

Evaluation of Neutrophil-Lymphocyte Ratio as Inflammatory Marker in Chronic Kidney Disease Stage 3 and 4

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ABSTRACT

Chronic kidney disease (CKD) is a worldwide health problem because of the significant morbidity and mortality which is mostly due to chronic inflammation and proteinuria. Early detection of inflammation and its proper management can prevent further CKD progression and complications. This study aims to observe the association of neutrophil-lymphocyte ratio (NLR) with inflammatory markers in chronic kidney disease stage 3 and 4. In this study, a total of 100 adult patients of CKD stage-3 and 4 were included as study subjects and patient with acute illness, known case of malignancy, cardiovascular and cerebrovascular disease were excluded from the study. From each patient all the relevant history, clinical and laboratory findings were recorded in the data collection sheet. Study subjects were divided into two groups according to NLR value; those who have NLR 0- 3 were in group normal NLR and subjects with NLR >3 in group high NLR. Then markers of inflammation ESR, CRP and serum albumin were compared between these groups. Statistical analysis was done by Statistical Package for Social Science (SPSS) version 22.0. The mean ESR of male and female patients was higher in high NLR subjects than normal NLR subjects. The mean CRP was higher in high NLR subjects than normal NLR subjects. The mean serum albumin was lower in high NLR subjects than normal NLR subjects. The difference of mean ESR, CRP was statistically significant between high NLR and normal NLR subjects but difference of mean serum albumin was not statistically significant. The study findings suggest that high NLR is significantly associated with inflammatory markers-ESR, CRP. Hence, it can be concluded that NLR could be used as an indicator of inflammation in CKD.

Keywords: Chronic Kidney disease, Inflammatory marker, Neutrophil-lymphocyte ratio.

Mugda Med Coll J. 2024; 7(1): 4-8

DOI: <https://doi.org/10.3329/mumcj.v7i1.73955>

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide health problem because of the significant morbidity and mortality. CKD is associated with age-related decline of renal function accelerated in hypertension, diabetes, obesity and primary renal disorders.¹

Proteinuria shows strong association to risk of progression to chronic renal failure.² The presence of

proteinuria generally reflects impaired glomerular filtration barrier or impaired tubular function, in which advanced immunoinflammatory activity has been found to play an important role.³ Proteinuria is the basic finding of renal damage and is an important indicator of development of fibrogenesis and glomerulosclerosis linked to the progression of several kidney diseases.⁴ It may cause an increase in

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morbidity and mortality in the general population. The effect of proteinuria is essentially due to an increase in inflammation that is already present. Evidence for this includes the amount of increased protein in the urine and is associated with increased amount of tubulointerstitial inflammatory cells, especially, T lymphocytes.⁴

Neutrophil lymphocyte ratio (NLR) is an indicator of inflammation in chronic kidney disease (CKD); it may not be an independent predictor of CKD progression except that the CKD is in a more advanced stage and reflects the associated inflammation. Classical risk factors such as DM and lower GFR are more powerful predictors of progression.⁵ Neutrophil lymphocyte ratio (NLR) is a strong indicator in determining inflammation in cardiac and noncardiac diseases.⁴

There is a graded inverse relationship between CVD risk and glomerular filtration rate (GFR) that is independent of age, sex and other risk factors.^{6,7} Decreased renal function is a predictor of hospitalization,¹ cognitive dysfunction and poor quality of life.^{8,9} The healthcare burden is highest in early stages due to increased prevalence, affecting around 35% of those over 70 years.¹⁰

Atherosclerosis, which develops as a result of inflammation, is the most important cause of morbidity and mortality in CKD.¹¹ Neutrophil counts are increased, whereas lymphocyte counts are decreased during inflammation and recent studies have emphasized that NLR could be used as an indicator for inflammation.¹² Other studies showed that NLR is increased in inflammation in cardiovascular disorders and can be used as an indicator of prognosis.^{13,14} Studies in patients with malignancies as well as cardiovascular disorders revealed that NLR and lifespan are correlated.¹⁵ Mahmoud et al¹² found that NLR is significantly higher in patients with CKD compared to healthy individuals and NLR is increased as the stage of kidney disease progressed.

Cardiovascular mortality risk due to atherosclerosis is 10–20-fold higher in CKD patients as compared to general population.¹⁶ In addition to conventional risk factors, CKD has nonconventional risk factors that accelerate atherosclerosis.¹⁷ Nonconventional risk factors include inflammation and thrombogenic factors. In addition to known conventional indicators of inflammation such as C-reactive protein (CRP), fibrinogen, erythrocyte sedimentation rate, several

interleukins and tumor necrosis factor alpha, several recent studies have shown that mean platelet volume (MPV) and neutrophil/lymphocyte ratio (NLR) are also increased during inflammation and may be associated with poor prognosis in CKD.¹⁸ In addition to increased morbidity and mortality, Neutrophil-Lymphocyte ratio (NLR) is a marker of inflammation. Some recent data suggest that NLR may predict the progression of CKD.⁵ Use of NLR as indicators of inflammation is very valuable as it can be evaluated by a simple blood count.

Therefore, aim of the study is to evaluate the NLR as inflammatory markers in patients with CKD stage 3 and 4.

METHODS

This cross-sectional study was conducted in the Department of Nephrology and Medicine out patient department, Dhaka Medical College Hospital, Dhaka for 12 months. After getting approval from the Research Review Committee of the Department of Nephrology and Ethical review committee of Dhaka Medical College, a questionnaire was prepared considering key variables like demographic data, clinical presentation and clinical findings. Then, informed written consent was taken from each patient. Total 100 adult patients of CKD stage-3 and 4 defined by MDRD formula were included as study subjects and patient with acute illness, known case of malignancy, cardiovascular and cerebrovascular disease were excluded from the study. After selection of the patient; aims, objectives and procedures of the study was explained with understandable language to the patient. Risks and benefits also were made clear to the patient. The patients were encouraged for voluntary participation and they were allow being free to withdraw themselves from the study. Then, relevant history, physical examination and laboratory findings were recorded in the data collection sheet. For convenience, study subjects were divided into two groups according to NLR value; subjects with NLR 0- 3 were in group normal NLR and subjects with NLR >3 in group high NLR. Then markers of inflammation ESR, CRP, serum albumin and also 24 hours urinary total protein were compared between these groups. Estimation of complete blood count, ESR, Serum Creatinine, serum albumin and CRP was done as laboratory parameters. Calculation of Neutrophil-Lymphocyte Ratio (NLR) was done dividing absolute neutrophils counts by absolute lymphocytes counts. eGFR was estimated by using MDRD formula. Statistical analysis was

done using Package SPSS version 22.0. For comparison of data, Kolmogorov–Smirnov test was used. Student’s *t*-test, Mann–Whitney U-test, Chi-square test used where applicable.

RESULTS

The mean serum albumin was lower in high NLR subjects than normal NLR subjects. The difference of mean ESR, CRP was statistically significant between high NLR and normal NLR subjects but difference of mean serum albumin was not statistically significant.

Table I: Distribution of the study population by Socio demographic parameters (n=100)

Socio demographic parameters	Number (%)
Age (in year)	
<40	10 (10.0)
41-50	28 (28.0)
51-60	40 (40.0)
61-70	15 (15.0)
>70	7 (7.0)
Mean ± SD	54.46±11.16
Range(min-max)	(35-87)
Sex	
Male	67 (67.0)
Female	33 (33.0)

Table II: Association of NLR with ESR (mm/1st hour) (n=100)

ESR (mm/1 st hour)	High NLR (N= 59) Number (%)	Normal NLR (N= 41) Number (%)	P value
Male			
High (>10)	35 (59.4)	24 (58.6)	
Normal (0-10)	1 (1.7)	7 (17.1)	
Mean±SD	30.03±13.81	23.16±8.63	0.005
Range(min-max)	10-82	10-37	
Female			
High (>20)	23 (38.9)	6 (14.7)	
Normal (0-20)	0 (0.0)	4 (9.8)	
Mean±SD	33.74±20.36	24.5±18.42	0.022
Range(min-max)	20-120	10-70	
P value reached from unpaired t-test			
high NLR (NLR>3)			

normal NLR (NLR 0-3)

Table III: Association of NLR with CRP (n=100)

CRP	High NLR (N= 59) Number (%)	Normal NLR (N= 41) Number (%)	P value
<6.0	1 (1.7)	0 (0.0)	
≤6.0	58 (98.3)	41 (100.0)	
Mean±SD	16.54±11.09	10.54±6.81	0.002
Range(min-max)	1-66	6-36	

P value reached from unpaired t-test

Table IV: Association of NLR with serum albumin (n=100)

Serum Albumin (gm/dl)	High NLR (N= 59) Number (%)	Normal NLR (N= 41) Number (%)	P value
Low (<3.5)	39 (66.1)	20 (48.8)	
Normal (3.5-5.5)	20 (33.9)	21 (51.2)	
Mean±SD	3.4±0.54	3.53±0.48	0.218
Range(min-max)	2.5-4.8	2.8-5	

P value reached from unpaired t-test

DISCUSSION

In present study, it was observed that more than one third 40 (40.0%) patients belonged to age 51-60 years. The mean age was 54.46±11.16 years with ranged from 35 year to 87 years. More than two third 67 (67.0%) patients were male and 33(33.0%) were female.

In this study, it was observed that 35 (59.4%) male patients had high ESR in high NLR subject and 24 (58.6%) patients in normal NLR subjects. The mean ESR of male patients was 30.03±13.81 mm/1st hour in high NLR and 23.16±8.63 mm/1st hour in normal NLR subject. 23 (38.9) female patients had high ESR in high NLR subject and 6 (14.7) patients in normal NLR subject. The mean ESR of female subject was 33.74±20.36 mm/1st hour in high NLR subjects and 24.5±18.42 mm/1st hour in normal NLR subject. The difference of mean ESR was statistically significant between high NLR and normal NLR subject in both male and female. Kocyigit et al¹⁸; Ju et al. (2015)¹⁶ stated that neutrophil/lymphocyte ratio (NLR) were

increased during inflammation and associated with poor prognosis in CKD. Yoshitomi et al¹⁹ reported that a high NLR was associated with poor renal outcomes, suggesting that NLR may be a useful marker for prognostic prediction in patients with CKD.

In present study, it was observed that 58 (98.3%) patients had high level of CRP in high NLR subject and 41 (100.0%) patients in normal NLR subject. The mean CRP was 16.54 ± 11.09 in high NLR subjects and 10.54 ± 6.81 in normal NLR subject. The difference of mean CRP was statistically significant between these two groups. Kocyigit et al¹⁸; Ju et al.¹⁶ stated that neutrophil/lymphocyte ratio (NLR) were increased during inflammation and associated with poorer prognosis in CKD. Yoshitomi et al¹⁹ reported that the high NLR group had significantly higher CRP level compared with the low NLR group.

It was observed that almost 39 (66.1%) patients had low serum albumin in high NLR subjects and 20 (48.8%) patients in normal NLR subjects. The mean serum albumin was 3.4 ± 0.54 gm/dl in high NLR subjects and 3.53 ± 0.48 gm/dl in normal NLR subjects. The difference of mean serum albumin was not statistically significant between these two groups. Hypoalbuminemia is a frequently found feature of chronic kidney disease (CKD).²⁰ Binnetoglu et al⁴ reported that there was a moderate positive correlation between proteinuria and NLR.

CONCLUSION

The study findings suggest that high NLR is significantly associated with inflammatory markers-ESR, CRP. So, it can be concluded that NLR could be used as an indicator of inflammation in CKD.

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