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.
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 (diluents), 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. 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 ≤ 15mls/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 ± 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**

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–33</td>
<td>30</td>
<td>25.4</td>
</tr>
<tr>
<td>34–49</td>
<td>39</td>
<td>33.1</td>
</tr>
<tr>
<td>50–65</td>
<td>32</td>
<td>27.1</td>
</tr>
<tr>
<td>&gt;65</td>
<td>17</td>
<td>14.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>118</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>sex</th>
<th>Patients</th>
<th>Control</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.5</td>
<td>&gt;1.5</td>
<td>&lt;1.5</td>
<td>&gt;1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td>46</td>
<td>57</td>
<td>13</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>30</td>
<td>38</td>
<td>10</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>42</td>
<td>76</td>
<td>95</td>
<td>23</td>
<td>236</td>
<td></td>
</tr>
</tbody>
</table>

\( t-10.456, df 117 \ p-value 0.000 \)

**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, Rafiaoglu 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 stress 30 while lower lymphocyte count indicates malnutrition 31.

Oxidative stress from reports in many studies has been observed to be associated with disease progression in CKD 32. 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. 34 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 population 45. NLR has also been associated with development of ischaemic heart disease (IHD) in predialysis 46 and dialysis patients 47. NLR also displays prognostic value for proteinuria 48 which is also a marker for CVD in CKD patients and an independent risk factor for progression of CKD to ESRD 49.
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.

REFERENCES


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