

# An Observational Study of Head and Neck Squamous Carcinomas from a Tertiary Cancer Centre of Marathwada Region, Maharashtra, India

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## ABSTRACT

**Introduction:** Head and neck cancer constitutes about one third of all the cancers in India. Head and neck squamous carcinoma is an important cause of morbidity and mortality with variability in geographical location, age, gender, habits, socio-economic status.

**Aim:** To identify changing trends in age, gender, sites involved and histopathological grades of malignant and analyse potentially malignant lesions in head and neck region in Marathwada region of Maharashtra, India.

**Materials and Methods:** This observational retrospective descriptive study was carried out in tertiary cancer hospital in Marathwada region of Maharashtra, India, over a period of two years which included 1008 cases. All the biopsy cases and biopsies obtained under ultrasound and also computed tomography (CT) guidance showing invasive squamous carcinoma and potentially malignant lesions of head and neck region with their histological analysis were studied. Relevant clinical and demographic details were noted and statistical analysis was done and results were explained in tables and percentage.

**Results:** Total 1008 cases were studied. The maximum number of cases were in the age group of 51-60 years. Males were more

affected than females. The buccal mucosa (29.5%) was most common site affected and maxilla (0.8%) the least. Histologically invasive tumour were well differentiated (17.65%), moderately differentiated (79.93%) and poorly differentiated (2.42%). Rest lesions were distributed in following categories: carcinoma-in-situ, verrucous neoplasm, dysplasia, atypical squamous proliferation, leukoplakia, pseudoepitheliomatous hyperplasia. Age-wise, site-wise, gender-wise distribution of cases and association between site of lesions and gender and grade of tumour were studied.

**Conclusion:** The associated risk factors, lifestyle patterns, habits, addictions and geographic and demographic factors, socio-economic status and evolving Human Papilloma Virus (HPV) association and pathogenesis are still topic of debate where much progress is still to be made. It deserves closer study. Apart from invasive squamous malignancies, precursor lesions if investigated at an earliest along with increasing awareness among population in relation to healthy lifestyle changes, habits followed by thorough clinical examination and histopathology and HPV association, possibility of planning specific strategies of prevention, diagnosis and treatment help reduce morbidity and mortality.

**Keywords:** Grade, Head and neck region, Trends

## INTRODUCTION

Head and neck cancer constitutes about one third of all the cancers in India [1,2]. Head and neck cancers are the cancers affecting upper aerodigestive tract which includes oral cavity, oropharynx, larynx, nasopharynx, hypopharynx [3,4]. Squamous cell carcinoma is one of the most common head and neck squamous malignancies and represents 90% of oral malignancies [5,6]. Changing trends in clinicopathological observations of head and neck squamous carcinomas needs substantial support of good quality epidemiological data. It poses significant health threat; increasing the morbidity and mortality among cancer patients. As the incidence of head and neck cancer varies with anatomical location and gender and also the countries, even specific regions of different countries, daily habits, awareness of hygienic practices, use of dentures, frequency of tobacco chewing and smoking with alcohol and weed smoking addictions, it makes studies on epidemiological data imperative in understanding the varying trends. Also, rising awareness of endemicity of viral infections like HPV and Epstein-Barr Virus (EBV), ultraviolet radiation exposure especially in a lip cancer, *Candida* infections, genetic predisposition and very rarely nutritional deficiencies are contributing factors for increased number of cases. Most commonly affected age group are adults and elderly, however its increasing incidence is observed in young adults as well [7,8]. Head neck squamous carcinomas incidence rate has reached

0.4-3.6% in patients below 40 years of age [4,9]. The demographic and clinicopathological findings of oral squamous cell carcinomas maybe similar in most studies, however difference is noted in few parameters among countries [10,11]. Also variability is noted in distribution of invasive malignancies at sites other than oral cavity. Hence, this study was carried out with an aim of understanding the distribution of invasive squamous malignancies and potentially malignant lesions in head and neck region along with identifying changing trends in age, gender, sites involved and histopathological grades of malignant tumours in head and neck region in Marathwada region of Maharashtra, India.

The management of head and neck cancers in India in most of the healthcare centres are surgery followed of radiotherapy or radiotherapy with no specific treatment protocol. Besides, these treatment modalities are available mostly in urban areas of the country. Many patients remain undiagnosed and untreated, because of lack of awareness and disparity in availability and affordability of the treatment. Also, hospitals does not have specialised head and neck units to establish specific approach to these cancer. Majority of the patients are managed by under resourced government funded regional cancer centres which are overburdened by patients and have a long waiting list for respective treatment modality depending on stage of the disease. Besides, the concept of health insurance is not well established in India and hence treatment takes heavy toll due

to lack of money. Even if few patients manage to take appropriate treatment, rehabilitation is another part which takes a backseat. With this understanding, even though there is no novel research in current topic an attempt was done to understand pathological aspect of head and neck cancer in our regional cancer centre.

## MATERIALS AND METHODS

This observational retrospective descriptive study was carried out in tertiary cancer hospital in Marathwada region of Maharashtra, India, over a period of two years (January 2019-December 2020). Data was collected from histopathology registers and computer records in July to August 2021 and was analysed in September 2021. The Institutional Ethics Committee (IEC) approval was received in a letter number dated IEC-GMCA/Approval/ 07/2022.

**Inclusion criteria:** 1008 biopsy cases of head and neck region diagnosed as invasive squamous carcinoma and potentially malignant lesions of head and neck region with their histological analysis were included in the study. All the biopsy cases and biopsy obtained under radiological guidance (ultrasound, CT) were included in the present study. The biopsy from laryngopharynx was obtained under local anaesthesia with direct laryngoscope and was also included in present study. Since it was non interventional observational, descriptive study, no prior consent was taken from patients.

**Exclusion criteria:** Surgical resection specimens with modified neck dissection, primary squamous malignancies of musculoskeletal system and thyroid lesions were excluded from the study. Slides/blocks received for second opinion were also excluded from study.

## Study Procedure

All the relevant clinical, radiological and previous pathology and other lab reports were taken into consideration while reporting all the cases. Specimen were examined and fixed in 10% neutral buffered formalin; thorough sampling and multiple serial and deep cut sections were given in cases where invasion was difficult to comment upon in histomorphology. Sections (5 µm) were cut from paraffin-embedded blocks and stained with Haematoxylin and Eosin (H&E) and then examined. Careful screening, contextual interpretation and deep cut sections were studied wherever needed. Immunohistochemistry (IHC) was not carried out in all the cases as diagnosis offered was unequivocal. Total 1008 cases were studied where sites of origin in the head neck region varied.

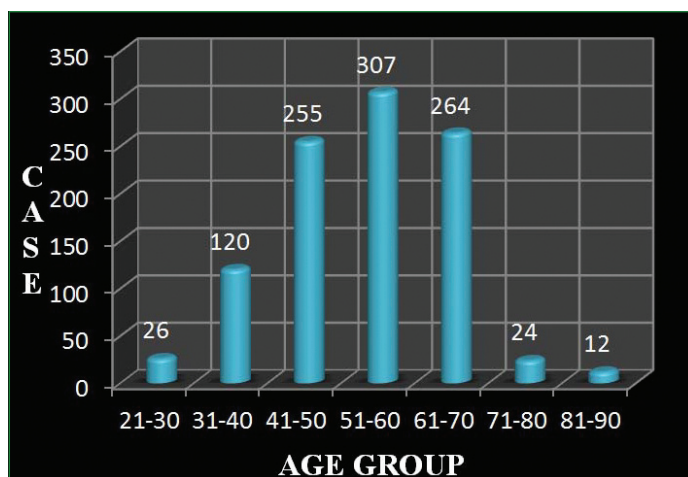
## STATISTICAL ANALYSIS

Descriptive analysis was done on the collected data and results were explained in tables, graph and percentage. The Chi-square test was used for statistical analysis and p-value <0.05 was considered to be statistically significant.

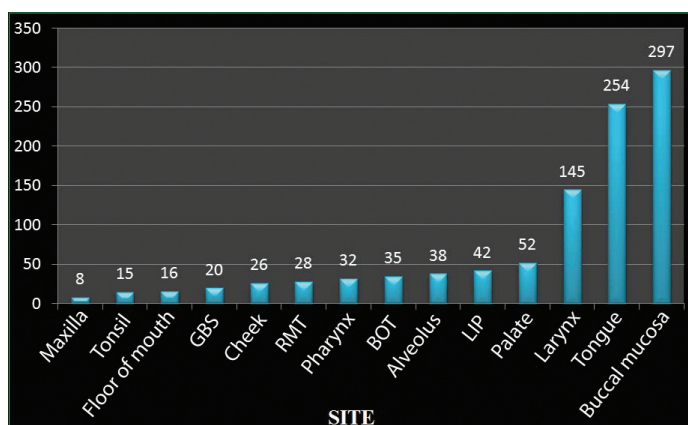
## RESULTS

Total cases of 1008 were included in the study. This represents 74.3% of all oral malignancies diagnosed in laboratory over duration of two years (January 2019 to December 2020). Males represented 77.2 (n=778) of all cases and females represented 22.8 (n=230) of all cases. Male to female ratio in present study is 3.3:1 [Table/Fig-1]. The maximum number of cases were seen in the age group of 51 to 60 years (n=307, 30.5%) and least number of cases were seen in the age group if 81 to 90 years (n=12, 1.2%) [Table/Fig-1]. Most common site involved was buccal mucosa (n=297, 29.5%) followed by tongue (n=254, 25.2%) and the least common involved site was maxilla (n=8, 0.8%) [Table/Fig-2].

Most of the invasive squamous malignancy cases had conventional histomorphology of squamous carcinoma except five cases of which three cases showed of sarcomatoid variant of squamous cell carcinoma and two cases of basaloid variant of squamous cell carcinoma. Out of 827 cases of invasive malignancies, the most common histological grade for these tumours was moderately



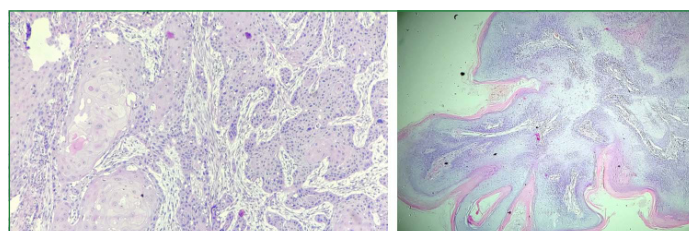
[Table/Fig-1]: Age wise distribution of cases.



[Table/Fig-2]: Site wise distribution of cases.

GBS: Gingivobuccal sulcus; RMT: Retromolar trigone; BOT: Base of tongue

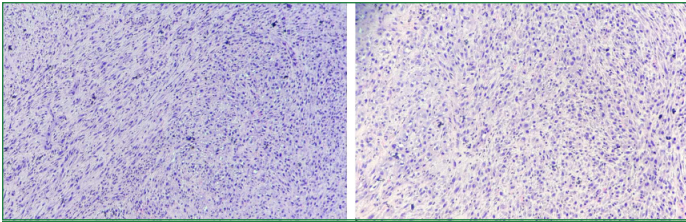
differentiated (grade 2, n=661, 79.93%) [Table/Fig-3] followed by well differentiated (grade 1, n=146, 17.65%) [Table/Fig-4] and least were poorly differentiated (grade 3, n=20, 2.42%) [Table/Fig-5,6]. The cases which did not show invasion or any microscopic findings contributing to invasive tumour were classified as, Carcinoma in situ [squamous intraepithelial lesions] (n=18, 1.79%), mild to moderate dysplasia (n=43, 4.27%), verrucous neoplasm (n=25, 2.48%), atypical squamous proliferation (n=71, 7.04%), leukoplakia (n=7, 0.69%), Pseudoepitheliomatous Hyperplasia (PEPH) (n=17, 1.69%).



[Table/Fig-3]: Microscopic examination shows polygonal to oval cells with abundant eosinophilic cytoplasm, high N:C ratio, prominent nucleoli, atypical mitoses in sheets; moderately differentiated squamous cell carcinoma (H&E, 400X). [Table/Fig-4]: Microscopic examination shows well differentiated hyperplastic squamous epithelium with orderly maturation, hyperplastic surface papillae with keratin and broad, blunt, downward pushing rete pegs; lymphoplasmacytic infiltrate in lamina propria suggests pseudoepitheliomatous hyperplasia (H&E, 100X). (Images from left to right).

Distribution of invasive tumours and potentially malignant lesions were studied and showed buccal mucosa (n=297, 29.5%) as most commonly affected site followed by tongue (n=254, 25.2%) and least affected site is maxilla (n=8, 0.8%) [Table/Fig-7].

The opinion from statistician was obtained and appropriate test was applied. The differences in the histological grade of the tumours when comparing each site results were not statistically significant (p>0.05). The Chi-square test showed significant difference between male and female gender as per their histological grading (p<0.05). [Table/Fig-8].



**[Table/Fig-5]:** Microscopic examination shows spindle to oval cells, eosinophilic cytoplasm, high N:C ratio, prominent nucleoli, atypical mitoses in sheets suggests sarcomatoid squamous carcinoma (poorly differentiated squamous cell carcinoma) (H&E, 100X). **[Table/Fig-6]:** Microscopic examination shows spindle to oval cells, eosinophilic cytoplasm, high N:C ratio, prominent nucleoli, atypical mitoses in sheets with focal individual cell keratinization suggests sarcomatoid squamous carcinoma (poorly differentiated squamous cell carcinoma) (H&E, 200X). (Images from left to right).

on timely diagnosis and help prevent further morbidity. The cases of squamous carcinoma were more common among males with various studies having male to female ratio ranging between 6:1 to 2:1 [12-15]. While in present study it was 3.3:1. This similar ratio was observed in eastern India [16]. [However, it was higher than that of a northeastern-India (2.9:1) [17] and lower than from northern India (3.8:1) [18]. This male to female ratio was reported to be lower in other studies from India [19,20] ranging from 1.5:1 to 2.1:1. Increasing exposure to carcinogens like tobacco smoke, weed smoke, nicotine in any form, active or passive smoke, betel quid (paan) and areca nut chewing, changing lifestyles and also due to the prevailing local socio-cultural mindset facilitating males to better healthcare accessibility leading to higher diagnosis in them.

Site of lesions	WD	MD	PD	Verrucous neoplasm	Carcinoma in situ	Dysplasia	Atypical squamous proliferation	Leukoplakia	PEPH	Total
Lip	03	29	02	01	01	01	04	01	0	42
Maxilla	0	06	0	0	0	02	0	0	0	08
Palate	08	29	03	01	0	05	05	0	01	52
Floor of mouth	03	08	0	01	01	01	02	0	0	16
Base of tongue	06	19	01	02	0	02	03	0	02	35
Larynx	16	101	03	03	04	05	09	0	04	145
Pharynx	06	19	0	0	01	02	04	0	0	32
Cheek	03	18	0	0	03	0	01	01	0	26
Retromolar trigone	06	16	0	0	01	03	02	0	0	28
Gingivobuccal sulcus	03	10	01	0	01	02	02	0	01	20
Alveolus	08	22	01	01	0	02	04	0	0	38
Tonsil	04	10	0	0	01	0	0	0	0	15
Tongue	40	165	05	07	01	07	22	02	05	254
Buccal Mucosa	40	209	04	09	04	11	13	03	04	297
Total	146	661	20	25	18	43	71	07	17	1008

**[Table/Fig-7]:** Distribution of lesions according to the site (N=1008).

WD-Well differentiated; MD-Moderately differentiated; PD-Poorly differentiated; PEPH-Pseudoepitheliomatous hyperplasia

Parameter site of lesions	Males	Females	Total
<b>Site of lesions</b>			
Lip	31	11	42
Maxilla	08	0	08
Palate	40	12	52
Floor of Mouth	11	05	16
Base of Tongue	26	09	35
Larynx	105	40	145
Pharynx	26	06	32
Cheek	21	05	26
Retromolar Trigone	22	06	28
Gingivobuccal Sulcus	14	06	20
Alveolus	26	12	38
Tonsil	10	05	15
Tongue	211	43	254
Buccal Mucosa	227	70	297
Total	778	230	1008
<b>Histological Grade</b>			
Well Differentiated (WD)	101	45	146
Moderately Differentiated (MD)	520	141	661
Poorly Differentiated (PD)	17	03	20
Total	638	189	827

**[Table/Fig-8]:** Distribution of lesions and tumors as per site and gender (n=1008).

## DISCUSSION

As per many studies squamous cell carcinoma is most common head and neck malignancy, however present study emphasises

Although bidi-smoking, betel quid (paan) and areca nut chewing is practiced among rural females, but to a lesser extent as compared to males along with increasing exposure to biological agents as HPV and EBV may have contributed cases with rise among females also when compared to other studies [21-24]. India also has the higher incidence of head neck cancers in females in comparison to other parts of world [25]. The duration of exposure to tobacco chewing and smoking either long past or present are important risk factors for oral squamous carcinoma [7]. The maximum number of cases were seen in the age group of 51 to 60 years which was similar to data from northeastern and northern India where it was 50-59 years and lower to eastern India [16].

In present study, it was observed that any part of oral mucosa was involved and when large tumours were noted even contiguous areas were also affected. Most common location affected with squamous carcinoma was buccal mucosa followed by lateral border of tongue, ventral aspect of tongue, alveolar/gingiva mucosa. Also affected are pyriform sinus mucosa, laryngeal mucosa, pharyngeal mucosa, maxillary mucosa, however its least affected site was maxilla in present study. Followed by oral cavity and oropharynx, larynx was the commonest site involved similar to north India. However northeast region in India reports oropharynx as the commonest site [16]. This may be attributed to smoking habits especially bidi which is a form of crude cigarette without filter. There are reports stating development of laryngeal cancers with smoking habits [19].

India has highest incidence of oral cavity and oropharynx malignancies among all malignancies [26]. The border of tongue is most common site of squamous cell carcinoma in America and Europe, the buccal mucosa is most common site in southeastern region due to habits of tobacco and areca-nut chewing [7]. The tongue and buccal mucosa were the two most common locations

for squamous cell carcinoma in Iran as discussed by Andisheh-Tadbir A et al., [27]. The study presented by Jaikittivong A et al., have reported that 50% of their oral squamous cell carcinoma affected gingiva and alveolar ridge, which was justified by different aetiological factors associated with the development of squamous carcinoma [28]. Kruse AL et al., reported that palate and alveolar mucosa were more affected sites in females, however could not justify this gender specific site predilection [29]. Even present study does not show any gender specific site predilection.

Majority of invasive squamous carcinomas are graded as moderately differentiated followed by well differentiated, as also shown by present study [12,27,28,30-33]. This contradicts, Effiom OA et al., study has showed that 47.6% of all cases were histologically classified as poorly differentiated, while well differentiated tumours represent 32.6% of their cases [22]. It was observed in present study during analysis that males were predominantly affected by moderately differentiated squamous carcinoma and poorly differentiated squamous carcinoma, while females were predominantly affected by well differentiated squamous carcinoma and moderately differentiated squamous carcinoma tumours. It was also observed that histological grade can also be possibly associated with the site of tumours. As squamous carcinomas affecting buccal mucosa and gingivobuccal sulcus and lip were usually well differentiated tumours, while tumours affecting tongue borders, floor of mouth, ventral tongue, alveolar mucosa, larynx, pharynx were moderately differentiated. However, the differences were not statistically significant. Literature mentions histological variants of squamous carcinoma and it is imperative to recognise them, as some histological subtypes and distinct clinicopathological entities need different treatment protocols and approach and have variable prognosis [31,33].

Many forms of tobacco are used. Probably the most common tobacco use is the smokeless-chewable khaini; which is an oral preparation of tobacco and slaked lime kept for long hours in the buccal sulcus. This habit is a potential risk factor for various potentially malignant conditions and oral cancer [16]. Gutkha is made of crushed areca nut, tobacco, catechu, paraffin and slaked lime with some flavourings and popular among young people. Betel quid (popularly known as paan) is a chewable preparation of betel leaf enclosing chopped areca nut, slaked lime, powered tobacco and catechu. Hookah is another form of smoking where flavoured tobacco smoke is passed through water and then inhaled. All these are equally popular among the affluent class of society also [16]. The difficulties in early detection of oral squamous cell carcinoma is a major problem and exact reasons including social and health related behaviour and tumour characteristics are not well understood [34]. Also oral potentially malignant disorders are relatively common, showing a global prevalence from 1-5% and their gender, age, site predilection similar to oral squamous carcinoma [7].

Although exact malignant transformation rate of these potentially malignant disorders is unknown, the morphological pattern of these lesions is encountered in invasive squamous malignancies [35]. These findings reinforce the importance of considering the possibility of squamous carcinoma when dealing with these conditions and the need for obtaining biopsy specimens from all lesions of this group. Besides, meticulous observant study was carried out in deep cut and recut serial sections wherever necessary along with careful evaluation of basement membrane was key in all cases, in order to confirm early invasion and tumour cell restriction upto papillary lamina propria especially in CA in situ, dysplasia, verrucous neoplasm, atypical squamous proliferation cases. A study have named verrucous neoplasm with minor foci of invasion as hybrid verrucous carcinoma [33], also known as well differentiated carcinoma, in present study these cases were classified as well differentiated carcinoma. Basaloid squamous cell carcinoma is a rare aggressive variant with male gender predominance, usually

associated with tobacco and alcohol use and presents as ulcerated exophytic mass [33]. Two cases diagnosed in present study affected males in sixties and seventies and tumours were located along cheek and buccal mucosa [33]. Three cases of sarcomatoid variant in present study were suggested IHC studies for confirmation as squamous carcinoma and further evaluated. All three cases showed male gender predilection, in seventies along buccal mucosa. Also, in present study majority of the cases did not have clinical stage mentioned on the requisition form, its corroboration with pathology parameters were difficult. In summary, head and neck squamous carcinoma show variable pattern of distribution as per age, gender, site and distribution in different regions and countries, ethnic groups and hence difference in different regions of same country. These differences can be attributed to various cultural patterns, habits, genetic factors and endemicity to certain viruses like HPV, EBV with upcoming fact of their association with them [36]. Hence, more studies are needed with new and in-depth outlook towards head neck squamous carcinomas along with demographic and clinical profile offering an enhanced comprehension of these tumors and the possibility of planning specific strategies of prevention, diagnosis and treatment.

### Limitation(s)

As this study was a single centre observational retrospective descriptive study it limits the generalisation of the findings on a larger scale because of selection bias, lack of follow-up data of these patients due to lack of resources and also limited correlation of surgical histopathology findings postoperatively. Also, majority of the cases did not have clinical stage mentioned on the requisition form, its correlation with pathology parameters were difficult.

### CONCLUSION(S)

The associated risk factors, lifestyle patterns, habits, addictions and geographic and demographic factors, socio-economic status and evolving HPV association and pathogenesis are still topic of debate where much progress is still to be made. It deserves closer study. Apart from invasive squamous malignancies, precursor lesions if investigated at an earliest along with increasing awareness among population in relation to healthy lifestyle changes, habits followed by thorough clinical exam and histopathology and HPV correlation, possibility of planning specific strategies of prevention, diagnosis and treatment help reduce morbidity and mortality.

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#### PLAGIARISM CHECKING METHODS: (Jain H et al.)

- Plagiarism X-checker: Feb 21, 2022
- Manual Googling: Apr 15, 2022
- iThenticate Software: May 26, 2022 (19%)

#### ETYMOLOGY: Author Origin

#### AUTHOR DECLARATION:

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- For any images presented appropriate consent has been obtained from the subjects. NA

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