



Original Research Article

Expression of CD44 and Ki-67 in oral squamous cell carcinoma

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ABSTRACT

Aim and Objectives: The present study was done to evaluate the immunohistochemical expression of CD44 and Ki-67 in cases of oral squamous cell carcinoma.

Materials and Methods: A Hospital based observational study was conducted at the Department of pathology, in a tertiary teaching hospital in western Uttar Pradesh. The study included specimens of oral lesions undergone incisional biopsies and/or radical complete surgical resection diagnosed as squamous cell carcinoma. Specimens were grossed, processed, paraffin embedded, appropriate sections were taken and Haematoxylin and eosin stained, then examined under microscope. Immunohistochemical markers-CD44 and Ki-67 were applied.

Results: Most common sites were tongue (40.0%) and buccal mucosa (35.0%). The correlation of CD44 and Ki-67 score with histological grades in Oral Squamous Cell Carcinoma were significant in all three grades i.e., grade 1, grade 2 and grade 3.

Conclusion: The immunoexpression of CD44 may have prognostic significance in determining the tumour's stage, grade, degree of invasiveness, and likelihood of metastasis. Ki-67 is a simple to use indicator of cell proliferation whose expression is positively correlated with the development of illness. As a result, it is a marker of carcinogenesis and malignant transformation in oral premalignant lesions. IHC methods may be costly and time-consuming, but their evaluation could be utilised to guide treatment choices for individuals with OSCC.

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1. Introduction

The most prevalent kind of cancer arises from the squamous epithelium of the upper aerodigestive tract. Head and neck cancer affects about 10.3% of all cases in India as in the year 2020. Lip and oral cavity cancers are second most common among the top ten malignancies in India.¹ One of the most frequent malignant tumours in the world is oral squamous cell carcinoma. In South East Asia, notably in India, it predominates significantly, accounting for 19% of all male cancer cases and 7% of female cancer cases.²

Variations in OSCC incidence, mortality, location, grade, histological type, and tumour stage at diagnosis have all been linked to differences in gender, race, and age.³ Cancers of the lip mucosa, tongue, gingiva, mouth's floor, palate, and others are considered to be oral cancers.^{4,5}

Oral squamous cell carcinomas (OSCC), are heterogeneous tumours that arise predominantly as a result of ongoing mutations brought on by genetic instability and environmental effects. The origin of OSCCs might be cancer stem cells, clonal evolution, or a combination of the two.⁶ The oral squamous cell carcinoma has the grading systems like TNM Staging, Broder's system and Anneroth's classification.⁷

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The cell adhesion molecule known as CD44 is a transmembrane protein that has a role in both cell-to-cell and cell-to-matrix contacts. In addition to this, it is a marker for cancer stem cells and possesses two different phenotypes: 1) The epithelial-mesenchymal transition phenotype, found in cancer stem cells that express the CD44 isoform and are resistant to proteolysis. 2) The cancer stem cells having an epithelial phenotype and express CD44v isoforms that are susceptible to trypsin. This helps in distinguishing between epithelial phenotype cancer stem cells and epithelial-mesenchymal transition phenotype, as epithelial phenotype cancer stem cells have a lower expression of CD44 than epithelial-mesenchymal transition phenotype cells.⁸

During the G1, S, G2, and M phases of the cell cycle, the big, non-histone protein known as Ki-67 has been utilised as a marker of proliferative activity. One of the indications for tumour invasion potential and the invasive activity of tumours connected to the degree of malignant neoplastic cells is the degree to which tumour cells express the protein Ki-67 through their proliferative activity. Expression of Ki-67 antigen is elevated in both dysplasia and SCC as compared to normal mucosa.⁹

It gives distinct reaction patterns that only involve proliferating cells, immunostaining with antibodies to Ki-67 antigen is well established as a method that is both quick and efficient for evaluating growth fractions of various tumour types.¹⁰ Tumours expressing higher Ki-67 carry poor prognosis. The present study was done to evaluate the immunohistochemical expression of CD44 and Ki-67 in histopathologically diagnosed cases of oral squamous cell carcinoma.

2. Materials and Methods

This Hospital based observational study was conducted at the Department of Pathology. Samples of oral lesions diagnosed as squamous cell carcinoma in the department of Pathology were taken. The study was conducted for duration of 18 month i.e., April 2021 to October 2022. Sixty cases were included in the study.

2.1. Study population

Oral lesions, 'histopathologically diagnosed' as squamous cell carcinoma, falling within specified duration of time in our hospital, were thoroughly evaluated for tumour grading and IHC expression of Ki-67 and CD 44. Clinical data records, blocks, slides etc were retrieved from archives of histopathology lab, Department of Pathology.

2.2. Inclusion criteria

Specimens of oral lesions undergone incisional biopsies and/or radical complete surgical resection diagnosed as squamous cell carcinoma.

2.3. Exclusion criteria

Tissues without adequate size and representative material and tissue biopsies of patients who had undergone radiotherapy and/or chemotherapy.

2.4. Study method

2.4.1. Histopathological examination

Processing of well labelled specimens were done in our department after fixation of the specimen in 10% neutral buffered formalin for 24-48 hrs. Specimens were grossed, processed, paraffin embedded, appropriate sections were taken and Hematoxylin and eosin stained, then examined under microscope.

2.4.2. Immunohistochemistry

CD44 and Ki-67 were applied on histologically diagnosed oral squamous cell carcinoma. Malignant cells were graded for CD44 membranous staining (Table 1)⁹ and malignant cells were graded for Ki-67 nuclear staining (Table 2).¹⁰

Normal tonsil was taken as a positive control for CD44 and lymph node was taken as positive control for Ki-67.

2.5. Statistical analysis

SPSS version 25.0 analysed the Excel data when it was loaded. Quantitative (numerical variables) data was given as mean and standard deviation, whereas qualitative (categorical variables) data was provided as frequency and percentage. If $p < 0.05$, it was statistically significant.

2.6. Ethics

Proper approval of institutional ethical committee was obtained before starting the study (MMC/IEC/2021/213).

3. Results

In the present study we studied 60 cases of Squamous Cell Carcinoma. Majority of the subjects belonged to 40-49 years (36.7%) followed by 30-39 years (20.0%), 50-59 years (15.0%) and above 70 years (13.3%). The mean age was 50.90 ± 14.08 years. There were 50 (83.3%) males and 10 (16.7%) females.

Out of 60 cases, Majority of cases i.e. 30 cases (50%) were showing ulcero-proliferative type of growth, followed by 18 cases (30%) showing proliferative growth and rest 12 cases (20%) were having ulcerative type growth.

Maximum number of cases i.e., 32 cases (53.3%) were that of grade 2, followed by 20 cases (33.3%) of grade 1, and 08 cases (13.3%) of grade 3. (Table 3)

On correlation of Ki 67 score with Histological grade, the mean Ki67 percentage was significantly more among poorly differentiated ($81.88\% \pm 5.94\%$) compared to moderately differentiated ($33.13\% \pm 15.44\%$) which was significantly

more than well differentiated ($23.50\% \pm 9.75\%$). On contrary, the correlation of CD 44 score with histological grade, the mean CD44 percentage was significantly more among well differentiated ($75.50\% \pm 11.46\%$) compared to moderately differentiated ($63.28\% \pm 25.39\%$) which was significantly more than poorly differentiated ($45.63\% \pm 16.57\%$). Correlation of Ki-67 and CD44 score with histological grades in OSCC was done. (Table 4, Figure 1). Correlation of Ki-67 and CD44 score with histological grades in OSCC revealed p value <0.05 i.e. statistically significant. On comparison, there was statistically significant difference among histological grades.

Table 1: Malignant cells were graded for CD44 membranous staining as follows⁹

| Score | Percentage |
|-------|-----------------------------------|
| 0 | <10% positive cells |
| 1 | Between 10 and 25% positive cells |
| 2 | Between 25 and 50% positive cells |
| 3 | Between 50 and 75% positive cells |
| 4 | >75% positive cells |

Table 2: Malignant cells were graded for Ki-67 nuclear staining (Ki-67 LI Labelling Index)¹⁰ was graded as

| Score | Percentage |
|-------|------------|
| 0 | LI=0% |
| 1 | LI=1%-25% |
| 2 | LI=26%-50% |
| 3 | LI=51%-75% |
| 4 | LI=>75% |

4. Discussion

Squamous cell carcinoma accounts for 95% of the malignant tumors of the oral cavity. More than 60% of the patients present with an advanced stage of the disease. According to Leite and Koifman's research, patients with carcinoma of the tongue died more frequently than those with carcinoma of the lip.¹¹ In addition, the superior gingivo-facial sulcus is associated with a worse prognosis because of the difficulty in assessing and treating local extension and the abundant lymphatic drainage in that area.¹²

Most of the tumors in this study were histological grade II i.e., 53.3% followed by 33.3% in grade I and 13.3% in grade III. The study bears close resemblance to studies done by Wangsa D et al,¹³ A R Gadbaile et al.¹⁴ all of which reported maximum cases in grade II followed by grade I and grade III i.e., moderately differentiated OSCC, followed by well differentiated OSCC, followed by poorly differentiated OSCC. The findings were in contrast with the study done by Takkem A et al.¹⁵ in which maximum number of cases were

seen in grade 3 i.e., poorly differentiated OSCC.

In our study of 60 cases of OSCC, Ki-67 Score 4+ was significantly more among poorly differentiated. The mean Ki-67 percentage was significantly more among Poorly differentiated ($81.88\% \pm 5.94\%$) compared to moderately differentiated ($33.13\% \pm 15.44\%$) which was significantly more than well differentiated ($23.50\% \pm 9.75\%$).

Thirty cases of OSCC were examined by Moghadam S et al¹⁶ for Ki-67 expression. For Well differentiated OSCC, the mean Ki-67 was 23.3, for Moderately differentiated OSCC, the mean was 41.2, and for Poorly differentiated OSCC, the mean was 64.1. Takeem A et al¹⁵ found that for well differentiated OSCC, the mean Ki-67 protein was 12.7, for moderately differentiated OSCC mean was 30.6, and for poorly differentiated OSCC mean was 53.5, it was determined that the expression of Ki-67 rose steadily with OSCC grade.

Mittal et al¹⁷ stated that the average number of positive nuclei per millimetre of length was significantly higher in Oral potentially malignant lesions (OPMLs) with a high proliferation rate than in OPMLs with a low proliferation rate. Within the Malignant lesions, PDSOC had the highest Ki67 LI (66.00 ± 8.4), followed by MDSCC (62.66 ± 8.02) and WDSOC (55.10 ± 6.1). Ki67 LI was shown to be statistically significant throughout all stages of malignancy, which is in line with the findings of Buch A et al¹⁸ and Tumuluri et al.¹⁹

Abdelbary et al²⁰ found that the mean Ki-67 protein was 21.3, for moderately differentiated OSCC mean was 31.3, and for poorly differentiated OSCC mean was 43.5. Verma R et al²¹ reported that the mean Ki-67 was 67.33 for Well differentiated OSCC, 75.5 for Moderately differentiated OSCC and 81.45 for Poorly differentiated OSCC.

Tumuluri V et al¹⁹ indicated that the histological grading of OSCC and the Ki-67 proliferative indices obtained were linked with each other. Whereas, Stoll et al²² revealed that the Ki-67 index was unable to predict survival in 107 patients with OSCC. These contradictory findings can be related to the tumour type or the immunohistochemical analysis technique (quantitative, qualitative or both). Additionally, population habits may be linked to sample heterogeneity, which could affect how the lesion behaves.

In comparison to well-differentiated OSCC, moderately differentiated OSCC had a greater overall Ki-67 staining.¹⁵ Ki-67 staining was diffuse in the majority of the central region of tumour islands, but nuclear Ki-67 positivity was seen at the periphery of poorly differentiated OSCC, indicating that these cells were less differentiated and in a more proliferative phase.¹⁵

Oral squamous cell carcinomas have been linked to heightened expression of the Ki- 67 protein in tumour tissues²³ The levels of the protein Ki-67 rise in Oral Epithelial Dysplasia and OSCC as tissue differentiation falls.¹⁵ Ki-67 protein is a potential therapeutic target in cancer due to its expression in all proliferating cells and

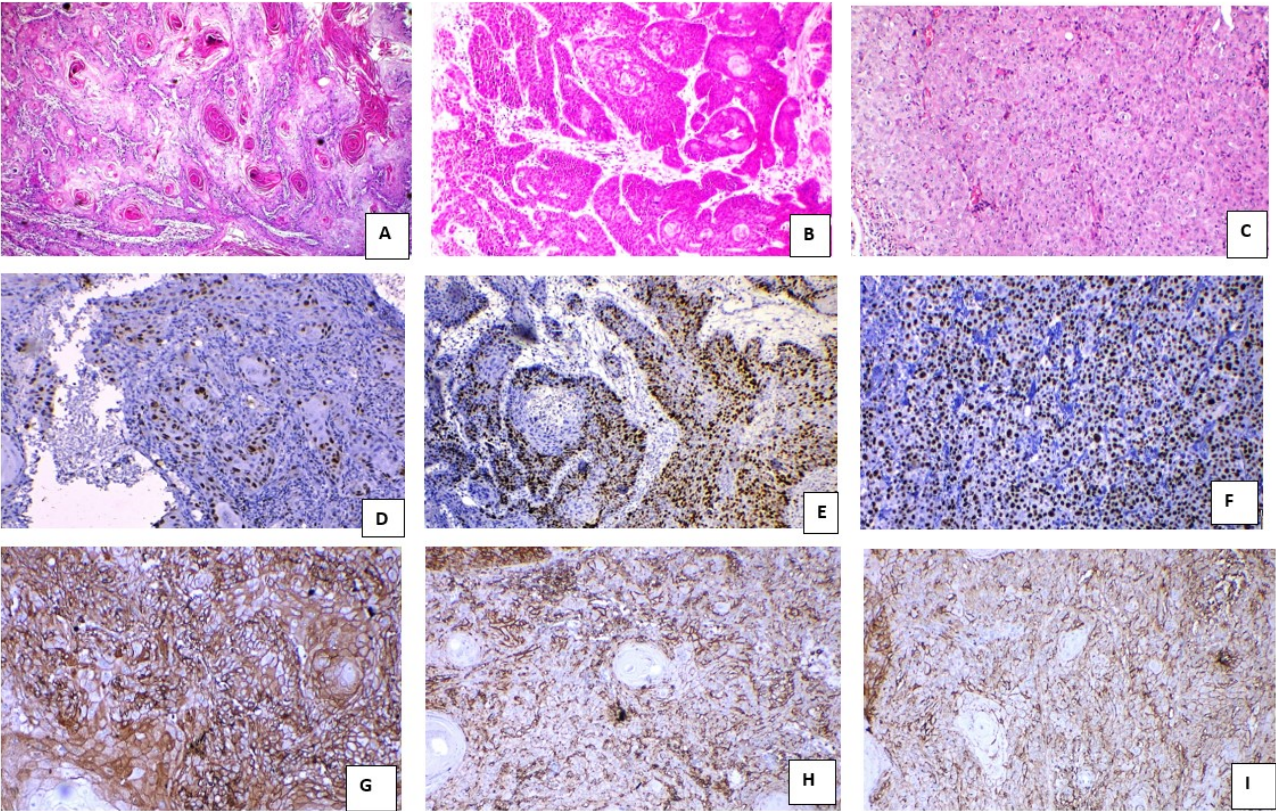


Figure 1: Photomicrograph showing| **A:** Well differentiated; **B:** Moderately differentiated and **C:** Poorly differentiated oral squamous cell carcinoma (H&E 100x); **D:** Well differentiated oral squamous cell carcinoma showing immunopositivity for Ki-67 score-1; **E:** Moderately differentiated oral squamous cell carcinoma showing immunopositivity for Ki-67 score-2; **F:** Poorly differentiated oral squamous cell carcinoma showing immunopositivity for Ki-67 score- 3; **G:** Well differentiated oral squamous cell carcinoma showing immunopositivity for CD44 score-4; **H:** Moderately differentiated oral squamous cell carcinoma showing immunopositivity for CD44 score-2; **I:** Poorly differentiated oral squamous cell carcinoma showing immunopositivity for CD44 score-2 (IHC 400x) respectively.

Table 3: Distribution of histological grades in OSSC cases

| Histological Grade | No. of Cases | Percentage |
|---------------------------|--------------|------------|
| Well Differentiated | 20 | 33.3% |
| Moderately Differentiated | 32 | 53.3% |
| Poorly Differentiated | 8 | 13.3% |
| Total | 60 | 100.0% |

Table 4: Correlation of Ki-67 and CD44 score with histological grades in OSCC

| Grade | Ki-67 Score | | | | CD-44 Score | | | | p-value |
|-------|-------------|---------|----------|----------|-------------|----------|-----------|------------|---------|
| | 1+ | 2+ | 3+ | 4+ | 1+ | 2+ | 3+ | 4+ | |
| 1 | 10(50%) | 10(50%) | 0(0%) | 0(0%) | 0(0%) | 0(0%) | 9(45%) | 11(55%) | 0.008** |
| 2 | 11(34.4%) | 16(50%) | 5(15.6%) | 0(0%) | 2(6.25%) | 8(25%) | 12(37.5%) | 10(31.25%) | 0.027* |
| 3 | 0(0%) | 00.0% | 1(12.5%) | 7(87.5%) | 2(25%) | 5(62.5%) | 1(12.5%) | 0(0%) | 0.039* |

the prognostic value of the Ki-67 marker in many cancers. Strategies that inactivate Ki-67 protein are a promising anti-proliferative approach, with potential application in cancer treatment.²⁴

Kaza et al²⁵ found that the mean value of CD44 immunopositive cells was found in well-differentiated squamous cell carcinomas compared to moderately and poorly differentiated squamous cell carcinomas. Immunostaining scores of 3 and 4, indicating the presence of 50-75% and above 75% positive cells, were consistently among well-differentiated squamous cell carcinoma.

Hema KN et al²⁶ revealed that CD44 expression by tumour cells in OSCC was statistically correlated with the tumour grade i.e., Higher mean was observed in well-differentiated squamous cell carcinoma (10.8), followed by Moderately differentiated squamous cell carcinoma (5.9) and poorly differentiated squamous cell carcinoma showed least CD44 immunopositivity (3.7).

Research by Stoll et al²² and Kanke et al²⁷ all support these results. The degree of cellular proliferation and differentiation was linked to the limited expression of CD44 in different stages of OSCC. The immunostaining expression of CD44 decreases as tumour grade rises, which may indicate a lack of cell-cell adhesion and contribute to the smooth disassembly of cells. Since poorly differentiated squamous cell carcinomas are characterized by highly pleomorphic cells that have little similarity to the parent tissue, low levels of CD44 immunostaining are often seen in these tumours.²⁵

Moraes et al²⁸ found that 30 out of 52 cases had positive membranous staining of CD44. The median rate of cell division, as measured by Ki-67, was 37.1% in malignancies. In poorly differentiated tumours in particular, Ki-67 was shown to be expressed all over the parenchyma of the tumour. So, Ki-67 appears to be crucial in the cellular growth of many cancers. Ki-67 has a relationship with both cellular differentiation and proliferation. Cell-cell adhesion, lymphocyte activation, and cell substrate interaction are only a few of the regular uses for the cell membrane molecule CD44. Hyaluronan is bound by CD44. As a result, CD44 may have minimal expression or not function at all, giving the tumour an advantage.²⁹

Expression of KI-67 and CD 44 has also been studied on cervical squamous cell carcinoma. About 73.1% and 26.9% of cases were strongly positive and positive, respectively, for Ki-67 expression. 65.4%, 30.8%, and 3.8% of cases were strongly positive, positive, and weakly positive, respectively, for CD44 expression. Ki-67, and CD44 expression between the three groups were statistically significant.³⁰

Cvema et al, revealed that CD44 intra-cytoplasmic and membranous expression can be recommended as an early indicator of signs of malignant transformation in non-homogeneous leukoplakia and possible loss of stemness.³¹

One of the reasons for OSCC therapy failure is the presence of a small pluripotent cell subpopulation identified as “cancer stem cells” (CSCs), which are considered to have a tumour-initiating and self-renewal ability. The transmembrane glycoprotein CD44 has been recognized as a characteristic CSC surface marker that may be used independently or in combination with other markers for the identification of CSCs in various cancers.³²

5. Conclusion

In order to diagnose OSCC, choose a course of treatment, and determine the prognosis, immunohistochemistry has become a routine procedure. Statistically significant differences among histological grades signifies that immunohistochemistry expression of Ki-67 and CD44 can be used for prognosis and treatment of patients. Thus, the IHC marker CD44 and Ki-67 have been proven to be particularly helpful in predicting the invasive behavior of OSCC. One of the major limitations of this study is small sample size. Thus, further more studies on a larger sample size are needed for generalization of the results of this study.

6. Source of Funding

None.

7. Conflict of Interest


None.


References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021;71(3):209–49.
2. Zhu DW, Liu Y, Yang X, Yang CZ, Ma J, Yang X, et al. Low Annexin A1 expression predicts benefit from induction chemotherapy in oral cancer patients with moderate or poor pathologic differentiation grade. *BMC Cancer.* 2013;13:301. doi:10.1186/1471-2407-13-301.
3. Funk GF, Karnell LH, Robinson RA, Zhen WK, Trask DK, Hoffman HT, et al. Presentation, treatment, and outcome of oral cavity cancer: A national cancer data base report. *Head Neck.* 2002;24(2):165–80.
4. Sankaranarayanan R, Ramadas K, Amarasinghe H, Subramanian S, Johnson N. Oral Cancer: Prevention, Early Detection, and Treatment. vol. 3. Washington (DC: The International Bank for Reconstruction and Development / The World Bank; 2015.
5. Mchugh JB, Goldblum JR, Lamps LW, McKenny JK, Myers JL. Upper aerodigestive tract. In: Rosai and Akerman's Surgical Pathology. vol. 2018. Elsevier; p. 1–146.
6. Mărgăritescu C, Pirici D, Simionescu C, Stepan A. The utility of CD44, CD117 and CD133 in identification of cancer stem cells (CSC) in oral squamous cell carcinomas (OSCC). *Rom J Morphol Embryol.* 2011;52:985–93.
7. Akhter M, Hossain S, Rahman QB, Molla MR. A study on histological grading of oral squamous cell carcinoma and its co-relationship with regional metastasis. *Journal Oral Maxillofacial Pathology.* 2011;15(2):168–76.
8. Biddle A, Liang X, Gammon L, Fazil B, Harper LJ, Emich H. Cancer stem cells in squamous cell carcinoma switch between two distinct phenotypes that are preferentially migratory or proliferative. *Cancer*


- Res. 2011;71(15):5317–5343.
9. Endl E, Gerdes J. The Ki-67 protein: fascinating forms and an unknown function. *Exp Cell Res*. 2000;257(2):231–7.
 10. Brown DC, Gatter KC. Monoclonal antibody Ki-67: its use in histopathology. *Histopathology*. 1990;17(6):489–503.
 11. Leite IC, Koifman S. 1998.
 12. Massano J, Regateiro FS, Januário G, Ferreira A. Oral squamous cell carcinoma: review of prognostic and predictive factors. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(1):67–76.
 13. Wangsa D, Ryott M, Åvall Lundqvist E, Petersson F, Elmberger G, Luo J, et al. Ki-67 expression predicts locoregional recurrence in stage I oral tongue carcinoma. *Br J Cancer*. 2008;99(7):1121–8.
 14. Gadbail AR, Sarode SC, Chaudhary MS, Gondivkar SM, Takade SA, Yuwanati M, et al. Ki67 Labelling Index predicts clinical outcome and survival in oral squamous cell carcinoma. *J Appl Oral Sci*. 2021;3:e20200751.
 15. Takkem A, Barakat C, Zakaraia S, Zaid K, Najmeh J, Ayoub M, et al. Ki-67 Prognostic Value in Different Histological Grades of Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma. *Asian Pac J Cancer Prev*. 2018;19(11):3279–86.
 16. Atarbashi-Moghadam S, Monji DY, Namdari M, Mokhtari S. Differential expression of cell proliferation and apoptosis markers in squamous cell carcinoma of the tongue in young and old patients. *Indian J Oral Health Res*. 2018;4(2):42. doi:10.4103/ijohr.ijohr_3_19.
 17. Mittal A, Awasthi S, Chauhan R, Ahmad F, Kumar A, Mitra N, et al. Ki-67 expression in oral potential malignant and malignant lesions and correlation of mitotic index with MIB-1 labeling index. *Acta Medica International*. 2022;9(1):14–20.
 18. Buch A, Halder N, Kheur S, Chandanwale S, Kumar H. Correlation between ki- 67 labeling index and mitotic index in oral squamous cell carcinoma. *Clin Cancer Investig J*. 2019;8(3):90–5.
 19. Tumuluri V, Thomas GA, Fraser IS. Analysis of the Ki-67 antigen at the invasive tumour front of human oral squamous cell carcinoma. *J Oral Pathol Med*. 2002;31(10):598–604.
 20. Abdelbary RM, Elzarka MS, Fouad HA, Fata MM. Expression of Ki-67 and CD105 markers in Oral Squamous Cell Carcinoma. *Alexandria Dent J*. 2019;44(1):117–22.
 21. Verma R, Singh A, Jaiswal R, Chandra A, Verma R, Tak J, et al. Association of Ki-67 antigen and p53 protein at invasive tumour front of oral squamous cell carcinoma. *Indian J Pathol Microbiol*. 2014;57(4):553–7.
 22. Stoll C, Baretton G, Soost F, Terpe HJ, Domide P, Löhns U, et al. Prognostic importance of the expression of CD44 splice variants in oral squamous cell carcinomas. *Oral Oncol*. 1999;35(5):484–9.
 23. He W, Xiao Y, Chen WM. Expression of Ki-67 and P53 protein in oral squamous cell carcinoma and its clinical significance. *Shanghai Kou Qiang Yi Xue*. 2015;24(2):228–31.
 24. Kausch I, Lingnau A, Endl E, Sellmann K, Deinert I, Ratliff TL, et al. Antisense treatment against Ki-67 mRNA inhibits proliferation and tumour growth in vitro and in vivo. *Int J Cancer*. 2003;105(5):710–6.
 25. Kaza S, Kantheti LP, Poosarla C, Gontu SR, Kattappagari KK, Baddam VR, et al. A study on the expression of CD44 adhesion molecule in oral squamous cell carcinoma and its correlation with tumour histological grading. *J Orofacial Sci*. 2018;10(1):42–9.
 26. Hema KN, Rao K, Devi HU, Priya NS, Smitha T, Sheethal HS, et al. Immunohistochemical study of CD44s expression in oral squamous cell carcinoma-its correlation with prognostic parameters. *J Oral Maxillofac Pathol*. 2014;18(2):162–8.
 27. Kanke M, Fujii M, Kameyama K, Kanzaki J, Tokumaru Y, Imanishi Y, et al. Clinicopathological significance of expression of CD44 variants in head and neck squamous cell carcinoma. *Jpn J Cancer Res*. 2000;94(4):410–5.
 28. De Moraes F, Lourenço SV, Ianez RC, De Sousa E, Silva MM, Damascena AS, et al. Expression of stem cell markers in oral cavity and oropharynx squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2017;123(1):113–22.
 29. Spafford MF, Koeppe J, Pan Z, Archer PG, Meyers AD, Franklin WA, et al. Correlation of tumor markers p53, bcl-2, CD34, CD44H, CD44v6, and Ki-67 with survival and metastasis in laryngeal squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg*. 1996;122(6):627–32.
 30. Mehdi HK, Raju K, Sheela SR. Association of P16, Ki-67, and CD44 expression in high-grade squamous intraepithelial neoplasia and squamous cell carcinoma of the cervix. *J Cancer Res Ther*. 2023;19:260–7. doi:10.4103/jcrt.jcrt_43_21.
 31. ICvema, Dzudzilo M, Kleina R, Franckevica I, Svirskis S. Correlation of Soluble CD44 Expression in Saliva and CD44 Protein in Oral Leukoplakia Tissues. *Cancers (Basel)*. 2021;13(22):5739. doi:10.3390/cancers13225739.
 32. Karisik MJ, Lazarevic M, Mitic D, Nikolic N, Markovic MM, Jelovac D, et al. Osteogenic and Adipogenic Differentiation Potential of Oral Cancer Stem Cells May Offer New Treatment Modalities. *Int J Mol Sci*. 2023;24(5):4704. doi:10.3390/ijms24054704.


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