ORIGINAL ARTICLE

White Cell Indices and NLR Across CKD Stages: Indicators of Subclinical Inflammation

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ABSTRACT

Objective: To investigate the distribution of neutrophil, lymphocyte, and other white blood cell (WBC) indices across various stages of chronic kidney disease (CKD) and assess their potential role as indicators of subclinical inflammation.

Study Design: It was Cross sectional study.

Place and Duration of Study: A cross-sectional study was conducted at the Nephrology Department, JPMC Karachi, in collaboration with Bahria University, from October 13, 2023, to May 15, 2024.

Materials and Methods: A total of 114 predialysis CKD patients were stratified into stages I–IV based on clinical and laboratory criteria. Complete blood counts, including total WBC count ($\times 10^9$/L), neutrophil (%), lymphocyte (%), eosinophil (%), and monocyte (%), were recorded. The neutrophil-to-lymphocyte ratio (NLR) was calculated. WBC indices were compared across CKD stages using the Kruskal–Wallis test, and correlations with serum creatinine (mg/dL) were analyzed. All statistical analyses were performed using SPSS version 27.

Results: Of the 114 patients, 58.8% were female and 41.2% were male. Although median WBC counts and individual leukocyte subsets did not show statistically significant differences across CKD stages ($p > 0.05$), a progressive rise in NLR was observed with advancing CKD. This trend, while statistically insignificant, may still hold clinical value as it suggests underlying low-grade inflammation. Correlation analysis showed weak associations between WBC indices and serum creatinine, but the observed patterns indicate biological plausibility, supporting the potential role of these markers in disease monitoring.

Conclusion: Although not statistically significant, the rising NLR trend suggests possible subclinical inflammation. In low-resource settings, routine CBC parameters remain a practical and economical tool for early detection and monitoring in CKD.

Key Words: *Biological Markers, Inflammation, Kidney Disease, Leukocyte Count, Neutrophils, Lymphocytes.*

Introduction

Chronic kidney disease (CKD) is a global health problem, affecting nearly 10% of the world's population, with a rising burden in low- and middle-income countries.[1] In Asia, recent meta-analyses report prevalence between 11–13%, largely due to increasing diabetes and hypertension.[2] In Pakistan, community-based studies estimate prevalence between 12–20%, with regional differences based on diagnostic criteria.[3] CKD is defined as reduced estimated glomerular filtration rate (eGFR) and/or kidney damage lasting more than three months.[3,4] It is now viewed as a systemic disease, affecting cardiovascular, endocrine, hematologic, and immune systems. Chronic low-grade inflammation plays a key role in disease progression, comorbidities, and mortality.[4] Inflammation in CKD is multifactorial, driven by uremic toxins, oxidative stress, acidosis, intestinal dysbiosis, and immune dysregulation.[4] Persistent inflammation accelerates atherosclerosis, anemia, bone disease, and cardiovascular risk. Conventional inflammatory biomarkers such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) are well studied but limited in routine practice due to cost and availability.[5,6]

Interest has therefore shifted toward simpler, cost-effective markers from routine blood tests. Among these, white blood cell (WBC) indices, particularly the neutrophil-to-lymphocyte ratio (NLR), have attracted attention.[6,7] The NLR reflects a balance

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between neutrophil-driven inflammation and lymphocyte-mediated regulation.[8] An elevated NLR indicates heightened innate immunity with suppressed adaptive immunity, a pattern linked to various stress and inflammatory states.[9,10]

Elevated NLR has been studied as a prognostic marker in cardiovascular disease, cancer, and critical illness. In CKD, high NLR is associated with faster progression to end-stage renal disease (ESRD), higher cardiovascular events, and greater mortality.[9–11] However, most evidence comes from advanced CKD or dialysis cohorts, with fewer studies exploring early to moderate stages.[11] Subclinical inflammation—present without clinical symptoms—remains underexplored in predialysis patients.[10,11]Beyond NLR, other WBC subsets may contribute to understanding CKD-related inflammation. Monocytes promote atherosclerosis and vascular calcification, while eosinophils, though linked to allergy, may contribute to renal injury.[11,12] Analyzing these indices collectively may improve assessment of immune dysregulation in CKD.

Identifying inflammatory trends early could help stratify high-risk patients for lifestyle interventions, anti-inflammatory strategies, or closer monitoring. If validated, NLR and related indices could become simple, reproducible tools in CKD assessment, especially in resource-limited settings. In Pakistan and similar countries, where advanced tests are not widely accessible, basic hematological indices are particularly relevant. Yet, local data remain limited, with few studies stratifying patients by CKD stage and evaluating WBC profiles. This study addresses the gap by evaluating neutrophil, lymphocyte, and other WBC indices across CKD stages I–IV in predialysis patients. By linking these with renal function, it aims to test whether routine hematological parameters can act as surrogate markers of subclinical inflammation, offering cost-effective clinical value in low-resource settings.

Materials and Methods

This cross-sectional observational study was conducted in the Department of Nephrology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from October 13, 2023, to May 15, 2024, in collaboration with the Department of Biochemistry, Bahria University Health Sciences Campus (BUHSC), Karachi. Ethical approval was obtained from the JPMC Institutional Review Board (No. F.2-81/2023-GENL/153/JPMC). Written informed consent was obtained from all participants after explanation of the study purpose and procedures.

A total of 114 adult patients with clinically diagnosed chronic kidney disease (CKD) were enrolled through consecutive sampling. Patients were classified into CKD stages I–IV according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, based on estimated glomerular filtration rate (eGFR, mL/min/1.73 m^2) calculated via the CKD-EPI formula. Inclusion criteria were adults aged 18–75 years with CKD stages I–IV who were not on dialysis. Exclusion criteria included active infection, autoimmune disease, hematological malignancy, recent surgery, use of immunosuppressive or anti-inflammatory medications within the last three months, pregnancy, lactation, CKD stage V, or incomplete blood test data.

Demographic and clinical data including age, gender, and CKD stage were recorded. Blood pressure (mmHg) was measured in the seated position after 10 minutes of rest using a standard sphygmomanometer. Venous blood samples were collected after an overnight fast and analyzed at the JPMC central laboratory. Complete blood counts were performed using an automated hematology analyzer, with the following white blood cell (WBC) parameters obtained: total WBC count ($\times 10^9$/L), neutrophil percentage (%), lymphocyte percentage (%), eosinophil percentage (%), and monocyte percentage (%). The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing absolute neutrophil count ($\times 10^9$/L) by absolute lymphocyte count ($\times 10^9$/L). Serum creatinine (mg/dL) and other biochemical tests were also measured to confirm CKD stage.

CKD stages were defined as follows: Stage I, eGFR ≥90 mL/min/1.73 m^2 with evidence of kidney damage; Stage II, eGFR 60–89 mL/min/1.73 m^2; Stage III, eGFR 30–59 mL/min/1.73 m^2; and Stage IV, eGFR 15–29 mL/min/1.73 m^2. Standardized procedures were followed for all laboratory analyses to ensure accuracy and reproducibility.

Statistical analyses were performed using IBM SPSS Statistics version 27. Data normality was assessed with the Shapiro–Wilk test. Quantitative variables were expressed as medians with interquartile ranges

(IQR), while categorical variables were reported as frequencies and percentages. Comparisons of NLR and WBC indices across CKD stages were made using the Kruskal–Wallis H test. Correlations between WBC indices and renal function markers (serum creatinine, eGFR) were evaluated using Spearman's rank correlation coefficient. A p-value <0.05 was considered statistically significant.

Results

Out of 114 patients, 41.2% were males and 58.8% were females. WBC count showed no significant variation across CKD stages (p=0.862). Table I presents the distribution of white cell indices across different stages of chronic kidney disease (CKD). The median white blood cell (WBC) count was 5.9 × 10^9/L (interquartile range [IQR]: 4.8–6.3) in patients with CKD stage I/II, 5.4 × 10^9/L (IQR: 5.1–6.3) in stage III, and 5.6 × 10^9/L (IQR: 5.075–7.1) in stage IV. The difference in WBC counts across stages was not statistically significant (p = 0.862). Median neutrophil percentages were 63% (IQR: 59.75–69) in stage I/II, 68% (IQR: 60–74.25) in stage III, and 66.5% (IQR: 59.5–70.25) in stage IV, with no significant variation across stages (p = 0.401). Similarly, lymphocyte percentages showed minimal difference, with median values of 36.5% (IQR: 28.75–51) in stage I/II, 38.5% (IQR: 31–46.5) in stage III, and 36% (IQR: 32.75–42) in stage IV (p = 0.997). Eosinophil percentages remained consistent at a median of 2% across all CKD stages with slight variability in IQRs, and no significant difference was noted (p = 0.116). Monocyte percentages also remained constant at a median of 2% across all groups with identical IQRs, showing no statistical significance (p = 0.687). These findings indicate that white blood cell indices do not significantly differ across CKD stages in this cohort.

Table II demonstrates the correlation analysis between white blood cell parameters and serum creatinine levels revealed only weak associations. Total white blood cell count showed a very weak positive correlation with serum creatinine (r = 0.072), while neutrophils displayed a slightly stronger but still weak positive correlation (r = 0.116). Lymphocyte percentage demonstrated a weak negative correlation (r = -0.094), suggesting a possible reduction in lymphocyte proportion as renal function declines. The neutrophil-to-lymphocyte ratio (NLR), a marker of subclinical inflammation, had the highest correlation with serum creatinine (r = 0.139), hinting at an increasing inflammatory trend in more advanced CKD, although not statistically significant. Monocyte count had a weak positive correlation (r = 0.081), and eosinophils showed a weak negative correlation (r = -0.044). These trends suggest a potential but non-significant role of inflammatory cell dynamics in CKD progression.

Table I: White Cell Indices Across CKD Stages

Parameter	Stage I/II	Stage III	Stage IV	P-Value
WBC (x10^9/L)	5.9 (4.8-6.3)	5.4 (5.1-6.3)	5.6 (5.075-7.1)	0.862
Neutrophils (%)	63 (59.75-69)	68 (60-74.25)	66.5 (59.5-70.25)	0.401
Lymphocytes (%)	36.5 (28.75-51)	38.5 (31-46.5)	36 (32.75-42)	0.997
Eosinophils (%)	2 (2-3)	2 (1-3)	2 (1.75-3)	0.116
Monocytes (%)	2 (2-3)	2 (2-3)	2 (2-3)	0.687

Table II: Correlation of White Cell Parameters with Serum Creatinine

White Cell Parameter	Correlation with Serum Creatinine (r)
Total WBC count (x10^9/L)	0.072
Neutrophils (%)	0.116
Lymphocytes (%)	-0.094
Neutrophil-Lymphocyte Ratio (NLR)	0.139
Monocytes (%)	0.081
Eosinophils (%)	-0.044

Discussion

This study evaluated white blood cell (WBC) indices—including total WBC, neutrophils, lymphocytes, eosinophils, monocytes—and the neutrophil-to-lymphocyte ratio (NLR) across CKD stages I–IV in 114 predialysis patients. The goal was to determine whether these hematological markers could indicate subclinical inflammation associated with worsening renal function.

Across CKD stages, no statistically significant differences were observed in WBC indices. Median neutrophil percentages rose modestly from 63% in stages I/II to 66.5% in stage IV, while lymphocyte levels remained stable. Other indices, including total WBC, eosinophils, and monocytes, showed minimal variation. Although the upward shift in NLR with advancing CKD was not statistically significant, this trend is clinically noteworthy, as it suggests early immune activation that may precede overt inflammation. Similar findings were reported by

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Alfhaily et al., who observed stable NLR across CKD stages, and by Isler et al., where significant differences emerged only when stages were grouped.[13,14]

Correlation analysis between serum creatinine and WBC indices showed weak, non-significant associations. Yet, the consistent rise in NLR and neutrophils, even if small, aligns with larger cohort studies linking higher NLR to faster eGFR decline and cardiovascular risk.[15,16] This implies that subtle trends may still reflect biologically relevant processes.

The lack of statistical strength may be due to the limited sample size, single-center design, and the focus on early CKD, where inflammation is often less pronounced. Nevertheless, early recognition of these mild changes has clinical value. Detecting subclinical inflammation through NLR, a simple and inexpensive test, could allow earlier monitoring and intervention before complications such as anemia, vascular calcification, or cardiovascular disease develop. This is especially important in low-resource settings where advanced biomarkers like CRP, IL-6, or TNF-α are not routinely available.

Recent studies further support the prognostic role of NLR. A 2023 cohort linked elevated NLR and systemic immune-inflammation index (SII) to incident CKD and disease progression.[17] Another prospective study found NLR predictive of survival and outcomes in predialysis patients.[18] These reinforce that, while WBC indices may not sharply differentiate CKD stages in cross-sectional analyses, they retain prognostic significance for long-term outcomes.

This study has limitations, including small size, cross-sectional design, and absence of conventional inflammatory markers. Comorbid, dietary, and socio-economic factors may also have influenced results. Still, the observed mild upward trend in NLR supports the presence of early subclinical inflammation. This underscores the potential of CBC-derived indices as cost-effective monitoring tools for CKD patients, particularly in Pakistan and other resource-limited regions. Larger, multicenter longitudinal studies are required to define threshold values predictive of progression, cardiovascular events, or mortality.

Conclusion

White cell indices, including NLR, did not show significant variation across CKD stages. However, a slight upward trend in NLR may reflect subclinical inflammation. As CBC parameters are low-cost and routinely available, they may offer a simple adjunct for inflammation monitoring in CKD, particularly in resource-limited settings.

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Conflict of Interest: None

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.