

Original research article

To determine the epidemiological profile and the pattern of cervical lymph node metastasis in patients with Oral Squamous Cell Carcinoma (OSCC)

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Abstract

Introduction: The Oral Squamous Cell Carcinoma (OSCC) is one of the most commonly encountered carcinomas in the head and neck region in this era, with increase in tobacco abuse. The incidence of OSCC is 1.9% to 3.5% of malignant tumour in the whole body and it accounts for 4.7% to 20.3% of head and neck malignancies, ranking second in head and neck cancers.

Material and Methods

Study Area: Patients diagnosed with Oral Squamous Cell Carcinoma who underwent surgery in the Department of ENT at Dr. Babasaheb Ambedkar Memorial Hospital, Byculla, Mumbai.

Observations & Result: On comparison of various subsites of oral cavity involved in our study we observed buccal mucosa (50%) was the most involved subsite, followed by tongue (23%) followed by lower alveolus (12%). clinically we observed that cT2 (38%) and cT3 (38%) were the most common stage of presentation and we observed that cNO (65%) was the most common stage of presentation. Out of 53 patients, 37 (70%) patients showed moderately differentiated tumour histology followed by poorly differentiated (19%) and well differentiated (11%). 24.5% patients had depth of invasion less than or equal to 5mm, 36.5% patients had 5 to 10mm, 40.4% patients had depth of invasion more 10mm. We observed only type 3 and type 4 Pattern of invasion in our study out of which 71.60% was type 3 and 28.30% was type 4.

Conclusion: We found that buccal mucosa (50%) was the most commonly involved subsite. Among the study population, most of the patients (65%) had clinically no occult neck metastasis. We observed that there is no significant association between well differentiated and moderately differentiated tumour histology and occult neck metastasis.

We observed that with increasing depth of invasion there was an increased risk of occult metastasis. Our study showed only type 3 and type 4 pattern of invasion.

Keywords: Oral cavity, carcinoma, metastasis

Introduction

The Oral Squamous Cell Carcinoma (OSCC) is one of the most commonly encountered carcinomas in the head and neck region in this era, with increase in tobacco abuse. The incidence of OSCC is 1.9% to 3.5% of malignant tumour in the whole body and it accounts for 4.7% to 20.3% of head and neck malignancies, ranking second in head and neck cancers [1, 2, 3].

OSCC affects males more frequently than females although the ratio is equalising and in recent times, increased number of cases is being reported in elderly females as well as young females [4, 5].

There are an estimated 657,000 new cases of cancers of the oral cavity and pharynx each year, and more than 330,000 deaths and the incidence are increasing exponentially worldwide [6].

The 5-year survival in patients with OSCC still remain poor, although there are many advances in the treatment and technology. The reason for increased mortality is due to failure in early diagnosis. The

main reason for this scenario is due to the fact that most oral cancers do not produce pain at early stage. Oral cancer can cause cervical lymph node metastasis. During the clinical examinations such as palpation and on imaging tools like ultrasonography, CT and MRI, the lymph nodes may appear uninvolved. But there can be micro metastasis in the draining lymph nodes. Such involvement is called occult lymphatic metastasis or/occult neck metastasis.

Tobacco abuse is the most important risk factor for OSCC and is responsible for approximately 22% of cancer deaths [7].

OSCC has a multifactorial etiology with majority of the cases are attributable to separate and combined habits of tobacco use (smoked and chewed), alcohol consumption, betel quid, areca nut and betel quid substitutes. A number of recent studies are confirming the putative role of Human Papilloma Virus, especially in the western world, which still needs to be investigated in our population [8].

Tobacco and alcohol are globally accepted and well documented strongest risk factors, most prevalent in the western countries with a multiplicative synergistic effect that has been shown in a number of studies [9, 10]. Developing Asian countries present a different scenario with greater prevalence of tobacco, betel quid, areca nut and its substitutes as major carcinogenic influences [11].

Even when the tumour is small (T1 and T2), OSCC carries a high risk of cervical lymph node metastasis. Thus, appropriate treatment of cervical lymph nodes is essential for locoregional control of the disease. Around 20 to 40% of early-stage oral cancer patients can have occult cervical lymph node metastasis [12].

Surgery continues to play a prominent role in the management of patients with oral cancer and neck dissection remains an integral part along with primary surgical resection [13].

Prognosis of OSCC depends on multiple factors and it is best determined by histological examination of resected lymph nodes. Clinico-radiological investigations have a sensitivity of 60 to 70% to detect nodal metastasis [14].

Aims and Objectives

*To determine the epidemiological profile and the pattern of cervical lymph node metastasis in patients with Oral Squamous Cell Carcinoma (OSCC).

*Evaluate the associations between various clinical parameters-differentiation of tumour, pattern of invasion, depth of invasion and lymphovascular emboli and presence of cervical nodal metastasis.

Material and Methods

Study Area: Patients diagnosed with Oral Squamous Cell Carcinoma who underwent surgery in the Department of ENT at Dr. Babasaheb Ambedkar Memorial Hospital, Byculla, Mumbai.

Study Population: Target population for the study included those patients diagnosed with Oral Squamous Cell Carcinoma who underwent surgery from July, 2019 to March, 2020 and satisfied the following inclusion criteria and who were willing to be a part of this study with written informed consent.

Study Design: Hospital based Prospective study.

Sample Size: 53 Patients of Oral Squamous Cell Carcinoma who underwent surgery from July, 2019 to March, 2020 and satisfied the inclusion criteria.

Study Duration: July 2019 to June 2020.

Inclusion Criteria

- Patients who underwent surgery for Oral Squamous Cell Carcinoma.
- Patients who are willing to give written informed consent.
- Patients between 18 and 75 years of age who had histologically proven OSCC that met the staging criteria of the American Joint Committee on Cancer (AJCC) 8th edition and who had undergone neck dissection at the time of primary tumour resection.
- Patients who had no prior history of head and neck cancer treatment.
- Patient who did not receive any neoadjuvant, concomitant chemoradiotherapy or radiotherapy.

Exclusion Criteria

- Patients who did not fulfil the inclusion criteria.
- Patients who were lost to follow up.
- Patients who were unwilling to give written informed consent.

Observations & Results

Observations

- The study included 53 patients out of which 74% were male and 26% were female.

- Around 34% of study population belong to age group of less than 50 years, 58% of study population were in age group of 50 to 60 years and 8% were from 60 years and above age group.
- On comparison of various subsites of oral cavity involved in our study we observed buccal mucosa (50%) was the most involved subsite, followed by tongue (23%) followed by lower alveolus (12%). Other subsites involved were upper alveolus 6%, RMT 8% and hard palate 2%.
- In our study we found that 98.22% of study population were chronic tobacco users.
- In our study clinically we observed that cT2 (38%) and cT3 (38%) were the most common stage of presentation followed by cT4a (21%). cT1 was the least common presentation.
- Among the buccal mucosa carcinoma, cT2 (44%) was the most common presentation followed by cT3 (33%), cT4a (19%), cT1(4%).
- Among the tongue carcinoma, cT2 (50%), cT3 (50%) were the most common presentation.
- Among lower alveolus carcinoma, cT3 (50%), cT4a (50%) were the most common presentation.
- Among Retromolar trigone carcinoma, cT2 (50%) was the most common presentation followed by cT3 (25%), cT4a (25%).

En compared with the P staging overall pT2 (21%) was the most common stage of presentation followed by pT3 (19%) and pT4a (11%).

- Among the buccal mucosa carcinoma, pT2 (44%) was the most common presentation followed by pT3 (37%), pT4a (15%), pT1(4%).
- Among the tongue carcinoma, pT2 (58%) was the most common presentation followed by pT3 (3%), pT4a (8%).
- Among lower alveolus carcinoma, pT3(50%), pT4a (50%) were the most common presentation.
- Among Retromolar trigone carcinoma, pT2 (50%) was the most common presentation followed by pT3 (25%), pT4a (25%).
- In our study, clinically we observed that cN0 (65%) was the most common stage of presentation followed by cN1(19%), cN3b (7%) cN2b (5.7%), cN2a (1.9%).
- Among the buccal mucosa carcinoma, cN0 (63%) was the most common presentation followed by cN1 (19%), cN3b (11%) and cN2b (7%).
- Among the tongue carcinoma, cN0 (75%) was the most common presentation followed by cN1 (17%), cN3b (8%).
- Among lower alveolus carcinoma, cN1 (50%) was the most common presentation followed by cN0 (17%), cN2a (17%), cN2b (17%).
- Among Retromolar trigone carcinoma, cN0 (100%) was the most common presentation.
- When compared with the P staging overall pN0 (52%) was the most common stage of presentation followed by pN1 (29%), pN3b (13.46%), pN2b (3.8%), pN2c (1.9%).
- Among the buccal mucosa carcinoma, pN0 (52%) was the most common presentation followed by pN1 (26%), pN3b (15%), pN2b (4%), pN2c (4%).
- Among the tongue carcinoma, pN0 (67%) was the most common presentation followed by pN1 (17%), pN3b (17%).
- Among lower alveolus carcinoma, pN1(50%) was the most common presentation followed by pN0 (17%), pN2b (17%), pN3b (17%).
- Among Retromolar trigone carcinoma, pN0 (50%), pN1(50%) were the most common presentation.
- Out of 53 patients, 37 (70%) patients showed moderately differentiated tumour histology followed by poorly differentiated (19%) and well differentiated (11%).
- In our study among the well differentiated histology, we observed that there was no clinical neck metastasis in all patients and pathologically there was no clinical neck metastasis in 83% and occult neck metastasis in 17%.
- In our study among the moderately differentiated histology, we observed that there was no clinical neck metastasis in 65% patients and occult neck metastasis in 35% patients and pathologically there was no clinical neck metastasis in 54% and occult neck metastasis in 46% patients.
- In our study among the poorly differentiated histology, we observed that there was no clinical neck metastasis in 50% patients and occult neck metastasis in 50% patients and pathologically there was no clinical neck metastasis in 30% and occult neck metastasis in 70% patients.
- 24.5% patients had depth of invasion less than or equal to 5mm, 36.5% patients had 5 to 10mm, 40.4% patients had depth of invasion more 10mm.
- In Patients with depth of invasion of 5mm or less we observed there was clinically no occult neck metastasis in 85% patients whereas 15% had occult neck metastasis. Pathologically 85% patients had no occult neck metastasis and 15% had occult neck metastasis.
- In patients with depth of invasion 5 to 10mm we observed there was clinically no occult neck metastasis in 79% patients whereas 21% had occult neck metastasis. Pathologically 63% patients had no occult neck metastasis and 37% had occult neck metastasis.
- In patients with depth of invasion more than 10mm, we observed there was clinically no occult neck metastasis in 43% patients whereas 57% had occult neck metastasis. Pathologically 24% patients

had no occult neck metastasis and 76% had occult neck metastasis.

- We observed that only one patient had lymphovascular emboli.
- We observed only type 3 and type 4 Pattern of invasion in our study out of which 71.60% was type 3 and 28.30% was type 4.
- In patients with type 3 Pattern of invasion, we observed there was clinically no occult neck metastasis in 68% patients whereas 32% had occult neck metastasis. Pathologically, 58% patients had no occult neck metastasis and 42% had occult neck metastasis.
- In patients with type 4 Pattern of invasion, we observed there was clinically no occult neck metastasis in 60% patients whereas 40% had occult neck metastasis. Pathologically, 40% patients had no occult neck metastasis and 60% had occult neck metastasis.

Discussion

Oral cavity is the most common site of carcinoma in head and neck region. Most common malignant tumour type in the oral cavity is squamous cell carcinoma. OSCC is frequently associated with poor prognosis. Around 30% of OSCC patients with clinically N0 neck can have occult metastasis. Therefore, cervical lymph node metastasis is one of the most significant independent prognostic factors as it reduces the rate of survival by 50%. Hence, we should aim to treat cervical lymph nodes to control the locoregional disease and improve disease free survival and better quality of life.

There has always been a debate between elective neck dissection and therapeutic neck dissection and various studies have revealed that elective neck dissection (END) is more beneficial in terms of survival rates. It also reduces the relapse rate and increase disease free survival and hence the overall survival.

There has been tremendous technological advancement in the field of radiology with computerized tomography (CT), High resolution ultrasonography, Magnetic resonance imaging (MRI), Positron emission tomography (PET-CT) all playing major role in preoperative staging of OSCC but due to significant variations in sensitivity and specificity rate, a single radiological modality cannot be used to confirm cervical nodal metastasis [15].

OSCC Surgical Protocol at Our Hospital

Initially, every patient is assessed by ENT consultant and is evaluated in relation to tumour size location and lymph node involvement through a thorough physical examination along with CT, MRI and PET-CT if needed and histological diagnosis is confirmed. Then patient is staged as per AJCC 8th edition and a treatment plan is devised. Primary tumour is resected along with a margin clearance of more than 1cm and selective neck dissection or modified radical neck dissection is done. Primary Specimen is oriented and sent for histological evaluation. Each level of lymph node is labelled separately and sent for histological evaluation in 10% buffered formalin solution. pTNM staging is evaluated as per post-operative final histological report and various parameters including T staging, margin clearance, lymph node involvement, pattern of invasion, depth of invasion, lymphovascular emboli, differentiation of tumour are evaluated. Patient is either kept under observation or planned for post-operative radiotherapy/chemotherapy. Patient is followed up at various post-operative intervals including once every 3 months in the 1st year and subsequent intervals as needed.



Fig 1: Separately labelled specimens of levels of lymph node excised

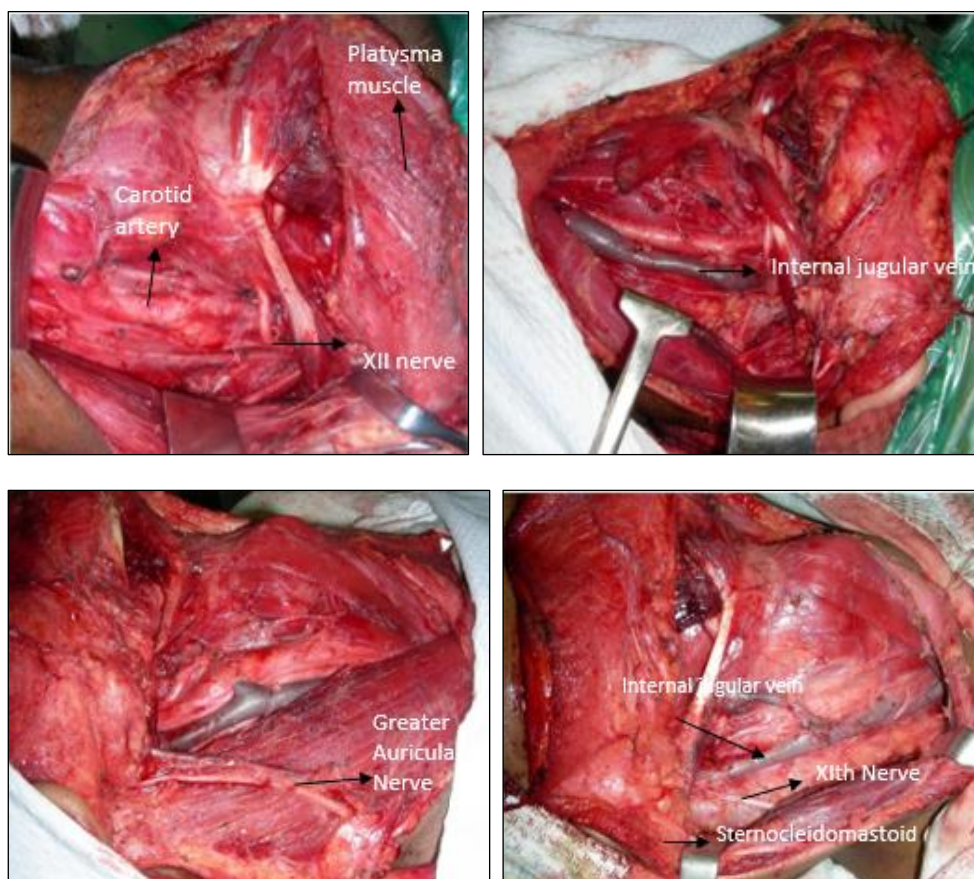


Fig 2: Various images of neck dissection showing various important structures in different cases

In our study, we evaluated 53 patients and determined the pattern of cervical lymph node metastasis in patients with Oral Squamous Cell Carcinoma and associations between various clinical parameters with occult nodal metastasis.

In the present study, increased incidence of OSCC was found in males (74%) than in females (26%) with a male to female ratio of 2.84 :1 which is consistent with other Indian study on oral cancer.

Conclusion

This study included 53 patients diagnosed with OSCC and underwent surgery at Department of ENT of Dr Babasaheb Ambedkar Memorial Central Railway Hospital, Byculla, Mumbai. The male to female ratio was 2.84: 1. Most of the patients belong to the age group of 50 to 60 years (58%). 34% with age less than 50 years and 8% with age more than 60 years. 98% had history of tobacco or betel quid chewing habit of more than or equal to 5 years. We found that buccal mucosa (50 %) was the most commonly involved subsite followed by tongue (23%), lower alveolus (12%), RMT (8%). We observed that overall cT2 and cT3 were the most common presentation (38%) followed by cT4a (21%). Histologically pT2 (42%) was the most common presentation followed by pT3 (36%), pT4a (24%). Among buccal mucosa carcinoma cT2 (44%) was the most common presentation followed by cT3, cT4a. On histological evaluation, same presentation was observed-pT2 (44%) was the most common presentation. We observed that most of the patients suffering from tongue carcinoma presented at an advanced stage. cT2, cT3 were the most common presentation among tongue carcinoma patients. Histologically pT2 was the most common presentation among tongue carcinoma. We found that pre-operative clinical staging was similar to histological staging suffering from carcinoma of lower alveolus. They presented at an advanced stage and were easily diagnosed using radiological tests with pT3 (50%), pT4a (50%).

Among the study population, most of the patients (65%) had clinically no occult neck metastasis. In the remaining 35% patients, 19% were cN1, 7% were cN3b, 5.7% cN2b and 1.9% cN2a. On histological comparison 52% had no occult neck metastasis. This showed that 48% of patients with OSCC have lymph node metastasis at the first visit. Similar findings were observed in buccal mucosa carcinoma, 63% patients had no clinical occult neck metastasis. But histologically 48% of patients had occult neck metastasis at the first visit. Among the tongue carcinoma patient, 75% of patients had no clinical neck metastasis and histologically 67% had no occult neck metastasis. 33% patients suffering from tongue carcinoma had histological neck involvement. 84% cases of lower alveolus carcinoma had neck involvement histologically. We only observed 4 cases suffering from RMT carcinoma out of which 50%

had occult neck metastasis.

References

1. Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, *et al.* Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology.* 2013;31:4550-9.
2. Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, *et al.* Cancer statistics in China, 2015. *CA Cancer J Clin.* 2016;66:115-32.
3. Siegel RL, Miller KD, Jemal A. Cancer Statistics. *CA Cancer J Clin.* 2017;67:7-30.
4. Koo K, Barrowman R, McCullough M, Iseli T, Wiesenfeld D. Non-smoking non-drinking elderly females: A clinically distinct subgroup of oral squamous cell carcinoma patients. *Int J Oral Maxillofac Surg.* 2013;42:929-33.
5. Toporcov TN, Znaor A, Zhang ZF, Yu GP, Winn DM, Wei Q, *et al.* Risk factors for head and neck cancer in young adults: A pooled analysis in the INHANCE consortium. *Int J Epidemiol.* 2015;44:169-85.
6. Oral cancer [Internet]. World Health Organization; c2020. [cited 22 September 2020]. Available from: <https://www.who.int/cancer/prevention/diagnosis-screening/oral-cancer/en/>
7. Risk Factors: Tobacco [Internet]. National Cancer Institute; c2020. [cited 22 September 2020]. Available from: <https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco>
8. Chaturvedi AK. Epidemiology and clinical aspects of HPV in head and neck cancers. *Head Neck Pathol.* 2012;6(1):S16-24.
9. Zygogianni AG, Kyrgias G, Karakitsos P. Oral Squamous cell cancer: early detection and the role of alcohol and smoking. *Head Neck Oncol;* c2011.
10. Saman D. A review of the epidemiology of oral and pharyngeal carcinoma: update. *Head & Neck Oncology,* 2012, 4(1).
11. Lambert R, Sauvaget C, De Camargo Cancela M, Sankaranarayanan R. Epidemiology of cancer from the oral cavity and pharynx. *Eur. J Gastroenterol Hepatol.* 2011;23(8):633-641.
12. Bittar RF, Ferraro HP, Ribas MH, Lehn CN. Predictive factors of occult neck metastasis in patients with oral squamous cell carcinoma. *Brazilian journal of otorhinolaryngology.* 2016;82:543-7.
13. Balasundram S, Mustafa WM, Ip J, Adnan TH, Supramaniam P. Conservative neck dissection in oral cancer patients: A 5-year retrospective study in Malaysia. *Asian Pac J Cancer Prev* 2012;13:4045-50.
14. Lim SC, Zhang S, Ishii G, *et al.* Predictive markers for late cervical metastasis in stage I and II invasive squamous cell carcinoma of the oral tongue. *Clin Cancer Res.* 2004;10(1 pt 1):166-172.
15. Sharma A, Kim J, Paeng J. Clinical analysis of neck node metastasis in oral cavity cancer. *Journal of the Korean Association of Oral and Maxillofacial Surgeons.* 2018;44(6):282.