Original Article

Neutrophil Gelatinase-Associated Lipocalin (NGAL) and Progression of Acute Kidney Injury (AKI): A Study in a Tertiary Care Hospital

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ABSTRACT

Background: Acute kidney injury (AKI) is a clinical problem with an estimated incidence of 7% in hospitalized patients. Acute renal failure (ARF) secondary to ischemic injury remains a common and potentially devastating problem in clinical nephrology, with a persistently high rate of mortality despite significant advances in supportive care. Here, we conducted a prospective, multicenter cohort study involving 1219 adults undergoing cardiac surgery to evaluate whether early postoperative measures of urine IL-18, urine neutrophil gelatinase-associated lipocalin (NGAL), or plasma NGAL could identify which patients would develop AKI and other adverse patient outcomes. Aim of the study: To evaluate theNeutrophil Gelatinase-Associated Lipocalin (NGAL) and progression of 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. AKI was not developed in 52 cases of which urinary NGAL was normal in 41(78.8%) cases and abnormal in 11(21.2%) cases. On the other hand 28 patients were developed AKI of which urinary NGAL was normal in 11(39.3%) cases and abnormal in 17(60.7%) cases. The crude odd ratio was 5.76with 2.10 to 15.80 of 95% CI. The relationship between the urinary NGAL and AKI was statistically significant (p=0.000). **Conclusion:** Urinary NGAL include a restoration of adequate kidney perfusion, the avoidance of potential nephrotoxins like nephrotoxic antibiotics, contrast media and therapeutic efforts that target the cause of AKI. It appears reasonable to speculate that an earlier institution of these measures will improve clinical outcomes.

Keywords: Kidney injury, Progression, Lipocalin, Clinical Problem, Neutrophil.

INTRODUCTION

Acute kidney injury (AKI) is a clinical problem with an estimated incidence of 7% in hospitalized patients.[1] Acute renal failure (ARF) secondary to ischemic injury remains a common and potentially devastating problem in clinical nephrology, with a persistently high rate of mortality despite significant advances in supportive care. AKI has long-term implications in AMI patients and it is being associated with CKD progression, recurrent AMI,

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heart failure progression and long-term mortality.[2] Hospitalized patients with AMI are subject to several procedures and complications related to AKI like coronary artery bypass grafting (CABG), catheterization, heart failure and drugs nephrotoxicity.[3] The reported incidence of ACS-associated AKI is extremely heterogeneous, ranging from 5.0% to 55.0%, and it varies with the criteria used for diagnosing AKI, the clinical setting and the investigated population.[4] AKI is a major clinical problem in hospitalized patients.[5] In essence, AKI is defined as the abrupt (within ≤48hours) increase in serum creatinine of ≥0.3mg/dL (26.4micromol/L) from baseline, a relative increase in serum creatinine ≥50%, or oliguria of <0.5ml/kg/hr for more than six hours.[6] The criteria of an absolute increase in serum creatinine of ≥0.3mg/dL (26.4 micromole/L) from baseline was derived from epidemiological data

demonstrating an 80% increase in mortality risk associated with this levelof serum creatinine increase.[7] Diagnosis of AKI currently depends on changes in serum creatinine and is usually made at least 24 to 48 hours after the initial renal insult.[8] This hinders formulation of possible early therapeutic strategies, which could otherwise reduce the clinical sequel of AKI. NGAL appears to be a promising marker for early detection of AKI and is likely to be adapted for wide scale clinical use in patient management as a point of care test.[9] To assess the usefulness of urinary neutrophil gelatinase associated lipocalin (uNGAL) for early detection of AKI in these patients, comparing to serum creatinine. Beyond other different biomarkers, urinary NGAL has probably deserved the greatest interest. It rises within 2 hours of renal insult and peaking at 6-12 hours. uNGAL also rises in some conditions such as sepsis, COPD, CKD, malignancy but this level of rising is much lesser than the level raised in AKI. Nakahashiet al,[9] have reported that acute kidney injury (AKI) is a frequent complication of cardiac surgery and increases morbidity and mortality. Here, we conducted a prospective, multicenter cohort study involving 1219 adults undergoing cardiac surgery to evaluate whether early postoperative measures of urine IL-18, urine neutrophil gelatinase-associated lipocalin (NGAL), or plasma NGAL could identify which patients would develop AKI and other adverse patient outcomes.

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: Comparison of Age with NGAL group

Age Group	NGAL		Total	P value
	Normal	High		
20 to 40 Years	9 (17.3%)	1 (3.6%)	10 (12.5%)	0.174
40 to 60 Years	29 (55.8%)	20 (71.4%)	49 (61.3%)	
More Than 60 Years	14 (26.9%)	7 (25.0%)	21 (26.3%)	
Total	52 (100.0%)	28 (100.0%)	80 (100.0%)	

Table 4: Comparison of Gender with NGAL group

Gender	NGAL		Total	P value
	Normal	High		
Male	34 (65.4%)	20 (71.4%)	54 (67.5%)	0.582
Female	18 (34.6%)	8 (28.6%)	26 (32.5%)	
Total	52 (100.0%)	28 (100.0%)	80 (100.0%)	

Table 5: Comparison of AKI group with Urinary NGAL group (n = 80)

NGAL Group	AKI Group		Total	OR(95% CI)	P value
	Non AKI	AKI			
Normal	41(78.8%)	11(39.3%)	52(65.0%)	5.76 (2.10 to15.80)	0.000
Abnormal	11(21.2%)	17(60.7%)	28(35.0%)		
Total	52(100.0%)	28(100.0%)	80(100.0%)		

Table 6: Correlation between ACS and AKI

Variables	N (%)	P Value
ACS	80 (100.0)	P<0.0001
AKI	28 (35.0)	

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 comparison of age with NGAL group. Out of 80 patients, 20 to 40 years of which urinary NGAL was normal in 9 (17.3%), high in1 (3.6%) and total in 10 (12.5%). 40 to 60 years of which urinary NGAL was normal in 29 (55.8%), high in 20 (71.4%) and total in 20 (71.4%). More than 60 years of which urinary NGAL was normal in 14 (26.9%), high in 7 (25.0%) and total in 21 (26.3%). All age group in the case, urinary NGAL was normal in 52 (100.0%), high in 28 (100.0%) and total in 80 (100.0%). The comparison of age with NGAL group was statistically significant (p=0.174). [Table 4] shows the Comparison of Gender with NGAL group. Male patients of which urinary NGAL was normal in 34 (65.4%), high in 20 (71.4%) and total I 54 (67.5%). Female patients of which urinary NGAL was normal in 18 (34.6%), high in 8 (28.6%) and total in 26 (32.5%). All the patients of which urinary NGAL was normal in 52 (100.0%), high in 28 (100.0%) and total in 80 (100.0%). The Comparison of Gender with NGAL group was statistically significant (p=0.582). Table V shows the comparison between the AKI group and the urinary NGAL group. It was found that AKI was not developed in 52 cases of which urinary NGAL was normal in 41 (78.8%) cases and abnormal in 11 (21.2%) cases. On the other hand 28 patients were developed AKI of which urinary NGAL was normal in 11 (39.3%) cases and abnormal in 17 (60.7%) cases. The crude odd ratio was 5.76with 2.10 to 15.80 of 95% CI. The relationship between the urinary NGAL and AKI was statistically significant (p=0.000).

DISCUSSION

A total number of 80 patients presented with acute coronary syndrome were recruited for this study. The distribution of patients according to age was recorded. 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,[10] observed the mean age was 54.38 ± 8.80 years. On the other hand, Kim et al,[11] has observed higher age in their study patients, where the mean age was 64.14±14.05 years. All age group in our study, urinary NGAL was normal in 52 (100.0%), high in 28 (100.0%) and total in 80 (100.0%). Similarly, Parikh et al,[12] have observed the higher age of their study patients undergoing CABG surgery with cardiopulmonary bypass. It could be due to geographical variations, racial and ethnic differences, genetic causes and different lifestyle in their study patients. In another study, Xin et al,[13] observed the mean age was found 37.04 ± 20.21 years. The distribution of patients by gender was recorded. 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,[12] found predominance of male. In our study, all the patients of which urinary NGAL was normal in 52 (100.0%), high in 28 (100.0%) and total in 80(100.0%). Similar observations with respect of sex male predominant is also found by Prabhu et al10, Tuladhar et al and Xin et al.[13,14] The distribution of patients according to the presence of AKI is recorded. In this study most of the patients were presented without AKI which was 52 (65.0%) cases and the rest of the 28 (35.0%) cases were presented with AKI. The comparison between the AKI group and the urinary NGAL group. It was found that AKI was not developed in 52 cases of which urinary NGAL was normal in 41 (78.8%) cases and abnormal in 11 (21.2%) cases. On the other hand 28 patients were developed AKI of which urinary NGAL was normal in 11 (39.3%) cases and abnormal in 17 (60.7%) cases. The crude odd ratio

was 5.76 with 2.10 to 15.80 of 95% CI. The relationship between the urinary NGAL and AKI was statistically significant (p=0.000).

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

Urinary NGAL include a restoration of adequate kidney perfusion, the avoidance of potential nephrotoxins like nephrotoxic antibiotics, contrast media and therapeutic efforts that target the cause of AKI. It appears reasonable to speculate that an earlier institution of these measures will improve clinical outcomes. However, the utility of NGAL may not be limited to making an early diagnosis of AKI but could extend to the excellent ability of this marker to assess the risk of an unfavorable clinical course in patients with established AKI.Large-scale study should be carried out.Multi-center study should be conducted to get the real situation of Bangladesh.

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