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Acute Coronary Syndrome: The Efficacy of NGAL as a Biomarker for Acute Kidney Injury (AKI)

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ABSTRACT

Background: Acute kidney injury (AKI) is common in patients hospitalized with an acute myocardial infarction (AMI) and it develops in 10.0% to 30.0%. In high-risk patients, such as those hospitalized for congestive heart failure, sepsis, and those who have undergone cardiac surgery, the incidence of AKI is high which is ranging from 10.0% to 25.0%. In experimental and clinical studies, NGAL has been investigated extensively and would appear to be one of the most frequently investigated and most promising early biomarkers of AKI. Aim of the study: To evaluate the efficacy of NGAL as a biomarker for Acute Kidney Injury (AKI). **Methods:** This cross-sectional study was conducted in the Department of Nephrology at National Institute of Kidney Diseases and Urology (NIKDU), National Institute of Cardiovascular Disease, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total number of 80 patients presented with acute coronary syndrome or heart failure were recruited for this study. This study population was selected by purposive sampling technique. Statistical analysis was done by using SPSS version 21.0 for Windows. Assumptions of normality and homogeneity of variance were initially checked. Prior to the commencement of this study, the Institutional Review Board, NIKDU, and Dhaka approved the thesis protocol. **Results:** Maximum patients were in the age group of 40 to 60 years, which was 49(61.3%) cases followed by more than 60 years and 20 to 40 years, which were 21(26.3%) cases and 10(12.5%) cases respectively. The mean age of the patients was 55.33±11.710 years with the range of 32 to 80 years. In this study male was predominant than female which was 54(67.5%) cases and 26(32.5%) cases respectively. The ratio of male and female was 2.1:1. The normal value of urinary NGAL was less than 131.7 ng/mL. The mean with SD of normal and abnormal urinary NGAL group were 68.83±44.10 ng/mL and 505.89±305.92 ng/mL respectively. The urinary UNGAL and development of AKI was positively correlated which was weak. **Conclusion:** In conclusion, the efficacy of urinary NGAL as a biomarker, for acute kidney injury (AKI) among patients with acute coronary syndrome has given a good result.

Keywords: Efficacy, Biomarker, Kidney injury, Lipocalin, Infarction.

INTRODUCTION

Acute kidney injury (AKI) is common in patients hospitalized with an acute myocardial infarction (AMI) and it develops in 10.0% to 30.0%.[1] In high-risk patients, such as those hospitalized for congestive heart failure, sepsis, and those who have undergone cardiac surgery, the incidence of AKI is high which is ranging from 10.0% to 25.0%.[2] The AKI incidence in patients in the coronary care unit has been reported to vary from 9.6% to 27.0% with mortality ranging from 20.0% to >50.0%.[3] NGAL is one of the most intensively investigated novel renal biomarkers with promising data from animal experiments and clinical studies comprising the populations at risk for AKI.[4] Therefore, it appears to fulfill many characteristics of an appropriate 'real-time' biomarker for AKI detection.[5] Urine NGAL has been found to be an early predictor for acute kidney injury.[6] Newer devices for early bedside detection of NGAL are now available. Since serum creatinine is known to be an inadequate and late marker of acute kidney injury (AKI), NGAL might soon emerge as an early marker for AKI.[7] Current evidence also suggests its role as a biomarker in a variety of other renal and non-renal conditions.[8] NGAL messenger RNA and protein expression are markedly induced in tubules of the damaged kidney, resulting in elevated urinary and plasma levels of NGAL. In addition, circulating NGAL is filtered in the glomerulus but undergoes rapid and effective proximal tubular reabsorption unless the proximal tubule uptake machinery is damaged.[9] In addition, NGAL is produced in neutrophils and, expectedly, increased NGAL levels have been observed in the urine of patients with urinary tract infections, but at lower levels when compared to those commonly observed in AKI.[10] An early marker of AKI, similar to troponin in acute myocardial disease, may permit the treatment, prevention of renal injury extension

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avoids glycopeptides, and amino-glycosides prevent or avoid contrast-induced nephropathy, maintain positive fluid balance and help physicians for the timing of renal replacement therapy.[11] Neutrophil gelatinase-associated lipocalin (NGAL) is a novel biomarker for which levels are increased within hours after a nephrotoxic, ischemic, or septic insult.[12] Furthermore, several studies suggested that elevated NGAL levels are predictive of poor clinical outcomes in AKI, including dialysis initiation and mortality, even when adjusted for conventional predictors, such as creatinine levels.[13] In experimental and clinical studies, NGAL has been investigated extensively and would appear to be one of the most frequently investigated and most promising early biomarkers of AKI.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Nephrology at National Institute of Kidney Diseases and Urology (NIKDU), National Institute of Cardiovascular Disease, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total number of 80 patients presented with acute coronary syndrome or heart failure were recruited for this study after fulfilling the inclusion and exclusion criteria. This study was carried out from July 2018 to June 2019 for a period of one (01) year. This study population was selected by purposive sampling technique. Informed consents were taken from all possible participants of the study. Detailed history and thorough examination was done of each patient. Laboratory measurement of serum creatinine was measured on 1st day of cardiac attack and daily for next 2 days. Urine sample was collected in a sterile non-heparinized tube immediately after admission in the CCU. Urine samples were centrifuged for 5 min at 2000g and the supernatant was collected at appendrop and stored in 0.5 ml aliquots at -800 C for subsequent analysis. Urine NGAL immunoassay was measured by a standardized clinical platform (ARCHITECT® analyser, Abbott Diagnostics) in the department of biochemistry, BSMMU. The remaining biochemical analyses (including S. Creatinine, S. RBS) were performed using standard kits and using an auto analyzer at the Department of Bio-Chemistry at NICVD & BSMMU, Dhaka. Some of the investigations were carried out in the laboratory of the Department of Biochemistry at NIKDU; however, some investigations were carried out outside the hospital. The study subjects were selected based on selection criteria from the patients of the Coronary Care Unit, NICVD & BSMMU Hospital. Statistical analysis was done by using SPSS version 21.0 for Windows. Assumptions of normality and homogeneity of variance were initially checked. Prior to the commencement of this study, the Institutional Review Board, NIKDU, and Dhaka approved the thesis protocol.

Inclusion Criteria

- Patients with acute coronary syndrome who are STEMI and NSTEMI and/or Troponin I positive.
- Patients more than 18 years of age.

Exclusion Criteria

- Patients with known CKD
- Patients with diagnosed COPD or Malignancy
- Patients with sepsis

RESULTS

Table 1: Distribution of Study Population According to Age (n = 80)

Age Group	Frequency	Percent
20 to 40 Years	10	12.5
40 to 60 Years	49	61.3
More Than 60 Years	21	26.3
Total	80	100.0
Mean ±SD (Range)	55.33±11.71(32 to 80)	

Table 2: Distribution of Study Population According to Gender (n = 80)

Gender	Frequency	Percent
Male	54	67.5
Female	26	32.5
Total	80	100.0

Table 3: Distribution of Serum Creatinine Level (n = 80)

Serum Creatinine	Mean± Std. Deviation	Median	Range	P value
Baseline	1.10±0.186	1.10	0.70 to 1.50	0.000697
After 24 Hrs	1.25±0.359	1.10	0.80 to 2.60	
After 48 Hrs	1.58±1.324	1.10	0.80 to 9.00	

Table 4: Distribution of study Population According to Urinary NGAL (n = 80)

AKI Group	NGAL (Mean± SD)	P Value
Non AKI (n=52)	68.83±44.10	0.000
AKI (n=28)	505.89±305.92	

Table 5: Correlation between Urinary NGAL and AKI

Variables	Value
Pearson Correlation value (r)	0.068
P Value	0.549

Maximum patients were in the age group of 40 to 60 years, which was 49 (61.3%) cases followed by more than 60 years and 20 to 40 years, which were 21 (26.3%) cases and 10 (12.5%) cases respectively. The mean age of the patients was 55.33±11.710 years with the range of 32 to 80 years [Table 1]. In this study male was predominant than female which was 54 (67.5%) cases and 26 (32.5%) cases respectively. The ratio of male and female was 2.1:1 [Table 2]. [Table 3] shows the distribution of serum creatinine level. The mean with SD of serum

creatinine level in baseline, after 24 hrs of admission and after 48 hrs of admission were 1.10±0.186 mg/dL, 1.25±0.359 mg/dl and 1.58±1.324 mg/dL respectively. The relationship of these three serum creatinine value were statistically significant (p=0.000697). [Table 4] shows the distribution of study population according to urinary NGAL. The normal value of urinary NGAL was less than 131.7 ng/mL. The mean with SD of normal and abnormal urinary NGAL group were 68.83±44.10 ng/mL and 505.89±305.92 ng/mL respectively. The difference between these two group was statistically significant (p=0.000). [Table 5] shows the correlation between Urinary NGAL and AKI. The urinary UNGAL and development of AKI was positively correlated which was weak. This correlation was statistically significant (p=0.549).

DISCUSSION

Maximum patients were in the age group of 40 to 60 years, which was 49 (61.3%) cases followed by more than 60 years and 20 to 40 years, which were 21 (26.3%) cases and 10 (12.5%) cases respectively. The mean age of the patients was 55.33±11.710 years with the range of 32 to 80 years. Similarly, in India Prabhu et al,[14] observed the mean age was 54.38 ± 8.80 years. On the other hand, Kim et al,[15] has observed higher age in their study patients, where the mean age was 64.14±14.05 years. In another study, Xin et al,[16] observed the mean age was found 37.04 ± 20.21 years. In this study male was predominant than female which was 54 (67.5%) cases and 26 (32.5%) cases respectively. The ratio of male and female was 2.1:1. Similarly, Parikh et al,[17] found predominance of male. Similar observations with respect of sex male predominant is also found by Prabhu et al,[14] Tuladhar et al,[18] and Xin et al.[16] The mean with SD of serum creatinine level in baseline, after 24 hrs of admission and after 48 hrs of admission were 1.10±0.186 mg/dL, 1.25±0.359 mg/dl and 1.58±1.324 mg/dL respectively. The relationship of these three serum creatinine value were statistically significant (p=0.000697). This result indicates that the serum creatinine level was increased after 48 hours. AKI was defined as an increase in serum creatinine after cardiac injury by more than 0.5 mg/dL (0.44 µmol/L) from baseline as defined by the 2003 acute renal failure consensus conference.[19] Similar to the present study, Xin et al,[16] have showed that serum creatinine levels at 12 h and 24 h after heart injury was increased due to acute coronary artery disease. Tuladhar et al,[18] have mentioned in their study that there is no significant difference in the baseline levels of creatinine after cardiac injury. Tuladhar et al,[18] defined AKI according to the acute renal failure consensus conference, which recommends an increase of 0.5 mg/dL. This is clinically important because it has been demonstrated that changes in serum creatinine of 0.3 mg/dL within the first 48 hours after cardiac injury are associated with a significant increase in intensive care and hospital duration. Kim et al,[15] showed the mean serum creatinine level was raised after cardiac surgery. The mean 24 hrs serum creatinine level after cardiac injury was found. The all above finding are comparable with the current study regarding the serum creatinine level status during baseline, after 6 hrs, after 24 hrs and after 48 hrs. The normal value of urinary NGAL was less than 131.7 ng/mL. The mean with SD of normal and abnormal urinary NGAL group were 68.83±44.10 ng/mL and 505.89±305.92 ng/mL respectively. The difference between these two group was statistically significant (p=0.000). In India, a study done by Prabhu et al,[14] found that the mean NGAL was 111.97 ± 19.41 ng/ml, which is consistent with the present study result. In another study, Tuladhar et al,[18] have observed that the plasma levels of NGAL was higher in patients who developed acute coronary disease. Kim et al,[15] have been showed that the mean immediate NGAL value was 216.28±49.25 ng/ml, which was similar to the present study result. The correlation between Urinary NGAL and AKI. The urinary UNGAL and development of AKI was positively correlated which was weak. This correlation was statistically significant (p=0.549). Similar to this result Prabhu et al,[14] have reported a positive significant Pearson's correlation value (r=0.488; p<0.05) between serum creatinine level and NGAL.

Limitations of the Study

1. The sample size was small and was not sufficient.
2. This was a single centered hospital based study, which indicated that there was a selection bias and this had given a biased result.
3. Study population did not reflect the whole country picture.

CONCLUSION

In conclusion, the efficacy of urinary NGAL as a biomarker, for acute kidney injury (AKI) among patients with acute coronary syndrome has given a good result. NGAL has moved from being a marker of undifferentiated systemic inflammation to become a possible marker for early detection of AKI. The present study suggests that urinary CyC and NGAL are superior to conventional and novel plasma markers in the early diagnosis of acute kidney injury following acute coronary syndrome. Large-scale study should be carried out. Multi-center study should be conducted to get the real situation of Bangladesh.

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