

Clinico-Pathological Features, Management, and Outcome in Patients with Carcinoma of Oral Cavity

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ABSTRACT:

Background: Oral carcinoma ranks 8th commonest carcinoma in the world.⁽¹⁾ In a developing country like India, it becomes the commonest cancers out of all by a gross margin of up to 40% cases annually among all type of cancers. Multiple risk factors and varying trends in the age and subsite demands active research in the field of oral carcinoma. Newer management modalities provide better prognosis than previous treatment protocols. Keeping this in mind, we have conducted and studied extensively on the age, sex, risk factors, subsites, investigations, management, and outcomes in case of carcinoma of oral cavity.

Aims: To evaluate the clinicopathological features, management, and outcome in carcinoma of oral cavity.

Materials and methods: A cross sectional observational study conducted in Santosh medical college during July 2021- June 2022 on 32 patients diagnosed with squamous cell carcinoma of oral cavity.

Results: Most of the patients were in the middle aged less than 5th decade with male predominance. Chewable tobacco had the highest association out of all risk factors in all the cases. Majority of the patients presented with ulcer and buccal mucosa being the commonest subsite of occurrence and having premalignant lesion of leucoplakia as the usual presentation. Majority of cases were presented in the advanced stage.

Conclusion: Oral cavity carcinoma invites serious threat to the Indian population as with the influence of tobacco predominantly chewing and alcohol. Serious association with lower socioeconomic status suggest better habitats and employment, education and awareness in the field of oral cavity carcinoma and their outcomes.

Keywords: Oral cavity carcinoma, tobacco, squamous cell carcinoma, buccal mucosa.

INTRODUCTION:

Oral and oropharyngeal carcinoma accounts for the one among the commonest carcinoma of head and neck worldwide and the commonest carcinoma in India with more than 40% of all carcinomas. ⁽¹⁾ Oral cancer was thought to be off consumption of tobacco and alcohol but with current update, HPV associated head and neck carcinoma is another entity upcoming with cause unknown. ⁽²⁾ There happens to be numerous risk factors in the occurrence of oral carcinoma which has varying prevalence depending on the country. Many cases in the developing world is related to the consumption of tobacco products as smoking or chewable as well as alcohol. But as of the recent advancements and studies, it is stated that in the developed world, the risk factors for oral carcinoma is in a varying trend with more association to viral infections like HPV, EBV etc. More predilections towards HPV virus. ⁽²⁾ In countries like India, being a developing world, the younger generation who are more socioeconomically poor will go for cheaper source of addictions such as chewable tobacco, alcohol which synergistically leads to oral carcinoma. Tobacco-specific N-nitrosamines, such as N-nitrosanornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone are found to be the causative factors either in smoking or chewable variants. Another product being areca nut which is added along with tobacco during consumption as chewable variety adds the carcinogenic property of tobacco. Seconding the risk factor being alcohol, has the polymorphism in the alcohol metabolising enzyme causing the risk towards oral carcinoma. More factors like inadequate oral hygiene, chronic trauma like in case of broken teeth, dentures, caries etc, genetic factors are other factors that as considered to be the causatives for oral carcinoma. Squamous cell carcinoma constitutes for nearly 90% of the carcinoma of oral cavity followed by other carcinomas that develop from salivary glands, melanocytes or metastasis. Carcinogens like Oral cavity carcinoma is further subdivided into 7 subsites; floor of mouth, buccal mucosa, retromolar trigone, alveolar ridge, oral tongue, hard palate, mucosal lip. Oral squamous cell carcinoma is found more common in men than females with 4:1 ratio. More of incidence in the elderly age group which currently is showing a reduction in the age of occurrence to much lower decades. ⁽³⁾ Oral tongue came out to be the commonest subsite for oral carcinoma as per the western studies whereas under Indian circumstances, buccal carcinoma has higher prevalence. ⁽⁴⁾

The OSCC develops over many years and throughout this period there are several neoplasial sites transforming and occurring in the oral cavity ⁽⁵⁾. Oral carcinogenesis is a highly complex multifactorial process that happens when epithelial cells are affected by multiple genetic

alterations⁽⁶⁾, such as key disorders on TP53, NOTCH1 (Notch homolog 1 genes are translocation-associated (Drosophila)), EGFR (epidermal growth factor receptor), CDKN2A (cyclin-dependent kinase inhibitor 2a), STAT3 (signal transducer and activator of transcription 3), Cyclin D1, Rb (retinoblastoma). Tumorigenesis necessitates multiple essential elements: a limitless replicative potential, self-sufficiency in growth signals, deficiency of sensitivity to anti-growth signals, the ability to evade apoptosis, raised

angiogenesis, invasion and metastasis.⁽⁷⁾ Most patients present in the later stages even when adequate measures for early identification and management are in place. A decreasing trend in this aspect is seen as recent trend suggests increasing incidence of early diagnosis comes closer to the those with later stage disease.

Recent AJCC 8th guideline update suggests new classification of oral cavity carcinoma based on HPV related and non-HPV related with inclusion of factors like depth of invasion rather than the old AJCC 7th staging which was taking into consideration the size of the tumor with infiltration into the adjacent structures along with nodal and distant metastasis. Suspected patients of oral cavity carcinoma are worked up with clinicopathological and radiological evaluation with the help of biopsy and imaging techniques like CECT face and neck or MRI Face are the proposed investigatory modalities prior to the obvious management. Gold standard treatment for oral cavity carcinoma is considered to be surgical management with plastic surgical reconstruction to maintain the adequacy of aesthetic and functional outcome to the patient. Oral cavity carcinoma is more or like managed with a multidisciplinary approach considering plastic surgical reconstruction for aesthetic and functional outcome with or without radiation therapy (external beam radiotherapy/ brachytherapy) and co adjuvant chemotherapy (chemotherapy with agents such as cisplatin, carboplatin, 5-fluorouracil, paclitaxel and docetaxel) also favours post operative outcome in patients who have wider infiltration to adjacent structures like mandible, maxilla, skull base etc.^(8,9) Most of the advanced stage tumors ends up in palliative management as they becomes unresectable due to proximity to vital structures or infiltration to the same.

METHODS:

This study was performed over a period of 1 year in 32 patients diagnosed with squamous cell carcinoma of oral cavity. Inclusion criteria: 1) Diagnosed case of Primary Carcinoma of Oral cavity of all subsites, 2) Patients of Both the genders, 3) Patients of all age groups. Exclusion criteria: 1) Patients who are not willing for the study, 2) Metastatic Carcinoma, 3) Carcinoma of Esophagus or any other site in Head & Neck. After taking informed consent from the patient, history of the case including the clinical presentation of their disease with likely etiology, subsites and risk factors will be taken and followed up with histopathological profile of the patient after doing FNAC/ biopsy and the imaging investigations were done as per the subsites of the lesions like CT of face and neck, USG primary lesion with neck, MRI face and neck, PET scan etc. According to the clinical staging and grade of tumor as per

AJCC 8th guidelines, treatment will be planned whether lone surgery or with surgery followed by chemoradiotherapy or palliative treatment. Immediate postop period is assessed for any surgery related complications and outcomes of treatment. The study was approved by the institutional ethics committee.

RESULTS:

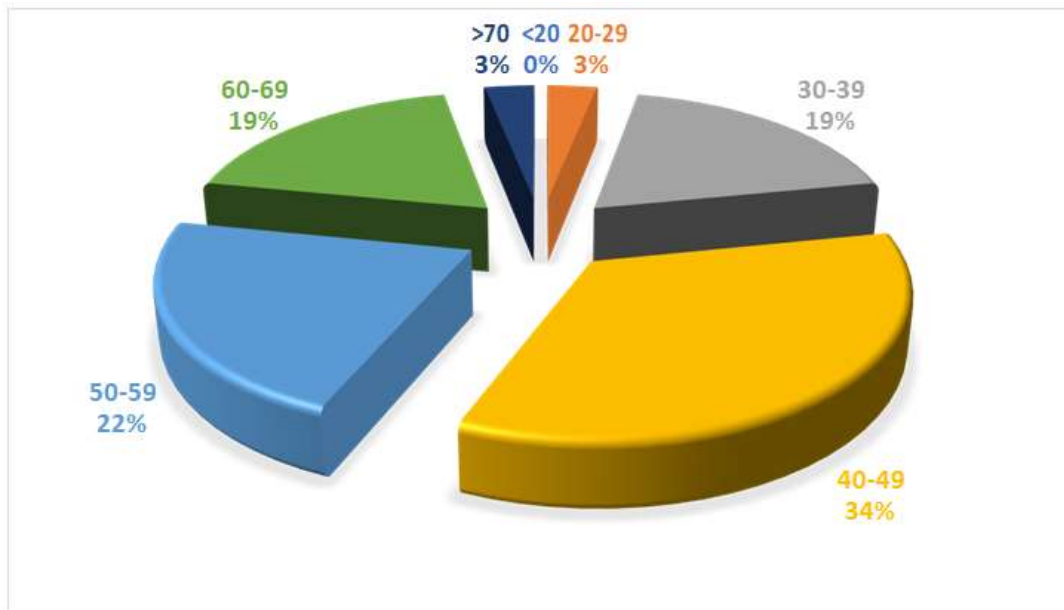


Figure 1 Age distribution

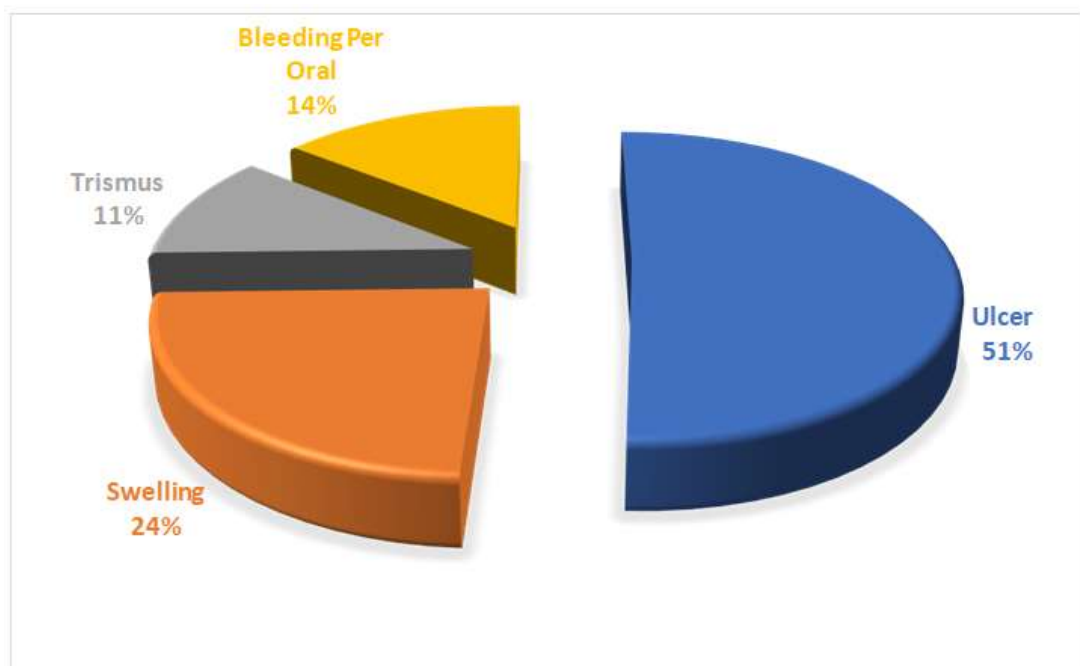


Figure 2 Distribution of Clinical presentation

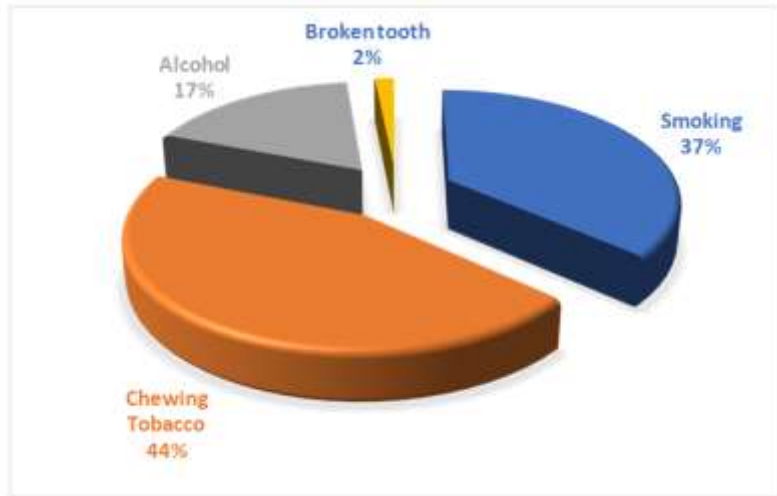


Figure 3 Risk factors

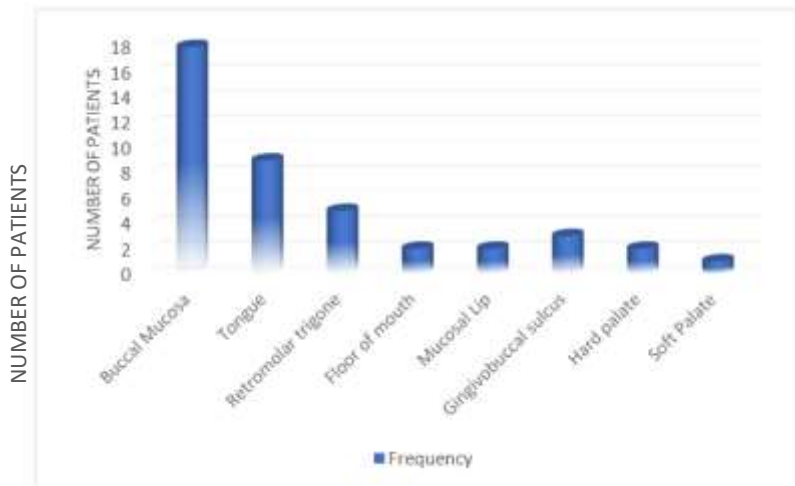


Figure 4 Subsites

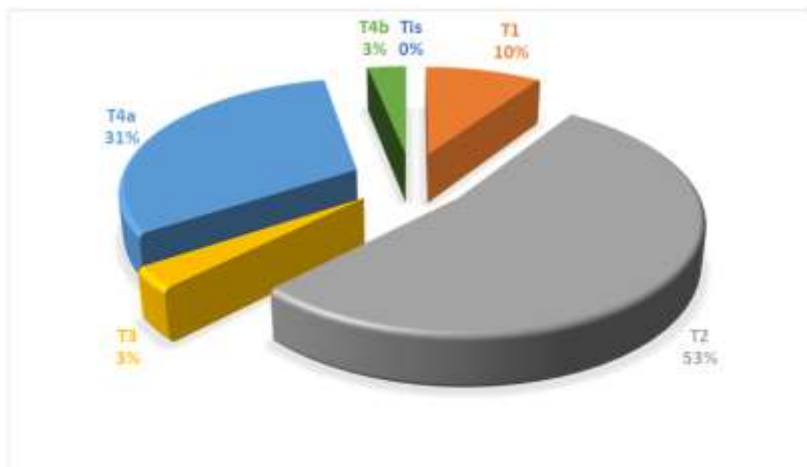


Figure 5 Tumor staging (AJCC 8th)

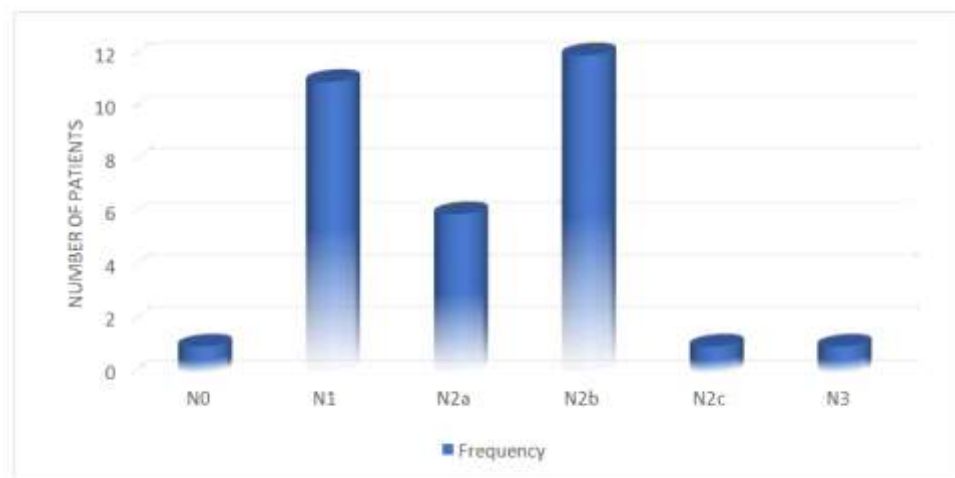


Figure 6 Nodal staging (AJCC 8th)

Out of 32 patients, most of the patients were (11 [34.3%]) 40-49 years of age which was statistically significant [p.00138] [Z=3.2026]. Male population (26 [81.3%]) was higher than the female population (6 [18.8%]). most of the patients had (32[100.0%]) Ulcer it was statistically significant [p<.00001] [Z=7.7538] followed by bleeding per oral at 28.1% and swelling of 21.8%. More number of patients had (28 [87.5%]) Chewing Tobacco which was statistically significant [p<.00001] [Z=6.7799] followed by smoking (23[71.8%]) and alcohol (11[34.3%]). Buccal mucosa was predominant (18[56.2%]) followed by tongue (9[28.1%]) and the rest followed. According to TNM staging as per AJCC 8th, T2 accounted for 17 cases with 53.1% followed by T4a in 10(31.2%) cases. Nodal status was found to be as N2b (12[37.5%]), N1in 11(34.3%). 24(75%) availed surgical treatment with significantly low complication rate in only 2 patients. 10(31.3%) availed chemotherapy out of which, 4(12.5%) availed palliative chemotherapy.

DISCUSSION:

The present study was a Cross-sectional observational Study. This Study was conducted from July 2021-June 2022 at Santosh Medical College and Hospitals. Total 32 patients were evaluated in this study.

In our study, out of 32 patients, most of the patients were (11[34.3%]) 40-49 years of age which was statistically significant [p.00138] [Z=3.2026]. We found that, the mean Age of patients was [48.4063± 11.3475]. Suggesting a decade earlier predominance of disease compared to the previous studies done on the same. Male population (26[81.3%]) was higher than the female population (6[18.8%]) which was statistically significant [p<.00001] [Z=5].

Our study showed that, most of the patients had Ulcer (32[100.0%]) it was statistically significant [p<.00001] [Z=7.7538] which was the commonest OPD presentation all over the world followed by bleeding per oral at 28.1% and swelling of 21.8%.

In our study, a greater number of patients had Chewing Tobacco (28[87.5%]) which was statistically significant [$p < .00001$] [$Z = 6.7799$] followed by smoking (23[71.8%]) and alcohol (11[34.3%]). Results were suggestive and significant enough to justify the most cases being diagnosed in case of those having chewable tobacco. In our Indian setup, most of the patient had habits of chewing tobacco or tobacco containing products like paan as it is an economical way of tobacco addiction compared to high priced cigarettes or cigars. It was found that, lower number of patients had leucoplakia (9[28.1%]), Erythroplakia (2[6.3%]) it was statistically significant [$p < .00001$] [$Z = 4.9498$].

In our study, more number of patients had buccal mucosa (18 [56.2%]) it was statistically significant [$p < .00001$] [$Z = 4.6511$] followed by tongue (9[28.1%]), retromolar trigone (5[15.6%]), gingivo buccal sulcus (3[9.3%]), floor of mouth (2[6.2%]), mucosal lip (2[6.2%]), hardpalate (2[6.2%]). In Indian subcontinent the oral cavity carcinoma had major preponderance in the buccal carcinoma as due to the habituation of lodging the chewable tobacco in the buccal mucosa with maximum direct contact in the buccal mucosa by the same.

Majority number of patients had well differentiated (28 [87.5%]) it was statistically significant [$p < .00001$] [$Z = 6.5127$] followed by moderately and poorly differentiated Tumours at 6.3% each. This was having good significance with post op outcome as many hadn't come with signs of recurrence during the study period and also post op complications were also near negligible.

More number of patients under TNM staging had T2 (17[53.1%]), followed by T4a (10[31.2%]) and T1 (3[9.3%]) value of z is 4.4483. The value of p is $< .00001$ and is significant. Nodal staging was done resulted in N1 (11[34.3%]), N2b (12[37.5%]), N2a (6[18.7%]) which was statistically significant [$p = .00062$] [$Z = 3.4176$]. All cases were evaluated for metastasis clinically and radiologically (32[100.0%]) M0 in TNM Staging. General staging was analysed as stage 4a (22[68.8%]), stage 3 (9[28.1%]) and stage 4b (1[3.1%]). The value of z is 5.4708. The value of p is $< .00001$. All cases were diagnosed in the advanced stage. Improved survival was attributable to early-stage diagnosis with negative lymph mets at time of diagnosis whereas late stage will inversely affect patient survival.

We observed that, higher number of patients had surgical treatment (24 [75.0%]) which was statistically significant [$p = .00006$] [$Z = 4$]. 34.3% had done surgery alone and not radiotherapy. Type of surgery done was based on the extend and site of tumour in the oral cavity. In cases of buccal mucosa, retromolar trigone, gingiva, the option of hemi and segmental mandibulectomy was sought according to the extend and infiltration of tumours to the mandible/ masseteric muscles, pterygoid muscle. Lower maxillectomy was sought in cases with superior extension of tumour in cases of hard palate, upper buccal mucosa tumours. Radiation therapy was given to 31.3% of the patients post op in those who had undergone surgery. Post operation, out of those patients undergone surgery 24 [75.0%], only 2 patients

had complication as 1 patient developed surgical site infection and another patient developed hematoma. Most of the patients had no (30 [93.8%]) no Complications which was statistically significant [$p < .00001$] [$Z=7.5$].

Few numbers of patients whose primary was advanced stage as in stage 4a and 4b and those who had unresectable Tumours had been given chemo therapy (10 [31.3%]) which was statistically significant [$p.0027$] [$Z=3$] out of which 4 patients [12.5%] received palliative chemotherapy and 4 patients [12.5%] had lost followup post chemotherapy. 4 patients [12.5%] who had unresectable tumours with higher extend of infiltration had ended up in palliative treatment.

CONCLUSION:

India being one among the developing nations face a serious threat from the rise in the cases of head and neck carcinoma, precisely oral carcinoma. There seems to be decline in the age of onset of disease compared to western nations due to consumption of tobacco products, alcohol in various forms. Its high time to develop a good campaign in promoting to quit the tobacco and alcohol products so as there will be higher chance of survival for middle aged population. Since oral carcinoma can be attributable to low socioeconomic status, awareness and support has to be conducted accordingly.

Newer tendency of HPV causing oral carcinoma is another analogue that has to be considered as it is the commonest cause of head and neck carcinoma in western world. So, promoting vaccination against HPV can help out in reducing the possible occurrence of HPV related oral carcinoma. Study had concluded the early detection of carcinoma in many a number of cases but near equal contribution is from the advanced disease group also. This has to be brought to a significant early presentation state over the next few years of time. Treatment strategies are being successful as the study suggest with far low complications with good aesthetic and functional recovery in post op period.

BIBLIOGRAPHY:

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018 Nov 1 [cited 2022 Oct 18];68(6):394–424. Available from: <https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21492>
2. Ludwig DC, Morrison SD, Dillon JK. The Burden of Head and Neck Cancer in the United States, 1990 - 2017. *Journal of Oral and Maxillofacial Surgery*. 2021 Oct 1;79(10):2162–70.
3. Pires FR, Ramos AB, de Oliveira JBC, Tavares AS, de Luz PSR, dos Santos TCRB. Oral squamous cell carcinoma: clinicopathological features from 346 cases from a

- single oral pathology service during an 8-year period. *J Appl Oral Sci.* 2013 [cited 2022 Oct 18];21(5):460–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/24212993/>
4. (PDF) Five year (1994-1998) consolidated report of Hospital Based Cancer Registries. [cited 2022 Nov 14]. Available from: https://www.researchgate.net/publication/275496733_Five_year_1994-1998_consolidated_report_of_Hospital_Based_Cancer_Registries
 5. Tanaka T, Ishigamori R. Understanding Carcinogenesis for Fighting Oral Cancer. *J Oncol.* 2011 [cited 2022 Dec 2];2011. Available from: </pmc/articles/PMC3136173/>
 6. Tumor Microenvironment and Myelomonocytic Cells - Google Books. [cited 2022 Dec 2]. Available from: https://books.google.co.in/books?hl=en&lr=&id=wn-ZDwAAQBAJ&oi=fnd&pg=PR11&ots=SpE7jsclAc&sig=c5hLGFBxDfG4R89bFeFgHTsF62A&redir_esc=y#v=onepage&q&f=false
 7. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell.* 2000 Jan 7 [cited 2022 Dec 2];100(1):57–70. Available from: <https://pubmed.ncbi.nlm.nih.gov/10647931/>
 8. Huang SH, O’Sullivan B. Oral cancer: Current role of radiotherapy and chemotherapy. *Med Oral Patol Oral Cir Bucal.* 2013 Mar 1 [cited 2022 Dec 2];18(2):e233. Available from: </pmc/articles/PMC3613874/>
 9. Yao M, Epstein JB, Modi BJ, Pytynia KB, Mundt AJ, Feldman LE. Current surgical treatment of squamous cell carcinoma of the head and neck. *Oral Oncol.* 2007 Mar [cited 2022 Dec 2];43(3):213–23. Available from: <https://pubmed.ncbi.nlm.nih.gov/16978911/>