

## ORIGINAL ARTICLE

## ASSESSING IN-HOSPITAL MORTALITY AND PREDICTORS IN PATIENTS WITH CONTRAST-INDUCED NEPHROPATHY FOLLOWING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

Rajesh Kumar, Kheraj Mal, Abiha Urooj, Barkha Luhana, Mohammad Rasool, Muhammad Yousuf Daud, Kubbra Rahooja, Maryam Samad, Uroosa Safdar, Ali Bin Naseer, Kalsoom Chachar, Muhammad Ishaq, Zahid Ur Rehman, Musa Karim

National Institute of Cardiovascular Diseases, Karachi-Pakistan

**Background:** The contrast-induced nephropathy (CIN) is a common complication of primary percutaneous coronary intervention (PCI) it has been reported to be associated with an increased risk of mortality. The study reported the in-hospital mortality among patients who developed CIN after primary PCI. **Methods:** This descriptive cross-sectional study was conducted on a sample of consecutive who developed CIN after primary PCI at a tertiary care cardiac hospital in Karachi, Pakistan. The CIN was defined as either a relative increase of 25% or an absolute increase of 0.5 mg/dL in post-procedure serum creatinine within 72 hours. The in-hospital mortality status was recorded and clinical and demographic predictors of in-hospital mortality were identified with the help of binary logistic regression analysis. **Results:** In the study sample of 402 patients, 74.1% (298) were male and the mean age of the study sample was 59.4±11.5 years. The in-hospital mortality rate was 9.7% (39). On multivariable analysis, an increased risk of mortality was found to be independently associated with inferior wall myocardial infarction (IWMI) with right ventricular (RV) infarction, intra-procedure arrhythmias, and pump failure with an adjusted odds ratio of 3.63 [95% CI: 1.31-10.08;  $p=0.013$ ], 5.53 [95% CI: 1.39-22.06;  $p=0.015$ ], and 8.94 [95% CI: 3.99-20.02;  $p<0.001$ ], respectively. **Conclusion:** In conclusion, there is a high rate of mortality for patients who develop CIN after primary PCI, and the risk of mortality is further aggravated by the presence of IWMI with RV infarction, intra-procedure arrhythmias, and pump failure.

**Keywords:** Iodinated contrast media; Percutaneous coronary intervention (PCI); Contrast-induced nephropathy (CIN); Mortality; Pakistan

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### INTRODUCTION

Among patients undergoing primary percutaneous coronary intervention (PCI), secondary to acute myocardial infarction (ACS),<sup>1-3</sup> a contrast medium is used to better visualize the cardiac vasculature. However, the use of contrast media can cause contrast-induced nephropathy (CIN), a condition where kidney function is impaired or worsened.<sup>4</sup> It is one of the most frequent causes of acute kidney injury acquired in hospitals, which is linked to higher rates of morbidity, mortality, and medical expenditures among patients undergoing PCI.<sup>4-8</sup> Patients with pre-existing kidney illness, diabetes, heart failure, hypotension, advanced age, and other factors<sup>4,5,9</sup> have an increased chance of getting CIN. For example, hydration,

the use of low- or iso-osmolar contrast agents, and the prescription of medications like statins or B-type natriuretic peptide<sup>5,9,10</sup> have all been suggested as prophylactic methods to lower the incidence of CIN.

Contrast-induced nephropathy-related mortality in patients undergoing PCI is a severe growing concern.<sup>11-14</sup> In-hospital mortality, long-term mortality, and poor cardiovascular outcomes are all elevated by CIN globally.<sup>11-16</sup> Depending on the nature of acute coronary syndrome (ACS), such as ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI), the risk of mortality from CIN may change.<sup>15,17-19</sup> According to one study, CIN was an independent predictor of in-hospital mortality in both

categories and was more common in patients with STEMI than NSTEMI (18.5% vs. 8.7%,  $p=0.036$ ).<sup>19</sup> A risk model was created in a different study<sup>15</sup> to forecast in-hospital mortality in patients receiving PCI, and it was discovered that CIN was one of the factors with a substantial effect on the risk score. As a result, it's critical to detect and prevent CIN in PCI patients, especially those with STEMI or other high-risk conditions.

In Pakistan, there is a severe scarcity of scientific evidence related to mortality due to CIN among patients undergoing primary PCI. This gap in knowledge needs to be filled in order to understand the CIN-related mortality, associated risk factors, and natural epidemiology of CIN after PCI among the Pakistani population. This knowledge can also play a major role in devising strategies to prevent such adverse events. Therefore, in this study, our aim was to evaluate the in-hospital mortality rate and to identify the clinical and demographic predictors of mortality among patients who developed CIN after primary PCI at a tertiary care cardiac center in Karachi, Pakistan.

## MATERIAL AND METHODS

This descriptive cross-sectional study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan between January and August 2021. Participants were patients who developed CIN after primary PCI through consecutive sampling. Inclusion criteria included patients of either gender and above 18 years of age, those with mortality within the catheterization laboratory were excluded from the study. Data were collected on 402 patients on baseline patient characteristics including age, sex, medical history, medications, and laboratory values (e.g., serum creatinine levels). Additionally, procedural details related to the PCI and post-procedure hospital events were also recorded, which include any event of access site complication, acute or sub-acute stent thrombosis, bleeding, cerebrovascular accidents, pump failure, or mortality. The CIN was defined as either a relative increase of 25% or an absolute increase of 0.5 mg/dL in post-procedure serum creatinine within 72 hours.

All the statistical analysis were performed with the help of IBM SPSS version 21. Patients were categorized based on in-hospital mortality status and demographic and clinical

data were compared between the two groups with the help of appropriate statistical tests such as Chi-square test or independent sample tests/ Mann-Whitney U test. Univariate and multivariable binary logistic regression analysis was performed to determine the predictors of in-hospital mortality.  $p$ -value of 0.05 was considered statically significant

Ethical approval was obtained from the institution review board of the National Institute of Cardiovascular Diseases (NICVD). Verbal informed consent was obtained from all participants, and confidentiality of patient data was ensured throughout the study.

## RESULTS

In the study sample of 402 patients, 74.1% (298) were male and the mean age of the study sample was  $59.4 \pm 11.5$  years. The in-hospital mortality rate was 9.7% (39). The association of demographic and clinical characteristics was assessed and the results are summarized in Table 1. We found that factors like low systolic blood pressure at the time of presentation ( $p < 0.001$ ), high random blood glucose at the time of presentation ( $p < 0.003$ ), higher Killip class III / IV ( $p < 0.001$ ), specific types of myocardial infarction (MI) (extensive anterior wall MI with right bundle branch block (RBBB) and inferior wall MI with right ventricular infarct), being intubated ( $p = 0.014$ ), arrhythmias on presentation ( $p = 0.010$ ), co-morbid conditions like diabetes mellitus ( $p = 0.009$ ), and chronic kidney disease ( $p = 0.007$ ) to be positively associated with in-hospital mortality.

The procedure characteristics and post-procedure outcomes are summarized in Table 2. The in-hospital mortality was found to be positively associated with Intra-procedural arrhythmias (15.4% vs. 3.0%;  $p < 0.001$ ), post-procedure pump failure (66.7% vs. 16.3%;  $p < 0.001$ ), and cerebrovascular accident/stroke (10.3% vs. 0.3%;  $p < 0.001$ ).

On multivariable analysis, an increased risk of mortality was found to be independently associated with inferior wall myocardial infarction (IWMI) with right ventricular (RV) infarction, intra-procedure arrhythmias, and pump failure with an adjusted odds ratio of 3.63 [95% CI: 1.31-10.08;  $p = 0.013$ ], 5.53 [95% CI: 1.39-22.06;  $p = 0.015$ ], and 8.94 [95% CI: 3.99-20.02;  $p < 0.001$ ], respectively (Table-3).

**Table-1: Comparison of baseline demographic and clinical characteristics between the patients' groups based on in-hospital survival status**

	Total	In-hospital Outcome		p-value
		Alive	Death	
<b>Total (N)</b>	<b>402</b>	<b>363 (90.3%)</b>	<b>39 (9.7%)</b>	-
<b>Gender</b>				
Male	298 (74.1%)	271 (74.7%)	27 (69.2%)	0.462
Female	104 (25.9%)	92 (25.3%)	12 (30.8%)	
<b>Age (year)</b>	59.4 ± 11.5	59.6 ± 11.4	57 ± 12.6	0.178
≤ 45 years	51 (12.7%)	43 (11.8%)	8 (20.5%)	0.297
46 to 64 years	209 (52%)	190 (52.3%)	19 (48.7%)	
≥ 65 years	142 (35.3%)	130 (35.8%)	12 (30.8%)	
<b>Ischemic time (min)</b>	410 [276-645]	410 [270-630]	385 [300-660]	0.799
<b>Systolic blood pressure (mmHg)</b>	129.4 ± 28.9	130.9 ± 28.2	115.3 ± 31.3	0.001
<b>Heart rate (bpm)</b>	91.8 ± 22.5	91.5 ± 22	94.6 ± 26.7	0.486
<b>Random blood sugar (mg/dL)</b>	197.5 [154-256]	191 [150-248]	226 [181-290]	0.003
<b>Body mass index (kg/m<sup>2</sup>)</b>	26.6 ± 3.7	26.5 ± 3.5	27.8 ± 4.6	0.038
<b>Killip Class</b>				
I	246 (61.2%)	225 (62%)	21 (53.8%)	0.001
II	51 (12.7%)	50 (13.8%)	1 (2.6%)	
III	69 (17.2%)	62 (17.1%)	7 (17.9%)	
IV	36 (9%)	26 (7.2%)	10 (25.6%)	
<b>Type of myocardial infarction</b>				
Anterior wall MI (AWMI)	224 (55.7%)	208 (57.3%)	16 (41%)	0.063
Extensive AWMI + RBBB	12 (3%)	9 (2.5%)	3 (7.7%)	
Isolated - Inferior wall MI (IWMI)	68 (16.9%)	63 (17.4%)	5 (12.8%)	
IWMI + RV Infarct	60 (14.9%)	49 (13.5%)	11 (28.2%)	
IWMI + posterior wall MI (PWMI)	25 (6.2%)	23 (6.3%)	2 (5.1%)	
Inferolateral wall MI	1 (0.2%)	1 (0.3%)	0 (0%)	
Isolated – Lateral wall MI (LWMI)	7 (1.7%)	6 (1.7%)	1 (2.6%)	
Isolated – PWMI	3 (0.7%)	3 (0.8%)	0 (0%)	
New Onset LBBB	2 (0.5%)	1 (0.3%)	1 (2.6%)	
<b>Intubated</b>	100 (24.9%)	84 (23.1%)	16 (41%)	
<b>Arrhythmia on presentation</b>	81 (20.1%)	67 (18.5%)	14 (35.9%)	0.010
<b>Co-morbid conditions</b>				
Previous PCI/CABG	38 (9.5%)	34 (9.4%)	4 (10.3%)	0.857
Hypertension	251 (62.4%)	224 (61.7%)	27 (69.2%)	0.357
Diabetes	197 (49%)	173 (47.7%)	24 (61.5%)	0.009
Smoking	87 (21.6%)	76 (20.9%)	11 (28.2%)	0.295
Chronic kidney disease	8 (2%)	5 (1.4%)	3 (7.7%)	0.007
History of cerebrovascular accident/stroke	7 (1.7%)	7 (1.9%)	0 (0%)	0.871
Obesity	64 (15.9%)	54 (14.9%)	10 (25.6%)	0.081

MI="myocardial infarction", RBBB="right bundle branch block", LBBB="left bundle branch block", RV="right ventricular", PCI="percutaneous coronary intervention", CABG="coronary artery bypass grafting"

**Table-2: Comparison of procedure characteristics and post-procedure outcomes between the patients' groups based on in-hospital survival status**

	Total	In-hospital Outcome		p-value
		Alive	Death	
<b>Total (N)</b>	<b>402</b>	<b>363 (90.3%)</b>	<b>39 (9.7%)</b>	-
<b>Left ventricular end-diastolic pressure (mmHg)</b>	25.6 ± 10.5	25.7 ± 10.4	25.1 ± 11.7	0.755
<b>Left ventricular ejection fraction (%)</b>	36.1 ± 8.8	36.1 ± 8.5	36.2 ± 11.1	0.995
<b>Temporary pacemaker implant</b>	25 (6.2%)	24 (6.6%)	1 (2.6%)	0.32
<b>Intra-aortic balloon pump implant</b>	29 (7.2%)	27 (7.4%)	2 (5.1%)	0.596
<b>Number of vessel involved</b>				
Single vessel disease	112 (27.9%)	101 (27.8%)	11 (28.2%)	0.684
Two vessel disease	147 (36.6%)	135 (37.2%)	12 (30.8%)	
Three vessel disease	143 (35.6%)	127 (35%)	16 (41%)	
<b>Culprit segment</b>				
Left main	8 (2%)	8 (2.2%)	0 (0%)	0.675
Proximal LAD	156 (38.8%)	144 (39.7%)	12 (30.8%)	
Non-proximal LAD	74 (18.4%)	66 (18.2%)	8 (20.5%)	
Right coronary artery (RCA)	116 (28.9%)	102 (28.1%)	14 (35.9%)	
Left circumflex	40 (10%)	36 (9.9%)	4 (10.3%)	
Diagonal	4 (1%)	4 (1.1%)	0 (0%)	
Ramus	3 (0.7%)	2 (0.6%)	1 (2.6%)	
SVG-RCA	1 (0.2%)	1 (0.3%)	0 (0%)	
<b>Pre-procedure TIMI (thrombolysis in myocardial infarction) flow grade</b>				
0	225 (56%)	203 (55.9%)	22 (56.4%)	0.402
I	44 (10.9%)	37 (10.2%)	7 (17.9%)	
II	65 (16.2%)	61 (16.8%)	4 (10.3%)	
III	68 (16.9%)	62 (17.1%)	6 (15.4%)	
<b>Slow flow/no-reflow during procedure</b>	131 (32.6%)	117 (32.2%)	14 (35.9%)	0.643
<b>Thrombus grade</b>				
I	23 (5.7%)	20 (5.5%)	3 (7.7%)	0.967
II	27 (6.7%)	24 (6.6%)	3 (7.7%)	
III	62 (15.4%)	57 (15.7%)	5 (12.8%)	
IV	65 (16.2%)	59 (16.3%)	6 (15.4%)	
V	225 (56%)	203 (55.9%)	22 (56.4%)	
<b>Post-procedure TIMI (thrombolysis in myocardial infarction) flow grade</b>				
0	1 (0.2%)	1 (0.3%)	0 (0%)	0.762
I	7 (1.7%)	6 (1.7%)	1 (2.6%)	
II	53 (13.2%)	46 (12.7%)	7 (17.9%)	
III	341 (84.8%)	310 (85.4%)	31 (79.5%)	
Total lesion length (mm)	26.8 ± 10.9	26.9 ± 11	26.1 ± 9.8	0.663
Maximum vessel diameter (mm)	3.3 ± 0.3	3.3 ± 0.4	3.3 ± 0.3	0.454
Reperfusion arrhythmias	62 (15.4%)	58 (16%)	4 (10.3%)	0.347
Intra-procedural arrhythmias	17 (4.2%)	11 (3%)	6 (15.4%)	<0.001
<b>Post-procedure in-hospital outcomes</b>				
Pump failure	85 (21.1%)	59 (16.3%)	26 (66.7%)	<0.001
<b>Bleeding</b>				
Non	394 (98%)	357 (98.3%)	37 (94.9%)	0.13
Minor	2 (0.5%)	2 (0.6%)	0 (0%)	
Major	6 (1.5%)	4 (1.1%)	2 (5.1%)	
Cerebrovascular accident/stroke	5 (1.2%)	1 (0.3%)	4 (10.3%)	<0.001
Access site complication	8 (2%)	7 (1.9%)	1 (2.6%)	0.787
Stent thrombosis	25 (6.2%)	21 (5.8%)	4 (10.3%)	0.272

LAD="left anterior descending artery", SVG="saphenous vein grafts"

**Table-3: Univariate and multivariable binary logistic regression analysis for in-hospital mortality**

	Univariate		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Female	1.31 [0.64-2.69]	0.463	-	-
Age	0.98 [0.95-1.01]	0.178	0.98 [0.95-1.02]	0.371
Total ischemic time	1.01 [0.97-1.06]	0.580	-	-
Systolic blood pressure	0.98 [0.97-0.99]	0.002	0.99 [0.98-1.01]	0.227
Random blood sugar ≥ 200	1.98 [1.00-3.94]	0.050	1.48 [0.64-3.46]	0.361
Killip class III/IV	2.41 [1.23-4.75]	0.011	1.43 [0.43-4.72]	0.558
Intubated	2.31 [1.17-4.57]	0.016	1.19 [0.37-3.83]	0.767
Arrhythmia on arrival	2.47 [1.22-5.01]	0.012	1.21 [0.50-2.92]	0.668
Extensive AWMi with RBBB	3.28 [0.85-12.65]	0.085	2.10 [0.41-10.71]	0.370
IWMI with RV Infarct	2.52 [1.18-5.38]	0.017	3.63 [1.31-10.08]	0.013
Previous PCI/CABG	1.11 [0.37-3.30]	0.857	-	-
Hypertension	1.40 [0.68-2.85]	0.358	-	-
Diabetes	1.76 [0.89-3.46]	0.103	1.55 [0.65-3.71]	0.325
Smoking	1.48 [0.71-3.12]	0.297	-	-
History of cerebrovascular accident/stroke	0.84 [0.11-6.7]	0.871	-	-
Obesity	1.97 [0.91-4.28]	0.086	1.67 [0.64-4.37]	0.292
Chronic kidney disease	5.97 [1.37-26.00]	0.017	1.40 [0.17-11.23]	0.753
Pre-procedure LVEDP (mmHg)	0.99 [0.96-1.03]	0.754	-	-
Ejection fraction ≤ 40%	0.74 [0.35-1.56]	0.431	-	-
Temporary pacemaker implant	0.37 [0.05-2.83]	0.339	-	-
Intra-aortic balloon pump	0.67 [0.15-2.94]	0.599	-	-
Multi-vessel diseases	0.98 [0.47-2.04]	0.960	-	-
High thrombus grade (≥4)	0.98 [0.47-2.04]	0.960	-	-
Total lesion length	0.99 [0.96-1.03]	0.662	-	-
Maximum vessel diameter	0.69 [0.26-1.83]	0.453	-	-
Slow flow/no-reflow during procedure	1.18 [0.59-2.35]	0.643	-	-
Intra-procedural arrhythmias	5.82 [2.02-16.74]	0.001	5.53 [1.39-22.06]	0.015
Pump failure	10.31 [5.01-21.21]	<0.001	8.94 [3.99-20.02]	<0.001

OR="odds ratio", CI="confidence interval", AWMi="anterior wall myocardial infarction", RBBB="right bundle branch block", IWMI="inferior wall myocardial infarction", RV="right ventricular", PCI="percutaneous coronary intervention", CABG="coronary artery bypass grafting", LVEDP="left ventricular end-diastolic pressure"

## DISCUSSION

The results of this study show that mortality is high among patients who undergo primary PCI and develop CIN, and that several factors are associated with increased risk of death. A number of studies have evaluated and reported different characteristics of PCI patients developing CIN in Pakistani population including comparison of different risk scores.<sup>6-8</sup> However this study investigated the burden of and factors associated with mortality among primary PCI patients who developed CIN. These factors included lower systolic blood pressure at admission and after the procedure, higher Killip class, diabetes, chronic kidney disease, pump failure, and bleeding complications. Lower systolic blood pressure may reflect cardiogenic shock, which is a major predictor of mortality in this setting. Higher Killip class indicates more severe heart failure and pulmonary edema, which can also worsen the prognosis. Diabetes and chronic kidney disease are known to increase the risk of cardiovascular events and complications in patients with acute coronary syndromes.<sup>20</sup> Pump failure and bleeding complications are common adverse events that can occur during or after coronary angioplasty, and they can also increase the mortality rate.<sup>21</sup> These findings suggest that these patients need

careful monitoring and management of their hemodynamic status, comorbidities, and complications during and after the intervention. Further studies are needed to identify the optimal strategies to improve the outcomes of these patients and to reduce the mortality rate. For example, studies could compare different types of stents, antithrombotic agents, or mechanical support devices in this population.

The results of this study show that several factors are associated with in-hospital mortality among patients who primary PCI and later developed CIN. These factors include lower systolic blood pressure, higher random blood sugar, higher body mass index, higher Killip class, intubation, arrhythmias, diabetes, chronic renal disease, cerebrovascular accidents, bleeding, and pump failure. These factors may reflect the severity of the myocardial damage, the presence of comorbidities, and the occurrence of complications during or after the procedure. However, on multivariable analysis, the presence of IWMI with RV infarction, intra-procedure arrhythmias, and pump failure were found to be the independent predictors of mortality. These findings are consistent with previous studies that have identified similar risk factors for mortality in this

population. These results can help clinicians to identify high-risk patients and to provide appropriate care and management to improve their outcomes. Further studies are needed to confirm these results and to explore the mechanisms underlying these associations.

Literature supporting our findings and conclusion state that Similar findings, A study by Gao *et al*<sup>22</sup> found that lower systolic blood pressure, higher Killip class, diabetes, chronic renal disease, cerebrovascular accidents, bleeding, and pump failure were risk factors for in-hospital death emergency percutaneous coronary intervention. Another study with similar findings by Wang *et al*.<sup>23</sup> Developed and validated a risk model for such patients and their findings were similar to ours. However the studies contradicted our findings reported, one of them by Li *et al*.<sup>24</sup> higher body mass index was associated with lower in-hospital mortality in patients with COVID-19, and that higher random blood sugar was not associated with mortality. They also discussed the role of ACE2, the receptor for SARS-CoV-2, in obesity and diabetes.

Single center coverage, observational nature of the study, and lack of long-term follow-up are the key limitation of current analysis and further studies are warranted to evaluate the causes of mortality in these patients as well as effect of various therapeutic options for the management of CIN and its impact on the survival of patients.

## CONCLUSION

In conclusion, there is a high rate of mortality for patients who develop CIN after primary PCI, and the risk of mortality is further aggravated by the presence of IWMI with RV infarction, intra-procedure arrhythmias, and pump failure. Clinicians can use these insights to identify high-risk patients and put proper care plans in place.

## AUTHORS' CONTRIBUTION

RK, KM: Conceived the idea, study design. AU, BD, MR, MYD, KR, MS, US, ABN, KC, MI, ZUR: Data collection. RK, ZUR, MK: Write-up. RK, MK: Review. RK: Supervised the entire project.

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### Address for Correspondence:

**Dr. Rajesh Kumar**, Assistant Professor of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Rafiqi (H.J.) Shaheed Road, Karachi- 75510-Pakistan.

**Email:** rajeshnarsoolal@gmail.com

**Cell:** +92 333 730 6090