Characteristics and in Hospital Clinical Outcome of Patients with Non St-Segment Elevation Myocardial Infarction with Chronic Kidney Disease

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Abstract

Key words:

Non ST-Segment Elevation Myocardial Infarction; Chronic Kidney Disease.

Background: *Nearly 40% of patients presenting with Non ST-Segment Elevation Myocardial Infarction (NSTEMI) have Chronic Kidney Disease (CKD). CKD is a powerful predictor of adverse events among NSTEMI patients. The purpose of the present study was to evaluate the in-hospital outcome of patients with Chronic Kidney Disease presenting with Non ST-Segment Elevation Myocardial Infarction.*

Methods: *In this prospective observational study a total of 128 patients with NSTEMI were enrolled. They were divided equally in group I (NSTEMI with CKD) and group II (NSTEMI with normal renal function) on the basis of estimated glomerular filtration rate. Patients were considered to have CKD if he/she had documented history of CKD or estimated glomerular filtration rate <60 mL/min/1.73 m². Presence of in-hospital complications was identified.*

Results: *Patients with CKD were significantly older, with a greater prevalence of hypertension, diabetes mellitus, lower left ventricular ejection fraction, and lower haemoglobin level compared with those without CKD. CKD patients had more atypical presentation during admission. In-hospital complications were significantly higher in CKD patients presenting with NSTEMI.*

Conclusion: *CKD strongly predicts adverse in-hospital outcome among NSTEMI patients.*

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Introduction:

We know that nearly 40% of patients presenting with Non ST-Segment Elevation Myocardial Infarction (NSTEMI) have Chronic Kidney Disease (CKD).[1] CKD is a powerful predictor of adverse events among NSTEMI patients.[2] CKD patients have a high prevalence of obstructive coronary artery disease (CAD). The severity of CAD and lesion complexity progressively increased as estimated GFR decreased.[3] Rapid risk stratification is crucial for appropriate management of these patients and for targeting more potent and invasive therapies for higher risk patients.[4] Objective of the study was to compare the in-hospital outcome among patients of Non ST-Segment Elevation Myocardial Infarction with Chronic Kidney Disease.

Methods:

This study was conducted in the Department of Cardiology of the National Heart Foundation Hospital and Research Institute, Dhaka, Bangladesh during the period of June 2010 to May 2011. A total of 128 patients with NSTEMI were enrolled. They were divided equally in group I (NSTEMI with CKD) and group II (NSTEMI with normal renal function) on the basis of estimated glomerular filtration rate.

Patients of both sexes with Non ST-Segment Elevation Myocardial Infarction with chronic kidney disease (eGFR <60mL/min/1.73m²) and without chronic kidney disease (eGFR ≥60mL/min/1.73m²) were included in the study. Patients with ST-Segment Elevation Myocardial Infarction, unstable Angina, prior MI, PCI, CABG, CHF, congenital and valvular heart

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disease, cardiomyopathy, end Stage Kidney Disease requiring Renal Replacement Therapy, extremely severe concomitant disease (severe dementia, advanced malignancy) were excluded from the study.

Acute NSTEMI was diagnosed according to the criteria of the ACCF/AHA.[5] Chronic kidney disease is defined as either kidney damage or glomerular filtration rate <60 ml/min/1.73 m2 for ≥3 months according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines 2002.[6] Informed written consent was taken from each patient before enrollment. Meticulous history was taken regarding symptoms (chest pain or dyspnoea) and detailed clinical examination was performed. Demographic data and risk factors were recorded for all patients. Patient's baseline 12 lead ECG and Echocardiography were performed. Blood sample was taken for biochemical investigations including Troponin I, Hb% and Serum creatinine. Serum creatinine, lean body weight, gender and age were used to determine estimated GFR by Cockcroft and Gault formula.[7] Patients were stratified into 2 groups according to estimated GFR. Patients were followed up throughout their hospital stay up to discharge and occurrence of MACEs and complications, if any noted.

All necessary approval to perform the study was obtained from the Academic Council of National Heart Foundation Hospital and Research Institute, Dhaka, Bangladesh.

All clinical and follow-up data were prospectively collected in a pre-designed data collection form. After processing of all available data, statistical analysis of their significance was done. Obtained data were expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups was done by Student's t-test for continuous variables. Categorical data were analyzed by Chi-square test and Fisher's exact test (as appropriate). The whole analyses were done with the help of computer based SPSS (Statistical Programme for Social Science) programme version 16.0. p-value of <0.05 was considered as significant.

Results:

The mean age of group I patients was 60.4 years and 49.9 years for group II patients. Hypertension was the commonest risk factor in both groups (75% vs. 40.6%). 37.5% of CKD patients complaints of shortness of breath during admission. But this complaint was 18.8% in patients with normal renal function.

Table-I
Distribution of the demographic profiles between the groups

Age group (years)	Group I (n=64)		Group II (n=64)		p value*
	n	%	n	%	
£40	0	0	11	17.2	
41-50	7	11	30	46.9	
51-60	29	45.3	15	23.4	
61-70	20	31.2	8	12.5	
≥71	8	12.5	0	0	
Mean ± SD	60.4 ± 8		49.9 ± 9.3		.001[S]
Range	45-74		31-70		

Group I = NSTEMI with CKD, Group II = NSTEMI without CKD, S = Significant
* t-test was done to measure the level of significance

Table-II
Distribution of risk factors between the groups (n=128)

Risk factor	Group I (n=64)		Group II (n=64)		p value*
	n	%	n	%	
Smoking					
Current Smoker	23	35.9	23	35.9	.425[NS]
Ex-smoker	29	45.3	7	11	
Non-smoker	12	18.8	34	53.1	
Hypertension					
Yes	48	75	26	40.6	.001[S]
No	16	25	38	59.4	
Dyslipidaemia					
Yes	37	57.8	25	39.1	.052[NS]
No	27	42.2	39	60.9	
Family H/O IHD					
Yes	14	21.9	14	21.9	1.000[NS]
No	50	78.1	50	78.1	
Diabetes mellitus					
Yes	42	65.6	17	26.6	.001[S]
No	22	34.4	47	73.4	

Group I = NSTEMI with CKD, Group II = NSTEMI without CKD,NS = Not Significant
S = Significant. *Chi-square test was done to measure the level of significance

Table-III

Clinical presentation of the study patients (n=128)

Variable	Group I (n=64)		Group II (n=64)		p value*
	n	%	n	%	
Chest pain					
Present	44	68.8	53	82.8	.063[NS]
Absent	20	31.2	11	17.2	
Shortness of breath					
Present	24	37.5	12	18.8	.018[S]
Absent	40	62.5	52	81.2	
Others					
Present	11	17.2	14	21.9.	504[NS]
Absent	53	82.8	50	78.1	

Group I = NSTEMI with CKD, Group II = NSTEMI without CKD, NS = Not Significant
S = Significant.   *Chi-square test was done to measure the level of significance

The mean left ventricular ejection fraction of group I patients was 54.8% and 58.5% for group II patients. The mean value of serum creatinine and estimated glomerular filtration rate was 1.7 mg/dl and 40.4 ml/min/1.73m² respectively in CKD group and 1.0 mg/dl and 76.3 ml/min/1.73m² respectively in non-CKD group. The mean value of Hb% was 11.1 and 12.1 gm/dl in group I and group II respectively.

Table-IV

Distribution of the study patients (n=128) by mean ejection fraction

LVEF%	Group I (n=64)		Group II (n=64)		p value*
	n	%	n	%	
≤40	6	9.4	0	0	
41-50	10	15.6	9	14.1	
51-60	36	56.2	28	43.8	
≥61	12	18.8	27	42.2	
Mean ± SD	54.8 ± 7.8		58.5 ± 7.5		.009[S]
Range	35-66		42-70		

Group I = NSTEMI with CKD, Group II = NSTEMI without CKD, S = Significant
*t –test was done to measure the level of significance

Table-V

Distribution of the study patients (n=128) by mean serum creatinine and estimated GFR

Variable	Group I (n=64)		Group II (n=64)		p value*
	Mean±SD	Range	Mean±SD	Range	
Serum creatinine (mg/dL)	1.7±0.2	1.5-2.8	1.0±0.1	0.7-1.4	.001[S]
Estimated glomerular filtration rate (mL/min/ 1.73m²)	40.4±8.8	23-59	76.3±1.4	60.7-131.9	.001[S]
Hb% (gm/dL)	11.1±1.2	8-13.2	12.1±1.1	10-15	.001[S]

Group I = NSTEMI with CKD,   Group II = NSTEMI without CKD , S = Significant
*t –test was done to measure the level of significance

32.8% of patients in group I and 14.1% patients in group II developed complications during their hospital stay. The development of heart failure (15.6%) and acute kidney injury (12.5%) were significantly higher among patients with CKD compared to those with normal renal function. Other complications, such as, persistent chest pain, cardiogenic shock and arrhythmias were also higher in CKD group, though not statistically significant. Among CKD patients, 3.1% died during their hospital stay. On the other hand, all the patients with normal renal function survived.

Table-VI

Distribution of the study patients (n=128) by duration of stay

Variable	Group I (n=64) Mean ± SD	Group II (n=64) Mean ± SD	p value*
CCU stay (days)	2.4 ± 2	1.7 ± 1.4	.001[S]
Hospital stay (days)	6.6 ± 4	5.2 ± 3.1	.001[S]

Group I = NSTEMI with CKD,Group II = NSTEMI without CKD,S = Significant
*t –test was done to measure the level of significance

Table-VII

Distribution of the study patients (n=128) by in-hospital complications

Complication	Group I (n=64)		Group II (n=64)		p value*
	n	%	n	%	
Present	21	32.8	9	14.1	.012[S]
Absent	43	67.2	55	85.9	

Group I = NSTEMI with CKD,   Group II = NSTEMI without CKD, S = Significant
*Chi-square test was done to measure the level of significance

Table-VIII

Distribution of selected variables by in-hospital complications

Variable	Complication		p value#
	Present (n=30)	Absent (n=98)	
Age (years)	59.2 ± 11*	53.9±9.6	.012^S
Hb% (gm/dL)	11.1±1.3	11.8±1.3	.015^S
LVEF(%)	53.6±8.3	57.6±7.5	.015^S
HTN	22 (73.3)*	52(53.1)	.049^S
DM	17 (56.7)	42(42.9)	.184^{NS}

*values indicate mean±SD, S = Significant, # t – test was done to measure the level of significance
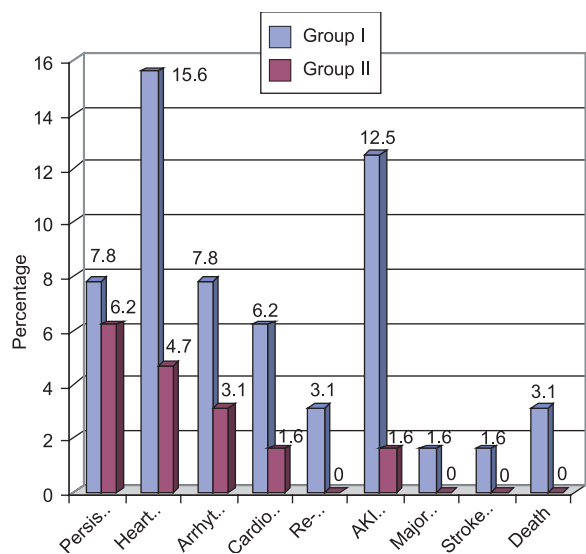
Fig.-1: *Bar diagram showing distribution of the study patients (n=128) by in-hospital outcomes*

Among various factors, univariate analysis showed that presence of hypertension (73.3% vs. 53.1%; p<0.05), age (59.2±11 years vs. 53.9±9.6 years; p<0.05), Hb% (11.11±1.3 gm/dL vs. 11.8±1.3 gm/dL; p<0.05), LVEF% (53.6±8.8% vs. 57.6±7.5%; p<0.05) were found to be important determinants of in-hospital complications. A step wise binary regression model was done with in-hospital complications as dependent and CKD group, age, HTN, LVEF% and Hb% as independent variables. However, only CKD remain in the final model in stepwise logistic regression. CKD patients had 2.98 times higher risk of developing in-hospital complications.

Table-IX

Result of multiple logistic regression analysis

Variable	B	Wald	Odds ratio	95.0% C.I. for odds ratio	p value
Constant	-1.26	31.89	0.28	-	.001
Presence of CKD	1.09	5.97	2.98	1.24-7.17	.015

Discussion:

This was a prospective observational study. By analyzing the estimated GFR using the Cockroft and Gault formula, patients were categorized in two groups: group I - patients with NSTEMI with CKD and Group II - patients with NSTEMI with normal renal function. A total of 128 patients were included in this study.

When age of the study patients were compared between the groups, it was found that the mean age in group I was 60.4±8 years and group II was 49.9±9.3 years. Mean age difference was statistically significant (p<0.05) between the groups. Nearly similar pattern of age distribution was reported in different studies in Bangladesh like Pasha and Awal, et al.[4,8] It was evident from the study that patients with CKD tended to be older than those with normal renal function. This observation was being consistent with the findings of different studies done in foreign countries. [1,9,10,11,12]

Hypertension was the commonest risk factor in both groups. Wong, et al. found that among NSTEMI patients with kidney dysfunction 62.2% were hypertensive, 45.6% were diabetic, 31.3% were dyslipidaemic and 14.6% were current smoker in Canadian ACS I registry.[10] Sarnak, et al., El-Menyar, et al., Fox, et al. and Kosuge, et al. observed hypertension as a commonest risk factor in their respective study.[1,12,14,15] So, the prevalence of risk factors in the present study was comparable with other studies.

During admission, chest pain was the presenting complaint in 68.8% in group I and 82.8% in group II. Absence of chest pain was higher (31.2%) in group I than in group II (17.2%). But the difference was not statistically significant (p>0.05). Shortness of breath was found 37.5% in group I and 18.8% in group II which was statistically significant (p<0.05). El-Menyar, et

al. observed that 26% of patients with chronic renal insufficiency complaints of shortness of breath and they were less likely to have chest pain at presentation which was statistically significant (p<0.001).[12] Finding of El-Menyar, et al. was consistent with this finding in that atypical presentation was more in patients with CKD than those without CKD. This was attributed to the fact that diabetic autonomic neuropathy or uraemic neuropathy, which may impair sensation of myocardial ischaemic pain, was more common among patients in NSTEMI with renal dysfunction.

The mean left ventricular ejection fraction was 54.8 ± 7.8% in group I and 58.5 ± 7.5% in group II. Mean ejection fraction was lower in group I than group II. This difference was statistically significant (p<0.05). Pasha also showed that mean ejection fraction was significantly lower in patients with impaired renal function than those with normal renal function (47.9±6.3% vs. 52.0±5.2%).[4] Kang, Jeong and Kim found that patients with NSTEMI with renal dysfunction had a significantly lower LVEF% (51±13% vs. 58±10%).[9] So, their findings were consistent with the findings of this study in that patients with CKD have reduced LVEF% than those with normal renal function.

The mean value of serum creatinine and estimated glomerular filtration rate were 1.7±0.2 mg/dL and 40.4±8.8 mL/min/1.73m² respectively in group I and 1±0.1 mg/dL and 76.3±1.4 mL/min/1.73m² respectively in group II. These differences were statistically significant (p<0.001). Hossain found identical mean serum creatinine and creatinine clearance rate (1.73 mg/dL and 39.9 mL/min respectively in 80 CKD patients) with the current study.[12] Nearly similar pattern of mean serum creatinine and estimated glomerular filtration rate distribution were reported in different studies like Kang, Jeong and Kim, Wong, et al. and El-Menyar et al.[9,10,12]

Anaemia is common in CKD patients; it usually correlates with the severity of renal failure and contributes to many of the non-specific symptoms of CKD. In this study, mean Hb% was 11.1±1.2 and 12.1±1.1 gm/dL in group I and group II respectively which was statistically significant (p<0.05). Hossain found mean Hb% was 11.6 gm/dL in 80 CKD patients.[13]

This study demonstrated that patients with NSTEMI and CKD had a relatively longer hospital stay than those with normal renal function. Mean length of CCU stay was 2.4 ± 2 and 1.7 ± 1.4 days in group I and group II respectively. Mean length of hospital stay was 6.6 ± 4 and 5.2 ± 3.1 days in group I and group II respectively. Statistically significant difference was found between the groups in terms of mean CCU stay and hospital stay (p<0.001). Nearly similar pattern of mean CCU and hospital stay (days) were reported in different studies like Freeman, et al., Kang, Jeong and Kim and El-Menyar, et al.[9,12,17] This finding demonstrates that CKD constitutes a further burden on hospital resources in patients with NSTEMI.

The total in-hospital complications were significantly higher in group I compared with those of group II. 21(32.8%) patients in group I and 9(14.1%) patients in group II developed complications during their hospital stay. Kang, Jeong and Kim found 32(34%) patients with renal dysfunction and 20(18.8%) patients without renal dysfunction developed complications (p<0.001).[9]

In this study, the most frequent complications in group I were heart failure (15.6%) followed by acute kidney injury (12.5%), arrhythmias (7.8%), persistent chest pain (7.8%), cardiogenic shock (6.2%), re-infarction (3.1%), death (3.1%), major bleeding (1.6%) and stroke (1.6%). The most frequent complications in group II were persistent chest pain (9.4%) followed by heart failure (4.7%), arrhythmia (3.1%), cardiogenic shock (1.6%) and AKI (1.6%). There was statistically significant difference between the groups in terms of heart failure and acute kidney injury (p<0.05). Other complications were also higher in patients with CKD than those with normal renal function, though the difference was not statistically significant (p>0.05). The lack of statistically significant difference between the groups might be due to small sample size. Moreover, high prevalence of comorbid conditions and metabolic derangements induced by the CKD state may contribute to poorer outcomes in patients with CKD after NSTEMI.

El-Menyar, et al. found that heart failure was 32% vs. 9%, cardiogenic shock was 7% vs. 2%, major bleeding was 1.6% vs. 0.5% and stroke was 1.9% vs. 0.3% among the patients with and without CKD in their study (p<0.001).[12] AKI was found in 12 patients; cardiogenic shock in 39 patients; major bleeding in 2 patients; arrhythmias in 13 patients with renal dysfunction while none had AKI; 15 had cardiogenic shock; 1 had major bleeding and 14 had arrhythmias with normal renal function in the study of Kang, Jeong and Kim.[9]

Higher prevalence of heart failure in CKD may be secondary to anaemia, volume overload and diastolic dysfunction. Pasha found heart failure was higher among patients with abnormal serum creatinine clearance (25.3%) compared to that with normal serum creatinine clearance (3.7%).[4] Freeman, et al. in their study regarding ACS and renal dysfunction found 16% and 37% patients with heart failure who had normal and impaired renal function respectively.[16] Fox, et al. found that patients with CKD were at higher risk of heart failure than patients with no CKD (12.5% vs. 4.4%).[1] All these findings were consistent with this finding in that heart failure was more in patients with CKD than those with normal renal function.

According to Acute Kidney Injury Network, 2007 an abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl, a percentage increase in serum creatinine of more than or equal to 50% (1.5 fold from baseline). Among 8 patients in group I who developed AKI, 5 patients developed AKI following admission and remaining 3 patients developed AKI following coronary interventions. Goldberg, et al. and Parikh, et al. found 9.6% and 19.4% of patients developed AKI during their hospital stay.[17,18] Lo, Liu and Hsu suggested that the association between AKI and adverse outcomes exists because patients who develop AKI have more severe pre-existing CKD than subjects who do not experience AKI. CKD also increases the risk of developing AKI after an acute illness.[19]

It is reported that around 14.5% of patients develop CIN (a form of AKI) after coronary angiography and intervention that results from both renal tubular toxicity and renal medullary ischaemia.[8] The most important risk marker for nephropathy after exposure of contrast media is pre-existing renal impairment and diabetes mellitus. Other markers associated with an increased risk of CIN include nephrotoxic drugs, anaemia, older age, preprocedural haemodynamic instability, volume depletion, heart failure and hypoalbuminaemia.[20]

In this condition, acute heart disease with ischemic injury (e.g., NSTEMI) might induce AKI through complex mechanisms, including hemodynamically mediated damage secondary to impaired cardiac output, anaemia, exogenous factors such as the contrast media used in coronary intervention, nephrotoxic effect of drugs (diuretics and rennin-angiotensin-aldosterone inhibitors), and humoral and immune-mediated damage to the kidney. These factors triggered activation of renal sympathetic nervous system which may contribute to decreased GFR with acute kidney hypo perfusion, reduced oxygen delivery, increased resistance to atrial natriuretic peptide and B-type natriuretic peptide, and increased cellular necrosis and apoptosis. Potential presences of a residual confounding factor in patients with CKD have been proposed to explain this clinically unfavorable association in subjects with NSTEMI developing AKI.

Freeman, et al. showed that ACS patients with abnormal renal function had significantly higher mortality compared to those with no renal impairment.[16] Pasha noticed death of 6(9.5%) patients with impaired renal function.[4] The mortality rate was 8% in patients with CKD compared with only 3.1% in patients without CKD in the study of Charytan, et al.[21] The estimated in-hospital death in patients with or without CKD was 16.8% and 0.8%, respectively, in the study of Kang, Jeong and Kim.[9] In hospital mortality was 6% vs. 0.7% in NSTEMI patients with or without chronic renal insufficiency in the study of El-Menyar, et al. which was statistically significant (p<0.001).[12] Several key articles described the increased mortality of patients with CKD in the acute MI setting and the relative underutilization of known cardio

protective therapies compared with patients without CKD.[1]

In this study, two patients (3.1%) died in group I. One patient was suffering from severe left main with double vessel coronary artery disease. Another patient was suffering from left main with triple vessel coronary artery disease with complete heart block. Both of them were waiting for CABG. Mortality rate was zero in group II and the difference between the groups in terms of mortality was not statistically significant (p>0.05). Small sample size and use of early invasive strategy in the study populations may explain this.

Conclusions:
CKD strongly predicts adverse in-hospital outcome among NSTEMI patients. Compared to patients with normal renal function, CKD patients were significantly older, with a greater prevalence of hypertension, lower left ventricular ejection fraction and lower haemoglobin level. CKD patients had more atypical presentation during admission. In-hospital complications were significantly higher in CKD patients presenting with NSTEMI.

Study limitations:
Sample size was small. All the patients with NSTEMI with CKD were not included due to different contraindications and co-morbid conditions. Follow-up was done only during hospital stay. Serum creatinine value might have been influenced by medications or clinical status.

Conflict of Interest - None.

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