



(RESEARCH ARTICLE)



NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF MORBIDITY AND MORTALITY IN LOW RESOURCE SETTINGS

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ABSTRACT

Background: Alternate laboratory investigations that could be used as prognosis-adjudicating tools or triage aids are either too invasive, or too expensive and therefore not fit to be used in a low-resource setting. The Neutrophil-to-lymphocyte ratio (NLR) is a simple inflammatory marker which is affordable, and can be calculated using a routine Full Blood Count. If a strong predictive effect is found using such lowly tools, it could transform the practice of medicine in the poorly served regions of Sub-Saharan Africa.

Methods: This study is a retrospective cohort study using secondary-tier healthcare data from Ughelli, Nigeria, and assesses the relationship between NLR and clinical outcomes among 213 participants. Demographic, clinical and haematological data were analysed using correlation and regression analysis. Descriptive statistics were used to summarize the demographic, clinical and haematological characteristics of the study population. Spearman's Rank Order correlation was used to assess the relationship between Neutrophil-to-lymphocyte ratio and selected clinical outcomes. The Mann-Whitney U test was used to compare Neutrophil-to-lymphocyte ratio between patients with shorter hospital stays and longer hospital stays.

Binary logistic regression was performed to determine the factors associated with prolonged hospital stay. Multiple linear regression was also used to assess whether the Neutrophil-to-lymphocyte ratio independently predicted the duration of hospital stay.

Results: The mean NLR was 2.93 ± 1.06 . NLR showed a weak positive correlation with duration of hospital stay ($r=0.149$, $p=0.030$). A one unit increase in NLR was associated with higher odds of prolonged hospital stay (adjusted OR=2.272, 95% CI: 1.349-3.826, $p=0.002$). However, NLR was not an independent predictor of the exact duration of hospital stay ($p=0.088$). The small number of deaths limited assessment of NLR as a predictor of mortality.

Conclusion: While a weak but statistically significant relationship was found between higher NLRs and increased morbidity, this relationship disappeared when controlling for confounders such as the total white blood cell count. The disappearance could suggest that patients who are judged to be very sick are either referred, or self refer to a tertiary facility. Further research into this would be potentially rewarding.

Keywords: Neutrophil; Lymphocyte; Morbidity; Mortality

1 INTRODUCTION

Neutrophils are the most abundant type of white blood cells in the human body, making up about 40% to 70% of all circulating white blood cells. [1] They act as the immune systems primary responders to infections, injuries and foreign invaders.

1.1 Neutrophils, Lymphocytes And Their Roles

Neutrophils are the most abundant type of circulating white blood cells which form an important part of the immune system. They are immediate responders to infections, injuries and diseases. Neutrophils act as the innate immune system's first line of defence via phagocytosis, granule release and extracellular trap formation. [2]

Lymphocytes are another type of white blood cells that form the backbone of the body's adaptive immune system. [3] Unlike neutrophils, lymphocytes provide a more specific defense and create a memory of pathogens in case of reoccurrence. They are the main functional cells of the immune system being responsible for the production of antibodies and direct cell mediated killing of virus. [4]

The Neutrophil-to-lymphocyte ratio is a mathematical approximation used as a clinical biomarker to measure systemic inflammation and physiological stress. Compared to other more exorbitant laboratory investigations, it can easily be calculated from a Full Blood Count which can be performed at an equivalent of \$2, making it potentially game changing for triage in developing nations. A normal Neutrophil-to-lymphocyte ratio typically ranges from 1-2 while values above 3.0 or below 0.7 indicate a pathological inflammatory state. [5]

2 METHODOLOGY

This study is a retrospective cohort study conducted across the secondary health level in Ughelli, Nigeria. Hospital records were used to assess the relationship between the Neutrophil-to-lymphocyte ratio and clinical outcomes specifically morbidity (having disease or undesirable side effect following medical treatment) [6,7] and mortality among patients in low resource settings. Research underscores that Neutrophil-to-lymphocyte ratio has great clinical value especially in developing countries like Ethiopia where there is a significant shortage of ICU, limited resources and manpower. [8] A total of 213 participants were included in the analysis. These participants had recorded haematological and clinical information such as neutrophil and lymphocyte counts which can be increased and decreased by high level of cortisol [9], total white blood cell count, packed cell volume, age, sex, and duration of hospital stay.

The participants met the inclusion criteria if they had available neutrophil and lymphocyte counts required to calculate the ratio, documented clinical and demographic information relevant to the study and a documented duration of admission in the hospital.

Participants were also excluded if they had incomplete or missing data and clinical information required for the analysis.

The clinical outcomes recorded included:

- Discharge
- Referral
- Discharge against medical advice

- Death

Duration of hospital stay was recorded in days and subsequently categorized into shorter hospital stay (less than or equal to 3 days) and longer stay (greater than or equal to 4 days).

The Neutrophil-to-Lymphocyte Ratio was calculated by dividing the neutrophil count by the corresponding lymphocyte count. The calculated values were used in assessing the relationship between the Neutrophil-to-lymphocyte ratio and duration of hospital stay. The main independent variable in the study was the neutrophil-to-lymphocyte ratio and the major clinical outcomes was duration of hospital stay.

Descriptive statistics were used to summarize the demographic, clinical and haematological characteristics of the study population.

Continuous variables were presented using mean and standard deviations, while categorical variables were presented as frequencies and percentages.

Spearman's Rank Order correlation was used to assess the relationship between Neutrophil-to-lymphocyte ratio and selected clinical outcomes.

The Mann-Whitney U test was used to compare Neutrophil-to-lymphocyte ratio between patients with shorter hospital stays and longer hospital stays.

Binary logistic regression was performed to determine the factors associated with prolonged hospital stay. Adjusted odd ratios with 95% confidence intervals were reported.

Multiple linear regression was also used to assess whether the Neutrophil-to-lymphocyte ratio independently predicted the duration of hospital stay as a continuous variable.

3 RESULT

Table 1: Socio-demographic and clinical characteristics of the study population (n = 213)

Variables	Frequency (n)	Percent (%)
Age (years)		
<25	61	28.6
25-44	113	53.1
45-64	29	13.6
>64	10	4.7
Mean age	33.54±14.23	
Sex		
Male	90	42.3
Female	123	57.7
Diagnostic category		
Infectious Diseases	62	29.1
Obstetric/Gynaecological	41	19.2
Trauma/Injury	29	13.6
Neurological/Cerebrovascular	23	10.8
Gastrointestinal	21	9.9
Toxicological/Substance-related	8	3.8
Cardiovascular/Hypertensive	6	2.8
Haematological	5	2.3

Respiratory	3	1.4
Endocrine/Metabolic	3	1.4
Psychiatric/Self-harm	3	1.4
Wound/Diabetic complications	3	1.4
Musculoskeletal/Spinal	2	0.9
Surgical	2	0.9
Urological	1	0.5
Hepatic	1	0.5
Comorbidity		
No comorbidity	197	92.5
Hypertension	9	4.2
Diabetes Mellitus	4	1.9
HIV	1	0.5
Diabetes + Hypertension	1	0.5
Hepatitis C	1	0.5
Outcome		
Discharged	178	83.6
Referred	18	8.5
DAMA	15	7
Death	2	0.9
Duration of stay	.	
Shorter stay (≤ 3 days)	177	83.1
Longer stay (≥ 4 days)	36	16.9

Table 1 shows the frequency and percentage distribution of the study population with respect to their socio-demographic and clinical characteristics. More than half of the study population, 113 (53.1%), were aged 25–44 years, with a mean age of 33.54 ± 14.23 years. Females constituted the majority of the study population, 123 (57.7%), while 90 (42.3%) were males. Infectious diseases constituted the largest proportion of the diagnostic categories, 62 (29.1%), followed by obstetric/gynaecological conditions, 41 (19.2%), and trauma/injury, 29 (13.6%). Most of the study population, 197 (92.5%), had no documented comorbidity, while hypertension was the most common comorbidity, occurring in 9 (4.2%) participants. The majority of the study population, 178 (83.6%), were discharged, while 18 (8.5%) were referred, 15 (7.0%) left against medical advice (DAMA), and 2 (0.9%) participants died. Regarding length of hospital stay, the majority, 177 (83.1%), had a shorter stay (≤ 3 days), while 36 (16.9%) had a longer stay (≥ 4 days).

Table 2: Haematological and clinical characteristics of the study population (n = 213)

Parameters	Minimum	Maximum	Mean	SD
Packed cell volume (%)	15.00	47.00	33.66	5.34
Total WBC count (mm^3)	7000.00	15500.00	9630.52	1474.20
Neutrophil count (%)	50.00	80.00	70.04	6.76
Lymphocyte count (%)	10.00	45.00	26.27	6.89
Neutrophil-to-lymphocyte ratio	1.11	8.00	2.93	1.06
Duration of stay (days)	1	28	2.44	2.90

Table 2 shows the descriptive statistics of the haematological and clinical characteristics of the study population. The mean packed cell volume was $33.66 \pm 5.34\%$, while the mean neutrophil and lymphocyte counts were $70.04 \pm 6.76\%$ and $26.27 \pm 6.89\%$, respectively. The mean total white blood cell count was $9,630.52 \pm 1,474.20$ cells/ μL , while the mean neutrophil-to-lymphocyte ratio was 2.93 ± 1.06 . The duration of hospital stay ranged from 1 to 28 days, with a mean duration of 2.44 ± 2.90 days.

Table 3: Spearman's rank-order correlation between NLR and selected clinical and haematological variables (n = 213)

Variable	NLR	Duration of Stay	Total WBC Count	PCV	Age
NLR	1.000	0.149*	0.770	-0.068	-0.273
Duration of Stay	0.149*	1.000	0.049	-0.133	-0.096
Total WBC Count	0.770	0.049	1.000	-0.103	-0.215
PCV	-0.068	-0.133	-0.103	1.000	0.215
Age (years)	-0.273	-0.096	-0.215	0.215	1.000

*p < 0.05.

Spearman's rank-order correlation analysis demonstrated a weak but statistically significant positive correlation between neutrophil-to-lymphocyte ratio (NLR) and duration of hospital stay ($p = 0.030$), indicating that higher NLR was associated with longer duration of hospital stay. NLR also demonstrated a strong positive correlation with total white blood cell count ($p < 0.001$) and a weak-to-moderate negative correlation with age ($p < 0.001$). No statistically significant correlation was observed between NLR and PCV ($p = 0.322$).

Table 4: Comparison of neutrophil-to-lymphocyte ratio according to duration of hospital stay (n=213)

Duration of hospital stay	Median (IQR) of NLR	Mean Rank	Mann-Whitney U	Z	p-value
Shorter stay (≤ 3 days)	2.69 (2.10–3.80)	103.84	2626.5	-1.661	0.097
Longer stay (≥ 4 days)	2.79 (2.44–3.93)	122.54			

The median NLR was slightly higher among patients with a longer hospital stay (2.79, IQR: 2.44–3.93) compared with those with a shorter stay (2.69, IQR: 2.10–3.80). However, the difference was not statistically significant (Mann-Whitney U = 2626.50, Z = -1.661, $p = 0.097$). This finding indicates that NLR does not significantly distinguish patients with shorter (≤ 3 days) from longer (≥ 4 days) hospital stays.

Table 5: Binary logistic regression analysis of factors associated with prolonged hospital stay

Predictor	B	SE	Wald	p-value	Adjusted OR	95% CI for OR
NLR	0.821	0.266	9.526	0.002	2.272	1.349–3.826
Age (years)	-0.012	0.015	0.651	0.421	0.988	0.958–1.018
Total WBC count	-0.001	0.000	6.069	0.014	0.999	0.999–1.000
PCV	-3.406	3.932	0.750	0.386	0.033	0.000–73.788
Sex (male vs female)	-0.754	0.458	2.710	0.100	0.470	0.192–1.154
Constant	3.146	2.372	1.758	0.185	23.242	—

Table 5 shows the binary logistic regression analysis of factors associated with prolonged hospital stay. NLR was significantly associated with prolonged hospital stay. For each one-unit increase in NLR, the odds of having a hospital stay of ≥ 4 days increased by approximately 2.27-fold (adjusted OR = 2.272, 95% CI: 1.349–3.826, $p = 0.002$), after adjusting for age, total white blood cell count, PCV and sex. Total white blood cell count was also statistically significant ($p = 0.014$), although its odds ratio was very close to 1. Age, PCV and sex were not statistically significant predictors of prolonged hospital stay ($p > 0.05$).

Table 6: Multiple linear regression analysis of factors associated with duration of hospital stay

Predictor	B	β	t	p	95% CI
NLR	0.438	0.159	1.714	0.088	–0.066 to 0.942
Age	0.004	0.022	0.315	0.753	–0.024 to 0.033
Total WBC	~0.000	–0.072	–0.771	0.441	–0.001 to 0.000
PCV	0.023	0.016	0.229	0.819	–0.178 to 0.225

NLR was not an independent statistically significant predictor of duration of hospital stay after adjustment for age, total WBC count, and PCV.

4 DISCUSSION

The study found a weak positive relationship between NLR and duration of hospital stay. Higher NLR was associated with increased odds of prolonged hospitalisation, suggesting that NLR may be a useful marker of disease severity. However, NLR was not an independent predictor of the exact duration of hospital stay, especially when confounders like the total white blood cell count were accounted for. The small number of deaths that occurred also limited assessment of its relationship with mortality. This pseudo-Berksonian bias is likely due to patients with greater morbidity removing themselves from the inclusion parameters and presenting at a tertiary facility. A larger, multicenter tertiary staged review would be ideal in deciphering if there is any juice worth the squeeze in using the Neutrophil-to-lymphocyte ratio as a prognostic and triage tool.

4.1 Clinical implications of an elevated Neutrophil-to-lymphocyte ratio

In a hospital or outpatient setting, a persistently elevated NLR could serve as an early warning prognostic beacon across several major categories of medicine. It signals a highly aggressive, potentially dysregulated response to an invading pathogen while in cardiovascular disease, it is a proxy for vascular inflammation, reflecting endothelial dysfunction and plaque instability.[10,11]

4.2 Limitations of The Study

The small number of deaths recorded made it difficult to properly assess whether Neutrophil-to-lymphocyte Ratio was associated with mortality.

Although NLR was associated with prolonged hospitalisation in the logistic regression, the multiple linear regression found that it did not independently predict the exact duration of stay.

Participants with incomplete or missing data were excluded. This could potentially affect how representative the final 213 participants were of the broader patient population.

5 CONCLUSION

While a weak but statistically significant relationship was found between higher NLRs and increased morbidity, this relationship disappeared when controlling for confounders such as the total white blood cell count. The disappearance could suggest that patients who are judged to be very sick are either referred, or self refer to a tertiary facility. Further research into this would be potentially rewarding.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors, Mojekwu Elochukwu John, Anayo Stellamaris Adaobi, Emedo Okechukwu Charles, Unini Collins Kelechi, Emenuga Chisom Olivia, Fab-Emerenini Eziokwu Bright, Owulezi Chigozie Leonard, and Anisiobi Promise Ugochukwu have no conflicts of interest regarding the study.

Statement of Informed Consent

Informed consent was obtained from all participants prior to data collection. To ensure confidentiality, all personal identifiers were removed from the dataset, and the study adhered to the ethical principles of the Declaration of Helsinki.

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