients at elevated risk for CIN post-PCI. Both markers are readily available through routine blood tests, enabling early intervention strategies.

LIMITATIONS

Several limitations should be considered when interpreting the findings of this study. Firstly, the relatively small sample size of 100 patients may affect the generalizability of the results, as a larger cohort would provide more robust data and support stronger conclusions. Secondly, the study population was limited exclusively to patients undergoing PCI, thereby excluding individuals undergoing non-coronary procedures involving contrast media. This restriction may limit the applicability of the findings to the broader population at risk for CIN in other clinical contexts. Lastly,

the study was a single-point observational study, which may not fully capture the dynamic changes in inflammatory markers or renal function over time.

CONCLUSION

CIN remains a significant complication following PCI, with implications such as prolonged hospitalization and increased mortality. This study emphasizes the role of systemic inflammation in the development of CIN, highlighting the predictive value of inflammatory markers like NLR and CAR. Patients with elevated NLR and CAR were found to be at significantly higher risk for CIN, indicating that these markers can aid in early identification of high-risk individuals. Incorporating NLR and CAR into routine pre-procedural assessments may enhance risk stratification and support the implementation of targeted preventive strategies. Continued research is warranted to strengthen predictive models and improve CIN management in high-risk populations.

REFERENCES

[1] Mohammed NM, Mahfouz A, Achkar K, et al. Contrast-induced Nephropathy. Heart Views 2013;14(3):106-16.
[2] Chen Y, Zheng X, Li N, et al. Impact of iodinated contrast media in patients received percutaneous coronary intervention: focus on thyroid disease. Front Endocrinol (Lausanne) 2022;13:917498.
[3] Rahman M, Shad F, Smith MC. Acute kidney injury: a guide to diagnosis and management. Am Fam Physician 2012 ;86(7):631-9.
[4] Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl 2006;(100):S11-5.
[5] He H, Chen XR, Chen YQ, et al. Prevalence and predictors of contrast- induced nephropathy (CIN) in patients with st-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI): a meta- analysis. J Interv Cardiol 2019;2019:2750173.
[6] Rear R, Bell RM, Hausenloy DJ. Contrast-induced nephropathy followingangiography and cardiac interventions. Heart 2016;102(8):638-48.
[7] Wu X, Ma C, Sun D, et al. Inflammatory indicators and hematological indices in contrast-induced nephropathy among patients receiving coronary intervention: asystematic review and meta-analysis. Angiology2021;72(9):867-877.
[8] Kaya A, Kaya Y, Topçu S, et al. Neutrophil-to- lymphocyte ratio predicts contrast-induced nephropathy in patients undergoingprimary percutaneous coronary intervention. Angiology 2014;65(1):51-6.
[9] Zengin Temel T, Satilmis D, Yavuz BG, et al. The value of C- reactive Protein/albumin ratio in the prediction of contrast-induced nephropathy in emergency department patients. Cureus 2023;15(5):e39230.
[10] Kurtul A, Yarlioglues M, Duran M, Murat SN. Association of neutrophil-to- lymphocyte ratio with contrast-induced nephropathy in patients with non-ST- elevation acute coronary syndrome treated with percutaneous coronaryintervention. Heart Lung Circ 2016;25(7):683-90.
[11] Karakurt A. The Predictive Value of C-reactive protein to albumin ratio to detect contrast-induced acute kidney injury in patients with acute myocardial infarction undergoing percutaneous coronary intervention. KAFKAS TIP BİL DERG 2021;11(2):231-43.
[12] Karabag Y, Çagdaş M, Rencuzogullari I, et al. The C- reactive protein to albumin ratio predicts acute kidney injury in patients with ST- segment elevation myocardial infarction undergoing primary percutaneouscoronary intervention. Heart Lung Circ 2019;28(11):1638-45.
[13] Rasheed JI, Razak MKA, Mahdi AG. Contrast- Induced Nephropathy after Coronary Angiography.IJSR. 2017;6 (6), 767-773.
[14] Ishikawa M, Iwasaki M, Namizato D, et al. The neutrophil to lymphocyte ratio and serum albumin as predictors of acute kidney injury after coronary artery bypass grafting. Sci Rep

2022;12(1):15438.

[15] Tanik VO, Cinar T, Velibey Y, et al. Neutrophil-to-Lymphocyte Ratio Predicts Contrast-Induced Acute Kidney Injury in Patients with ST-Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention. J Tehran Heart Cent 2019;14(2):59-66.