Assessment of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio as Inflammatory Markers among Sudanese Patients with Chronic Kidney Disease in Kordofan state- 2024

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Abstract:

Background and Objective: Low grade chronic inflammation is one of the central pathophysiological factors in chronic kidney disease (CKD). The complete blood count is a routine, inexpensive and easy test that provides information about formed blood contents. Neutrophil/lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) are simple parameters and novel inflammatory marker, which may be used in many diseases for predicting inflammation. The aim of this study is to assess the utilization of NLR And PLR as inflammatory markers in patient with CKD.

Methods: A cross- sectional descriptive study including 59 participants at different stage of CKD which was conducted. CKD was assessed based on glomerular filtration rate (GFR). Quantitative C-reactive protein (CRP) was analyzed by a fluorescence immunochromatographic methods as the bench inflammatory marker. NLR and PLR were calculated after complete blood count was performed.

Results: Based on CRP value the participants were subdivided into two groups the first is group without inflammation (CRP <1) and the second with inflammation (CRP > 1). The study revealed the mean of NLR was slightly higher (3.08) in the group that had inflammation, unlike other (2.78). while the mean PLR within normal range in two groups (inflamed = 132.5, non-inflamed = 151.7). our study was showing positive correlation between NLR and CRP (R= 0.05, P= 0.000). with regards to PLR and CRP the correlation was not significant.

Conclusion: Depending of these results, it can be concluded that NLR, together with CRP, may serve as a marker of systemic low-grade inflammation in patients with CKD. Larger prospective cohort studies in various ethnic groups are required to assess the possibility of using NLR as an alternative marker for CRP in patients with CKD.

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Introduction:

Chronic kidney disease (CKD) is an irreversible disease, characterized by abnormal renal structure/function for three or more months. Typically, in CKD patients renal damage markers are detected such as albuminuria, tubular-associated lesions, histological and imaging abnormalities with or without a decrease in glomerular filtration rate (GFR), or GFR < 60ml/ (min·1.732) ≥ 3 months 1. The progression of CKD can eventually lead to irreversible End-Stage Renal Disease (ESRD), which has become a significant public health concern in Sub-Saharan Africa in recent years 2. The aim of this study to assess the utilization of NLR And PLR as inflammatory markers in patient with CKD.

Materials and Methods: This is a cross-sectional descriptive study. The study was conducted at Eljemah Hemodialysis Center and Elobeid International Hospital in Elobeid town in the capital of North Kordofan state. Ninety-five patients with chronic kidney disease were selected randomly from patient attended to the Eljemah Hemodialysis Center and Elobeid International Hospital. All patients who were diagnosed with chronic kidney disease and various disease stages were included in this study. Patients with long-term use of hormones and associated immunosuppressants, with severe heart failure, malignant tumor, pregnancy, mental illness, tuberculosis, with recent surgical treatment and with incomplete/missing clinical data were excluded from the study. Patients with chronic kidney disease who attended Eljemah Hemodialysis Center and Elobeid international hospital during June to July 2024 were included and interviewed using data collection sheet focusing on personal and clinical data including (age, address, occupation, duration of dialysis, chronic diseases). The medical records of each patient were reviewed to identify the cause of CKD. Ethical clearance was obtained from the Ethics Review Committee of the Eljemah Hemodialysis Center and Elobeid international hospital. EDTA blood samples were collected from each participant after obtaining informed consent. Laboratory investigations of white blood cell (WBC), platelet, and leukocyte differential counts were preform using full automated hematological analyzer Zybio (Z3). Also heparinized blood samples were collected for biochemical testing include urea, creatinine and C-reactive protein using semi- automated biochemical analyzer (BTS 350) and fluorescence immunochromatography analyzer (XER110) for CRP. The NLR was calculated by dividing the absolute neutrophil count (ANC) by the absolute lymphocyte count (ALC); likewise, PLR was calculated by dividing the absolute platelet count by absolute lymphocyte count. The study was approved by the ethics committee of the Eljemah Hemodialysis Center. Verbal informed constant was obtained for all participants. Statistical Package for the Social Sciences (SPSS) version 24 was used for data analysis.

Results:

Ninety-five (59) participants were enrolled in this study. Amongst the total participants, males were predominant (57%), with a mean age of 51.2 years. According to the possible causes of the CKD, the most of participant had hypertension with percentage 37.3% followed by unknown causes 28.7%. Severity analysis

based on the GFR (mean= 7.7$\pm$ 5.7 ml/min/1.73m2) revealed that 81.4% and 19% of CKD patients were in stages4 (n=48) and stage5 (n=11) respectively. Anemia was common among CKD patients with means Hb 7.8$\pm$1.6 g/dl. Otherwise, the TWBCs within normal range (mean= 6.6$\pm$3.17). The means of variables NLR, PLR and MPV among all participants were 3$\pm$1.5 ,137$\pm$55.5 and 8.8$\pm$0.97 respectively.

The mean of CRP was 14.8$\pm$29.5 μg/dl and based on these inflammatory markers the participants subdivided into two groups the first is group with CKD without inflammation (CRP <1 mean=0.6) and the second with inflammation (CRP >1 mean= 18.9). The revealed a difference in the means of NLR, PLR and MPV between the two groups, such that the mean of NLR was higher (3.08 $\pm$1.5) in the group that had inflammation, unlike the others (mean = 208$\pm$1.1), while the mean of PLR (132.5$\pm$54) in the first group (inflamed) was lower than in the second group (mean= 151.7$\pm$58). Pearson's correlation test between these two groups showed that the inflamed group had a positive correlation with NLR and CRP (r=0.53 p=0.00), and there was a non-significant relationship for both PLR(p=0.85) and MPV (0.76) with CRP, while the non-inflamed group showed that there was no significant relation between NLR (p=0.13) and PLR (p=0.40) with the CRP and there was positive correlation between MPV and CRP (r=0.58 p=0.038).

Pearson correlation conducted between the variables NLR, PLR and MPV with the CRP variable for all participant and we found that there is a positive correlation between NLR and CRP (r=0.5 p=0.000) and there are insignificant relations between PLR (P= 0.89) and MPV (p= 0.80) with the CRP variable.

Based on the classification of participants according to the stage of the disease, the study revealed that the relation between NLR and CRP became stronger for those in stage5 (r=58 p=0.000), unlike those with stage4 the relationship between NLR and CRP became insignificant (p=0.86). In addition, there is insignificant relation between PLR and MPV with the CRP in the two stages.

Discussion:
The association of renal disease and certain social and economic factors suggests that lack of timely preventive health care interventions focused on these factors may aggravate this problem. However, in the present socioeconomic status, it is important that we seek cost-effective biological markers. NLR is a cheap, routinely used, and repeatable test, and many studies have found that it can be an indicator of systemic inflammation 3. This biomarker indicates an imbalance between effector cells (neutrophils) that reflect oxidative stress and regulatory cells (lymphocytes)that reduce the pro-inflammatory state 4. NLR, as a new biomarker of inflammation, reflects both the adaptive immune response (lymphocyte-mediated) and the innate immune response (neutrophil-mediated). A high neutrophil count primarily reflects infection, while a low lymphocyte count indicates poor general health and physiological stress 5. On other side the PLR is also a cheap and readily available laboratory test that reflects an increased systemic inflammatory status. The aim of this study to assess the neutrophil lymphocyte ratio and

platelet lymphocyte ratio as inflammatory marker in patients with chronic kidney disease. Present study revealed positive correlation between NLR and CRP (r=0.5 p=0.000). However, there was non-significant difference between the mean of NLR in the two groups that were classified based on CRP as inflamed (3.16) and non-inflamed (2.78). We also found that it was elevated in both groups. This result can be explained by the fact that the increase in NLR after acute physiological stress is earlier (<6 hours) than other laboratory parameters such as CRP or white blood cell count 5. In addition, the normal cutoff value of NLR is still under debate. In normal adult population, it may vary between 0.78 to 3.92 and may be higher in elderly, males, HIV, active hematological disorder, or exogenous steroid intake. Normal range of total leucocytes and neutrophiles are known to be lower in African and may explain the lower NLR in black 6. In Nigeria, Uduagbamen et al found a median NLR of 1.5 (range 0.9 - 2.1) in healthy adults with a mean age of 46 years 7. However, we need more studies to determine the normal value of NLR and take into consideration the different ages and nationalities present in Sudan to make these markers more effective. Indeed, in Sudan, Mohamed and et al, identified reference range of NLR between 0.3 to 2.9 in a cohort of three hundred participants aged from 5 to 85 years 8. Although these studies were conducted in Sudan, the average age was younger (mean was 37) than the average age in our study was 51.2 year.

With regards to PLR, the study showed the correlation between PLR and CRP was not significant. Similar results were obtained by the study of Nermina Klapuh-Bukvić et al, where they reported a slight increase in PLR value with the progression of renal impairment, but the correlation between PLR and CRP was not significant8.

The present study shows no significant relation between NLR and GFR. Opposite to some studies have found a negative correlation between the NLR and the glomerular filtration rate. Tonyali et al. found that an NLR >3.18 in patients undergoing radical or partial nephrectomy was associated with an increased risk (almost 3 times) of developing CKD (defined by a glomerular filtration rate <60ml/min/1.73m2) 9.

Conclusion: The present study showed an increase in CRP and NLR values in CKD patients. A significant positive relationship between CRP values and NLR was established in our study. In contrast of these results, it can be concluded that NLR, together with CRP, may serve as a marker of systemic low-grade inflammation in patients with CKD.

Recommendations: Larger prospective cohort studies in various ethnic groups are required to assess the possibility of using NLR as an alternative marker for CRP in patients with CKD.

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