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Neutrophil-Lymphocyte Ratio And Platelet Indices Value As Predictive Markers of Anaemia of Chronic Diseases/ Inflammation

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ABSTRACT

Background: Anaemia of chronic diseases (ACD) is a prevalent condition among patients with chronic illnesses. Neutrophil-lymphocyte ratio (NLR) and platelet indices (PI) have been suggested as potential biomarkers for ACD. This study aimed to assess the predictive value of NLR and PI in patients with chronic diseases attending hospitals in South-Western Nigeria.

Materials and Methods: A cross-sectional comparative study was conducted among 87 participants, including individuals diagnosed with HIV, HBV, chronic kidney disease (CKD), diabetes mellitus (DM), and a control group. Blood samples were collected, and NLR and PI were measured using an automated blood counter (Sysmex KX-21N). Statistical analysis was performed using ANOVA and unpaired t-tests, with significance set at $p \leq 0.05$.

Results: The mean NLR values showed no statistically significant difference between anaemic and non-anaemic subjects ($p > 0.05$). ROC analysis indicated limited discriminatory power for NLR (AUC = 0.577) and PLR (AUC = 0.536) as diagnostic tools for anaemia. Platelet indices, including PLT, MPV, PDW, and P-LCR, also revealed no significant differences between study groups.

Conclusion: The study found that NLR and PI have limited utility as predictive markers for ACD. Further studies are recommended to explore alternative biomarkers and refine diagnostic tools for ACD in chronic disease patients.

Keywords: Neutrophil-lymphocyte ratio, Platelet indices, Anaemia of chronic diseases, Chronic inflammation, Biomarkers, Predictive markers.

INTRODUCTION

Anaemia of chronic diseases (ACD) or anaemia of inflammation (AI) is one of the most common forms of anaemia encountered in patients with chronic infections, autoimmune diseases, malignancies, and other long-standing inflammatory conditions. The condition is characterized by impaired erythropoiesis and iron homeostasis, which results in inadequate erythrocyte production despite sufficient iron stores (1). Chronic inflammation in ACD is typically mediated by cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), which inhibit iron mobilization from macrophages and reduce erythropoietin production (2). These immunological alterations influence hematologic parameters and cellular responses, including neutrophil-lymphocyte ratio (NLR) and platelet indices.

The neutrophil-lymphocyte ratio has emerged as a widely recognized marker of systemic inflammation and stress response in various clinical conditions, including cardiovascular

diseases, cancers, and chronic inflammatory diseases (3). NLR reflects the balance between neutrophil-driven inflammatory responses and lymphocyte-mediated immune regulation. In the context of anaemia of chronic diseases, increased NLR levels have been associated with poor clinical outcomes and more severe inflammatory states, which may provide insight into the extent of inflammatory anaemia (4).

Similarly, platelet indices, such as mean platelet volume (MPV) and platelet distribution width (PDW), have been investigated as potential biomarkers in a range of inflammatory and haematologic disorders (5). Platelet activation is closely linked to inflammatory responses, and alterations in platelet indices may reflect the underlying inflammatory process present in anaemia of chronic diseases (6). In ACD patients, platelet hyperactivity and increased MPV values are often observed, which can contribute to the pathophysiology of the disease (7). These hematologic changes can serve as early indicators of the severity of inflammation and the degree of anaemia in affected patients.

The predictive value of NLR and platelet indices in ACD has been a subject of growing interest. Multiple studies have suggested that elevated NLR and altered platelet indices are correlated with disease progression and inflammatory burden in chronic diseases, including rheumatoid arthritis, systemic lupus erythematosus, and chronic kidney disease (8,9). Additionally, these parameters have been explored for their prognostic value in anaemic patients, providing clinicians with non-invasive and cost-effective tools for early diagnosis and disease monitoring.

Despite the potential of NLR and platelet indices as predictive markers of ACD, their clinical utility in routine practice is still under investigation. This research aims to explore the significance of these markers in patients with ACD and inflammation, contributing to the existing body of knowledge on haematologic predictors of chronic disease anaemia. By examining the association between NLR, platelet indices, and ACD, the study hopes to offer insight into their diagnostic and prognostic value, facilitating more targeted therapeutic interventions.

MATERIALS AND METHODS

Study Design

This study research was a cross-sectional comparative study designed to determine the potential effects of Neutrophil-Lymphocyte ratio and platelet indices value in patients with anaemia of chronic diseases. The study was carried out among infected patients attending Babcock University Teaching Hospital (BUTH), Ilishan-Remo, and State Hospital Ijebu Ode for a period of five months. Babcock University Teaching Hospital (BUTH), Ilishan-Remo, and State Hospital Ijebu Ode are both situated at South-Western Nigeria.

Sample Size Determination

The sample size was determined using the Cochran formula for estimating proportions in a population outlined by Onyemereze et al. (10):

$n = (Z^2 (Pq))/e^2$

where n = minimum sample size

Z = 1.96 at 95% confidence level,

P = known/expected prevalence

e = error margin tolerated at 5% = 0.05

q = 1 - p

The existing prevalence is 6.0%.

P = 6.0% = 0.06

q = 1 – p

= 1 – 0.06

= 0.94

$n = ((1.96)^2 (0.06 \times 0.94))/(0.05)^2$

$n = (3.8416 \times (0.0564))/0.0025$

n = (0.21667)/(0.0025) = 86.67

The sample size was 87, thus 87 participants were recruited for this study

Ethical Consideration

Before the commencement of the study, ethical approval was obtained from the Babcock University Health Research Ethics Committee (BUHREC) with reference number BUHREC455/23

Informed Consent

Informed consent was obtained from participants before recruiting them for the study. The aim, purpose, objectives, nature, and benefit of the study were properly

explained to each participant. They were assured of confidentiality, protection, free will to participate and freedom to withdraw from the study at any time. The participants were requested to complete a consent questionnaire.

Selection Criteria

For participants to be qualified for selection, several factors were considered during this study

Inclusion Criteria

Participants with confirmed cases of chronic disease

Participants were both male and female

Participants that consent to the study

Exclusion Criteria

Participants that did not consent to the study.

Samples Collection

With all proper aseptic precautions, 2 ml of venous blood was collected from antecubital vein by disposable syringe in a sterile test tube containing EDTA anticoagulant.

Laboratory Analysis

The use of an automated blood counter (Sysmex KX-21N). Additionally, peripheral blood smears were stained with Leishman stain. The use of Interleukin-6 reagent using Enzyme linked Immunosorbent Assay was used to determine the amount of IL-6 present. All procedures were according to the manufacturer's instruction.

Statistical Analysis

Data obtained from the study were expressed as Mean ± SEM for control and the test group. Analysis of variance (ANOVA) was used between all the groups. Significant differences were taken at $p \leq 0.05$ and performed using Statistical Package for Social Sciences (SPSS) version 20.

RESULTS

The demographic distribution of the study subjects (Table 1) shows that individuals with HIV had the highest representation across age groups, particularly among those aged 36-45 years (16.1%), followed by those aged >55 years (11.5%). In contrast, subjects diagnosed with HBV and CKD had fewer participants, especially within the younger age groups (<25 years). Additionally, females (31%) were more represented in the HIV group compared to males (12.6%), whereas CKD patients had a higher proportion of males (8.0%) than females (4.6%).

In Table 2, the distribution of anaemia across different diagnoses reveals that CKD patients had the highest proportion of moderate and mild anaemia (45.5% each), whereas all HBV patients were non-anaemic. HIV patients had moderate (15.8%) and mild anaemia (10.5%), but the majority (73.7%) remained non-anaemic. For diabetes mellitus (DM) patients, 75% had mild anaemia, and none had moderate or severe anaemia. In the control group, 50% of subjects were non-anaemic, while 33.3% had mild anaemia. The chi-square test indicated a significant relationship between anaemia status and chronic disease diagnosis ($p = 0.002$).

Regarding the neutrophil-lymphocyte ratio (NLR), Figure 1 shows no significant difference between the NLR values in anaemic and non-anaemic subjects ($p = 0.7442$). This result is consistent across study groups, as reflected in Table 3, where NLR values did not show a statistically significant relationship with anaemic status ($p = 0.200$).

The ROC curve analysis in Figure 2 shows an area under the curve (AUC) of 0.577 for NLR as a diagnostic tool for anaemia, suggesting that NLR has limited predictive value for distinguishing anaemic from non-anaemic subjects.

For platelet indices (Table 4), there were no statistically significant differences in platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet large cell concentration (P-LCC), and platelet large cell ratio (P-LCR) between anaemic and non-anaemic subjects. The p-values ranged from 0.129 to 0.903, indicating that platelet indices were not significantly influenced by anaemic status.

Similarly, the platelet-lymphocyte ratio (PLR) showed no significant differences between the chronic disease and control groups ($p = 0.6639$), as seen in Figure 3. The AUC for PLR (0.536) also suggests poor discriminatory power as a diagnostic tool for anaemia (Figure 4).

Table 1: Demographic Distribution in relation to study group

HIV		DIAGNOSIS				
		HBV	CKD	DM	CONTROL	
AGE (Years)	<25	2(2.3%)	1(1.1%)	0(0%)	1(1.1%)	1(1.1%)
	26-35	5(5.7%)	1(1.1%)	1(1.1%)	0(0%)	3(3.4%)
	36-45	14(16.1%)	0(0%)	0(0%)	0(0%)	9(10.3%)
	46-55	7(8%)	1(1.1%)	2(2.3%)	2(2.3%)	9(10.3%)
	>55	10(11.5%)	1(1.1%)	8(9.2%)	1(1.1%)	8(9.2%)
GENDER	Female	27(31%)	2	4(4.6%)	3(3.4%)	19(21.8%)
	Male	11(12.6%)	2(2.3%)	7(8.0%)	1(1.1%)	11(12.65)

Table 2: Anaemia distribution in respect to different diagnosis of chronic disease and Control

Chronic diseases investigated	Anaemic status				Chi-square	p-value
	Severe	Moderate	Mild	Normal	31.062	0.002*
HIV	0(0%)	6(15.8%)	4(10.5%)	28(73.7%)		
HBV	0(0%)	0(0%)	0(0%)	4(100%)		
CKD	0(0%)	5(45.5%)	5(45.5%)	1(9.1%)		
DM	0(0%)	0(0%)	3(75%)	1(25%)		
CONTROL	2(6.7%)	3(10%)	10(33.3%)	15(50%)		

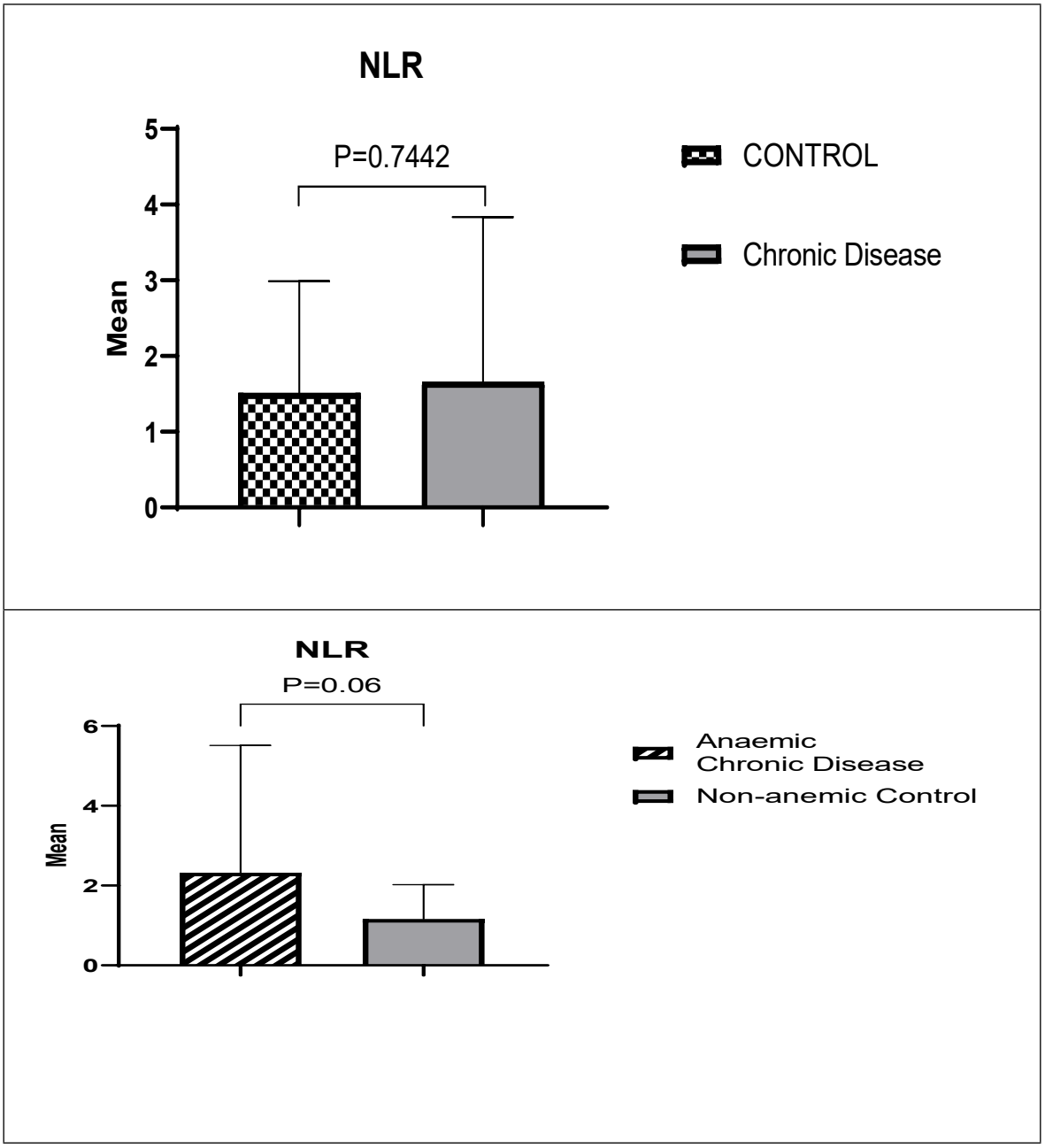
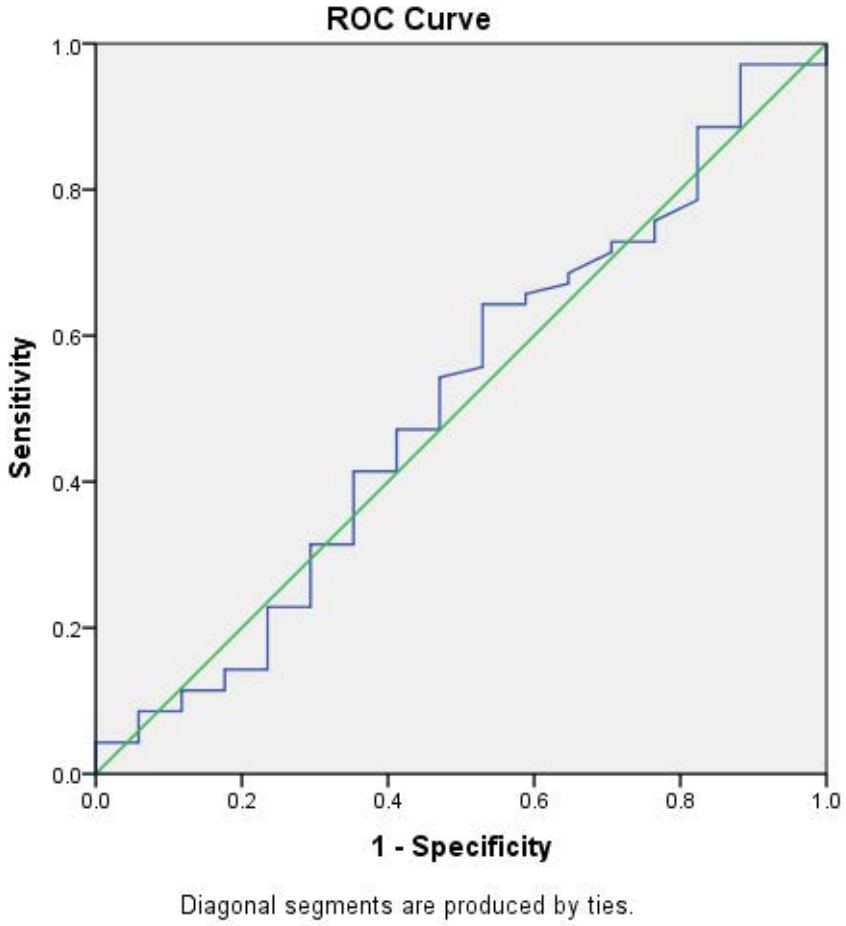


Figure 1: comparison of NLR between anaemia and non-anaemic subject.

Table 3: Distribution of NLR in relation to anaemic status

	NLR		Chi-Square	P-Value
	1-2	>2	4.647	0.200
Severe	1(50)	1(50)		
Moderate	10(71.0)	4(28.6)		
Mild	18(81.8)	4(18.2)		
Normal	44(89.8)	5(10.2)		



Area Under the Curve	
Test Result Variable(s)	Area
NLR	0.577

Figure 2: ROC curve indicating NLR as a diagnostic tool for Anaemia among study subjects.

Table 4: Comparison of platelet indices among study subjects

	Study group	N	Mean	Std. Deviation	P-Value
PLT (10^9/L)	**Non-anaemic**	**15**	**263.26**	**101.26**	**0.903**
	anaemic	**23**	**258.56**	**123.29**	
MPV (fl)	**Non-anaemic**	**15**	**11.65**	**1.22**	**0.431**
	anaemic	**23**	**11.26**	**1.63**	
PDW	**Non-anaemic**	**15**	**15.97**	**0.29**	**0.129**
	anaemic	**23**	**15.74**	**0.52**	

PCT (%)	**Non-anaemic**	**15**	**.30**	**0.11**	**0.665**
	anaemic	**23**	**.29**	**0.12**	
P-LCC (10^9/L)	**Non-anaemic**	**15**	**95.20**	**37.27**	**0.453**
	anaemic	**23**	**86.13**	**35.15**	
P-LCR (%)	**Non-anaemic**	**15**	**37.23**	**9.06**	**0.675**
	anaemic	**23**	**35.85**	**10.29**	

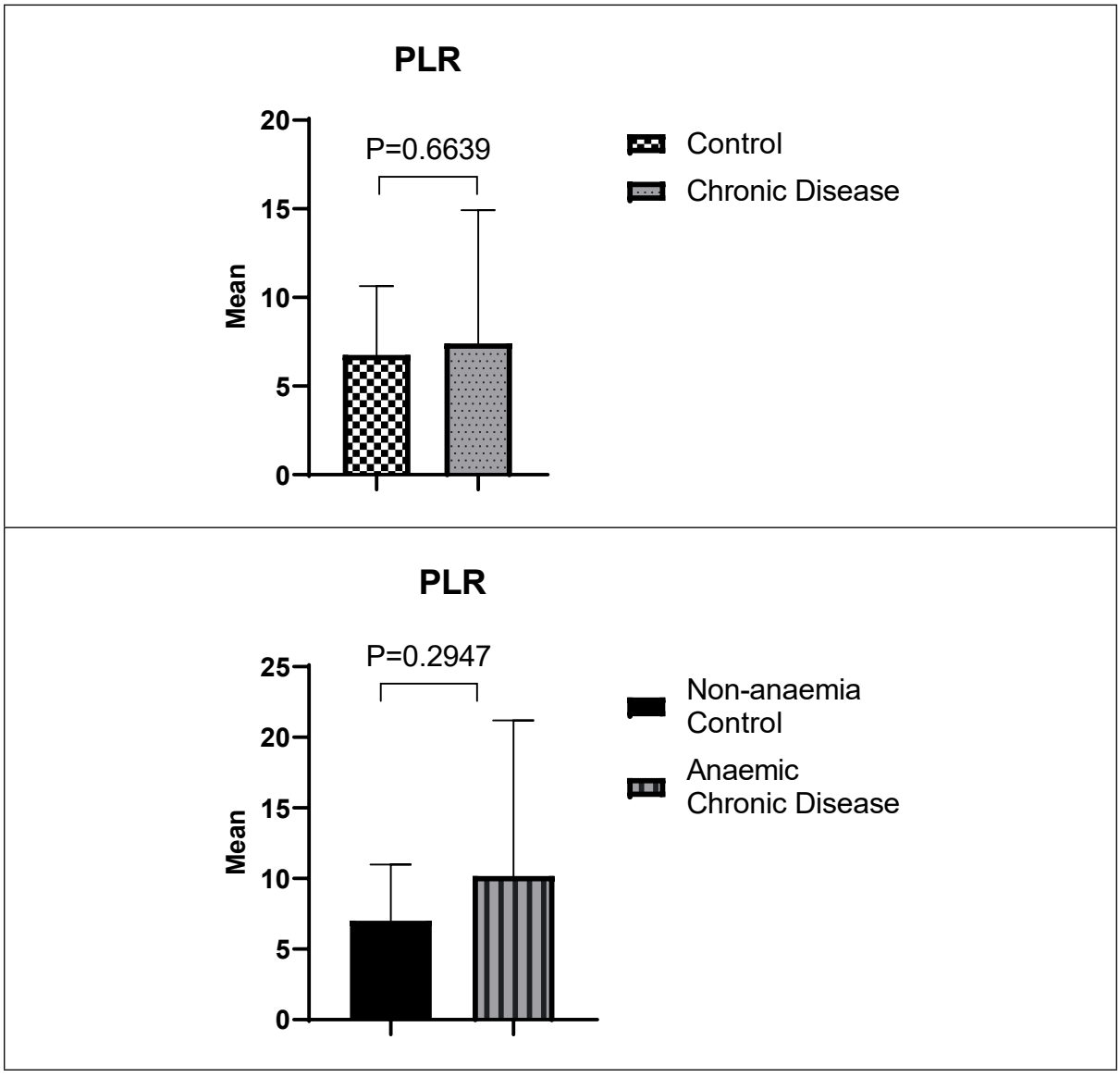
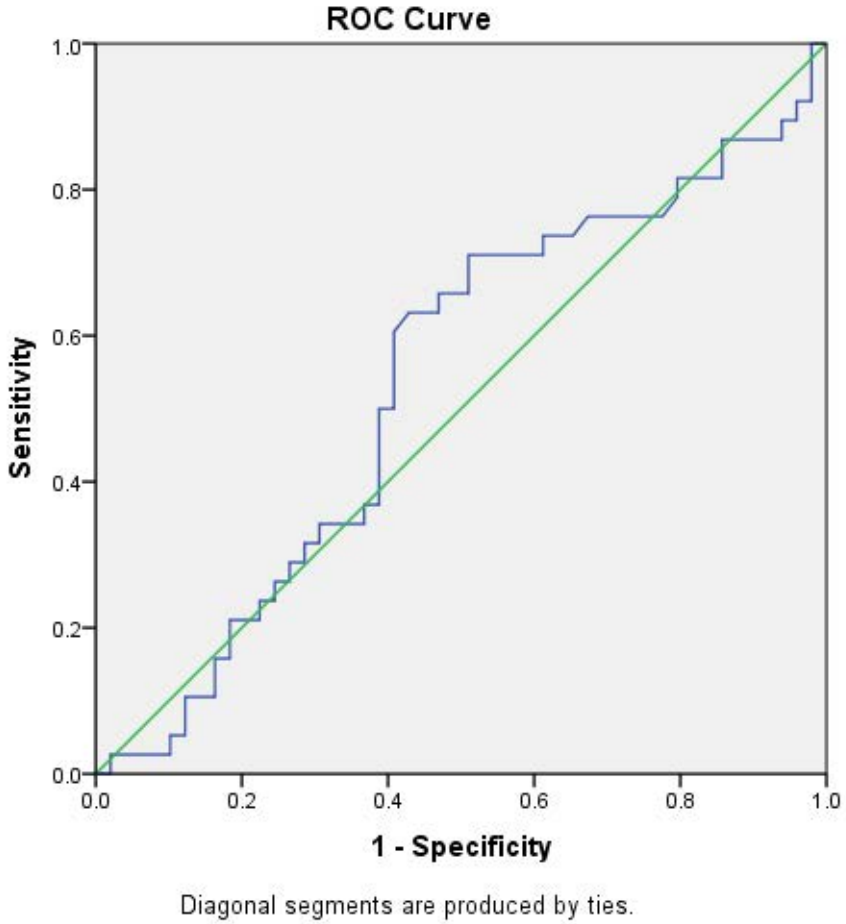


Figure 3: comparison of PLR among the study groups.



Area Under the Curve	
Test Result Variable(s)	Area
NLR	0.536

Figure 4: ROC curve indicating PLR as a diagnostic tool for Anaemia among study subjects.

DISCUSSION

The current study evaluates the predictive value of the neutrophil-lymphocyte ratio (NLR) and platelet indices in diagnosing anaemia of chronic diseases (ACD) and inflammation, comparing them with control subjects. The demographic data presented in Table 1 demonstrates a significant concentration of chronic disease diagnoses among older age groups (>46 years), particularly for HIV and chronic kidney disease (CKD). This trend is consistent with previous studies, which report that chronic diseases such as CKD, HIV, and diabetes mellitus (DM) are more prevalent in older populations due to longer exposure to risk factors and the cumulative effect of age-related declines in organ function (11). Moreover, the gender distribution, with a higher proportion of females, particularly for HIV, aligns with studies that have identified a higher

prevalence of anaemia among women with HIV due to factors such as menstruation and pregnancy (12).

The anaemia distribution, illustrated in Table 2, indicates that CKD patients exhibited the highest frequency of moderate to mild anaemia, followed by HIV patients, while no anaemia was observed among those with HBV. This aligns with the literature which has consistently shown that CKD is highly associated with anaemia due to decreased erythropoietin production and iron metabolism dysregulation (13). The absence of anaemia in HBV patients supports findings from previous research suggesting that while HBV can cause liver disease, it is less directly associated with haematological disorders compared to other chronic diseases like CKD and HIV (14).

The analysis of NLR between anaemic and non-anaemic groups did not yield statistically significant results, with p-values exceeding 0.05 (Figure 1). This lack of significance was also reflected in the comparison of NLR between chronic disease patients and control subjects. These results are consistent with several studies which suggest that while NLR can be elevated in certain inflammatory conditions, it may not always serve as a reliable marker for anaemia in chronic diseases (15).

The distribution of NLR in relation to anaemic severity (Table 3) shows no clear trend, with mild and moderate anaemia showing a higher percentage of NLR values between 1-2. This contrasts with studies that have shown a more pronounced elevation in NLR among patients with severe inflammatory responses (16). However, the absence of significant trends in NLR could be attributed to the specific chronic conditions studied here, which may not elicit the same degree of neutrophil and lymphocyte activation.

The ROC curve for NLR (Figure 2) shows an area under the curve (AUC) of 0.577, suggesting that NLR has limited power to differentiate between anaemic and non-anaemic patients. This finding is lower than AUC values reported in studies focusing on conditions like sepsis and malignancies, where NLR has been shown to have better discriminatory ability (3). The weak discriminatory power observed in this study could indicate that NLR may not be as useful in detecting anaemia of chronic disease, particularly when compared to its use in acute inflammatory or infectious states.

The comparison of platelet indices between anaemic and non-anaemic groups (Table 4) revealed no statistically significant differences. Platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) values were comparable across both groups. This is in contrast to previous research, which has found that platelet indices, particularly MPV and PDW, can be altered in conditions associated with inflammation and chronic disease (17). The lack of significant differences in the current study could be due to the specific chronic diseases being investigated, which may have a lesser effect on platelet morphology than more acute inflammatory conditions.

The ROC analysis for PLR (Figure 4) yielded an AUC of 0.536, indicating weak diagnostic power for PLR as a marker of anaemia. This result aligns with the findings for NLR and suggests that PLR may not serve as a strong predictive tool for anaemia in chronic disease populations. Similar to NLR, PLR has been shown to be more effective in acute inflammatory conditions such as infections or malignancies, where the platelet response is more pronounced (18). The chronic nature of the diseases studied here, such as HIV and CKD, may explain the limited variation in platelet indices.

The weak association of both NLR and PLR with anaemia of chronic disease in this study contrasts with previous research that has shown stronger relationships between these markers and inflammation. For instance, a study by Kocak et al. (19) demonstrated a significant elevation of NLR and PLR in patients with chronic inflammatory diseases such as rheumatoid arthritis, highlighting the role of these ratios in more overtly inflammatory conditions. The relatively modest inflammatory responses observed in chronic diseases like CKD and HIV, however, may contribute to the lack of statistical significance in the current study.

Furthermore, while platelet indices have been proposed as markers of inflammation, several studies have noted that the sensitivity of these indices can vary significantly depending on the population and disease under study. For example, in a study by Beyan et al. (6), MPV and PDW were significantly elevated in patients with inflammatory bowel disease, but similar findings were not observed in patients with CKD. This highlights the disease-specific nature of platelet responses, which may explain the lack of significant findings in this study.

CONCLUSION

This present study finds that both NLR and platelet indices, including PLR, show limited diagnostic utility as markers for anaemia of chronic disease or inflammation in the investigated population. While these markers have been shown to be valuable in acute inflammatory conditions, their effectiveness in chronic diseases appears to be more constrained. Future studies could benefit from larger sample sizes and a broader range of chronic diseases to more accurately assess the predictive value of NLR and platelet indices in these contexts.

RECOMMENDATIONS

From the findings of this study, the following recommendations are made:

Incorporation of Additional Biomarkers: Given the limited discriminatory power of NLR and PLR observed in this study, future studies should incorporate additional inflammatory and haematological biomarkers such as C-reactive protein (CRP) and ferritin. This could provide a more comprehensive assessment of the predictive capacity for anaemia in chronic diseases.

Exploration of Disease-Specific Variations: The differences in NLR and PLR between various chronic conditions such as HIV, HBV, CKD, and DM should be explored further. This would allow for the development of disease-specific predictive models for anaemia, which could improve targeted clinical interventions.

Longitudinal Studies to Track Progression: Conducting longitudinal studies could provide insights into how changes in NLR and platelet indices correlate with the progression of anaemia in patients with chronic diseases. This approach may help in early diagnosis and timely management of anaemia in these patients.

Clinical Application in Resource-Limited Settings: The potential utility of NLR and PLR as cost-effective, non-invasive screening tools for anaemia should be explored further, particularly in resource-limited settings where advanced diagnostic facilities are scarce. Future studies could focus on validating these indices in such environments to improve clinical decision-making.

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