

# Neutrophil to Lymphocyte Ratio: Prognostic Marker for OSCC

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## ABSTRACT

**Introduction:** Tumor microenvironment is infiltrated by innate and adaptive immune system cells particularly T lymphocytes that assist tumors to mimic inflammatory conditions seen in normal tissues. Tumor microenvironment plays an important role in determining the biological behavior of cancers like proliferation, invasion, metastasis and therapeutic resistance. Study aimed to estimate and compare the neutrophil to lymphocyte ratio (NLR) in patients with oral squamous cell carcinoma (OSCC) and in normal healthy individuals.

**Material and method:** A case control study was conducted on 15 cases of oral squamous cell carcinoma (OSCC) and 15 cases of normal healthy individuals. Neutrophil to lymphocyte ratio (NLR) was determined by the examination of peripheral blood smear in each case.

**Results:** In the present study, significant increased in the absolute neutrophil count and decreased in the absolute lymphocyte count were observed along with high neutrophil to lymphocyte ratio in OSCC patients than that of healthy controls.

**Conclusion:** Neutrophil to lymphocyte ratio can be used as a feasible, cost-effective, and potential marker for determining the aggressive behavior of OSCC and may also benefit in prognostic prediction.

**Keywords:** Carcinoma, Prognosis, Oral Squamous Cell Carcinoma

## INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common head and neck carcinomas arising from the mucosa of the upper aerodigestive tract, with increasing morbidity and mortality worldwide. Oral squamous cell carcinoma (OSCC) is the sixth most common cancer worldwide,<sup>1</sup> with epidemiologic variations amongst different geographic regions. In India, it ranks the third most common malignancy, which accounts for more than 30% of all cancers listed in the country.<sup>2,3</sup> Squamous cell carcinoma (SCC) is the most common neoplasm accounting for more than 90% of all oral malignancies and occurs with a growing incidence rate in young and middle-age population.<sup>4</sup> Oral squamous cell carcinomas generally follow clinically detectable potentially malignant disorders including oral leukoplakia, erythroplakia, and oral submucous fibrosis, which histologically represent the process of oral epithelial dysplasia (OED).<sup>5</sup> OSCC occurs as a result of tobacco exposure, alcohol, immunodeficiency, human papilloma virus, multiple mutations, genetic and epigenetic changes.<sup>6</sup>

The outcome of the disease is predisposed by various factors modulating tumor as well as host response.<sup>7</sup> Cancer-related inflammation are considered as one of the markers

with an essential role in the modulation of the tumour microenvironment.<sup>8,9</sup> Tumour-associated inflammatory cells include myeloid dendritic cells, macrophage subtypes (M1 and M2), a TIE2-expressing monocyte subset, mast cells, neutrophils, and T and B lymphocytes. These cells secrete chemokines, prostaglandins, proteinases, and complement components as well as play an important role in the tumour genesis process and progression by promoting cancer cell proliferation and survival, angiogenesis, and tumour metastasis, as well as impacting tumour response to systemic therapies.<sup>10</sup> Lymphocytes have been recognized to play an essential role in cancer immune surveillance, that are hypothesized to suppress tumour maturation.<sup>11</sup>

Hence, neutrophils, thrombocytes, and lymphocytes are the host inflammatory markers and determined as an independent prognostic factor in different malignancies.<sup>12,13</sup> The aim of the present study was to estimate and compare the neutrophil to lymphocyte ratio (NLR) in patients with oral squamous cell carcinoma (OSCC) and in normal healthy individuals.

## MATERIAL AND METHODS

A case control study was conducted in the IDST College, Modinagar in the year 2016-17 and the study was approved by the ethical committee. The study group comprised of 15 cases of oral squamous cell carcinoma (OSCC) and 15 cases of normal healthy individuals (control).

Patients with inflammatory, autoimmune, acute or chronic infectious diseases, hematological disorders, diabetes, hypertension, obstructive sleep apnea, corticosteroid therapy history or chronic renal failure have been excluded in this study. Neutrophil to lymphocyte ratio (NLR) was determined by the examination of peripheral blood smear in each case. The blood was collected from the median cubital vein under aseptic technique. The total leucocytes count and the differential leucocyte count was determined by the examination of peripheral blood smears. From the total

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Parameters	Group	Mean	T-test	P-value
Absolute neutrophil count	OSCC	5762.05	4.421	0.001
	Control	4308.9		
Absolute lymphocyte count	OSCC	2267.96	-2.140	0.026
	Control	2487.34		
Neutrophil to Lymphocyte ratio	OSCC	2.72	6.280	<0.001
	Control	1.89		

OSCC- Oral squamous cell carcinoma

**Table-1:** Comparison of Neutrophil to Lymphocyte ratio between OSCC patients and healthy individuals.

leucocytes counts and differential leucocytes counts, absolute counts were obtained for neutrophils and lymphocytes. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The data was analysed by using statistical software (SPSS version 19.0). Mean were calculated for each individual group. Independent t-test and Chi-square test were used. A probability value (p) of  $\leq 0.05$  was considered to be statistically significance.

## RESULTS

In the present study, majority of the subjects were males and above 40 years of age. The mean absolute neutrophil counts in OSCC and in control were 5762.05 and 4308.9 respectively. A p-value was found to be statistically significant between OSCC and control individuals. The mean absolute lymphocyte counts in OSCC and in control were 2267.96 and 2487.34 respectively. A p-value was found to be statistically non-significant between mean absolute lymphocyte counts in OSCC and control individuals. The mean neutrophil to lymphocyte ratio in OSCC and control individuals was 2.72 and 1.89 respectively with a statistically significant difference. In the present study, neutrophil to lymphocyte ratio was found to be significantly higher in OSCC patients as compared to healthy controls (Table 1).

## DISCUSSION

Inflammation, in the form of local and systemic inflammatory responses, is a main factor for oral carcinogenesis. The connection between inflammation and carcinogenesis was first listed by Rudolf Virchow in 1863.<sup>14</sup> Evidences suggest that the systemic inflammatory response is associated with variations in circulating white blood cells and indicates the presence of neutrophilia with a relative lymphopenia. The interaction between tumor cells and related stroma characterize a strong relationship which affects disease initiation and progression, as well as patient prognosis.<sup>15</sup>

In the current study, absolute neutrophils and lymphocytes counts along with its ratio in the peripheral blood of OSCC patients were assessed and compared with healthy controls. In this study, significant increased in the absolute neutrophil count and decreased in the absolute lymphocyte count were observed along with high neutrophil to lymphocyte ratio in OSCC patients than that of healthy controls which signified systemic inflammatory response in OSCC patients. Increased neutrophil to lymphocyte ratio might reflect increased inflammation and/or decreased immune reaction in these patients. The result in this present study was in accordance

with the study done by Shayma et al in 2017<sup>15</sup> and Phulari et al in 2019.<sup>16</sup> Yu et al in their study determined that head and neck cancer patients with an elevated pretreatment neutrophil to lymphocyte ration in the peripheral blood were prone to local invasion and distant recurrence and had a poor prognosis.<sup>17</sup>

In tumor microenvironment, tumors secrete chemotactic factors that actively recruit mononuclear cells mainly lymphocytes and macrophages to tumor sites.<sup>18,19</sup> Neutrophils are considered to be a key source of vascular endothelial growth factor (VEGF) which promotes angiogenesis that in turn promotes metastasis. Neutrophil to lymphocyte ratio is increased in initial tumors as a result of host response to the recognition of the foreign nature of tumor in the connective tissue zone. In advanced stages there is also suppression of lymphocytes that further leading to relative increase in neutrophil to lymphocyte ratio. Increased neutrophil in advanced stage suggest that tumor might associated with greater proportions of immature cells and altered functional status which eventually promotes tumor growth.<sup>15</sup>

## CONCLUSION

The present study determined lymphopenia and neutrophilia with high neutrophil to lymphocyte count in OSCC patients. Thus, neutrophil to lymphocyte ratio can be used as a feasible, cost-effective, and potential marker for determining the aggressive behavior of OSCC and may also benefit in prognostic prediction.

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