



**Intraoral Trauma and Traumatic Ulcer in OSMF and Its Malignant Potential**

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**Abstract**

**Aim:** The aim of study is to evaluate malignant potential role of trauma and traumatic ulcer in Oral submucous fibrosis with Oral squamous cell carcinoma.

**Materials & Method:** The study consisted 60 patients of OSMF with ulcer. OSMF with aggravating factors such as Defective teeth, ill-fitting dentures and/or parafunctional habits were included in study. Study patients were analysed for demographic details, tobacco habit in detail as well as OSMF & ulcer were examined in detail. All cytological & histological reports were assessed in details.

**Result:** 54 male patients (90%) were reported between 31 to 60 years of age. 96.67% patients had habit of tobacco, among them 67.24% had habit of gutkha chewing. Traumatic ulcers reported about 60% followed by carcinoma in situ (20%) and carcinomatous

ulcers (20%). 50% ulcer present on buccal mucosa. Highly significant result reported between aggravating factor & grade of OSMF. The relationship between OSCC location and histological grade was not statistically significant.

**Conclusion:** Buccal mucosa, partially erupted maxillary and mandibular third molars, and sharp teeth are the most common sites of OSMF malignant transformation. Any ulceration linked to OSMF should be reported by the patient since it has a significant risk of malignancy. Being aware of the aggravating factor and eliminating it is one method for halting the development of malignant potential for both patient as well as clinician.

**Keywords:** Oral Submucous Fibrosis, Aggravating Factors, Traumatic Ulcer/ Carcinomatous Ulcer

## Introduction

In 1952, Schwartz for the first time reported a case of “Atrophica idiopathica mucosae oris” occurring in Indians in East Africa. Lal and Joshi first described this condition in India and coined the term OSMF. The possible precancerous nature of oral submucous fibrosis was first mentioned by Paymaster in 1956, who described the development of slow-growing oral squamous cell carcinoma in one third of the cases with submucous fibrosis <sup>(1,2)</sup>. OSMF has a malignant transformation rate of 7-30% <sup>(3)</sup>.

The strongest risk factor for OSMF is the chewing of betel quid containing areca nut. OSMF is seen most frequently in community’s resident in the Indian sub-continent and has a reported incidence of between 0.2–1.2 percent of the urban population attending dental clinics. The condition predominantly affects women with a female: male ratio of 3:1 and characteristically first presents in adulthood between the ages of 45–54 years. After comparing the risk ratio, it has been estimated that people with OSMF are 19.1 times more likely to develop oral cancer than those without it <sup>(4,5)</sup>.

Chronic mechanical irritation (CMI) of the oral mucosa is the result of repeated injuring by the mechanical action of an intraoral injury agent. Defective teeth (malposition or with sharp or rough surfaces because of decay or fractures), ill-fitting dentures (sharp or rough surfaces, lack of retention, stability or overextended flanges) and/or parafunctional habits (e.g. oral mucosa biting or sucking, tongue interposition or thrusting), acting individually or together, could all be responsible for any mechanical irritation. Chronic trauma may increase in a cell undergoing division turn them susceptible to DNA damage, also promoting malignant cell growth. The overexpression of several mediators in chronic inflammation offers an explanation of the

potential role of chronic inflammation in cancer initiation, promotion, conversion and progression <sup>(6)</sup>.

The aim of study is to evaluate malignant potential role of trauma and traumatic ulcer in OSMF with OSCC.

## Material and Method

The study was conducted in oral medicine and radiology department of Government dental college and Hospital, Ahmedabad and consisted 60 patients of OSMF with ulcer. Ethical approval (IEC GDCH/ OMR.21 /2021) was taken for the study as well as informed consent was obtained from all subject. OSMF patients with ulcer suspected for carcinoma in situ or carcinoma were selected for the study. OSMF with aggravating factors such as Defective teeth (malposition or with sharp or rough surfaces), ill-fitting dentures and/or parafunctional habits (e.g. oral mucosa biting or sucking) were included in study. Patients of OSMF with ulceration other than trauma were excluded from the study such as aphthous ulcer, viral ulcer or any other. Study patients were analyzed for demographic details, tobacco habit in detail as well as OSMF & ulcer were examined in detail.

After selection on patients of OSMF with ulceration were treated first for ulcer, all cases were managed by conservative approach that is removal of causative factor (polishing of sharp cusp, adjustment of prosthesis, correct bushing technique, change in oral hygiene products, removal of ill-fitting denture) with non-steroidal anti-inflammatory mouthwash/ spray (benzylamine hydrochloride 1.5 mg/ml) four times a day and topical anesthetics (choline salicylate) three times a day before meal. Followed up was done after 7 days & if ulcer is responded with conservative therapy, they were followed up for 4 weeks duration. After 4 weeks of followed up ulcer is not responded to conservative management, they all were evaluated by

cytological & histological examination. All cytological & histological reports were assessed in details.

### Clinical Diagnostic Criteria

**Oral submucous fibrosis (OSMF)** was clinically examined & graded based on complain of hot & spicy food, blanched/fibrous mucosa, extension of fibrosis, vesicle/ulceration, & mouth opening measurement <sup>(7,8)</sup>.

**Traumatic ulcer** was examined for size, shape (round/elliptical), margins (well/ill-defined), floor, base, tenderness, induration & surrounding area (yellowish slough/ red erythematous halo) <sup>(9)</sup>. **Carcinoma in situ** was clinically examined as mixed red & white lesion, with irregular margin, indurated surface with or without papillary projection, bleeding tendency & mobility of adjacent teeth <sup>(10,11)</sup>. **OSCC** was clinically appears as non-healing ulcer or ulcero-proliferative growth as mixed red & white lesion, with irregular margins, indurated surface, with or without papillary projection, bleeding tendency, mobility of adjacent teeth & lymphadenopathy <sup>(10,11)</sup>.

### Result

Present study comprises of total 60 patients of OSMF with ulcer (traumatic ulcer/ carcinoma in situ/carcinomatous ulcer). 54 male patients (90%) & 6 female (10%) were reported. The maximum patients were reported between 31 to 60 years of age (68.33%) (table 1). 96.67% patients had habit of tobacco, among them 67.24% had habit of gutkha chewing (table 2). Traumatic ulcers reported about 60% followed by carcinoma in situ (20%) and carcinomatous ulcers (20%). 50% ulcer present on buccal mucosa followed by 38.33% on tongue. Non-significant result reported between site & ulceration (table 3). Sharp teeth as aggravating factors reported 31.67% followed by 21.67% parafunctional habit aggravating factors. Mandibular/maxillary 3<sup>rd</sup> molar partially eruption act as

aggravating factor in 75% advanced OSMF. 31.67% reported with early as well as moderate stage of OSMF. Highly significant result reported between aggravating factor & grade of OSMF (table 4). Cytological grade 2 was reported in 45.83% of cases, whereas cytological grade 1 was reported in 20.83% of cases (table 5). In 73.68% of cases, a well-differentiated OSCC was found, whereas in 21.05% of cases, a moderately-differentiated OSCC. Buccal mucosa was reported by 78.6% of well-differentiated OSCC, 75% of moderately-differentiated OSCC. Tongue was reported by 100% of poorly-differentiated OSCC. The relationship between OSCC location and histological grade was not statistically significant (table 6).

### Discussion

The World Health Organization subsequently defined OSMF as “a slowly progressive disease in which fibrous bands form in the oral mucosa, ultimately leading to severe restriction of movement of the mouth, including the tongue.” <sup>(1,4)</sup> It has been reported mainly from India, but has also been diagnosed in Srilanka, Malaysia, Nepal, South Vietnam, and Thailand <sup>(1)</sup>—OSMF is a premalignant condition mainly associated with the practice of chewing betel quid containing areca nut, a habit common among South Asian people <sup>(12)</sup>. OSMF incidence of malignant transformation is as 7.6% with a follow up of 17 years <sup>(13)</sup>. Carcinogenesis is multifactorial in humans. Tobacco and alcohol are often considered as the major risk factors for oral cancer <sup>(6)</sup>. However, they could not cause the entirety of cancers, and also there are individuals unexposed to those factors that could develop malignant lesions. This fact implies that there are other factors in oral cancer, and among them, chronic mechanical irritation (CMI) has been reported as aggravating factor <sup>(6)</sup>.

Chronic mechanical irritation (CMI) could generate changes in the healthy mucosa or intensify previous oral diseases<sup>(13)</sup>. CMI produces several alterations related to its duration and intensity. Effects could range from a hyperproliferative epithelial response if the stimulus is mild (frictional keratosis), to several levels of tissue injury (atrophy, erosion, ulcer) if it is intense or is of longer duration (chronic traumatic ulcer), often with fibrous connective tissue growth (Reactive hyperplasia, e.g. Denture-induced fibrous hyperplasia)<sup>(6)</sup>. CMI factors were registered in three groups: dental (tooth malposition, diastema, sharp or broken tooth, sharp or rough fillings or fixed prosthesis), prosthetic (sharp or rough dentures, defective retainers, overextended flanges, denture without stability and/or retention) and functional (tongue interposition, lip/cheek/ tongue biting or suction, dentures stabilization with tongue, etc.)<sup>(6)</sup>

Maximum patients reported were male (90%) (table 1). Warnakulasuriya<sup>(14)</sup> and Wang et al<sup>(15)</sup> found that males were more commonly seen OSCC associated with OSMF. Pindborg<sup>(16)</sup> found female develop OSCC associated with OSMF. Higher incidence of OSCC among male patients between the age of 31 to 60 year of age. Not a single patients reported between 1- 15 years of age (Table 1). That means that lack of nutritional care which increase the susceptibility to develop the OSCC relative risk increases approximately 12-folds from the third to seventh decade.

Maximum patients reported with smokeless tobacco habit (table 2). The Indian subcontinent has one of the highest incidences of oral cancer in the world, mainly due to the high prevalence of chewing or combination of smokeless tobacco & areca nut. In India, several market preparations are available such as gutka, khaini, mawa, and paan that contain smokeless tobacco<sup>(4)</sup>. Parental education also has an effect over the development of oral

adverse habits. It has been seen that higher parental education prevents the development of oral adverse habits in their offspring. Illiteracy or lower education status encourages the development of oral adverse habits. The incidence of OSMF was high in low socioeconomic status<sup>(13)</sup>.

Maximum ulceration present at buccal mucosa (50%). As an aggravating factor, partially erupted 3rd molars of maxilla and mandible repeatedly irritate the mucosa, leading to recurrent ulceration. Due to the aggravating factor of sharp teeth, the tongue was the second most prevalent location for ulceration. In present study non-significant result reported between site & ulceration (table 3). Many of the OSMF patients have shrunken cheeks with reduced cheek fullness and poor pliability of tissues. Once the cheek biting starts, the inflammation increases and the edematous tissue faces further trauma leading to a vicious cycle<sup>(17)</sup>. Areca nut causes DNA damage by direct acting alkylating agents, tumour induction by nitrosamines produced by nitrosation of areca alkaloids and tumor promotion by arecaidine. Additionally, its genotoxic and mutagenic effects are attributed to polyphenols and alkaloids as well as presence of areca nut-specific nitrosamines like N-nitrosoguvacoline, Nnitrosoguvacine, 3-propionaldehyde, and 3-propionitrile<sup>(1,3,15,18,19)</sup>. Dayal (2000) reported 13% of squamous cell carcinoma and 23% of epithelial dysplasia in OSMF due to traumatic injury. It is suspected that the trauma increases the permeability of tissue to carcinogens causing malignant transformation of susceptible cells. Furthermore, ectopic eruption of third molars especially in the maxilla is risk factor for malignant transformation of OSMF due to persistent impingement of OSMF tissue against the coronoid process<sup>(20)</sup>.

Highly significant result found between aggravating factors & grade of OSMF (table 4). OSMF patient has very restriction mouth opening in sharp teeth as well as impacted teeth (mandibular/ maxillary) were reported 75% cases. In such patients, owing to the stiffness of mucosa and constant trauma from occlusion due to malposition of lower and upper third molar, the OSCC could precipitate owing to chronic irritation. The posterior buccal mucosa was the most commonly involved site. Moreover, it was observed that such patients often reported with advanced stage of the disease extending to the retromolar trigon. So, all the patients of OSMF undergo for radiographic evaluation to find out status of impacted tooth & should be warned about the potential role in developing carcinomatous ulcer & they should be removed. Valley et al. <sup>(21)</sup> reported significant increase risk of OSCC associated with secondary ill-fitting denture. lockhart reported OSCC association with mechanical irritation from teeth, or denture <sup>(21)</sup>

As the OSMF grade transformed from early to advanced stage, blood vessels are obliterated or narrowed, constricted with collagen is completely hyalinized and change in inflammatory cells are mainly lymphocytes and plasma cell. So, chances of conversion of malignant potential increase with advanced grade of OSMF. Repeated trauma causes continuous inflammation produces repeated cycles of cell injury & compensatory proliferation. The increase in a cell undergoing division turn them susceptible to DNA damage, also promoting malignant cell growth, overexpression of several mediators in chronic inflammation offers an explanation of the potential role of chronic inflammation in cancer initiation, promotion, conversion & progression <sup>(20,21)</sup>.

Maximum patients showed class 2 atypical cytological grading (table 5). A total of 24 patients evaluated for

cytological examination and were advised to have their histopathology evaluation, however only 19 patients had their histopathology assessed since 5 of the patients weren't ready for incisional biopsies. Maximum patients reported as a well differentiated OSCC as maximum ulceration present on the buccal mucosa. Only one patient reported with poorly differentiated OSCC which was involved lateral border of tongue. Non-significant result reported between site of ulceration & histological grade of OSCC in present study (table 6). OSCC without OSMF preferentially involves the ventral surface of the tongue and floor of mouth, about 50% of all cases <sup>(22)</sup>. OSCC of tongue is most likely to associated with smoking habit. Pack and LeFevre & Copenhagen HJORTING-HANSEN OSCC arising from OSMF showed buccal mucosa most common about 53.43% <sup>(23,24)</sup>. Chaturvedi et al (2012). reported most common site of OSMF-OSCC Gingivobuccal complex about 38.3% by buccal mucosa accounted for 38.3% <sup>(24,25)</sup>.

### Conclusion

Oral Submucous Fibrosis is a symptomatic condition, the patient can recognize the disease process at an early stage. Hence, proper counseling and education of the patient regarding the devastating effects may help or reduce the incidence of malignant transformation of OSMF. Buccal mucosa, partially erupted maxillary and mandibular third molars, and sharp teeth are the most common sites of OSMF malignant transformation. Any ulceration linked to OSMF should be reported by the patient since it has a significant risk of malignancy. Being aware of the aggravating factor and eliminating it is one method for halting the development of malignant potential for both patient as well as clinician. Chances of development of OSCC in OSMF patients increase due to chronic trauma & traumatic factor as aggravating factors.

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### Legend Figures & Tables



Figure 1:

Site: Posterior buccal mucosa

Aggravating factors: partially erupted maxillary 3<sup>rd</sup> molar

Clinically appear: traumatic ulceration on posterior buccal mucosa.



Figure 2:

Site: buccal mucosa

Aggravating factor: sharp teeth

Clinically appear: carcinoma in situ

Cytological: cytological grade 4



Figure 3:

Site: buccal mucosa

Aggravating factors: sharp maxillary & mandibular teeth

Clinically appear: proliferative growth,

Histopathological: well differentiated OSCC

Table 1: Distribution of the patients according to age and gender

Age Group	Male (N=54) (90%)	Female (N=6) (10%)	Total (N=60)
01-15	0	0	0
16-30	14(25.93%)	2(33.33%)	16(26.67%)
31-45	22(40.74%)	1(16.67%)	23(38.33%)
46-60	16(29.63%)	2(33.33%)	18(30%)
>60	2(3.70%)	1(16.67%)	3(5%)

Table 2: Distribution according to type of habit

Habit	Total (N=60)	
Smokeless (N=58)(96.67%)	Areca nut	12 (20.68%)
	Pan masala chewing	7 (12.06%)
	Tobacco	16 (27.57%)
	Gutkha chewing	23 (67.24%)
Combined (N=2)(3.33%)	Smokeless+ Smoking	2

Table 3: Distribution of ulcer according to site

	Traumatic ulcer (N=36) (60%)	Carcinoma in situ (N=12)(20%)	OSCC (N=12) (20%)	Total (N=60)
Buccal mucosa	17(47.22%)	6(50%)	7(58.33%)	30(50%)
Gingivobuccal sulcus	1(2.78%)	0	1(8.33%)	2(3.33%)
Palate	2(5.56%)	1(16.67%)	0	3(5%)
Pterygomandibular raphe	1(2.78%)	1(16.67%)	0	2(3.33%)
Tongue	15(41.67%)	4(33.33%)	4(33.33%)	23(38.33%)
Chi square value	5.157			
Significance	0.741(NS)			

Table 4: Distribution according to grade of OSMF with aggravating factors

	Very early (N=10)(16.67%)	Early stage (N=19)(31.67%)	Moderate stage (N=19)(31.67%)	Advanced stage (N=12)(20%)
Sharp teeth (N=19) (31.67%)	5(50%)	8(42.10%)	6(31.6%)	0
Maxillary/ Mandibular partially erupted teeth (N=12) (20%)	0	0	3(15.8%)	9(75%)
Ill-fitting denture (N=4)(6.67%)	1(10%)	1(5.3%)	2(10.52%)	0
Cheek biting (N=12) (20%)	1(10%)	6(31.6%)	3(15.8%)	2 (16.7%)
Parafunctional Habit [bruxism](N=13) (21.67%)	3(30%)	4(21.1%)	5(26.31%)	1(8.33%)
Chi square value	34.588			
Significance	0.001(HS)			

Table 5: Distribution according to cytological diagnosis

Grade of cytological diagnosis	Number of patients (N=24)
Grade 1	5 (20.83%)
Grade 2	11 (45.83%)
Grade 3	4 (16.67%)
Grade 4	4 (16.67%)

Table 6: Distribution according to histological diagnosis

Site	Well differentiated OSCC (N=14) (73.68%)	Moderately differentiated OSCC (N=4) (21.05%)	Poorly differentiated OSCC (N=1) (5.26%)
Buccal mucosa(N=14)	11(78.6%)	3(75%)	0
Gingivobuccal sulcus(N=1)	1(7.1%)	0	0
Tongue(N=2)	0	1(25%)	1(100%)
Palate(N=2)	2(14.3%)	0	0
Chi square value	13.358		
Significance	0.344(NS)		