

Neutrophil: Lymphocyte ratio and oral squamous cell carcinoma: A preliminary study

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Abstract

Introduction/Background: It is well-established that host response plays a vital role in the determination of biological behavior of tumors. Inflammatory response against tumors has been a focus of research in recent years. There has been extensive research regarding inflammatory reaction in oral squamous cell carcinoma (OSCC) in tissue specimens. However, there is no much data regarding systemic inflammatory response in OSCC. It was recently reported that an elevated neutrophil:lymphocyte ratio (NLR) may correlate with aggressive biological behavior in various malignancies including head-and-neck tumors. Thus, the study was undertaken with the aim of evaluation of NLR in peripheral blood of patients suffering from OSCC.

Materials and Methods: The research was a prospective, case-control study. Hundred patients suffering from OSCC and 100 healthy individuals were included in the study, after obtaining informed consent. NLR was determined from the differential leukocyte count obtained from complete blood count in each case. Comparison of NLR was made among two groups.

Results: The mean value of absolute neutrophil count was found to be significantly higher in OSCC cases than in controls ($P < 0.01$). The mean value of NLR in OSCC was found to be 2.84, and in controls, it was 1.95. This difference was found to be statistically significant ($P < 0.001$).

Conclusion: NLR and other hematological parameters may serve as surrogate marker for potential aggressive behavior of OSCC and may help in prognostic prediction of these cases.

Keywords: Behavior, carcinoma, neutrophil: lymphocyte ratio, oral, prognosis

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common cancers worldwide. Despite the availability of promising treatment modalities, the overall 5-year survival rate of these patients is not improved. Locoregional metastasis further decreases the survival rate.^[1]

It is well established that host response plays a vital role in the determination of biological behavior of tumors. There has been extensive research regarding the local inflammatory reaction in OSCC, in tissue specimens.^[1] However, there is no much data regarding systemic inflammatory response to OSCC. It is recently hypothesized that an elevated neutrophil:lymphocyte ratio (NLR) may correlate with

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aggressive biological behavior in various malignancies including head-and-neck tumors.^[2]

The inflammatory reaction against tumor increases angiogenesis, brings about DNA damage and prevents apoptosis and thus facilitates the proliferation of tumor cells and increases the potential for metastasis. Recent studies have shown correlations between the degree of systemic inflammatory response and outcomes in various tumors.^[3] NLR is a validated marker of systemic inflammation. Published data suggest that an elevated preoperative NLR may correlate with an increased risk of recurrence, tumor aggressiveness, poorer prognosis, propensity for metastasis and death in various malignancies such as ovarian tumors, breast cancer and laryngeal squamous cell carcinomas (LSCCs).^[3]

In a study on pretreatment NLR in epithelial ovarian cancer with patients of benign ovarian tumors, benign gynecological disease and healthy controls, it was found that preoperative NLR in ovarian cancer participants was significantly higher than that in benign ovarian tumor participants, benign gynecologic disease participants and healthy controls.^[4] In a study conducted to evaluate the usefulness of the NLR in predicting short- and long-term mortality in breast cancer patients, it was found that patients in the highest NLR quartile had higher 1- and 5-year mortality rates compared with those in the lowest quartile, thereby indicating that NLR is an independent predictor of short- and long-term mortality in breast cancer patients.^[5]

In a previous study to evaluate whether NLR could be used as an inflammatory marker to differentiate LSCC patients from benign laryngeal lesion (BLL) and precancerous laryngeal lesion (PLL) patients, it was found that of paired comparisons made to determine the group that caused the difference, the mean NLR of the patients with PLL and LSCC was significantly higher than the patients with BLL. It was contemplated that NLR is an inexpensive, reproducible and widely available blood test, and it could be a useful inflammatory marker to differentiate LSCC patients from BLL and PLL patients.^[3]

Despite many studies on NLR in various tumors, very few studies have been done in OSCC. The current study was undertaken with the aim of evaluation of NLR and other hematological parameters such as hemoglobin percentage, absolute neutrophil count and absolute lymphocyte count in peripheral blood of patients suffering from OSCC to evaluate the usefulness of NLR as a prognostic biomarker in OSCC. Despite routine blood investigations and complete blood count taken in OSCC patients before

biopsy, very few studies have been done to evaluate the ratio of blood cells (NLR), so as to correlate and evaluate its usefulness as a biomarker. The objectives of the present study were to assess the NLR and to find the relationship between NLR and severity of malignancy so as to evaluate if it could be used as a prognostic biomarker.

MATERIALS AND METHODS

The study was undertaken as a prospective, case-control study. The study protocol was approved by the Institutional Ethical Committee. Patients with clinical suspicions of OSCC were subjected to the evaluation of complete blood count and incisional biopsy with informed consent. Thus, 100 histopathological proved cases of OSCC were included in the study. The patients with conditions such as autoimmune, acute or chronic infectious diseases, hematological disorders, history of corticosteroid therapy or chronic renal insufficiency and recurrence cases of OSCC were excluded from the study. NLR was obtained by the examination of peripheral blood smear in each case. The blood was collected from the median cubital vein with aseptic technique. The differential leukocyte count was obtained by the examination of peripheral blood smears stained with Field's stain. From the differential counts, absolute counts were obtained for neutrophils and lymphocytes and NLR was calculated for each case thereafter. Hundred healthy individuals were selected as controls and NLR was calculated in each case of control group by the above-mentioned method. Independent *t*-test and Chi-square test were used for statistical analysis.

RESULTS

The current study was undertaken with an aim to evaluate whether there is any significant difference between NLR in cases of OSCC and controls and to find out if NLR may correlate with aggressive behavior of OSCC. A total of 200 individuals were included in the study, 100 cases of OSCC and 100 healthy controls. The Chi-square test showed that OSCC occurs more significantly in males than in females ($P < 0.08$) [Figure 1]. The mean white blood cell count was higher in OSCC cases than in controls. The hemoglobin percentage was found to be higher in controls than in OSCC cases [Figure 2]. The mean value of absolute neutrophil count was found to be significantly higher in OSCC cases than in controls ($P < 0.01$). However, the differences between mean values of absolute lymphocyte count of two groups were not statistically significant ($P = 0.035$) [Table 1]. The mean value of NLR in OSCC was found to be 2.84, and in controls, it was 1.95. This difference was found to be statistically

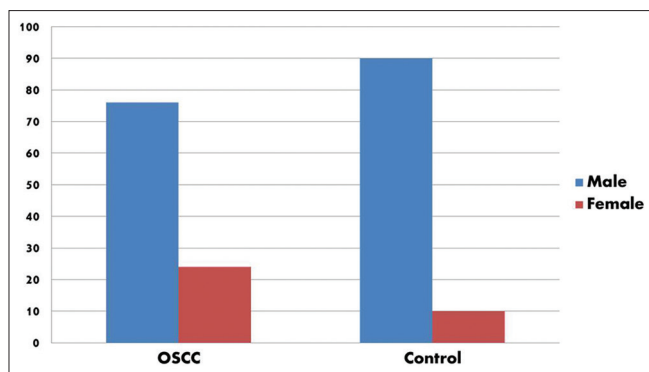


Figure 1: Gender-wise distribution of the study groups

significant (was < 0.001). Thus, in the current study, that NLR was found to be significantly higher in OSCC patients in comparison with healthy controls.

DISCUSSION

Previous studies have indicated a possible relation between NLR and malignancy. However, very few studies have been done to evaluate the prognostic significance of preoperative NLR and its effect on survival rate in cases of OSCC. The objective of the present study was to assess the NLR and other selective hematological parameters among healthy controls and OSCC patients.

Inflammation has a very important role in tumor prognosis. Causes of inflammation include autoimmune diseases, malignant and benign tumors and other pathologies which result in infiltration of inflammatory cells at specific sites in the body. Inflammation is believed to promote development and progression of various cancers, and inflammation in the body can be detected in peripheral blood. According to recent studies, there is a link between the inflammatory microenvironment of a tumor and systemic responses induced by the tumor. The increased count of neutrophils and/or decreased count of lymphocytes may suppress lymphokine-activated killer cells. These may be the possible mechanisms for decreased survival in cancer patients.^[6] In cancer, lymphocytopenia may indicate a generalized state of immune depression.^[7] Survival maybe affected by the depressed immune function. Various animal experiments have shown that deficiency in the development and/or function of CD4⁺ Th1 helper cells, CD8⁺ cytotoxic T cells or natural killer (NK) cells makes the host more susceptible to cancer development.^[8] NLR may show the two opposing inflammatory and immune pathways existing together in cancer patients.^[5]

Study done on epithelial ovarian cancer patients gave similar results to the present study, indicating an increased

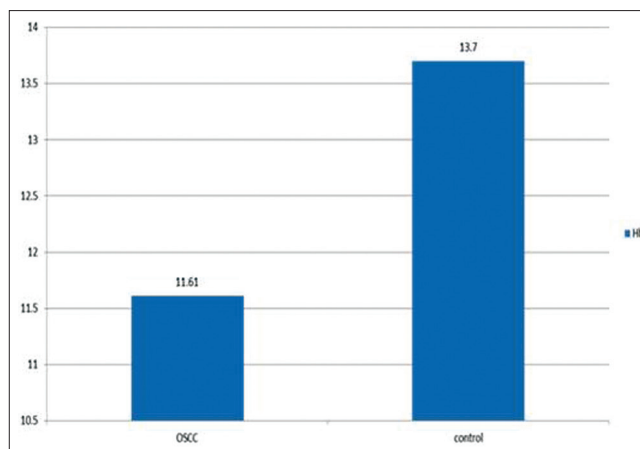


Figure 2: Mean hemoglobin percentage of oral squamous cell carcinoma and control groups

Table 1: Results of independent t-test for absolute neutrophil count, absolute lymphocyte count and N:L ratio

	Group	Mean	t	P
Absolute Neutrophil count	OSCC	6119.81	4.496	<0.001
	Control	4751.55		
Absolute Lymphocyte count	OSCC	2287.31	-2.129	0.035
	Control	2503.11		
N:L ratio	OSCC	2.84	7.243	<0.001
	Control	1.95		

OSCC: Oral squamous cell carcinoma, N:L: Neutrophil:lymphocyte

preoperative NLR in ovarian cancer participants compared to benign ovarian tumors.^[4] Similar to the present study, NLR has been indicated to be a good prognostic factor in nasopharyngeal carcinoma.^[9] In contrast to our study, Dutta *et al.* showed no correlation between NLR and esophageal cancer; the present study showed a relation between NLR and prognosis in cases of OSCC.^[10] Previous studies showed a relation between papillary thyroid carcinoma and NLR, similar to the present study.^[11] Relation between soft-tissue sarcoma and NLR was shown with respect to prognosis and survival rate similar to the present study.^[12]

CONCLUSION

In the present study, the patients underwent evaluation of complete blood count by collection of venous blood. NLR was determined from the differential leukocyte count and comparison of NLR and other hematological parameters was made among two groups. Statistical analysis showed that males were more affected than females. The overall absolute neutrophil count was found to be increased in OSCC cases ($P < 0.001$) which was statistically significant although absolute lymphocyte count was not found to be statistically significant ($P = 0.035$) and there was decrease in lymphocyte count which maybe suggestive of immunodepression. NLR values were obtained from absolute counts and were found to be higher in OSCC cases

than in healthy controls. Therefore, our results suggest that NLR has a relationship with malignant transformation of oral epithelium. In future, NLR can prove as an important prognostic biomarker before operative procedures. Longitudinal studies with 5-year survival rate will also be more helpful to study the relationship between NLR and biological behavior of OSCC cases. Thus, NLR may serve as an important prognostic parameter in future.

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Conflicts of interest

There are no conflicts of interest.

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