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Neutrophil to Lymphocyte Ratio as a Predictor of Outcomes in Orofacial Infections in Patients Admitted to Kenyatta National Teaching and Referral Hospital in Nairobi, Kenya

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Abstract

Background: Untreated and progressive orofacial infections pose a great health risk due to local and distant spread, which often leads to increased morbidity and mortality. These infections can be of either odontogenic or non-odontogenic origin. Early definitive diagnosis allows for early intervention, thereby ultimately reducing the associated morbidity and mortality. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are the most commonly used markers of severity, prognosis and treatment response of severe orofacial infections in our setup. The neutrophil to lymphocyte ratio (NLR) has been demonstrated to be a useful, inexpensive diagnostic and prognostication tool in infections in other parts of the body. Its utility in orofacial infections remains largely unexplored. **Aim**: To determine the utility of NLR as an independent predictor of outcomes in orofacial infections. **Design**: This was a cross-sectional study carried out in patients admitted with orofacial infections to the oral & maxillofacial, otorhinolaryngology and ophthalmology clinics at the Kenyatta National Teaching and Referral Hospital (KNH) in Nairobi, Kenya between November 2023 and July 2024. **Methods**: Demographic and relevant clinical data were obtained from consenting eligible patients at admission. The values of the absolute counts of neutrophils, lymphocytes and C-reactive proteins were also obtained, and the Neutrophil-Lymphocyte Ratio (NLR) calculated. Length of hospital stay, admission to intensive care unit

(ICU) and mortality were recorded. The Mann Whitney U test was used to establish whether there was a significant difference in NLR and CRP among outcomes. Spearman rank order correlation was used to establish the relationship between NLR values and length of stay. **Results**: Only 80 patients were recruited into the study. The participants ranged form <5 to >60 year with an interquartile range of 33.8 years and a median age of 26.3 years. Most participants were male (71.2%, n = 57). NLR was significantly associated with the length of hospital stay with a p-value of 0.029 before adjustment. Participants with normal NLR had 8.21 times higher odds of disease resolution compared to those with abnormal. **Conclusion**: NLR had a significant association with mortality and disease severity and was comparable to CRP in ability to predict disease outcomes in orofacial infections. Participants with resolved disease had significantly lower levels of NLR compared to those who were admitted to the ICU. Similarly, participants who died or were admitted to the ICU had significantly higher levels of CRP compared to those with resolved disease. NLR can be an easily accessible and good predictor of disease outcomes.

Keywords

Neutrophil Lymphocyte Ratio, C-Reactive Protein, Orofacial Infections

1. Introduction

Orofacial infections are infections arising from the oral cavity and face. They are either odontogenic or non-odontogenic in origin, with the vast majority being bacterial in nature. Orofacial infections are of particular concern because severe infections are prone to spread locally and regionally through fascial spaces of the head and neck, and haematogenous spread leading to systemic infection. Untreated severe orofacial infections have high morbidity and mortality. Rapid diagnosis, patient assessment and institution of definitive treatment are therefore important in ensuring positive treatment outcomes.

Neutrophils form part of the innate immune system and are the most abundant granulocytes accounting for 50% - 70% of all white blood cells. They are phagocytic and are the hall mark of acute inflammation, being among the first responders to the site of inflammation through chemotaxis, especially in bacterial infection [1] [2]. Neutrophil to lymphocyte ratio (NLR) is used in clinical practice to evaluate systemic inflammation. It is elevated in certain conditions and has been found to be a valuable predictor of outcomes in a variety of diseases including cardiovascular disease, pulmonary arterial hypertension, schizophrenia, and hearing loss [3] [4].

Whereas C-Reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin have been used routinely as inflammatory markers and prognostic indicators, NLR has not gained popularity in clinical practice, more so in orofacial infections. NLR is calculated from the absolute values of neutrophils and lympho-

cytes obtained from full blood count by dividing neutrophil count by lymphocyte count. This eliminates the need for additional test requests as would be necessary for CRP, ESR or procalcitonin levels. The ratio has been used to prognosticate mortality, progression to severe disease, increased odds and duration of intubation, risk of severe disease in intubated patients, and the need for intensive care [5].

The NLR ratio has been used to predict mortality, with specificity and sensitivity comparable to that of CRP and ESR in conditions such as pneumonia, cancer and sepsis [6]. In the head and neck region, NLR has been successfully used in the management of malignancies to demonstrate the association between chemoradiation therapy and the development of grade three mucositis [7] [8]. Increased NLR has also been associated with increased length of hospital stay and duration of antimicrobial treatment in infections. Conversely, it has been shown to decrease to values approaching those of normal persons after successful treatment for infection [9] [10].

2. Methodology

This was a cross-sectional study on NLR as a predictor of outcomes in patients with orofacial infections at the Kenyatta National Teaching and Referral Hospital (KNH) in Nairobi, Kenya. Patients with a diagnosis of orofacial infections and a pre-treatment full blood count available were recruited between November 2023 and July 2024. Information on participant demographics, diagnosis, prior antibiotic use, and comorbidities was recorded. Pretreatment values of absolute neutrophil, lymphocyte counts, as well as CRP were recorded. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The cut off for NLR was set at 2, with values above this being considered abnormal. The outcome of the treatment in terms of hospital stay, admission to the ICU or mortality was recorded at the time of discharge.

The data were analysed with R version 4.1.2. Normality was assessed using the Shapiro-Wilk test. Continuous data were described using mean and standard deviation, and median and interquartile range. Categorical data were summarised using frequencies and proportions. The Kruskal-Wallis test was used to establish any significant difference in NLR among the various outcomes. Spearman rank order correlation was used to establish the relationship between NLR values with the recorded length of hospital stay. Mortality was expressed both as an absolute count and as a proportion by dividing the number of deaths by the sample size. Logistic regression was used to assess whether NLR was associated with the outcomes. A p-value of less than 0.05 was considered statistically significant.

3. Results

Out of 135 patients with orofacial infections 80 met the inclusion criteria and were recruited into the study. Of the 80 participants, 17 (21.2%) were under 5 years of age, 13.7% (11) were aged 6 - 17 years, 32.5% (26) were aged 18 - 35years, 21

(26.3%) were 36 - 60 years, and 5 (6.3%) were more than 60 years old. Most of the participants were male (71.2%, n = 57) (Table 1).

Table 1. Sociodemographic characteristics.

Characteristics	Description	Frequency (n = 80)	Percent
Age in years	Under 5	17	21.2
	6 to 17	11	13.7
	18 to 35	26	32.5
	36 to 60	21	26.3
	>60	5	6.3
Gender	Female	23	28.8
	Male	57	71.2

3.1. Diagnoses among Participant with Orofacial Infections

The most frequent diagnosis among the study participants was Ludwig's angina with 17 participants (21.3%), followed by orbital and periorbital infections (20.0%, 16). Other diagnoses included 11 cases of submandibular abscess, 5 of necrotizing fasciitis, 3 mental abscesses, 2 peritonsillar abscesses, and 2 parotid abscesses.

Ludwig's angina and orbital/periorbital infections were the most frequent lesions, with 17 (21.3%) and 16 (20%) participants respectively. Submandibular abscesses were the third commonest lesion with 11 participants (13.8%). Other lesions included necrotizing fasciitis, and mental, peritonsillar and parotid abscesses (Table 2).

Table 2. Diagnoses among patients with orofacial infections.

Diagnosis	Frequency (n = 80)	Percent
Ludwig's angina	17	21.3
Impending Ludwig's angina	11	13.8
Submandibular abscess	11	13.8
Orbital and Periorbital infections	16	20.0
Necrotizing fasciitis	5	6.3
Submental abscess	3	3.8
Parotid abscess	2	2.5
Retropharyngeal abscess	2	2.5
Dentoalveolar abscess	2	2.5
Peritonsillar abscess	3	3.8
Acute rhinosinusitis with left eye cellulitis	1	1.3
Canine and buccal space abscess	1	1.3
Deep neck spaces infection, empyema thoracis, sepsis with acute kidney injury	1	1.3
Fronto temporal abscess	1	1.3

Continued

Necrotic tongue	1	1.3
Retropharyngeal abscess with mediastinum involvement	1	1.3
Rhino sinusitis with orbital complications	1	1.3
Right Canine space and periorbital abscess with diabetic ketoacidosis	1	1.3

3.2. Haematological Profiles of the Study Participants

Majority of the participants (73.8%, n = 59) had elevated white blood cells (WBC). Two thirds (68.8%, n = 55) had elevated neutrophil count of more than 7 mm^3 cells/L (normal range 2 - 7 mm^3 cells/L). Three fifths of the participants (61.2%, n = 49) had normal lymphocyte levels, while a fifth (20%, n = 16) had low count and just under a fifth (15 participants, 19%) had elevated counts above 4 (normal range 0.8 - 4^9 cells/L). Almost all the participants who had CRP readings available (94.1%, 48 out of 51) had elevated CRP levels (Table 3).

Table 3. Haematological characteristics of the study participants (n = 80).

Blood type	Description	Frequency (%)
White blood cells (mm^3)	4.0 to 10/mm^3	21 (23.3%)
	>10/mm^3	59 (73.8%)
Neutrophil count (%)	<2	2
	2 - 7	23 (28.8%)
	>7	55 (68.8%)
Lymphocytes (%)	<0.8	16 (20%)
	0.8 - 4	49 (61.2%)
	>4	15 (18.8%)
C-reactive protein (CRP) at Admission		
CRP (mg/dL)	≤4.0	3
	>4.0	48 (94.1%)

3.3. NLR and Its Association with the Length of Hospital Stay

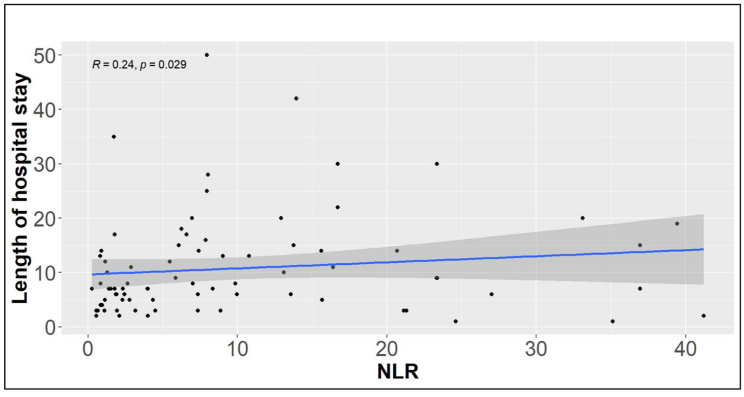

Figure 1. Correlation between NLR and the length of hospital stay.

The median NLR from this study was 6.43 with an interquartile range of 1.94 to 13.81. The minimum and maximum NLR observed were 0.27 and 41.20, respectively. The results from this study showed a weak positive correlation between NLR and the length of hospital stay with a Spearman correlation coefficient of r_s (78) = 0.24, (p-value = 0.029) (Figure 1).

3.4. Association between the NLR and Mortality

Ten deceased participants (12.5.%) had a slightly higher NLR than the survivors, although Wilcoxon signed-rank test was not statistically significant (W = 0.051, z = +1.94, p = 0.051, n = 80) (Figure 2).

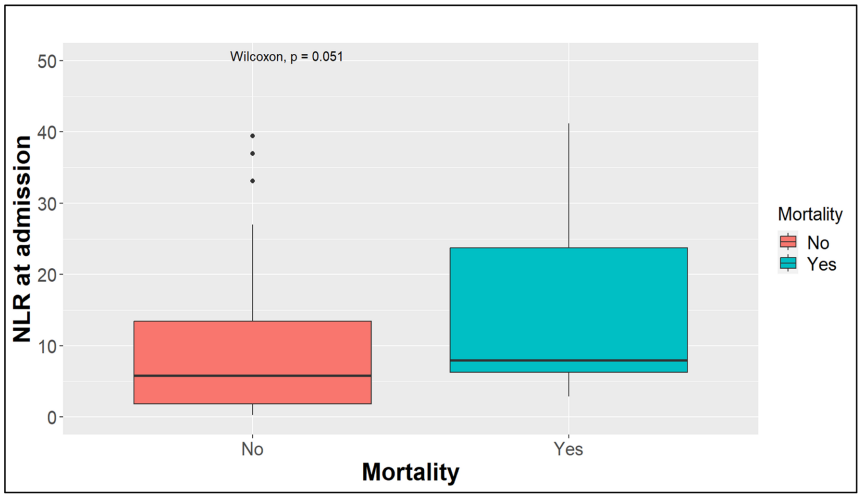

Figure 2. Association between NLR and mortality.

3.5. Association between the NLR and Other Outcomes

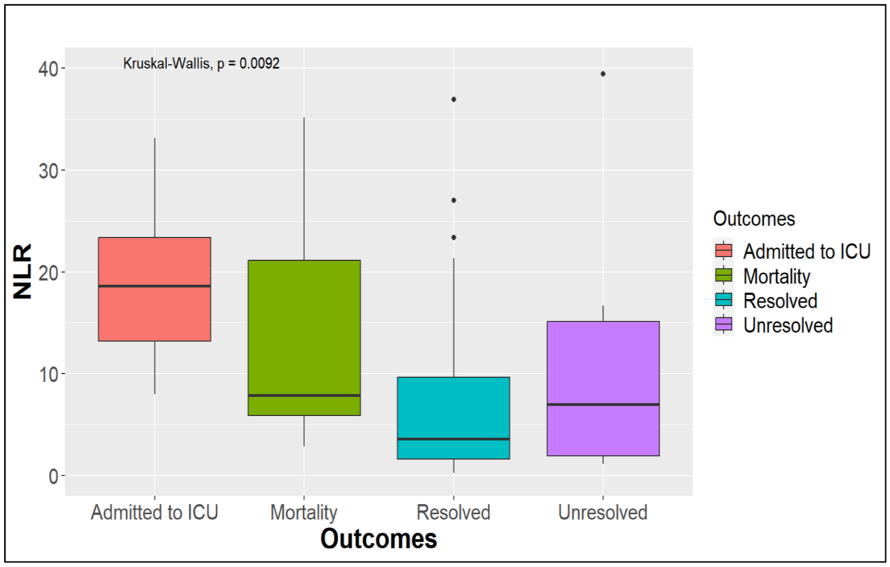

Figure 3. Association between NLR and the various outcomes among patients with orofacial infections.

Kruskal-Wallis test (H = 49, p-value = 0.0092 d f = 4) showed that there was significant difference in NLR among the outcomes of unresolved disease (admission to the intensive care unit and/or mortality), and resolved disease (Figure 3). To identify the significant outcome from the results obtained by Kruskal Wallis test, a pairwise comparison test was done using the Tukey test, which showed a significant difference in NLR between admission to the intensive care unit (ICU) and resolved disease (p-value = 0.039).

3.6. Association between C-Reactive Protein and Outcomes

There was a significant difference in the CRP levels in at least one outcome of participants with orofacial infections from Kruskal Wallis test (H = 49, p-value = 0.011). To determine the outcomes with significant differences, a pairwise comparison using the Tukey test revealed substantial differences in CRP levels between admission to the ICU and resolved disease, and mortality and resolved disease with p-values of 0.042 and 0.004 respectively (Table 4).

Table 4. Pairwise comparison of differences between outcomes of patients with orofacial infections and C-reactive proteins.

Outcomes	P value
Unresolved-Resolved	0.117
Admitted to ICU-Resolved	**0.042**
Mortality-Resolved	**0.004**
Admitted to ICU-Unresolved	0.874
Mortality-Unresolved	0.492
Mortality-Admitted to ICU	0.943

3.7. NLR and CRP Utility in Predicting Outcomes of Orofacial Infections

Neither CRP nor NLR was significantly associated with mortality. However, the logistic regression test showed that patients with normal NLR had 82% lower odds of mortality compared to those with abnormal NLR (Table 5).

Table 5. Association between mortality and CRP/NLR.

		Mortality			
Predictor	Description	No	Yes	Adjusted OR (95% CI)	P value
C-reactive protein	Abnormal	41	7	Reference	
	Normal	3	0	NA	0.997
NLR	Abnormal	44	9	Reference	
	Normal	26	1	0.18 (0.01, 1.05)	0.123

3.8. Length of Hospital Stay

A multiple linear regression to determine whether there was an association between NLR and CRP levels versus the length of hospital stay. The results revealed no association between the two predictor variables and the length of hospital stay. From the odds ratio, the data showed that one unit increase in CRP increased the length of hospital stay by 3% while one unit increase in NLR increased the length of hospital stay by 10%. Under bivariate analysis, there was a significant positive relationship between NLR and the length of hospital stay ($p < 0.05$) (**Table 6**).

Table 6. Neutrophil to lymphocyte ratio and C-reactive protein utility in predicting outcomes of orofacial infections.

Variable	Adjusted OR (95% CI)	P value
C-reactive protein	1.03 (1.00, 1.06)	0.064
NLR	0.90 (0.69, 1.18)	0.453

4. Discussion

The finding that male participants were the most affected by orofacial infections is in agreement with two studies but contradicts another study that showed no gender predilection [11]-[13]. The observation of a significant proportion of young adults with orofacial infection has been reported elsewhere [11]. Literature posits that men are generally more prone to neglecting their oral health, maintaining poorer oral hygiene, facing higher rates of periodontal disease, and sustaining dental injuries. In contrast, women typically have more positive attitudes towards dental visits, possess greater oral health literacy, and engage in better oral health practices [14]. Mortalities higher in male participants, agrees with Omeje *et al.*, 2016 where 73.1% of the mortalities were men [11]. The foregoing observation fits well in the explanations given by behavioural models on health-seeking behaviour between males and females, where females have better health-seeking behaviour and practices, thus seek intervention early and prevent progression of disease in early stages. The findings that the most common comorbidities associated with orofacial infections were diabetes mellitus, HIV, and hypertension match those of Shweta *et al.* [15].

The findings on the WBC, neutrophils, and CRP are consistent with existing knowledge that they tend to increase during an infection [16]. Length of hospital stay among participants with orofacial infections was significantly associated with increase in NLR. In agreement with the current study, a systematic review of NLR in patients with odontogenic infections revealed that an increase in the ratio was significantly associated with longer duration of hospital stay in addition to more severe disease and the need for higher doses of antibiotics after surgery [17] [18]. These findings are supported by others who have reported a significant association in length of hospital stay among patients with higher levels of NLR [9] [19] [20]. During bacterial infections, the body's inflammatory response is marked by

an increase in neutrophils and a relative decrease in lymphocytes. This shift in balance between inflammatory cells is reflected in the NLR, a reliable indicator for diagnosing bacterial infections. The more severe the infection, the longer the hospital stay, and the higher the values will be in the laboratory tests [21]. This study showed that admission to the intensive care unit (ICU) was associated with higher levels of NLR. There was a statistically significant difference in NLR in the disease outcomes (ICU admission, mortality), indicating a strong association. The finding that the lowest NLR levels were associated with disease resolution is corroborated by other authors, as is the finding that higher NLR indicates more severe disease [21]. Higher levels of NLR have been associated with more severe disease, which can then explain the increase in mortality with higher levels of NLR [14] [18].

The current study did not reveal a significant association between mortality and NLR, probably due to a smaller sample size compared to other studies [14] [18], although this study showed that participants with normal NLR had lower odds of mortality compared to those with abnormal NLR, in line with findings elsewhere that NLR can significantly predict mortality among patients with odontogenic infections [18]. The lack of significance in the current study could be due to a low sample size.

The current study revealed a significant difference in NLR between participants who died and those with resolved disease among participants with orofacial infections. Similarly, CRP was also significantly different between participants who died or were admitted to the ICU and those with resolved disease. Participants with normal NLR of 2 had significantly higher odds of disease resolution compared to those with abnormal NLR. It can therefore be deduced that NLR is as good as CRP in predicting outcomes in orofacial infections, which is the standard of care in our setup. In fact, this study has shown that NLR is an independent predictor of disease resolution in orofacial infections.

5. Conclusion

NLR had a significant association with mortality and disease severity and was comparable to CRP in ability to predict disease outcomes in orofacial infections. Participants with resolved disease had significantly lower levels of NLR compared to those who were admitted to the ICU. Similarly, participants who died or were admitted to the ICU had significantly higher levels of CRP compared to those with resolved disease. NLR can be an easily accessible and good predictor of disease outcomes.

Ethical Approval and Consent to Participate

The study protocol had ethical approval from the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee (No. P591/07/2023). Permission to conduct the study was obtained from the management of Kenyatta National Hospital. Informed consent was obtained from the participants at admission and where the participant was a minor, consent was obtained from the parent

or the guardian.

Conflicts of Interest

The authors declare that they have no competing interest.

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