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Original Research Article

Cancer of tongue-our fixed entity

C. V. Srinivas, Julie P. R.*

Department of Otorhinolaryngology and Head Neck Surgery, DR B. R. Ambedkar Medical College and Hospital, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Julie P. R.,
E-mail: juliedony1993@gmail.com

ABSTRACT

Background: Oral cancer ranks the top three of all cancers in India. This study aimed to determine etiologic factors for squamous cell carcinoma (SCC) of the tongue and its management.
Methods: This longitudinal retrospective study was conducted with 30 patients of biopsy- proven SCC of tongue diagnosed in our hospital between the years of 2010-2022. Medical records, including history of abuse of alcohol, betel nuts, tobacco products and human papillomavirus (HPV) infection were recorded. The patients details including tumour size, location, node metastasis, grade, disease recurrence, other primary cancers, delay time until diagnosis, therapy course were noted. Patients were analyzed based on etiology and management undertaken.
Results: Among 30 patients with SCC tongue, 25 (83.33%) were males, 5 (16.66%) were females. Smoking was significantly higher in males (20 patients), in those 5 alcoholics. Chronic mechanical trauma was observed in 5 patients. HPV infection was observed in 2 males, 3 females had betel nut chewing habit and use of smokeless tobacco. Among 30 cases alcohol abuse, smoking, chronic mechanical traumas, HPV infection and betel nut chewing appeared as significant etiologic factors of which smoking was the most common etiology (50%). Surgical excision with neck dissection followed by radiotherapy was treatment undertaken in our study patients based on SCC tongue stage.
Conclusions: our study concluded that smoking is the most common etiology of SCC tongue, the definitive treatment is surgery combined with radiotherapy based on TNM staging.

Keywords: Tobacco, SCC, Tongue

INTRODUCTION

Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer in the country. Age-adjusted rates of oral cancer in India is high, that is, 20 per 100,000 population and accounts for over 30% of all cancers in the country. The carcinoma of the tongue represents up to 50% of all cases of OSSC, with the lateral borders and the anterior two thirds the most commonly affected locations.[1]

High incidence of tongue cancer in some population groups are due to cultural habits, like chewing of tobacco in South Asia and alcohol use in parts of Western Europe.[2]

Tobacco contains up to 50 potential carcinogens, such as nitrosamines and polycyclic aromatic hydrocarbons.[3] Some of them may cause mutations of the p53 tumour-suppressor gene or other genes that disrupt cell-cycle regulation and modulation of the immune system.[4]

Alcohol can cause cancer by altering epithelial intracellular metabolism at the target site during its rapid passage through the mucosa and metabolism in the liver prior to elimination.[5,6,7,8]It may also act as a solvent,

increasing permeability of the oral mucosa and enhancing flow of carcinogens through cellular membranes.[9]

Known major avoidable risk factors of oral cancer include tobacco, alcohol.[1,10] Many studies on etiologic factors including HPV 16-18, diet and nutrition, genetics, oral hygiene, dental trauma still continue.[11-13]

Early-stage tongue carcinoma (T1 or T2) can be treated successfully with single-modality therapy, namely surgery or radiation. patients with advanced disease (T3 or T4) have a poor response to single-modality treatment. Two independent clinical trials found that postoperative adjuvant chemoradiation offered improved survival when compared to single-modality therapy in these patients.

Surgical interventions range from simple wide local excision and primary closure in small tumours to composite resections of tongue/floor of mouth/mandible in advanced tumours with the need for locoregional flaps or microvascular free flap reconstruction.

This study aimed to discuss the etiololgy of tongue SCC and treatment modalities.

METHODS

Our study was conducted in DR. B. R. Ambedkar medical college and hospital with 30 patients diagnosed with SCC of tongue between a period of 2010 to 2022.

Study design

This study was a longitudinal retrospective study.

Inclusion criteria

Patients with biopsy proven SCC of tongue were included in study.

Exclusion criteria

Patients who are not given consent for study and incomplete follow-up were excluded.

Sample size

Patients of biopsy proven SCC of tongue by consecutive sampling from hospital records, sample size of 30 were obtained for conducting the study.

Sampling method

The sampling method was consecutive sampling.

Ethical approval

This longitudinal retrospective study conducted with 30 patients of biopsy-proven SCC of tongue diagnosed in Dr. B. R Ambedkar medical college and hospital, Bangalore, between years of 2010-2022.

Study compliant with ethical standards.

Statistical methods and tools

Statistical methods and tools included context chart, analysis table.

We took patients' tobacco smoking habits details into consideration from hospital records-years of cigarette usage, number of cigarettes per day. Similarly collected data regarding alcohol consumption like duration of alcohol drinking and number of standard glasses consumed per day, week/month and type of beverage. Checked other substance abuse history like betel nut chewing and h/o dental trauma and HPV infection.

Details of patient group, including tumour size, location (base of tongue, mobile tongue, floor of mouth), node metastasis, grade, recurrence of disease, other primary cancers, delay time until diagnosis, therapy course were noted. Staging of tumours was noted based on pathologic TNM classification according to American joint committee on cancer system. Treatment modalities undertaken for patients who gave consent also recorded.

RESULTS

Among 30 patients with SCC tongue from hospital records, 25 (83.33%)-males and 5 (16.66%)-females. Smoking was significantly higher in male patients (20 patients), in those 5 patients alcoholics. Chronic mechanical trauma observed in 5, 3-males, 2-females.

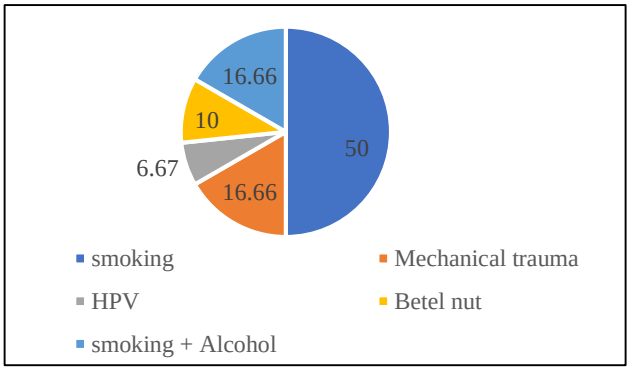

Figure 1: Common etiologies of squamous carcinoma of tongue.

HPV infection observed in 2 males similarly 3 females had habit of betel nut chewing. On analysis, alcohol abuse, smoking, chronic mechanical trauma, infection and betel nut chewing appeared as significant etiologic factors. Two patients had base of tongue SCC. Among 30 patients 5 recorded as given treatment consent, one base of tongue SCC was inoperable referred for radiotherapy, another base of tongue SCC managed by wide local

excision with supra omohyoid neck dissection followed by PMMC flap reconstruction followed by radiotherapy.

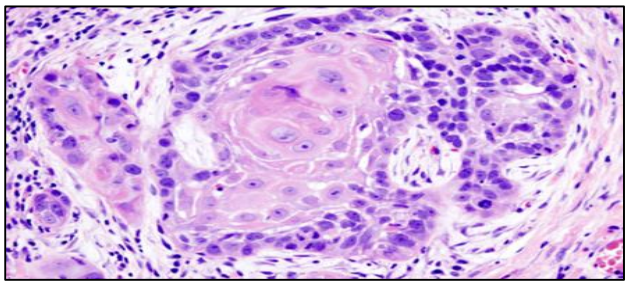

Figure 2: Histopathology of SCC of the tongue.

Figure 3: SCC of right lateral border of tongue.

Table 1: Distribution of risk factors among study subjects.

Risk factors	N
Smoking	15
Both smoking and alcohol	5
Mechanical trauma	5
HPV	2
Betel nut chewing	3

Table 2: Possible indications for post-operative RT.

S. no.	Close or positive margins
1	An affected lymph node > 3 cm
2	Multiple lymph nodes involved
3	Patients who had an open biopsy of a suspicious neck node and did not undergo neck dissection at the time
4	Extra capsular extension (ECE)
5	Perineural invasion, lymphovascular space invasion, invasion of cartilage, bone d/eep soft tissues
6	Recommendation of the surgeon due to intraoperative findings

Rest 3 patients with lateral border of tongue ca, 1 patient underwent wide local excision, another underwent right hemiglossectomy with right neck dissection (level 2 to 3) followed by radiotherapy, 1 patient with bilateral lateral border and anterior border of tongue undergone wide local excision with bilateral supraomohyoid neck dissection followed by radiotherapy.

Table 3: Summary of adjuvant treatment of oral cavity cancers, extracapsular extension.

Risk based on factors for treatment failure	Management
Low risk	No adjuvant radiations
Intermediate risk (-margin, -ECE)	Radiation therapy (60 Gy)
High risk (+ Margin and/or + ECE)	Chemo radiation (60-66 Gy) with cisplatin

Table 4: TNM classification of oral cavity cancer primary tumour.

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
T1	Tumour ≤ 2 cm in greatest dimension, ≤ 5 mm depth of invasion (DOI)
T2	Tumour ≤ 2 cm, DOI > 5mm and ≤ 10 mm or tumour > 2 cm but ≤ 4 and ≤ 10 mm DOI
T3	Tumour > 4 cm in greatest dimension, or any tumour > 10 mm DOI
T4a	Local disease moderately advanced: (Lips)- Tumour invades cortical bone cortical, inferior alveolar nerve, floor of the mouth or skin of the face (chin) (Oral cavity)- Tumour invades only adjacent structures (for example, cortical bone cortical, [mandible or maxilla], extrinsic muscle of the tongue, maxillary sinus or skin of face)
T4b	Local disease very advanced: Tumour invades masticator space, pterygoid plates, base or the skull and / or encases internal carotid artery

Table 5: TNM classification of oral cavity cancer.

NX	Region lymph nodes cannot be assessed
N0	No region lymph nodes metastasis
N1	Metastasis in single ipsilateral lymph, ≤ 3 cm in greatest dimension ENE (-)
N2	Metastasis in single ipsilateral lymph, > 3 cm, but ≤ 6 cm in greatest dimension ENE (-)
N2a	Metastasis in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension ENE (-).
N2b	Metastasis in bilateral or contralateral lymph nodes, none >6 cm greatest dimension ENE (-)
N2c	Metastasis in single ipsilateral lymph, > 3 cm, but ≤ 6 cm in greatest dimension ENE (-).
	Metastasis in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension ENE (-)
	Metastasis in bilateral or contralateral lymph nodes, none >6 cm greatest dimension ENE (-)
N3	Metastasis in a lymph node > 6 cm in greatest dimension ENE (-) or metastasis in any node (s) and clinically overt ENE (+)
N3a	Metastasis in a lymph node > 6 cm in greatest dimension ENE (-)
N3b	Metastasis in any node (s) and clinically overt ENE (+)

Lymph nodes (N), ENE (Extra nodal extension).

Table 6: Anatomical staging and prognostic groups.

Staging	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
11	T2	N0	M0
111	T3	NO	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
1V A	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N1	M0
1V B	Any T	N3	M0
	T4b	Any N	M0
1V C	Any T	Any N	M1

Table 7: TNM staging of 5 cases in our study and management.

Case no.	TNM staging	Management
1	T2N0MX	Anterolateral glossectomy with bilateral SOND followed by radiotherapy
2	T1NOMX	Wide local excision of right lateral border of tongue lesion
3	T2N0MX	Right hemiglossectomy+R sided selective neck dissection (II -III) followed by radiotherapy
4	T4aN0MX	WLE+ right hemimandibulectomy+right alveolectomy+right extended SOND+reconstruction with PMMC flap followed by radiotherapy
5	T4bN1M1	Radiotherapy

DISCUSSION

Oral cancer is the sixth most common malignancy worldwide with 90% of oral malignancies being SCC.[14] Among the different sites within the oral cavity, carcinoma of the tongue is the most seen.[15,16]

Exposure to cigarette use, a complex mixture of more than 4000 particulate and volatile components, increases the incidence of oral carcinogenesis especially in particular areas, which collect resoluble carcinogens such as floor of mouth and lateral border of tongue of oral cavity.[16,17]

Another known and preventable etiological factors include alcohol abuse, HPV, dental trauma.[16,18]

SCC of the tongue especially occurs in men.[12,17,19] In study group, the male: female ratio is 25:5.

The difference can be attributed to the possible differences in habitual actions such as smoking and drinking between males and females. From our study we found that among 30 patients with tongue SCC 50% were smokers and were males and 16.66% had additional alcohol abuse.

Chronic trauma of tongue and its causative role on oral carcinogenesis is a dilemma. Some authors suggested it as a cause of oral cancer; on the other hand, others suggest it is a result of the increase in volume of the tumour.[20]

In our study, results show mild association between chronic trauma and tongue cancer: 16.6% of the patients with tongue cancer had chronic trauma. Our results are consistent with the hypothesis that chronic physical irritation of the tongue squamous epithelium by a broken tooth or an inappropriately fitted denture may promote dysplasia and carcinogenesis, and this is independently of other risk factors.[21]

In our study among 5 females with SCC tongue 60% had habit of betel nut chewing and smokeless tobacco use. Chewing snuff is the leading cause of SCC of the oral cavity and oropharynx in India, part of Southeast Asia, China, and Taiwan, especially when consumed with betel containing areca nut.[22]

The relationship of HPV with oropharyngeal cancer has been well-documented, but rates of HPV are apparently much lower in oral cavity cancers. Machado et al recently found that oral cancers only infrequently harbor HPV, with an incidence of 4%.[23] Liang et al examined 51 patients with oral tongue SCC and found only one who was positive for HPV.[24] In our study 2 patient were positive for HPV and concluded that HPV infection is an etiology for tongue SCC but of least prevalence.

Verrucous carcinoma is a slow growing, well demarcated, exophytic variant of SCC with a characteristic verrucous presentation. Within the oral cavity it localises most commonly in the gingival and buccal mucosa and more rarely in the hard palate and floor of the mouth. Localisation within the tongue is very rare. The change is usually painless. Prognosis is very good and the 5-year survival is from 80 to 90%, although recurrences happen in 8% of patients. Metastases with verrucous carcinoma are very rare.[25]

Jadwiga Waskowska et al study on a 62-year patient admitted to the out-patient clinic of the department and clinic of dental surgery, SUM in Katowice with exophytic tongue lesion reported as verrucous carcinoma on histopathological examination.[26] Verrucous carcinoma has a significant link with tobacco products. Surgical excision is the standard of treatment and many years of

follow-up are required to capture additional foci. Because verrucous carcinoma is multicentric in nature and recurrent lesions may prove to be more poorly differentiated than their predecessor.[27] We didn't had any reported case of verrucous carcinoma in our study.

Treatment of tongue cancers requires a multidisciplinary team made up of an ENT head and neck surgeon specialized in head and neck cancers, dentist, prosthodontist, plastic reconstructive surgeons, medical oncologist, radiation oncologist, speech therapist, physical rehabilitation therapist, social worker, and psychologist. The treatment depends on the site, the extent of the primary tumour, and lymph node status, and include surgery alone, Radiation therapy alone or combination of both.[28-30] If primary tumour is treated with radiation, regional lymph nodes "at risk "are incorporated into the field of treatment.[31]

Larger cancers may require composite resections with reconstruction of the defect by pedicle flaps and often require adjuvant therapy with radiation and chemotherapy.[32,33]

For lesions of the oral tongue, surgery should remove all macroscopic evidence of the disease because of possibility of microscopic extension. If positive nodes present, cervical lymph node dissection is usually done in the same procedure. Neck dissection must be standardized (i.e., complete anatomical dissections, instead of random biopsies) in these situations to prevent incomplete surgery. Elective neck dissection is recommended for patients who have an oral cavity tumour with a minimum thickness of 4 mm.[31]

Supraomohyoid neck dissection is recommended in patients with a clinical stage N0 who are treated surgically. In our study 2 cases with clinically N0 stage underwent supraomohyoid neck dissection.

Bilateral neck dissection is performed in one case where tumour was present in bilateral anterior and lateral border of tongue abutting the midline.

Radiation therapy for cancer of the oral cavity may be administered as external beam radiotherapy (EBRT) or interstitial implantation alone. Larger lesions are frequently managed using external beam radiotherapy, which includes the primary site and regional lymph nodes (even if not clinically affected).[29]

The definitive indications for postoperative radiotherapy are positive margins, multiple positive nodes with metastatic disease, and extra capsular nodal extension.[34,35] Less certain indications include lymphovascular space invasion, perineural spread, single encapsulated positive lymph node, and thick tumors.[35]Tumours with a thickness between 3 to 9 mm have 44% subclinical node positivity and a 7% local recurrence rate and tumours with a thickness greater than 9mm thickness have 53% subclinical node positivity and a 24% local recurrence rate.[35] Among the 4 cases we operated 3 had a tumour thickness between 3 to 9 mm and had undergone post-surgery external beam radiation.

Postoperative radiotherapy (60 to 70 Gy in 6-7 weeks) reduces the rate of local and regional recurrence from 50-15% for tumours with pathologic features that predict a high local and regional failure rate.[36-38]

Two randomised clinical trials conducted in 2004 demonstrated the effectiveness of chemoradiotherapy with cetuximab only in patients with extracapsular extension and/or microscopically involved surgical margins.[37,39] In our study among 4 patients who had undergone surgery, none of them had extracapsular extension or positive tumour margin and had not undergone chemotherapy. The adjuvant treatment for patients with oral tongue cancers is summarized in Table 2.

Limitations

Incidence of SCC needs to be calculated in two separate cohorts who had risk factors and without risk factors.

CONCLUSION

From our study we concluded that smoking is the most common etiology of SCC of tongue and its prevalence increased in additional alcoholics and the definitive treatment is surgery of primary with or without neck dissection based on TNM staging.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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