



Neutrophil to Lymphocyte Ratio in Patients with End-stage Renal Disease in Benue State University Teaching Hospital, Makurdi, Nigeria

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ABSTRACT

Chronic Kidney Disease (CKD) leads to end-stage renal disease (ESRD) and cardiovascular events. An important determinant of progression in CKD is chronic systemic inflammation which can be evaluated using the neutrophil to lymphocyte ratio (NLR). We aimed to investigate the value of NLR in patients with ESRD compared with healthy subjects. This was a retrospective study which analyzed data from patients with end-stage renal disease and equal number of age and sex matched control (healthy subjects) seen at Benue State University Teaching Hospital Makurdi from October 1st 2012 to 31st December 2015. Out of the 118 patients studied 70(59.3) were males while 48 (40.7) were females. The mean age of the study population was 45.9 ± 16.4 . The mean NLR for patients with ESRD was 3.55 ± 4.01 while that of healthy subjects was 1.29 ± 0.25 . The mean NLR for patients was 3.47 ± 4.01 for males and 3.68 ± 4.06 for females while for the healthy subjects the mean NLR was 1.30 ± 0.27 for males 1.27 ± 0.22 for females. This study revealed elevated NLR in patients with ESRD. NLR reflects systemic inflammation. The availability of this ratio (NLR) can help improve outcome of patients with CKD.

Keywords: End Stage Renal Disease, Inflammation, Neutrophil-to-Lymphocyte Ratio

INTRODUCTION

Chronic Kidney Disease (CKD) is a global health problem. The prevalence and incidence of CKD is increasing in both developed and developing countries.^{1,2} The major cause of mortality in patients with CKD including end stage renal disease (ESRD) is cardiovascular disease (CVD). Many factors account for the increased risk of CVD in ESRD patients. They include both traditional and novel risk factors. The major cardiovascular event in these patients is atherosclerotic vascular disease. Traditional risk factors such as diabetes mellitus, hypertension, dyslipidaemia and obesity cannot

completely explain the increased risk of these patients for CVD.³ It has been shown that novel risk factors for CVD like inflammation and protein energy wasting (PEW) which are common in patients with ESRD play a crucial role in CVD in these patients.⁴ Chronic systemic inflammation has been shown to contribute to CKD progression and fibrosis.⁵ The neutrophil count reflects inflammation while the lymphocyte count is related to malnutrition and general stress. Neutrophil provides information that NLR is a complementary prognostic marker for evaluating the cardiovascular risk in CKD

patients.⁶ Several studies revealed that an increase in neutrophil count predicts mortality in haemodialysis and peritoneal dialysis patients.^{7,8}

Also in CKD patients, NLR has been shown to play a central role in deterioration of renal function and progression.⁹ NLR as a simple marker of chronic systemic inflammation predicts progression in CKD as well as patients with higher CVD risk.¹⁰ It is well known that about 30 – 50% of patients undergoing haemodialysis has chronic systemic inflammation.^{11,12,13} In CKD, inflammation may be induced by many causes including dialysis related factors such as membrane bio-incompatibility and back filtration of endotoxins from the dialysate and non-dialysis related factors such as non- access related infections and comorbidities. Even with advanced dialysis techniques that has substantially decreased dialysis related factors, the rate of infection has not diminished. Infectious disease in patients with ESRD depends on the condition of the patient such as immune dysfunction, PEW, comorbid conditions, dental illness, use of immunosuppression drugs and presence of vascular access devices.^{11,12}

Other factors that can contribute to inflammation in patients with ESRD include bacterial translocation from gastrointestinal tract as well as unrecognized opportunistic pathogens. NLR is a novel, simple and inexpensive index for assessing inflammation in cardiac and non-cardiac disorders and also been shown to have prognostic and predictive values in those with systemic inflammation as we have in ESRD.^{11,12,13} Emerging evidence suggests that increased NLR is a potential marker of poor prognosis in multiple tumours^{14,15} and CVD in general population.^{16,17,18} Isaac *et al*¹⁹ reported that NLR was associated with mortality among medical in patients with multiple chronic conditions. Ahbap *et al*²⁰ found a significant positive correlation of NLR with his CRP levels in ESRD patients. An *et al*²¹ reported that NLR was a strong predictor for overall and cardiovascular mortality in peritoneal dialysis patients. Queltet *et al*²² reported that NLR is a predictor of all- cause survival in haemodialysis patients. Since NLR is a relatively available result from full blood count, studies about its value in CKD patients are encouraging hence the aim of this study was to investigate the value of NLR in ESRD compared with healthy subjects.

MATERIALS AND METHODS

This was a retrospective study where records of 118 patients managed for ESRD between October 1st 2012 and December

31st 2015 were retrieved and reviewed. Inclusion criteria were patients with ESRD and those who gave their consent to participate in the study. Exclusion criteria were clinical evidence of heart failure, acute coronary syndrome, cerebrovascular accident, autoimmune disease, malignancy, active infection. Ethical clearance was obtained from the ethics committee of Benue State University Teaching Hospital. The records of all patients with ESRD seen by the Nephrology unit of Benue State University Teaching Hospital from 1st October 2012 to 31st December, 2015 were reviewed. Records of equal number of age and sex matched individuals attending the General Outpatient Department for medical fitness certificate within the same period were also reviewed and used as control.

Benue State University Teaching Hospital is a tertiary healthcare facility located in Makurdi, North Central Nigeria serving all the general hospitals in the state as well as receiving referrals from neighboring states of Nassarawa, Taraba and Kogi. Data obtained from each patient and control included age, gender, weight, full blood count and differentials. Full blood count was done using an autoanalyser with its reagents including cell pack (diluent), stromatolyser (WBC and RBC lyse reagent), cell clean, printer paper, light source and sample mixer. Neutrophil-to-lymphocyte was obtained by dividing absolute neutrophil to lymphocyte count.^{8,9} Estimated Glomerular Filtration Rate (eGFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine equation. CKD Stage 5 (ESRD) was defined as $eGFR \leq 15 \text{mls/min}$ or patients already undergoing dialysis or has had renal transplant.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS Inc. Chicago II) version 21.0 statistical software was used for data analysis. Quantitative variables were expressed as means \pm standard deviation while categorical variables were expressed as proportions. The t-test and the chi-square test were used in the comparison of means and proportions respectively. P-value <0.05 was considered statistically significant.

RESULTS

The study population comprised 118 subjects, 70(59.3%) were males while 48.(40.7%) were females. The mean ages of males and females were 47.1 ± 17.7 and 45.9 ± 19.4 years respectively (Table 1). There was no statistically significant

difference between the two values. 69% of the study population was less than 50 years of age. The mean NLR for patients with ESRD was 3.21 ± 2.57 while that of healthy subjects was 1.29 ± 0.25 .

The mean NLR for patients was 3.40 ± 2.80 for males and 2.86 ± 2.20 for females while for the healthy subjects the mean NLR was 1.30 ± 0.27 for males 1.27 ± 0.22 for females. The NLR of patients with ESRD was significantly higher than that of healthy subjects. 72(61%) of patients with ESRD had NLR > 1.5 compared with 23(19.5%) of healthy subjects (control group) Table 2 The result was statistically significant.

Table 1 : Age Distribution of ESRD Patients

Age Range	Frequency	Percentage
18-33	30	25.4
34-49	39	33.1
50-65	32	27.1
>65	17	14.4
Total	118	100

Table 2: Neutrophil-to-lymphocyte Ratio of Patients and Control

sex	Patients		Control		Total
	<1.5	>1.5	<1.5	>1.5	
Male	24	46	57	13	140
Female	18	30	38	10	96
Total	42	76	95	23	236

t-10.456, *df* 117 *p*-value 0.000

DISCUSSION

Age distribution of patients with ESRD revealed that most of them were in their productive years of less than 50 years (Table 1) This is similar to studies done in Nigeria, Africa and developing countries^{23,24,25} This is due to a number of reasons including high prevalence of childhood infections like glomerulonephritis, Human immunodeficiency Virus (HIV) infections, use of nephrotoxic agents such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and herbal medications as well as use of mercury containing soaps and creams.^{23,24,25} This study revealed that patients with End Stage Renal Disease (ESRD) have higher neutrophil-to-lymphocyte ratio

(NLR) compared with healthy subjects. (3.55 ± 4.01 compared with 1.29 ± 0.25).

This is similar to what was reported in several studies.^{12,13,14,16,26,27,28} For instance Abe T *et al*²⁶ in 2015 reported that higher NLR is associated with higher risk of CVD in incident dialysis patients. In 2004, Rafaioglu *et al*²⁷ reported that NLR was higher in patients with Behcet disease compared with healthy subjects and also came up with the finding that increased NLR correlated with disease activity. Additionally Posul E *et al*²⁸ in 2005 reported that high NLR in patients with ulcerative colitis was associated with active phase of the disease. Salciccioli JD *et al*²⁹ investigated 5000 patients treated at the intensive care unit in a large clinical database and reported that high NLR was significantly associated with mortality. Several factors could account for this increase in NLR in Patient with ESRD. It has been shown that increased neutrophil count reflects oxidative stress³⁰, while lower lymphocyte count indicates malnutrition³¹. Oxidative stress from reports in many studies has been observed to be associated with disease progression in CKD³². Malnutrition also has been implicated with adverse renal outcomes.³³ In CKD decline in glomerular filtration rate (GFR) is associated with increased risk for cardiovascular events and progression to ESRD.^{34,35}

Chronic systemic inflammation plays a key role in the outcome of CKD patients because inflammation is one of the important initiator of progressive tubule- interstitial fibrosis which leads to ESRD.^{36,37} Several studies have also reported that inflammation plays a key role in reduction in kidney function and initiation of cardiovascular events especially atherosclerotic vascular disease.³⁸ Several inflammatory cytokines such as C-reactive protein (CRP), Interleukin 6 and tumour necrosis α (TNF- α) are mainly used for research and not readily available for clinical practice therefore, NLR is more readily available and could be a reliable marker for detecting the extent of systemic inflammation in chronic diseases like CKD.³⁹ NLR is the now being used as an inflammatory marker in many diseases to identify high risk patients including CKD.^{40,41,42} NLR has been shown to be useful in predicting mortality and cardiovascular events in patients with CVD and malignant tumours.^{43,44} NLR is associated with ischaemic risk in the general population⁴⁵. NLR has also been associated with development of ischaemic heart disease (IHD) in predialysis⁴⁶ and dialysis patients⁴⁷. NLR also displays prognostic value for proteinuria^{48,49} which is also a marker for CVD in CKD patients and an independent risk factor for progression of CKD to ESRD.⁵⁰

CONCLUSION

This study showed elevated NLR in patients with ESRD. NLR is now seen as a marker for detecting high risk patients with chronic inflammatory disease including those with end stage renal disease. The availability of NLR with appropriate intervention can help improve outcome of patients with CKD.

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