

## THE ROLE OF NEUTROPHILS- LYMPHOCYTES RATIO (NLR), LYMPHOCYTES - MONOCYTES RATIO (LMR), PLATELETS- LYMPHOCYTES RATIO (PLR) IN ORAL CANCER AND ACUTE DENTAL INFECTIONS

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**Objectives:** The present study was a cross-sectional observational study, which was carried out on patients reported to the Department of Oral Medicine and Radiology. This study aims to evaluate the hemogram parameters NLR, LMR, and PLR among 90 Patients.

**Methods:** Patients were divided into 3 groups: Group A consists of 30 patients with histopathological confirmed oral cancer. Group B consists of 30 patients who presenting acute dental infections. Group C consists of 30 patients clinically healthy subjects. The hemogram parameters NLR, LMR and PLR were compared in the 3 groups and we studied their correlation to the clinical prognostic indicators like T stage, to the presence or absence of lymph node metastasis, and to differentiation of cancer. After obtaining personal informed consent, a thorough examination of the oral cavity and the lesion was conducted with an illuminated light and mouth mirror. Blood tests were performed on all the subjects before treatment. Under aseptic conditions, Venous blood (2 ml) was collected by venepuncture of the median cubital vein in the cubital fossa of the forearm using a disposable syringe with a 24-gauge needle. The withdrawn blood was transferred into an EDTA-containing test tube. Haematological parameters were analysed using an automated haematology analyzer. NLR, LMR, and PMR were calculated as the ratio of absolute peripheral neutrophil to lymphocyte, lymphocyte to monocyte, and platelet to lymphocyte count, respectively.

**Results:** The present study revealed that NLR is significantly elevated in oral carcinoma compared to healthy individuals, but is lesser than in patients with acute dental infections. LMR is higher in oral carcinoma than in acute dental infections and healthy individuals, but no statistically significant difference was detected among the groups. PLR is higher in oral carcinoma than in Acute dental infections and healthy individuals, and it is statistically significant. There are significant correlations in oral carcinoma between NLR, LMR, and PLR. NLR has a positive correlation with PLR and a negative correlation with LMR, which showed clinical significance as determined by the Spearman correlation coefficient. In Acute dental infections and healthy individuals, there is a significant correlation of NLR with LMR and PLR but no significant correlations between LMR and PLR and vice versa. NLR, LMR, and PLR were correlated to clinical prognostic indicators like T stage, presence or absence of lymph node metastasis, and differentiation of cancer. There is no significant difference in NLR, LMR, or PLR ratios concerning Clinical T staging since the p-value is greater than 0.05 for NLR, LMR, and PLR ( $p = 0.072, 0.446, 0.446$ , respectively). A statistically significant difference is found in LMR to the clinical presence or absence of Lymph node metastasis since the p-value is less than 0.05 only for LMR ( $p = 0.018$ ). The mean values of LMR in N0, N1, and N2 were 9.49, 5.65, and 4.40, respectively; this implies that the mean value of LMR decreases in advanced oral carcinoma as the nodal stage increases with lymph node metastases. A statically significant difference is found in NLR ( $p = 0.011$ ) and PLR ( $p = 0.013$ ) for differentiation of tumour (p-value is less than 0.05), which implies NLR & PLR values are elevated in moderate differentiated oral carcinomas when compared to well-differentiated oral carcinoma.

**Conclusions:** A significant elevation exists in haematological parameters like NLR, LMR, and PLR in oral carcinoma and acute dental infections.

**Keywords:** Dental infections, Platelets to Lymphocytes ratio, Monocytes to Lymphocytes ratio, Neutrophils to Lymphocytes ratio, Oral Cancers.

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**Conflicts of interest:**

The authors declare no conflicts of interest.

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## LE RÔLE DU RAPPORT NEUTROPHILES-LYMPHOCYTES (NLR), DU RAPPORT LYMPHOCYTES - MONOCYTES (LMR), DU RAPPORT PLAQUETTES-LYMPHOCYTES (PLR) DANS LES CANCERS DE LA BOUCHE ET LES INFECTIONS DENTAIRES AIGUËS

**Objectifs:** La présente étude est une étude observationnelle transversale, réalisée sur des patients du département de médecine bucco-dentaire et de radiologie. Cette étude vise à évaluer les paramètres de l'hémogramme NLR, LMR et PLR chez 90 patients.

**Méthodes:** Les patients ont été divisés en 3 groupes : Le groupe A est composé de 30 patients atteints d'un cancer de la bouche confirmé histo-pathologiquement. Le groupe B est composé de 30 patients présentant des infections dentaires aiguës. Le groupe C est composé de 30 patients cliniquement sains. Les paramètres de l'hémogramme NLR, LMR et PLR ont été comparés chez les 3 groupes, et leur corrélation étudiée avec des indicateurs pronostiques cliniques tels que le stade T, la présence ou l'absence de métastases ganglionnaires et la différenciation du cancer. Après avoir obtenu le consentement éclairé personnel, un examen approfondi de la cavité buccale et de la lésion a été réalisé avec une lumière éclairée et un miroir buccal. Des analyses de sang ont été réalisées sur tous les sujets avant le traitement. Dans des conditions aseptiques, du sang veineux (2 ml) a été prélevé par ponction veineuse de la veine cubitale médiane dans la fosse cubitale de l'avant-bras à l'aide d'une seringue jetable munie d'une aiguille de calibre 24. Le sang prélevé a été transféré dans un tube à essai contenant de l'EDTA. Les paramètres hématologiques ont été analysés à l'aide d'un analyseur d'hématologie automatisé. NLR, LMR et PMR ont été calculés comme le rapport absolu des neutrophiles périphériques aux lymphocytes, des lymphocytes aux monocytes et du nombre de plaquettes aux lymphocytes, respectivement.

**Résultats:** La présente étude a révélé que le NLR est significativement élevé dans les cas de carcinome buccal comparé aux individus en bonne santé, mais il est moindre que chez les patients à infections dentaires aiguës. Le LMR est plus élevé dans le carcinome buccal que dans les infections dentaires aiguës et chez les individus en bonne santé, mais aucune élévation significative n'existe entre les groupes. Le PLR est plus élevé dans le carcinome buccal que dans les infections dentaires aiguës et chez les individus en bonne santé, et il s'agit d'une élévation statistiquement significative entre les groupes. Il existe des corrélations significatives dans le carcinome buccal entre NLR, LMR et PLR. Le NLR a une corrélation positive avec le PLR et une corrélation négative avec le LMR, déterminée par le coefficient de corrélation de Spearman. Dans les infections dentaires aiguës et chez les individus en bonne santé, il existe une corrélation significative entre le NLR et le LMR et le PLR, mais aucune corrélation significative entre le LMR et le PLR et vice versa. NLR, LMR et PLR étaient corrélés à des indicateurs pronostiques cliniques tels que le stade T, la présence ou l'absence de métastases ganglionnaires et la différenciation du cancer. Il n'y a pas de différence significative dans les ratios NLR, LMR ou PLR concernant le stade clinique T puisque la valeur p est supérieure à 0,05 pour NLR, LMR et PLR ( $p = 0,072, 0,446, 0,446$ , respectivement). Une différence statistiquement significative est trouvée entre le LMR et la présence clinique ou l'absence de métastases ganglionnaires puisque la valeur p est inférieure à 0,05 uniquement pour le LMR ( $p = 0,018$ ). Les valeurs moyennes du LMR dans N0, N1 et N2 étaient respectivement de 9,49, 5,65 et 4,40 ; cela implique que la valeur moyenne du LMR diminue dans le carcinome buccal avancé à mesure que le stade ganglionnaire augmente avec les métastases ganglionnaires. Une différence statistiquement significative est trouvée entre le NLR ( $p = 0,011$ ) et le PLR ( $p = 0,013$ ) pour la différenciation de la tumeur (la valeur de p étant inférieure à 0,05), ce qui implique que les valeurs du NLR et du PLR sont élevées dans les carcinomes buccaux modérément différenciés par rapport à carcinome buccal bien différencié.

**Conclusions:** Il existe une élévation significative des paramètres hématologiques tels que le NLR, le LMR et le PLR dans le carcinome buccal et les infections dentaires aiguës.

**Mots clés:** Infections dentaires, rapport plaquettes/lymphocytes, rapport monocytes/lymphocytes, rapport neutrophiles/lymphocytes, cancers buccaux.

## Introduction

Oral cancer is the sixth most common cancer in the world; more than 90% are oral squamous cell carcinomas (OSCC) [1]. Cancer is closely associated with inflammation; its relationship has been among the most researched topics in the last decade [1]. Inflammatory responses, including initiation, progression, and metastasis, are critical in tumour development [1-5]. Inflammatory cells are important components of the cancer microenvironment [6]. Chronic infections are known to contribute to cancer initiation and progression by promoting angiogenesis [6]. The neutrophil-to-lymphocyte ratio (NLR) is a critical haematological parameter in inflammatory responses [6]. Elevated NLR has been linked to poor survival in cancers of the oesophagus, lung, breast, and colorectal cancers. There is growing evidence that NLR may play a diagnostic and prognostic role in head and neck cancers [6-8]. Inflammatory markers such as the neutrophils to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), and platelet to lymphocyte ratio (PLR) are used as predictive markers for various tumours and important measure of systemic inflammation as it is cost-effective, readily available [9]. Patients with odontogenic infections must be closely monitored due to the high risk of lethal complications due to the anatomical connectivity of potential spaces [9-11]. The aim of the study was to evaluate the hemogram parameters NLR, LMR, and PLR in oral cancer patients. The null hypothesis states that there the hemogram parameters are not indicators of presence of oral cancer.

## Materials and Methods

Ethical approval was obtained from the institutional ethical committee with IEC/ approval No.188. Study design: The present study was a cross-sectional observational study on patients who had report-

ed to the outpatient department of Oral Medicine and Radiology from March 2021 to January 2023, within the age group of 25-70 years. Patients were divided into 3 groups: Group A consists of 30 patients with clinically diagnosed & histopathologically confirmed oral cancer. Patients who haven't undergone any treatment for oral cancer. Group B consists of 30 Patients with acute dental infections like acute periapical abscess, acute dentoalveolar abscess, and space infections. Group C consists of 30 clinically healthy subjects. Exclusion criteria: 1- Patients with less than 25 years and more than 70 years of age, 2- Medically compromised patients with history of uncontrolled diabetes, 3- uncontrolled hypertension, coronary heart disease, 4- chronic renal failure and blood dyscrasias, 5- Patients who are currently under antibiotics therapy recently for a week, 6- Patients on anticoagulant therapy, 7- Patient undergoing chemotherapy, radiotherapy or who had received any cancer treatment, 8- Patients with acute or chronic systemic inflammatory conditions, 9- Pregnant and lactating mothers and 10- Patients not willing to participate or consent in the study. Patients with the above criteria were screened, and after their personal informed consent, a thorough clinical examination of

the oral cavity was performed (Armamentarium: Mouth mirror, Explorer, Periodontal probe, Tweezer, Spirit, Cotton, Gloves, 3 ml disposable syringe, EDTA Containing test tube), and the lesion was recorded with an illuminated light and mouth mirror. Patient were made to undergo all the haematological tests with utmost care and aseptic precautions with use of sterile diagnostic instruments and well sterilized laboratory apparatus. Cross infections between doctor and patients would be prevented by the use of disposable double gloves, mouth mask and head cap. Blood tests were performed on all the subjects before treatment. Under aseptic conditions, Venous blood (2.5 ml) was collected from patients using a venepuncture in a median cubital vein in the middle cubital fossa of the left forearm with a disposable syringe of 21-gauge needle.

The withdrawn blood was transferred into an EDTA-containing test tube. Haematological parameters were analysed using an automated haematology analyzer (Mindray BC-5000) after placing them in rollers for uniform mixing of the blood sample (Figure 1).

The results of the whole blood count of individual blood samples were obtained in the screen of the

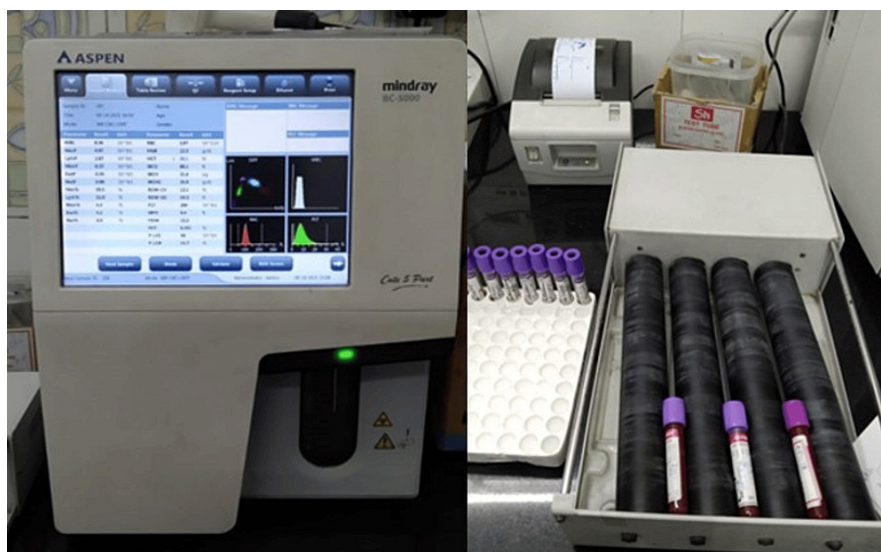


Figure 1. Haematological Autoanalyzer Mindray BC-5000



haematological autoanalyzer and were noted. The NLR, LMR, and PMR were calculated as the ratio of peripheral absolute neutrophil to lymphocyte, lymphocyte to monocyte, and platelet to monocyte count, respectively. The recorded data was compiled and entered into a Microsoft Excel spreadsheet, and statistical analysis was done using IBM SPSS (Statistics Package for Social Sciences, version 21). The descriptive statistics included computation of percentages, means and standard deviation.

The Kolmogorov-Smirnov test was used to determine the normality of the distribution followed by ANOVA test and post hoc test to compare the study groups. The Spearman rank correlation was used to determine any correlation between the variables.

## Results

49 males and 41 females were included in this study. Out of 49 males, 14 had oral cancer, 16 had acute dental infections, and 19 were healthy individuals. Out of 41 females, 14 had oral cancer, 16 had acute dental infections, and 11 were healthy individuals. 30 were oral cancer patients (Group A), 30 were Acute Dental infections (Group B), and 30 were healthy individuals (Group C). In Group A, 16 males & 14 females; in Group B, 14 males & 16 females; in Group C, 19 males & 11 females were studied.

The age-wise distribution of study subjects in all three groups was divided into five categories (up to 30, 31-40 years, 41-50 years, 51-60 years and above 60) (Figure 2).

30% had oral carcinoma between 41-50 age, 30% between 51-60 age, 60% of oral carcinoma occurs between 40-60 age. In Acute Dental infections, more than 50% occur between 31 and 50 age. The present study showed that the most common site is the buccal mucosa, followed by an alveolar ridge. 8% had oral carcinoma in the buccal muco-

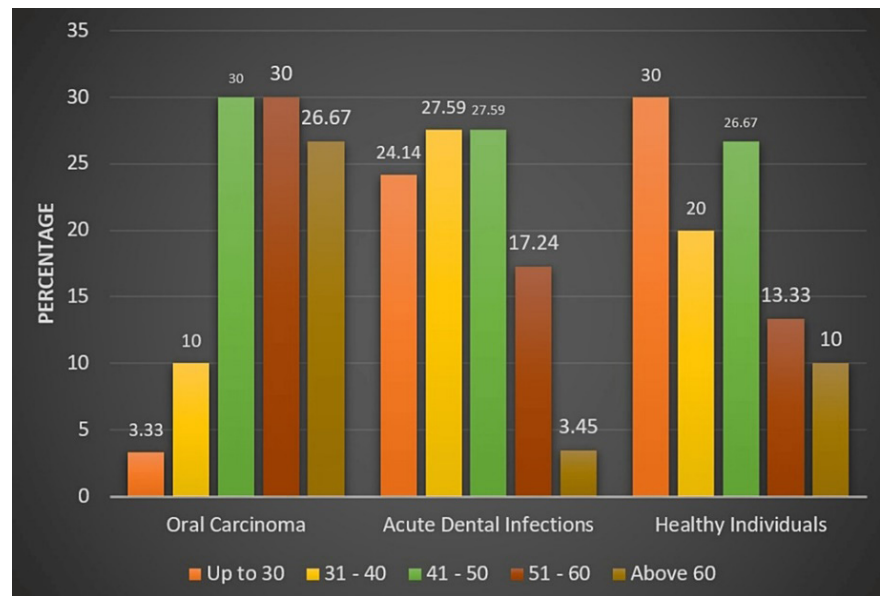


Figure 2. The Age wise distribution of the study subjects

sa, 7% had in alveolar mucosa, 5% had retromolar trigone, 4.13% in tongue, 2.6% in the palate. Clinical prognostic indicators like T stage, presence or absence of lymph node metastasis, and differentiation of cancer are recorded. The size and extent of the primary tumour determine tumour staging. Lymph node involvement in cancer is a significant parameter considered while staging the cancer. All the subjects in this study had clinical Lymph node involvement. clinical T staging showed T2- 53.33%, T3-26.67%, T1 & T4 - 10%. Lymph Node Metastasis showed 66.67% of N1, 23.33% of N2, 10% of N0. The tumours are graded based on how similar the tumour cell structure and organization are to normal cells. If the tumour cells are very similar to the normal cells, the tumour is graded as 'Well-differentiated'. The lesser the differentiation, the more aggressive or advanced the cancer. The most common histopathological grading in Group A was well-differentiated squamous cell carcinoma (73%) & moderately differentiated squamous cell carcinoma (27%) in acute dental infections, which includes four patients of acute irreversible pulpitis, 11 patients of acute periapical abscess, eight patients of acute dentoalveolar abscess, and seven

patients of space infections. The result of the normality test is shown in table 1.

The Mean value of Neutrophils-Lymphocytes Ratio (NLR) in oral carcinoma, Acute dental infections and healthy individuals are 2.66, 2.83 and 2.09 respectively (Figure 3).

Mean value of Lymphocytes-Monocytes Ratio (LMR) in oral carcinoma, Acute dental infections and healthy individuals are 5.74, 5.11 and 5.6 respectively (Figure 4).

The mean value of Platelets-Lymphocytes Ratio (PLR) in oral carcinoma, acute dental infections and healthy individuals are 142.07, 135.85 and 113.23 respectively (Figure 5).

Comparison of mean Neutrophils-Lymphocytes Ratio (NLR), Lymphocytes-Monocytes Ratio (LMR), Platelets-Lymphocytes Ratio (PLR) is shown (Table 2).

The NLR, LMR, and PLR were compared to clinical prognostic indicators like size and extent of primary tumour (T1, T2, T3, T4) stage, presence or absence of lymph node metastasis (N0, N1, N2), and differentiation (moderately/ well-differentiated) oral carcinoma by using ANOVA and post Hoc test.

Table 1. Test summary by One-sample Kolmogorov Smirnov Test for the Normality of the distribution (asymptomatic significances are displayed. The significance level is .05)

Null Hypotheses	Test	Sig	Decision
The distribution of Neutrophils- Lymphocytes Ratio (NLR) is normal with mean 2.51 and standard deviation 1.12	One-sample Kolmogorov Smirnov Test	0.175	Normal Distribution
The distribution of Lymphocytes- Monocytes Ratio (LMR) is normal with mean 5.51 and standard deviation 2.22	One-sample Kolmogorov Smirnov Test	0.210	Normal Distribution
The distribution of Platelets- Lymphocytes Ratio (PLR) is normal with mean 130.00 and standard deviation 48.51	One-sample Kolmogorov Smirnov Test	0.155	Normal Distribution

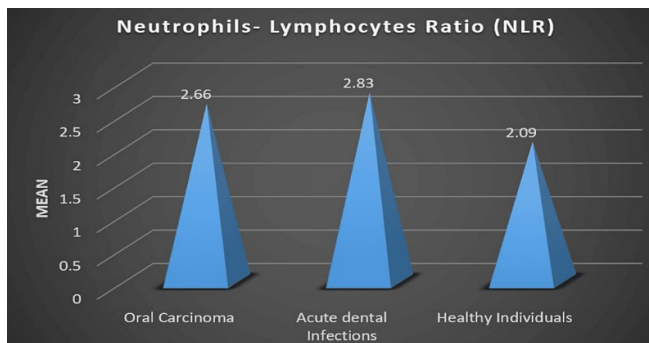


Figure 3. The Mean value of Neutrophils- Lymphocytes Ratio (NLR) in oral carcinoma, Acute dental infections and healthy individuals

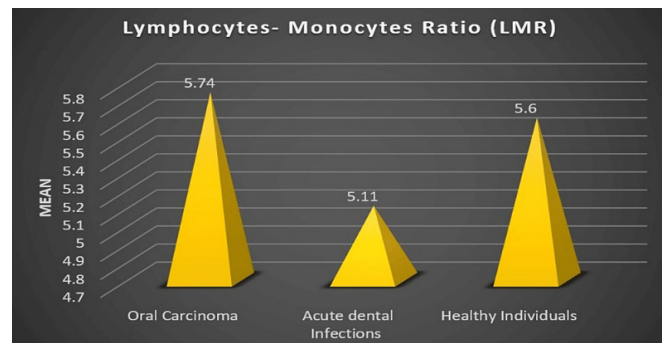


Figure 4. Mean value of Lymphocytes- Monocytes Ratio (LMR) in oral carcinoma, Acute dental infections and healthy individuals

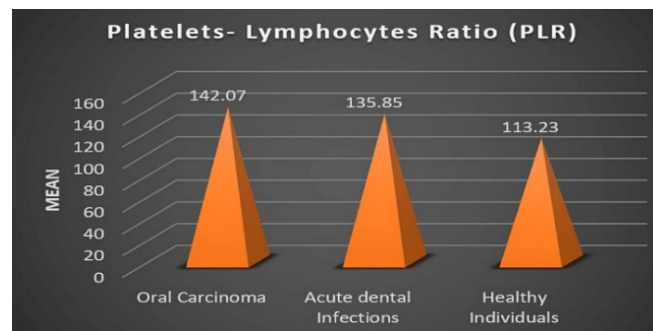


Figure 5. The mean value of Platelets- Lymphocytes Ratio (PLR) in oral carcinoma, acute dental infections and healthy individuals

There is no significant difference in NLR, LMR, or PLR ratios concerning Clinical T staging since the p-value is greater than 0.05 for NLR, LMR, and PLR ( $p = 0.072, 0.446, 0.446$ , respectively) (Table 3).

Relation of NLR, LMR, PLR with

presence or absence of lymph node metastases. Since p value is less than 0.05 only for LMR it is found that there is significant difference is found in LMR with respect to Clinical Presence/Absence of Lymph Node Metastasis.

The mean values of LMR in N0, N1, and N2 were 9.49, 5.65, and 4.40, respectively; this implies that the mean value of LMR decreases in advanced oral carcinoma as the nodal stage increases with lymph node metastases (Table 4).

Table 2. Comparison of mean value of Haematological parameters Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes-Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in oral carcinoma, acute dental infections and healthy individuals

Ratio	Groups	N	Mean	SD	SE	ANOVA	p value
NLR	Oral Carcinoma	30	2.66 <sup>a</sup>	1.16	0.211	3.83	0.025*
	Acute Dental Infections	30	2.83 <sup>a</sup>	1.32	0.240		
	Healthy Individuals	30	2.09 <sup>b</sup>	0.66	0.120		
	Total	90	2.53	1.11	0.117		
LMR	Oral Carcinoma	30	5.74	2.72	0.496	0.66	0.519
	Acute Dental Infections	30	5.11	1.88	0.343		
	Healthy Individuals	30	5.60	1.98	0.362		
	Total	90	5.48	2.22	0.233		
PLR	Oral Carcinoma	30	142.07 <sup>a</sup>	56.43	10.303	3.06	0.052*
	Acute Dental Infections	30	135.85 <sup>a,b</sup>	47.30	8.637		
	Healthy Individuals	30	113.23 <sup>a</sup>	36.94	6.743		
	Total	90	130.38	48.65	5.128		

(\* statistically significant) (SD: Standard Deviation - SE: Standard Error)

Table 3: Relation of Neutrophils- Lymphocyte Ratio (NLR), Lymphocytes -Monocytes Ratio (LMR), Platelets - Lymphocytes Ratio (PLR) with clinical T staging

Clinical T staging		N	Mean	SD	SE	ANOVA	p
Neutrophils- Lymphocytes Ratio (NLR)	T1	3	1.33	0.48	0.27	2.62	0.072
	T2	16	3.05	1.11	0.28		
	T3	8	2.28	1.18	0.42		
	T4	3	2.90	0.79	0.46		
	Total	30	2.66	1.16	0.21		
Lymphocytes- Monocytes Ratio (LMR)	T1	3	7.11	3.20	1.85	0.92	0.446
	T2	16	5.07	2.22	0.56		
	T3	8	6.70	3.34	1.18		
	T4	3	5.43	3.23	1.86		
	Total	30	5.74	2.72	0.50		
Platelets- Lymphocytes Ratio (PLR)	T1	3	91.18	3.94	2.28	0.92	0.446
	T2	16	147.12	42.89	10.72		
	T3	8	145.98	79.95	28.27		
	T4	3	155.63	74.59	43.06		
	Total	30	142.07	56.43	10.30		

Table 4: Clinical relation of Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) with nodal metastases.

Ratio	Clinical Presence/ Absence of Lymph Node Metastasis	N	Mean	SD	SE	ANOVA	p
Neutrophils- Lymphocytes Ratio (NLR)	N0	3	2.01	1.30	0.75	0.69	0.511
	N1	20	2.65	1.24	0.28		
	N2	7	2.95	0.86	0.32		
	Total	30	2.66	1.16	0.21		
Lymphocytes- Monocytes Ratio (LMR)	N0	3	9.49	3.98	2.30	4.66	0.018*
	N1	20	5.65	2.49	0.56		
	N2	7	4.40	1.25	0.47		
	Total	30	5.74	2.72	0.50		
Platelets- Lymphocytes Ratio (PLR)	N0	3	108.21	87.41	50.47	0.69	0.511
	N1	20	142.91	55.45	12.40		
	N2	7	154.18	48.61	18.37		
	Total	30	142.07	56.43	10.30		

(\* statistically significant)

Table 5: Correlation of Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) with Differentiation of Tumour

Ratio	Oral carcinoma	Acute dental infections	Healthy individuals	P Value	T Staging	Clinical Presence/ Absence of Lymph Node Metastasis	Differentiation of tumor
NLR	2.66	2.83	2.09	0.025*	0.072	0.511	0.011*
LMR	5.74	5.11	5.60	0.519	0.446	0.018*	0.639
PLR	142.07	135.85	113.23	0.052*	0.446	0.511	0.013*

(\* statistically significant)

Table 6. Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in oral carcinoma, acute dental infections and healthy individuals and Correlation of Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) With Clinical Staging and Lymph node metastases.

Differentiation of Tumour		N	Mean	SD	SE	t	p
NLR	Moderately differentiated	8	3.52	1.18	0.42	2.72	0.011*
	Well differentiated	22	2.34	1.00	0.21		
LMR	Moderately differentiated	8	5.35	2.99	1.06	0.47	0.639
	Well differentiated	22	5.89	2.67	0.57		
PLR	Moderately differentiated	8	183.48	55.15	19.50	2.67	0.013*
	Well differentiated	22	127.01	49.93	10.65		

(\* statistically significant)



Since p value is less than 0.05 for NLR and PLR, a significant difference is found in NLR and PLR with respect to differentiation of tumour (Table 5).

Since p value is greater than 0.05 for NLR, LMR, PLR no significant difference is found with respect to Clinical T staging. A statistically significant difference is found in LMR to the clinical presence or absence of Lymph Node Metastasis, since the p-value is less than 0.05 only for LMR ( $p=0.018$ ). A statically significant difference is found in NLR ( $p=0.011$ ) and PLR ( $p=0.013$ ) for differentiation of tumour (p-value is less than 0.05), which implies NLR & PLR values are elevated in Moder-

ately differentiated oral carcinomas when compared to well-differentiated oral carcinoma (Table 6).

The scatter plot shows the Neutrophils- Lymphocytes Ratio (NLR) and Lymphocytes- Monocytes Ratio (LMR) correlation among three groups: oral carcinoma, acute dental infections, and healthy individuals (Figure 6).

The scatter plot shows the Lymphocytes- Monocytes Ratio (LMR) and Platelets- Lymphocytes Ratio (PLR) correlation among three groups: oral carcinoma, acute dental infections and healthy individuals (Figure 7).

The correlation of Neutrophils-Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in oral carcinoma by spearman rank correlation (Table 7).

The correlation of Neutrophils-Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR) and Platelets- Lymphocytes Ratio (PLR) in acute dental infections by Spearman rank correlation (Table 8).

The correlation of Neutrophils-Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in healthy individuals by spearman rank correlation (Table 9).

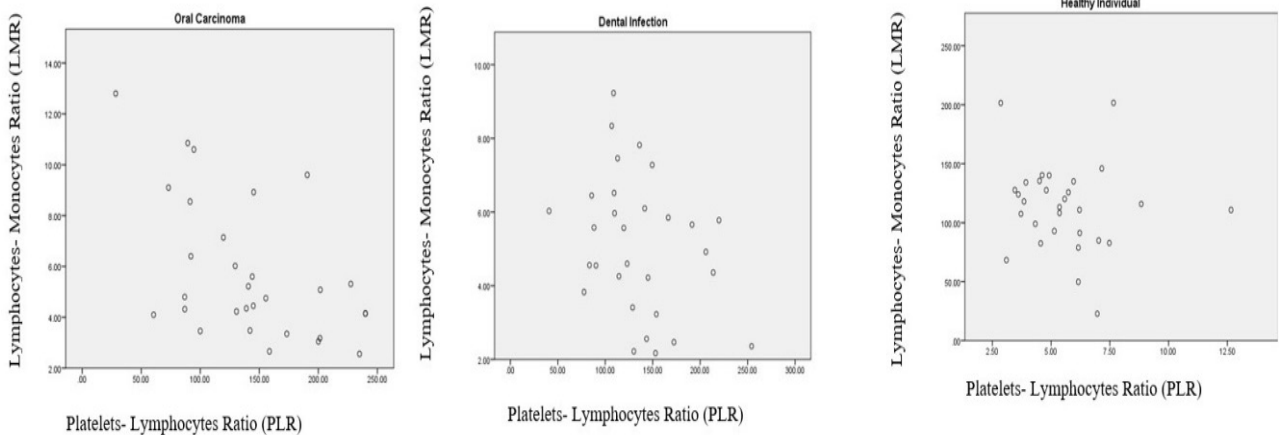


Figure 6. Scatterplot diagram shows the correlation of Neutrophils-Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR) in oral carcinoma, acute dental infections and healthy individuals

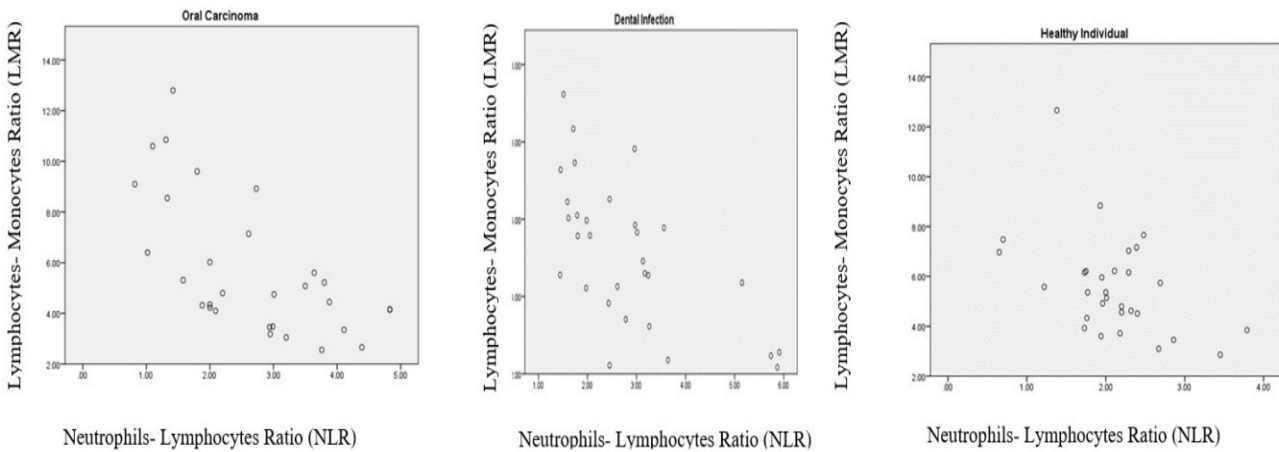


Figure 7. Scatter plot diagram showing the correlation of Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in oral carcinoma, dental infections and healthy individuals

Table 7. Correlation of Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in oral carcinoma by spearman correlation

Correlations –Group 1 Oral carcinoma				
Ratio		NLR	LMR	PLR
Neutrophils- Lymphocytes Ratio (NLR)	r	1.000	-.644**	.664**
	p	-	0.001	0.001
Lymphocytes- Monocytes Ratio (LMR)	r	-.644**	1.000	-.517**
	p	0.001	-	0.003
Platelets- Lymphocytes Ratio (PLR)	r	.664**	-.517**	1.000
	p	0.001	0.003	-
	N	30	30	30

(\*\* highly significant correlation)

Table 8. Correlation of Neutrophils- ymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR) and Platelets- Lymphocytes Ratio (PLR) in acute dental infections by spearman correlation.

Correlations – Group 2- Acute Dental Infections				
Ratio		NLR	LMR	PLR
NLR	r	1.000	-.640**	.537**
	p		0.001	0.002
LMR	r	-.640**	1.000	-0.303
	p	0.001		0.103
PLR	r	.537**	-0.303	1.000
	p	0.002	0.103	
	N	30	30	30

(\*\* highly significant correlation)

Table 9. Correlation of Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), Platelets- Lymphocytes Ratio (PLR) in healthy individuals by spearman's correlation.

Correlations – Group 3 -Healthy individuals				
		NLR	LMR	PLR
NLR	r	1.000	-.477**	.470**
	p		0.008	0.009
LMR	r	-.477**	1.000	-0.138
	p	0.008		0.469
PLR	r	.470**	-0.138	1.000
	p	0.009	0.469	
	N	30	30	30

(\*\* highly significant correlation)

There are significant correlations in oral carcinoma between Neutrophils- Lymphocytes Ratio (NLR), Lymphocytes- Monocytes Ratio (LMR), and Platelets- Lymphocytes Ratio (PLR). Neutrophils- Lympho-

cytes Ratio (NLR) has a positive correlation with Platelets- Lymphocytes Ratio (PLR) and a negative correlation with Lymphocytes- Monocytes Ratio (LMR). In Acute dental infections and healthy individuals, there

is a significant correlation of Neutrophils- Lymphocytes Ratio (NLR) with Lymphocytes- Monocytes Ratio (LMR) and Platelets- Lymphocytes Ratio (PLR) but no significant correlations between Lymphocytes-

Monocytes Ratio (LMR) and Platelets- Lymphocytes Ratio (PLR) and vice versa.

## Discussion

In 1863 the German physician and pathologist Rudolf Ludwig Karl Virchow hypothesized that cancer originated at sites of chronic inflammation after discovering leukocyte infiltration in neoplastic tissues, thus causing the first link between inflammation and cancer [1]. As a result, tumour-associated inflammation has been recognized as a crucial characteristic (hallmark) of cancer [2]. More recent research has focused on understanding tumour-elicited inflammation, the inflammatory response that occurs after tumour development and is found in nearly all solid malignancies [3, 4]. In the Meta-analysis done by Yang (2018), an increased NLR was also linked to lymph node metastases, a higher T stage, advanced tumour stage, tumour differentiation, and perineural invasion [5]. It is well established that systemic inflammation triggered by cancer cells contributes to tumour growth by encouraging angiogenesis. Neutrophils and lymphocytes appear to have the opposite impact on the development and spread of cancer cells [6].

T-lymphocytes prevent tumour cell's growth and metastatic spread by producing cytokines and causing cytotoxic cell death. Neutrophils are involved in the immune response against tumours [6]. Meanwhile, vascular endothelial growth factor (VEGF), primarily increased by neutrophils, promotes the growth and spread of cancer cells by increasing angiogenesis. As a result, a high NLR caused by relative neutrophilia and lymphopenia is frequently seen in cases of cancer [7]. It is widely recognized that intrinsic and extrinsic pathways regulate the inflammatory state of cancer. These pathways encourage the development and maintenance of a favourable pre-malignant inflammatory tumour mi-

croenvironment, which aids in cancer growth and spread. Along with the angiogenic cytokines interleukin-8 (IL-8) and vascular endothelial growth factor, neutrophils also produce matrix metalloprotein-9 (MMP-9) (gelatinase B), which causes tumour cells to become angiogenic. The depth of invasion and tumour differentiation is associated with neutrophil gelatinase-associated lipocalin. In addition to neutrophils, tumour-associated macrophages, and other leukocytes have been linked to aggressive tumour behaviour, including invasion and metastasis, through MMP-2 by inducing extracellular matrix remodelling. As a result, a high pre-treatment neutrophil-lymphocyte ratio (NLR) may indicate an underlying favourable microenvironment for tumour cell development and aggressiveness, favouring tumour dissemination/micro metastasis and, ultimately, recurrence.

The present study showed increased NLR and PLR in oral carcinoma compared to healthy individuals. This is in accord with a study done by Düzlü et al. (2016) in which NLR was significantly elevated in oral carcinoma [7]. Petrescu et al. (2020) study stated the mean NLR and PLR were found to be greater in malignant tumours than in benign lesions [8]. Imtiaz F (2012) stated that neutrophil-lymphocyte ratio is prevalent in chronic infections [9]. Dogruel F (2017) stated that Neutrophil-lymphocyte ratio is a marker for severe dental infections [10].

Tazeen et al. (2020) study concluded that PLR was preferable to NLR since both ratios on oral squamous cell carcinoma were shown to be increased and significant in predicting the prognosis of cancer [11].

High PLR may be related to a worse prognosis because platelets can promote tumour growth by promoting angiogenesis and increasing microvascular permeability, allowing tumour cells to extravasate into the bloodstream. Second, they interact with tumour cells through ligands or receptors that promote

tumour development or invasion. The adhesion molecule P selectin allows tumour cells to connect to platelets directly and can speed up tumour spread. Thirdly, platelets are hypothesized to protect tumour cells from NK cells by lowering their cytolytic activity. Patients with high PLRs also have relative lymphocytopenia, which could cause decreased immunity and weaker resistance to malignancy. So, Inflammatory indicators such as neutrophils, lymphocytes, monocytes, and platelets, as well as their ratios, can be utilized to predict prognosis [12]. Pursuing new mechanisms underlying potential cancer cures and prevention included studies of the immune system in various directions, including cancer vaccines and armoured anti-cancer immune cells, various types of immunotherapies, anti-cancer antibodies, and biological therapies. It is now clear that the immune system can play important pro- and anti-tumorigenic roles throughout the tumorigenesis process [13].

Lee S et al. (2020) stated elevated NLR or PLR can be used as a pre-operative clue to identify individuals at risk of shorter survival and greater recurrence of oral cancer [13]. Ashraf F. (2018) stated that Pre-treatment NLR was a reliable predictor of prognosis for patients with OSCC and provided an easy and observable sign of outcome [14]. Malik A, Mishra A, Mair M, et al. (2019) study proved NLR and PLR can be utilized to predict survival and prognosis in patients with oral cavity cancer. PLR is an excellent predictor of unfavourable clinicopathological variables and survival. NLR can only predict survival in a subgroup of individuals who have taken chemotherapy [15]. Wu et al. (2021) concluded high pre-treatment NLR was an independent unfavourable risk factor for both Overall survival and distant control in patients with oral cavity squamous cell carcinoma who underwent surgery and postoperative radiotherapy [16].

The present study showed increased LMR in oral carcinoma but,

contrary to the study done by Petrescu et al. (2020), where LMR was lower in malignant tumours than in benign lesions [8]. The study done by Ong HS (2017) concluded that Low pre-treatment LMR and high PLR indicate poor survival in patients with early tongue cancer [17]. Caldeira PC (2015) showed increased NLR in T3-T4 tumours compared to T1-T2. The present study showed no significant differences between clinical T staging [18].

According to Valero et al. (2021), higher NLR had more nodal features. In the present study, NLR is unrelated to the nodal features, But LMR decreases with nodal involvement [19]. Phulari RGS. (2019), stated that the mean NLR value in OSCC was 2.84, while it was 1.95 in controls [20]. NLR was found to be considerably greater in OSCC patients than in healthy controls, and this difference was statistically significant ( $p < 0.001$ ). This study is by a present study, which revealed NLR was 2.66 in oral cancer while in healthy individuals, it was 2.09. These ratios are inflammatory markers that are major prognostic factors in many inflammatory conditions. Through this study, we have attempted to calculate the NLR, LMR, and PLR in acute dental infection cases, which have not been previously studied. The

present study showed increased NLR, PLR, and decreased LMR in acute dental infections than healthy individuals. Dogruel F (2017) was the first to investigate the N/L ratio in odontogenic infections and concluded that NLR is elevated and can be used as a prognostic marker for patients with odontogenic infections [10]. The present study was in accord with the above study. NLR was elevated in acute dental infections. The present study agreed with the above study concerning increased NLR in acute dental infections compared to healthy individuals.

The present study showed increased NLR in oral carcinoma compared to healthy individuals but less than that of acute dental infections. PLR is elevated in oral carcinoma compared to both acute dental infections and healthy individuals. So, the present study showed elevated levels of NLR and PLR in oral carcinoma that are significant. So, these ratios serve as a prognostic tool in oral carcinoma and acute dental infections, where LMR is insignificant.

### Limitations

The study is unicentric confined only to one population. More research with larger samples is required to establish NLR, LMR, and

PLR as definitive diagnostic and prognostic markers in cases of oral cancer and acute dental infections.

### Conclusion

A significant elevation exists in haematological parameters like NLR, LMR, and PLR in oral carcinoma and acute dental infections. These ratios help assess the host's immune response in cases of oral carcinoma and acute dental infections. In this study, we have attempted to calculate the NLR, LMR, and PLR in acute dental infection cases that have not been previously studied. NLR, LMR, and PLR are simple, inexpensive haematological parameters recently used as diagnostic tools for oral carcinoma. They have been linked to nodal staging and tumour differentiation in oral carcinoma and are useful in dental infections. In addition, these ratios play a role as prognostic and predictive markers for oral carcinoma and dental infections. More research with larger samples is required to establish NLR, LMR, and PLR as definitive diagnostic and prognostic markers in cases of oral cancer and acute dental infections. Shortly, NLR, LMR, and PLR may be considered important biomarkers for diagnostic and prognostic roles in oral cancer.

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