DOI: 10.7860/JCDR/2026/86053.24237

Original Article

Pathology Section

Immunohistochemical Expression of FOXP3 and CD8 in Oral Squamous Cell Carcinoma: A Cross-sectional Study

SHARJUBALA KHUMANTHEM[1], TN SURESH[2], D ASWATHAPPA[3]

ABSTRACT

Introduction: In India, Oral Squamous Cell Carcinoma (OSCC) is among the top three malignancies. Tumour-Infiltrating Immune Cells (TIIC), as key elements of tumour microenvironment have recently been demonstrated to be crucial to the development and spread of cancer. The immune infiltrates of tumours is predominantly lymphocytes with T cells being major cell type.

Aim: To determine FOXP3 and CD8 immunohistochemical expression in OSCC and its correlation with Tumour -Node-Metastasis (TNM) staging and lymph node metastases.

Materials and Methods: The present cross-sectional laboratory based study was conducted in the Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar, Karnataka, India from April 2023 to April 2025. A total of 86 histologically confirmed cases of OSCC were screened for lymph node metastases, graded and TNM staged using the current American Joint Committee on Cancer (AJCC) staging criteria. The cases were then immunohistochemically stained using FOXP3 and CD8. Data analysis was done using Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 22 (IBM SPSS Statistics, Somers, NY, USA). Chi-square test/Fischer's exact test was employed as the test of significance. The Pearson's correlation coefficient was used to perform correlations. A p-value <0.05 was deemed statistically significant.

Results: The study patients were predominantly females and the mean age of the patients was 52 years. Nodal metastases were present in 37 (43%) of patients. Among the cases studied, 3 (3.5%), 18 (20.9%), 23 (26.7%),30 (34.9%) and 12 (14%) belonged to stage I, II, III, IVA and IVB, respectively. High CD8+IM (invasive margin) was associated with node negative cases (p=0.0074). Low CD8+IM (invasive margin) was associated with higher TNM stages (p=0.0092). Increased CD8+IM/FOXP3+ ratio was associated with lower TNM stages (p=0.023).

Conclusion: The quantity, location and roles of Tumour Infiltrating Lymphocytes (TIL) are dynamic in nature. CD8+ IM (invasive margin)/FOXP3+ ratio is a promising biomarker in cancer research. Modulating this ratio could enhance anti-tumour immunity and improve treatment outcomes.

Keywords: Cluster of differentiation 8, Forkhead box P3, Lymph node metastasis, Oral cancer, Tumour infiltrating lymphocytes, Tumour microenvironment

INTRODUCTION

Cancer of oral cavity is the most frequent among men in India and second among women. It accounts for 29.66% of cancer cases in Kolar, Karnataka, India [1]. Majority of the cases are Squamous cell Carcinoma (SCC) [2]. Despite a number of treatment options which includes immunotherapy, chemotherapy, radiation and surgery, OSCC has 50% overall survival [3,4]. In order to improve oncological risk stratification, it is noteworthy that recent research indicates an increasing interest in combining the pathogenic and immunological characteristics of different malignancies [5]. Also, the infiltration of immune cells in different compartments of tissue is ambiguous and not uniform in OSCC.

The tumour cells surround the stromal cells causing an inflammatory response that recruits various immune cells to aid in the cancer progression [6]. The immune system has a complex relationship with cancer cells and can either inhibit or promote tumour growth [7]. TIICs are myeloid and lymphoid cells that enter the tumour from the vasculature. Majority of TILs are T-lymphocytes with T-helper cells, cytotoxic T-cells and regulatory T-cells (Treg) subpopulations [8]. These are primarily cytotoxic T lymphocytes that are CD8 positive. Nodal negativity and better outcomes are all favourably connected with high CD8+T cells in a number of human malignancies, including SCC of head and neck [9].

Diverse subsets of immunosuppressive T cells make up regulatory T cells (Treg). FOXP3, a regulatory protein belonging to the fork head/winged-helix family contributes to the development and function of Treg. By inhibiting self-antigen reactive T cells, Tregs can mediate peripheral tolerance [10]. T lymphocytes that are receptive to tumour antigens are inhibited by Tregs posing as a barrier to antitumour immunity because majority of tumour antigens are self-antigens [11]. Some studies have linked increased intratumoural FOXP3+ expression to worse clinical outcomes [12], while other studies showed contradictory findings with increased infiltration of FOXP3+ regulatory T-cells in OSCC, particularly among never-smokers and never-drinkers, which was paradoxically associated with improved survival [13]. Therefore, the present study was conducted to evaluate the immunohistochemical expression of FOXP3 and CD8 in OSCC and to analyse their association with clinicopathological parameters, particularly including tumour stage and nodal involvement.

MATERIALS AND METHODS

The present cross-sectional laboratory based study was done in the Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar, Karnataka, India from April 2023 to April 2025 (Institutional Ethical Clearance number: DMC/KLR/IEC/11/2023-24). The study included a total of 86 histopathologically diagnosed cases of OSCC.

Sample size calculation: Sample size was estimated based on CD8 expression of 66.6% in OSCC as reported in the study done by De Meulenaere A et al., and considering an absolute error of 10% with 95% confidence interval [14]. These cases were screened for lymph node metastases, graded and TNM staged using the current AJCC staging criteria followed by immunohistochemical staining using FOXP3 and CD8 [15,16].

Inclusion and Exclusion criteria: The study included histopathologically diagnosed cases of OSCC treated with composite resection and cervical lymph node dissection.Patients who underwent

neoadjuvant radiation and/or chemotherapy before surgery and having second primary cancers were excluded.

Study Procedure

Tissue sections fixed in 10% formalin were subjected to Immunohistochemistry (IHC) staining. Incubation with primary rabbit monoclonal antibody against CD8 (Clone:EP 334, PathnSitu) and primary rabbit monoclonal antibody against FOXP3 (Clone:EP 340, PathnSitu) were done. Sections from tonsil served as positive control for both CD8 and FOXP3.

CD8+ and FOXP3+ IHC scoring: Grading of immunostaining was done according to the criteria used by Mukherjee G et al., where CD8 was scored based on the percentage-based method [16]. However, for FOXP3, universally accepted or standardised scoring system was not identified in the literature. To maintain methodological uniformity and enable direct comparison between immune cell populations within the same tumour microenvironment, the same percentage-based scoring approach for both CD8 and FOXP3 expression was adopted. Membranous staining and nuclear staining were considered positive for CD8 and FOXP3, respectively. In each slide, two compartments of the tissue sections were considered i.e., invasive margin of tumour (tumour and normal tissue interface) and the tumour centre (any region within tumour other than the invasive margin). Each section was first inspected at low power magnification to select five hotspots, then viewed under 400x magnification and a mean percentage of immunopositivity score was calculated for each of the sites. It was scored as: low (0-25%), intermediate (26-50%) and high (51-100%). Association of CD8+ and FOXP3+ immunohistochemical score were done with tumour thickness (<40 mm, ≥40 mm) [17], grade of tumour, depth of invasion, lymph node metastases, tumour staging, perineural invasion, bone invasion and lymphovascular invasion.

STATISTICAL ANALYSIS

Microsoft Excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) was used for analysis of data. Chi-square test/Fischer's exact test was employed as the test of significance. The Pearson's correlation coefficient was used to perform correlations. A p-value <0.05 was deemed statistically significant.

RESULTS

The age of the patients included in the present study ranged from 33 to 94 years (mean 52 years), with the majority 62 (72.1%) being female. The tumour subsites were classified as the buccal mucosa 53 (61.6%), gingivobuccal sulcus 21 (24.4%), tongue 9 (10.5%) and retromolar trigone 3 (3.5%). 74 (86%) cases were well-differentiated and 12 (14%) cases moderately-differentiated. Among the cases studied, 3 (3.5%) cases, 29 (33.7%) cases, 30 (34.9%) cases and 24 (27.9%) cases belonged to AJCC classification T1, T2, T3 and T4a stages respectively. 37 (43%) cases had presence of nodal metastasis. 3 (3.5%) cases, 18 (20.9%) cases, 23 (26.7%) cases and 42 (48.9%) cases belonged to stage I, II, III, IV, respectively.

CD8+ (IM: invasive margin and TC: tumour centre) and FOXP3+ scoring were correlated with different clinicopathological parameters such as tumour thickness, depth of invasion, histological grade, lymph node status, tumour staging, pathological TNM staging, lymphovascular invasion, perineural invasion and bone invasion [Table/Fig-1,2]. Low CD8+IM scoring 33 (80.4%) was noted in

Variables	Number of patients	CD8+IM			r-value	p-value	CD8+TC			r-value	p-value	FOXP3+			r-value	p-value
		Low	Intermediate	High			Low	Intermediate	High			Low	Intermediate	High		
Tumour staging (pT)																
T1	3	3	0	0	0.23	0.0562	3	0	0	0.008	0.9437	3	0	0	0.048	0.6708
T2	29	13	12	4			26	2	1			27	2	0		
T3	30	11	9	10			26	3	1			29	0	1		
T4a	24	14	9	1			21	3	0			23	1	0		
Lymph node status																
N+	37	21	15	1	0.29	0.0074	33	3	1	0.01	0.9304	37	0	0	0.14	0.2052
N_0	49	20	15	14			43	5	1			45	3	1		
Pathological stage (pTNM)																
I	3	3	0	0	0.28	0.0092	3	0	0	0.07	0.5271	3	0	0	0.071	0.5170
II	18	5	9	4			15	2	1			16	2	0		
III	23	9	5	9			20	3	0			22	0	1		
IVA	30	19	10	1			29	1	0			29	1	0		
IVB	12	5	6	1			9	2	1			12	0	0		

[Table/Fig-1]: Associations between CD8 invasive margin, CD8 tumour centre and FOXP3 with tumour stage, lymph node status and pathological TNM stage in the cohort of 86 OSCC patients.
*CD8+ (IM: invasive margin & TC: tumour centre), pT: pathological tumour stage, N+ -presence of lymph node metastasis, N_0- absence of lymph node metastasis

Variable	Number of patients	CD8+IM			r-value	p-value	CD8+TC			r-value	p-value	FOXP3+			r-value	p-value
		Low	Intermediate	High			Low	Intermediate	High			Low	Intermediate	High		
Grade of tumour																
WDSCC	74	34	27	13	0.054	0.62	64	8	2	0.092	0.3995	70	3	1	0.04	0.7117
MDSCC	12	7	3	2			12	0	0			12	0	0		
Tumour thickness																
<40 mm	42	21	15	6	0.037	0.7489	37	4	1	0.0004	0.9969	40	2	0	0.073	0.5126
≥40 mm	44	20	15	9			39	4	1			42	1	1		
DOI																
0-5 mm	20	12	5	3	0.039	0.7264	19	1	0	0.174	0.1077	20	0	0	0.051	0.6432
6-10 mm	37	15	15	7			35	1	1			34	2	1		
>10 mm	29	14	10	5			22	6	1			28	1	0		

LVI															
Present	13	8	5	0	0.14	0.1878	12	1	0	0.027	0.8083	13	0	0	0.044	0.6883
Absent	73	33	25	15			64	7	2			69	3	1		
PNI															
Present	8	5	3	0	0.10	0.3749	8	0	0	0.064	0.5597	8	0	0	0.027	0.8064
Absent	78	36	27	15			68	8	2			74	3	1		
BI															
Present	13	9	3	1	0.13	0.23	12	1	0	0.027	0.8083	13	0	0	0.044	0.6883
Absent	73	32	27	14			64	7	2			69	3	1		

[Table/Fig-2]: Associations between CD8 invasive margin, CD8 tumour centre and FOXP3 with various other clinicopathological parameters in the cohort of 86 OSCC patients. *CD8+ (IM: invasive margin & TC: tumour centre), WDSCC: Well-differentiated squamous cell carcinoma, MDSCC: Moderately differentiated squamous cell carcinoma, DOI: Depth of invasion, LVI: Lymphovascular invasion, PNI: Perineural invasion, BI: Bone invasion

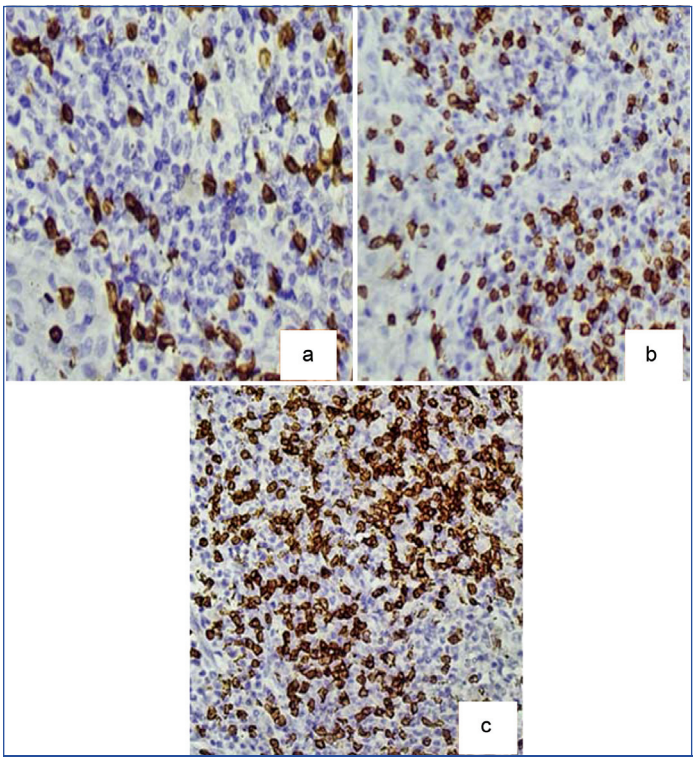
higher TNM stages (stage III & IV) with a p-value of 0.0092. High CD8+IM (invasive margin) was associated with node negative cases (p=0.0074). No significant correlation was noted among the other parameters. The IHC staining of CD8 and FOXP3 is shown in [Table/Fig-3,4] respectively.

Significant association (p=0.023) was noted between the CD8+IM/FOXP3+ ratio and pathological TNM stage. As the CD8+ IM/FOXP3+ ratio increases, the tumour stage tends to decrease [Table/Fig-5]. This inverse relationship between the immune ratio (CD8+ IM/ FOXP3+) and tumour stage could mean that higher immune activity is associated with lower stage tumours, suggesting a better prognosis or stronger immune response in earlier stages.

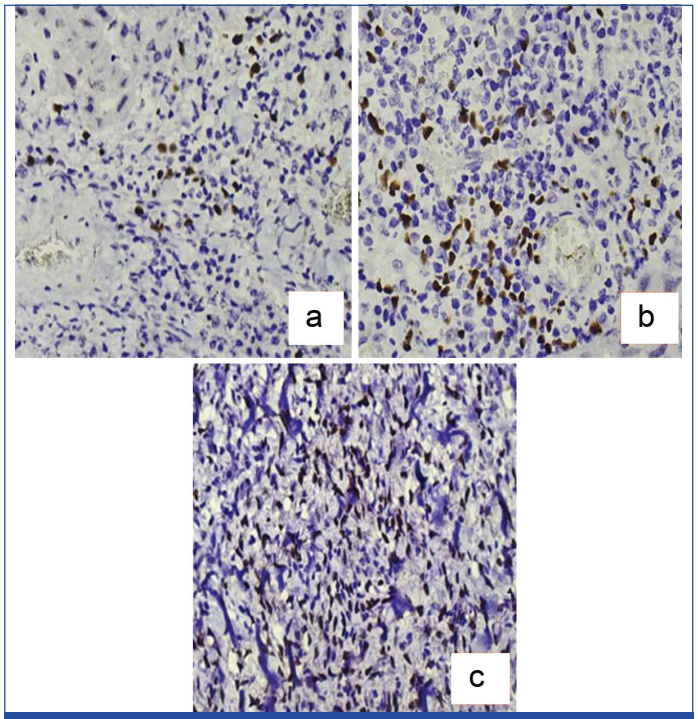
No statistically significant correlation (p=0.055, r=0.209) was found between CD8+TC/FOXP3+ ratio and tumour stage. The correlation analysis suggests a weak negative correlation between the CD8+IM/FOXP3+ ratio and lymph node positivity. However, it was found to be not significant (p=0.093, r=0.181).

DISCUSSION

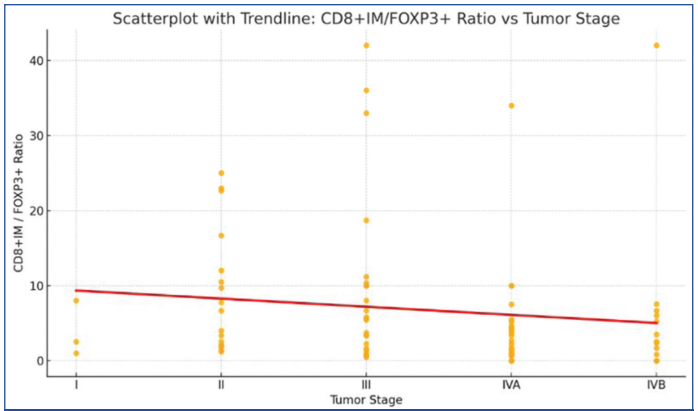
Over the past few decades, research on a variety of prognostic histopathological indicators has been captivated by the aggressiveness of OSCC. It also influences the choice of adjuvant treatment. Tumour thickness, depth of invasion, nodal metastasis and pathological TNM stage are the most well-known evaluable important variables linked to survival in OSCC [18].



[Table/Fig-3]: Immunohistochemical staining of CD8 showing: a) Low; b) Intermediate; c) High membranous staining (400 x magnification).



[Table/Fig-4]: Immunohistochemical staining of FOXP3 showing: a) Low; b) Intermediate; c) High nuclear staining (400 x magnification).



[Table/Fig-5]: Scatterplot showing CD8+ IM / FOXP3+ ratio vs TNM stage.

There is mounting evidence that distinct types of TILs are present in various locations, including peritumoural or intratumoural sites. Thus, the prognosis of individuals may also be influenced by the placement of CD8+T cells. A patient's baseline tumour immune profile is a major factor for immunotherapy effectiveness [19]. Three categories of TME are currently recognised: "immune hot, immune cold and immune altered" [20]. CD3+ and CD8+T cells accumulation is seen in the invasive margin and tumour centre in hot immune tumours, only in invasive margin for immune altered tumours whereas cold immune tumours have no T cells [21].

It was observed in the present study that both CD8+IM and CD8+TC low scoring were noted in higher T stages. Even though it

was not statistically significant, similar findings were noted in studies done by Lequerica-Fernandez P et al., [22] and Mukherjee G et al., with regards to CD8+ infiltration in invasive margin [16]. Meanwhile, CD8+ scoring in tumour centre showed opposite findings to a study done by Lequerica-Fernandez P et al., [22]. This could be attributed to difference in the scoring method used. Present study findings on CD8+ TC with regards to T stage correlates with a study done by Mukherjee G et al., [16]. These findings suggest how cytotoxic CD8+ T cells contribute to host anti-tumour response.

On comparing FOXP3+ results of the present study, it was not concurrent with other studies done by Lequerica-Fernandez P et al., Song JJ et al., and Hayashi T et al., [22-24]. Present study observed low FOXP3+ scoring found in higher T stages meanwhile other studies suggested otherwise. This could be due to the distinct scoring systems used and FOXP3+ expression varying within tumours affecting the results which can also explain tumour heterogeneity.

High CD8+ scoring at invasive margin was associated with node negative cases (p=0.0074). Similar findings were noted in study done by Mukherjee G et al., [16]. In the present study, we observed that low FOXP3+ expression was associated with node negative cases (p=0.2052) which was a contradictory finding when compared to studies done by Lequerica-Fernandez P et al., Song JJ et al., Hayashi T et al., and Ni Y et al., [22-25]. Since there is no established standard method for scoring FOXP3, different studies have used different methods of scoring.

It was observed that both CD8+IM (p=0.0092) and CD8+ TC (p=0.5271) low scoring was associated with higher TNM stages. This finding was consistent with Lequerica-Fernandez P et al., study findings when scoring was done in invasive margins [22].

Also, increased CD8+ IM/FOXP3+ ratio was found to be associated with lower TNM stages (p=0.023). This finding strongly concurred with a study done by Ni Y et al., [25]. The CD8+IM/FOXP3+ ratio is a promising biomarker in cancer research. Modulating this ratio could enhance anti-tumour immunity and improve treatment outcomes. Understanding the relationship between FOXP3+ expression and tumour stage can help in better understanding of cancer biology.

Lequerica-Fernandez P et al., in their study of 125 OSCC cases evaluated both stromal and tumoural FOXP3+ and emphasised on superiority of FOXP3 with respect to clinical outcomes [22]. A considerably better prognosis was linked to higher concentrations of stromal and tumoural FOXP3 (p=0.03 and p=0.03, respectively) among his study group. Meanwhile, low tumoural CD8+/FOXP3+ ratio was also found to significantly associated with a better prognosis (p=0.04) and a low stromal CD8+/FOXP3+ ratio was significantly associated with well-differentiated tumours (p=0.03). These findings were different from studies done by Kirchner J et al., and Kakkar A et al., where they observed high CD8+/FOXP3+ ratio correlating with good clinical outcomes [26,27].

In the present study, CD8+IM correlated with nodal metastasis and TNM staging. Meanwhile, when considered as a ratio between the two, increased CD8+IM/FOXP3+ ratio associated with lower TNM stages (p=0.023). This shifts the focus on importance of estimating the ratio between the different subpopulations of TILs rather than considering them each independently.

These results underline the notion that the quantity, location and roles of TILs are dynamic in nature and support the existence of various TIL subtypes in OSCC tumour microenvironment interacting with one another to exercise their effects.

Limitation(s)

Being an Institutional based study, the patient population included may not fully represent the broader demographic or clinical spectrum of OSCC, as regional factors could influence disease characteristics. The small sample size may also limit the study's generalisability and differences in methods of immunohistochemical scoring may affect the results. Multicenter studies involving diverse populations are needed to validate these findings and assess their broader applicability.

CONCLUSION(S)

FOXP3 and CD8 expression in OSCC may serve as prognostic biomarkers and their interplay in different sites of tumour can shape the TME. With CD8+IM being significantly correlated with nodal metastasis and pathological TNM staging, it signifies its prognostic value in oral cancer. Positive correlation between high CD8+IM/FOXP3+ ratio and lower TNM stages may also shed light on how tumour cells evade the immune system, with FOXP3 Treg cells potentially contributing to immune suppression and CD8+T cells playing a role in anti-tumour immunity.

REFERENCES

[1] Kalyani R, Das S, Bindra Singh MS, Kumar H. Cancer profile in the Department of Pathology of Sri Devaraj Urs Medical College, Kolar: A ten years study. Indian J Cancer. 2010;47:160-65.

[2] Suresh TN, Hemalatha A, Harendra Kumar ML, AzeemMohiyuddin SM. Evaluation of histomorphological and immunohistochemical parameters as biomarkers of cervical lymph node metastasis in squamous cell carcinoma of oral cavity: A retrospective study. J Oral Maxillofac Pathol. 2015;19(1):18-24.

[3] Sasahira T, Kirita T. Hallmarks of Cancer-Related Newly Prognostic Factors of Oral Squamous Cell Carcinoma. Int J Mol Sci. 2018;19(8):2413.

[4] Jiang M, Li B. STAT3 and its targeting inhibitors in oral squamous cell carcinoma. Cells. 2022;11(19):3131.

[5] Galon J, Mlecnik B, Bindea G, Angell HK, Berger A, Lagorce C, et al. Towards the Introduction of the "Immunoscore" in the Classification of malignant tumours. J Pathol. 2014;232:199-209.

[6] Ruiz-Ranz M, Lequerica-Fernandez P, Rodriguez-Santamarta T, Suarez-Sanchez FJ, Lopez-Pintor RM, Garcia-Pedrero JM, et al. Prognostic implications of preoperative systemic inflammatory markers in oral squamous cell carcinoma, and correlations with the local immune tumour microenvironment. Front Immunol. 2022;13:941-51.

[7] Schreiber RD, Old LJ, Smyth MJ. Cancer immunoediting: Integrating immunity's roles in cancer suppression and promotion. Science. 2011;331(6024):1565-70.

[8] Fu Q, Chen N, Ge C, Li R, Li Z, Zeng B, et al. Prognostic value of tumour infiltrating lymphocytes in melanoma: A systematic review and meta-analysis. OncoImmunology. 2019;8(7):e1593806.

[9] Uppaluri R, Dunn GP, Lewis JS Jr. Focus on TILs: Prognostic significance of tumour infiltrating lymphocytes in head and neck cancers. Cancer Immun. 2008;8:16-24.

[10] DiPaolo RJ, Glass DD, Bijwaard KE, Shevach EM. CD4+CD25+ T cells prevent the development of organ-specific autoimmune disease by inhibiting the differentiation of autoreactive effector T cells. J Immunol. 2005;175(11):7135-42.

[11] Sakaguchi S. Naturally arising Foxp3-expressing CD25+ CD4+ regulatory T cells in immunological tolerance to self and non-self. Nat Immunol. 2005;6:345-52.

[12] Stasikowska-Kanicka O, Wągrowska-Danilewicz M, Danilewicz M. Immunohistochemical analysis of Foxp3+, CD4+, CD8+ cell infiltrates and PD-L1 in oral squamous cell carcinoma. Pathol Oncol Res. 2018;24(3):497-505.

[13] Fiedler M, Off A, Eichberger J, Spoerl S, Schuderer JG, Taxis J, et al. OSCC in never smokers and never-drinkers is associated with increased expression of tumour-infiltrating lymphocytes and better survival. Cancers (Basel). 2023;15(10):268-78.

[14] De Meulenaere A, Vermassen T, Aspeslagh S, Zwaenepoel K, Deron P, Duprez F, et al. Prognostic markers in oropharyngeal squamous cell carcinoma: Focus on CD70 and tumour infiltrating lymphocytes. Pathology. 2017;49(4):397-404.

[15] Almangush A, Makitie AA, Triantafyllou A, de Bree R, Strojan P, Rinaldo A et al. Staging and grading of oral squamous cell carcinoma: An update. Oral Oncology. 2020;107:104799.

[16] Mukherjee G, Bag S, Chakraborty P, Dey D, Roy S, Jain P et al. Density of CD3+ and CD8+ cells in gingivo-buccal oral squamous cell carcinoma is associated with lymph node metastases and survival. PLoS One. 2020;15(11):e0242058.

[17] Alqutub S, Alqutub A, Bakhshwin A, Mofti Z, Alqutub S, Alkhamesi AA, et al. Histopathological predictors of lymph node metastasis in oral cavity squamous cell carcinoma: A systematic review and meta-analysis. Front Oncol. 2024;14:1401-21.

[18] Kademani D, Bell RB, Bagheri S, Holmgren E, Dierks E, Potter B et al. Prognostic factors in intraoral squamous cell carcinoma: The infuence of histologic grade. J Oral Maxillofac Surg. 2005;63:1599-605.

[19] Tumeh PC, Harview CL, Yearley JH, Shintaku IP, Taylor EJ, Robert L, et al. PD-1 blockade induces responses by inhibiting adaptive immune resistance. Nature. 2014;515(7528):568-71.

[20] Kolenda T, Przybyla W, Kapalczynska M, Teresiak A, Zajaczkowska M, Blizniak R, et al. Tumour microenvironment-Unknown niche with powerful therapeutic potential. Rep Pract Oncol Radiother. 2018;23(3):143-53.

[21] Galon J, Bruni D. Approaches to treat immune hot, altered and cold tumours with combination immunotherapies. Nat Rev Drug Discov. 2019;18(3):197-218.
[22] Lequerica-Fernandez P, Suarez-Canto J, Rodriguez-Santamarta T, Rodrigo JP, Suarez-Sanchez FJ, Blanco-Lorenzo V, et al.. Prognostic relevance of $CD4^+$, $CD8^+$ and $FOXP3^+$ TILs in oral squamous cell carcinoma and correlations with PD-L1 and cancer stem cell markers. Biomedicines. 2021;9(6):653-62.
[23] Song JJ, Zhao SJ, Fang J, Ma D, Liu XQ, Chen XB, et al. Foxp3 overexpression in tumour cells predicts poor survival in oral squamous cell carcinoma. BMC Cancer. 2016; 26;16:530-42.
[24] Hayashi T, Yoshikawa K, Suzuki S, Gosho M, Ueda R, Kazaoka Y, et al. Tumour-infiltrating FoxP3+ T cells are associated with poor prognosis in oral squamous cell carcinoma. Clin Exp Dent Res. 2022;8(1):152-59.
[25] Ni Y, Zhang X, Lu Z, Huang XF, Wang ZY, Yang Y, et al. Tumour-Infiltrating CD1A+ DCs and CD8+/FoxP3+ ratios served as predictors for clinical outcomes in tongue squamous cell carcinoma patients. Pathol Oncol Res. 2020;26(3):1687-95.
[26] Kirchner J, Plesca I, Rothe R, ResagA, Lock S, Benesova I, et al. Type I conventional dendritic cells and $CD8^+$ T cells predict favorable clinical outcome of head and neck squamous cell carcinoma patients. Front Immunol. 2024;15:1414-18.
[27] Kakkar A, Thakur R, Roy D, Sood R, Sharma A, Malhotra RK, et al. Tumour-infiltrating lymphocyte subsets and their individual prognostic impact in oral squamous cell carcinoma. J Clin Pathol. 2024;77(12):822-28.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar, Karnataka, India.
2. Professor and Head, Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar, Karnataka, India.
3. Professor and Head, Department of Surgical Oncology, Sri Devaraj Urs Medical College, Tamaka, Kolar, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. TN Suresh,
Professor and Head, Department of Pathology, Sri Devaraj Urs Medical College, Tamaka-563103, Kolar, Karnataka, India.
E-mail: Sureshtn.path@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 28, 2025
- Manual Googling: Apr 29, 2026
- iThenticate Software: May 01, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Dec 24, 2025**
Date of Peer Review: **Feb 27, 2026**
Date of Acceptance: **May 04, 2026**
Date of Publishing: **Sep 01, 2026**