

Original Research Article

## Is OSMF is an independent variable to affect cervical metastasis in OSCC associated with OSMF

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**Abstract:** There has been increased incidence of concomitant association of OSCC & OSMF in recent times. The aim of study is to determine whether OSMF is independent factor to determine the cervical metastasis in patients of OSCC with OSMF. Authors prospectively investigated total 100 patients which were divided into two groups (OSCC-OSMF and OSCC) with 50 patients in each group. Patients of both the group underwent surgery for OSCC with curative intent. In the study, males were predominantly affected in both the groups. In OSCC-OSMF group most commonly affected age group was of 31-40 (32%) and 41-50 years (32%). Whereas, in OSCC group, most commonly affected age group was of 51-60 years (30%). Buccal mucosa was the most frequently involved site in both the groups, accounting for 40% cases in each group. Most of the tumors were moderately differentiated in OSCC-OSMF group, where as in OSCC group most of them were well differentiated. Most of the patients in OSCC-OSMF group had grade three and grade four diseases. Cervical metastasis in OSCC-OSMF group was 34% whereas in OSCC group was 26%. Level Ib lymph nodes were most frequently involved in both the groups (OSCC-OSMF:22% and OSCC:18%). Correlation between OSMF grading and cervical metastasis was not significant. OSCC with OSMF affects younger population showing, predominantly involving buccal mucosa. OSMF did not have any independent impact on cervical metastases. However a study with larger sample size is required to arrive at a logical conclusion.

**Keywords:** Oral submucous fibrosis, Oral squamous cell carcinoma, cervical metastasis

**INTRODUCTION**

OSMF is a condition which would expose the entire oral cavity to malignant changes, the most common reason are the reduced elasticity of the oral mucosa subjects the mucosa to trauma mainly due to a malposed teeth, a sharp edge, special to mention a impacted third molar. More dangerous to mention is habit of betel-nut mixed with tobacco in which apart from development of condition, there is always risk of lesion because of tobacco. There has been increased incidence of concomitant association of OSCC & OSMF in recent times. Malignant transformation rate of OSMF was found to be in the range of 7-13% [1].

Oral cancer is the most common cancer in Indian males (13% of all malignancies) and is the third most common cancer in Indian females [2]. OSCC has loco-regional ramifications. It has a greater tendency to metastasize to regional lymph nodes in a predictable

manner. The overall 5-year survival of patients with OSCC is less than 50% [3]. Concomitant association of OSMF with OSCC is remarkable in that the dense fibrosis and less vascularity of the corium, in the presence of an altered cytokine activity creates a unique environment for carcinogens from both tobacco and areca nut to act on the epithelium. In patients having OSCC with OSMF, dense fibrosis and less vascularity of the corium, in the presence of an altered cytokine activity creates a unique environment for carcinogens from both tobacco and areca nut to act on the epithelium. Less vascularity may deny the quick absorption of carcinogens into the systemic circulation and this reduced and blocked submucosal vascularity may have a beneficial effect on overall prognosis [4].

The purpose of this study is to evaluate the effect of OSMF and compare the cervical metastasis in

patients with OSCC associated with and without OSMF.

**MATERIAL AND METHODS**

The present prospective, observational audit was designed and implemented between April 2013 and June 2016 at AVBRH. This study was a prospective audit without any special/ different interventions, for which the necessary institutional ethics committee waiver/exemption was obtained. All the patients with a non-healing ulcer of oral cavity with or without features of OSMF (intolerance to hot and spicy foods, pale looking oral mucosa, palpable fibrous bands, and chronic progressive trismus) were subjected to biopsy for conformation of OSCC. Patients with non-epithelial malignancy, multiple index tumours, history of chemotherapy, radiotherapy ± surgery and Second primary tumours were excluded. A total of 100 consecutive patients fulfilling the above criteria were included in the study. Patients were divided into two groups (OSCC-OSMF group and OSCC group) with 50 patients in each group.

The following clinical and pathologic findings were recorded: age, sex; habit history, primary site of disease according to various subsites (alveolus, tongue,

buccal mucosa, GB complex, retromolar trigone [RMT] and maxilla); clinical and pathologic tumor classification (cT and pT); clinical and pathologic nodal status (cN and pN). All patients underwent comprehensive pre-surgical evaluation, which included a medical history and complete physical examination, complete blood count, routine blood biochemistry, magnetic resonance imaging (MRI) scans of the head and neck, chest radiographs. The staging of OSCC was assigned according to pathological status at presentation for primary surgical treatment.

All patients underwent standard treatment i.e. Wide local excision of lesion, Supraomohyoid neck dissection for N0 neck and modified radical neck dissection for N+ neck followed by appropriate adjuvant treatment based on histopathologic parameters. Fibrotomy, coronoidectomy ipsilateral ± contralateral side and reconstruction with suitable flap. Resected specimen (index tumour) and resected levels of lymph nodes were assessed, grossed, labeled and subjected to intra operative frozen section, Step serial sectioning and Immuno-histochemical (IHC) evaluation with Pancytokeratin.

**RESULTS**

**Table-1: Correlation between OSMF grading and cervical metastasis**

		OSCC-OSMF	OSCC	P value
Age	Mean	43.24	51.94	0.0020
	Range	24-70	35-78	
Gender	Male	44(88%)	39(78%)	0.18
	Female	6(12%)	11(22%)	
Site	Alveolus	4(8%)	8(16%)	0.69
	Buccal Mucosa	20(40%)	20(40%)	
	Tongue	10(20%)	5(10%)	
	GB Complex	14(28%)	15(30%)	
	Maxilla	1(2%)	1(2%)	
	RMT	1(2%)	1(2%)	
TNM staging	I	1(2%)	0(0%)	0.50
	II	3(6%)	1(2%)	
	III	11(22%)	14(28%)	
	Iva	35(70%)	35(70%)	
Cervical metastasis	Positive	17(34%)	13(26%)	0.38
	Negative	33(66%)	37(74%)	
Histopathological grading	Well	16(32%)	28(56%)	0.033
	Mod	32(64%)	19(38%)	
	Poor	2(4%)	3(6%)	
Correlation between OSMF grading and cervical metastasis (N+) by Pearson's Linear Correlation				
	Correlation Coefficient(r)	95% confidence interval	p-value	Significant or not
OSCC-OSMF	0.229	0.0061-0.213	0.109	Not Significant

A total of 100 patients with 50 patients in each group (OSCC-OSMF and OSCC) were examined. Among the patients included for the study, males were predominantly affected in both the groups i.e. 88% (n=44) in OSCC-OSMF and 78% (n=39) in OSCC. In OSCC-OSMF group most commonly affected age

group was of 31-40 (32%) and 41-50 years (32%), followed by 21 – 30 years (16%). Whereas, in OSCC group, most commonly affected age group was of 51-60 years (30%) followed by 41-50 years (26%). Buccal mucosa was the most frequently involved site in both the groups, accounting for 40% cases in each group.

Most of the tumors were moderately differentiated in OSCC-OSMF group, whereas in OSCC group most of them were well differentiated. Most of the patients in OSCC-OSMF group had grade three and grade four diseases. Cervical metastasis in OSCC-OSMF group was 34% whereas in OSCC group was 26%. Level Ib lymph nodes were most frequently involved in both the groups (OSCC-OSMF: 22% and OSCC:18%). Correlation between OSMF grading and cervical metastasis was not significant [Table 1].

## DISCUSSION

In most countries around the world, oral cancer is more common in males than in females; likewise, oral submucous fibrosis is also more common in males for obvious reasons of prevalent betel nut chewing habit. In certain parts of India betel nut chewing habit is more of custom than a taboo. In the present study, both the groups (OSCC-OSMF and OSCC) showed higher incidence of malignancy in males (88% and 78% respectively) as compared to females (12 and 22% respectively). This can be explained by the fact that the incidence of chewing tobacco and betel nut is higher among males. This study is in accordance with the study of Chaturvedi *et al.* [5] Sharma *et al.* [6]. There is increasing evidence that trends are changing and that the usual male dominance is not the case in younger patients. The difference seen previously was probably a reflection of the differences in habits between males and females although this gap is narrowing. Jones *et al.* [7] reported female patients with carcinoma of tongue outnumbering males by almost 2:1 in patients under 40 years old and similar findings have been reported by McGregor *et al.* [8].

Site of oral squamous cell carcinoma has bearing on overall outcome of disease like malignancy of tongue and floor of mouth behave more aggressively when compared with buccal or labial mucosa malignancy. In OSCC-OSMF group, buccal mucosa (40%) was most commonly involved followed by gingivobuccal sulcus (28%) sulcus; also, buccal mucosa (40%) was most commonly involved in OSCC group followed by gingivobuccal sulcus (30%) both the group showed similar site predilection. Tongue was more frequently involved in the OSCC-OSMF group. Chaturvedi *et al.* [5]. They mention that, higher involvement of buccal mucosa in Indian population is related to a peculiar habit of placing the smokeless tobacco/areca nut product in the lower buccal vestibule. Moreover buccal mucosa is the site which is in direct and most frequent contact with the irritant. Oral tongue is commonly involved in OSMF and many patients show atrophy of tongue papillae, which are keratinized structures, causing a smooth or bald appearance. This loss of papillae may perhaps predispose to carcinogenesis because of loss of protective barrier.

One of the determinant factors for survival in patients of oral cancers is metastasis and recurrence.

Metastasis unequivocally signifies that tumor is malignant. The presence or absence of metastatic disease in cervical lymph nodes of oral cancer patients is the single most important determinant of therapy as well as the prognosis of the patient. In the present study, OSCC-OSMF group showed higher cervical metastasis as compared to OSCC group to various levels. And the correlation between OSMF grading and cervical metastasis was nonsignificant ( $p = 0.109$ ). Hashmi G S *et al.* [9] stated that, initial stage of nodal metastasis was predominant in cases of OSCC with OSMF. However, Chaturvedi *et al.* [Error! Bookmark not defined.] stated that lesser incidence of nodal metastases in cases of OSCC with OSMF. Zhou *et al.* [10] showed that patients with OSCC with OSMF had no neck node metastases. The results of this study were not in accordance with the above mentioned studies. The reason could be, most of the lesions in this study were advanced with increased depth of infiltration there by increasing the chances of cervical metastases. Contrary to the hypothesis stated by Chaturvedi *et al.* [Error! Bookmark not defined.] that the lesser incidence of lymph node metastases is because of the blockage of submucosal lymphatics as a result of fibrosis we would like to highlight that this hypothesis might be relevant for the early lesion in OSMF associated OSCC but the moment the depth of invasion by tumor cells increase it would confront larger diameter lymphovascular channels and the progress of the disease with respect to cervical metastases would be same as in OSCC. Further the knowledge of progression of submucous fibrosis explains that the phenomenon of fibrosis seldom extend and involves lamina propria, hence tumor infiltrating deeper to this barrier should behave as routine OSCC leading to similar rates of cervical metastases.

In both the groups (OSCC-OSMF and OSCC) Level Ib (22% and 18% respectively) lymph node was most commonly involved. This was in accordance with the Jochen A and Werner *et al.* [11] who stated that, the dense lymphatic system of the gingiva-buccal complex drains primarily into the submandibular lymph node through 8 to 10 collectors that extend through the buccal muscle. Essig H *et al.* [12] found that incidence of lymph node metastasis in level I was high as compared to other levels of lymph node from carcinoma of the buccal mucosa.

## CONCLUSION

OSCC with OSMF affects younger population showing, predominantly involving buccal mucosa. OSMF did not have any independent impact on cervical metastases, may be because of the presence of advance lesions in most of the cases (i.e. stage III and IV), as the moment the depth of invasion by tumor cells increase it would confront larger diameter lymphovascular channels and the progress of the disease with respect to cervical metastases would be same as in OSCC.

However a study with larger sample size is required to arrive at a logical conclusion.

#### REFERENCE

1. Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ, Warnakulasuriya S. Oral submucous fibrosis: review on aetiology and pathogenesis. *Oral oncology*. 2006 Jul 31; 42(6):561-8.
2. Notani PN. Global variation in cancer incidence and mortality. *CURRENT SCIENCE-BANGALORE*. 2001 Sep 10; 81(5):465-74.
3. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral oncology*. 2009 May 31;45(4):309-16.
4. Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ, Warnakulasuriya S. Oral submucous fibrosis: review on aetiology and pathogenesis. *Oral oncology*. 2006 Jul 31; 42(6):561-8.
5. Chaturvedi P, Vaishampayan SS, Nair S, Nair D, Agarwal JP, Kane SV, Pawar P, Datta S. Oral squamous cell carcinoma arising in background of oral submucous fibrosis: a clinicopathologically distinct disease. *Head & neck*. 2013 Oct 1; 35(10):1404-9.
6. Sharma P, Saxena S, Aggarwal P. Trends in the epidemiology of oral squamous cell carcinoma in Western UP: an institutional study. *Indian Journal of Dental Research*. 2010 Jul 1; 21(3):316.
7. Jones JB, Lampe HB, Cheung HW. Carcinoma of the tongue in young patients. *The Journal of otolaryngology*. 1989 Apr; 18(3):105-8.
8. McGregor GI, Davis N, Robins RE. Squamous cell carcinoma of the tongue and lower oral cavity in patients under 40 years of age. *The American Journal of Surgery*. 1983 Jul 1;146(1):88-92.
9. Hashmi GS, Ahmed SS, Khan S, Athar H. Incidence of submucous fibrosis in oral cancer patients. *Biology and Medicine*. 2011; 3(2):207-14.
10. Zhou S, Qu X, Yu Z, Zhong L, Ruan M, Ma C, Wang M, Zhang C, Jian X. Survivin as a potential early marker in the carcinogenesis of oral submucous fibrosis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2010 Apr 30; 109(4):575-81.
11. Werner JA, Dünne AA, Myers JN. Functional anatomy of the lymphatic drainage system of the upper aerodigestive tract and its role in metastasis of squamous cell carcinoma. *Head & neck*. 2003 Apr 1;25(4):322-32.
12. Essig H, Warraich R, Zulfiqar G, Rana M, Eckardt AM, Gellrich NC, Rana M. Assessment of cervical lymph node metastasis for therapeutic decision-making in squamous cell carcinoma of buccal mucosa: a prospective clinical analysis. *World journal of surgical oncology*. 2012 Nov 22; 10(1):253.