

**ASSOCIATION BETWEEN THE RISK FACTORS AND CLINICAL SEVERITY OF  
ORAL SUBMUCOUS FIBROSIS: A CROSS SECTIONAL STUDY**Neeraj Kumar<sup>1\*</sup> (M.D.S), Richa Kumari<sup>2</sup> (M.D.S) and Piyush Mishra<sup>3</sup><sup>1</sup>Assistant Professor, All India Institute of Medical Sciences Bilaspur, Himachal Pradesh India.<sup>2</sup>Ex Tutor, ESIC Rohini, New Delhi, India.<sup>3</sup>Statistician, Nand Kumar Chauhan Government Medical College Khandwa, Madhya Pradesh India.**\*Corresponding Author: Dr. Neeraj Kumar (M.D.S)**

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**ABSTRACT**

**Background:** Oral submucous fibrosis (OSMF) is a chronic, progressive, high risk precancerous condition of the oral mucosa seen primarily in the Asian countries. But in recent years, more severe form of the disease in younger age group has been observed. The aim of the present study was to evaluate the association of the various risk factors with the severity of the disease. **Materials and Methods:** A cross sectional study was done in 152 diagnosed cases of OSMF over a period of 22 months. The detailed demographics, history related to the duration and frequency of tobacco chewing habits were recorded and clinical examination was carried out. The observations were tabulated and analysed using Chi-square/Fisher exact test through software R version 3.6.3. **Results:** Out of 152 cases of OSMF, 129 were males and 23 were females. The most common age group affected with the OSMF was 21-40 years and males were the majority affected. The duration and frequency of the gutkha/supari/tobacco consumption was significantly associated with the severity stages of the OSMF ( $p=0.05$ ). Mouth opening was decreased as the severity of the OSMF increases. **Conclusions:** The duration and frequency of the chewing habits were associated with the severity of the disease. As the younger age group was mostly affected with the stage III of OSMF, young people need to receive health education regarding prevention of OSMF.

**KEYWORDS:-** Oral sub mucous fibrosis, Risk factors, Precancerous condition, Chewing habits.

**INTRODUCTION**

Oral sub-mucous fibrosis (OSMF) is an oral precancerous chronic progressive condition which presents with burning sensation, rigidity of palate, buccal and labial mucosa and retromolar pad area leading to decreased mouth opening and restricted tongue movement. OSMF is most prevalent in the South Asians countries, with overall prevalence rate was found to be about 0.2% -0.5 % in India and varying from 0.2-2.3% in males and 1.2-4.57% in females respectively.<sup>[1]</sup> Areca nut/betel nut is possibly the second most consumed carcinogen after tobacco in the Indian subcontinent. The malignant potential of OSMF to oral cancer /squamous cell carcinoma transformation has been reported to be 7-30%.<sup>[2]</sup>

There are regional variations in the type of areca nut products used in different parts of India. Areca nut is chewed for variety of reasons such as mouth freshener, concentration improver, stress reliever and a digestive following food. The withdrawal symptoms of these products includes mood swings, loss of concentration, sleep disturbance, anxiety, irritability and craving.<sup>[3]</sup> The areca nut contains many alkaloids, arecoline being the

most abundant, which have been shown to stimulate the fibroblastic activity which lead to increased collagen synthesis. There is involvement of the sub epithelial connective tissue and inflammatory cell infiltrate deposits in the juxta-epithelial connective tissue. This could be due to the lysyl oxidase activity which stimulate cross linking of the collagen leading to fibrosis.<sup>[4]</sup>

Over the past several years, different researchers worked on different aspects of OSMF. There are limited studies in present scenario which correlates the role of a habit such as duration, frequency, type of tobacco consumption to the clinical grading of OSMF. This cross sectional survey was carried out to find the association between the risk factors and the severity of the OSMF.

**MATERIAL AND METHODS****Study design and settings**

The descriptive cross sectional survey was carried out at the private hospital in district Khandwa, Madhya Pradesh from June 2018 to March 2020. The permission was taken from the director of the private hospital to collect the data. The patients reported to the out-patient

department of dental were enrolled in the survey as per the following inclusion and exclusion criteria.

#### **Inclusion criteria**

- a. Diagnosed cases of OSMF
- b. Patients between the age range from <20 to >60  
Patients with OSMF having a history of chewing guthka/supari/tobacco products  
Exclusion criteria:
  - a. Patient diagnosed with syndromes or mental retardation
  - b. Mouth opening limited due to other causes like space infection or pericoronitis

The patients reported with sign and symptoms of OSMF were examined clinically and based on the clinical signs and symptoms cases were diagnosed by the chief investigator (NK). The diagnosed OSMF patients between <20 to >60 who volunteered and gave consent to participate in the survey were included in the study. A total of 152 patients diagnosed with OSMF were included in the study. The demographic details of the enrolled patients like age, sex and occupation were recorded on a specially prepared proforma. The clinical details related to the chewing habits like guthka/supari with or without tobacco, type of tobacco consumption, frequency of tobacco/guthka/ supari consumption per day and duration in years, mouth opening, severity of the OSMF lesion, presence or absence of fibrous bands, burning sensation and location of fibrous bands were also recorded.

#### **Clinical diagnosis and functional staging of OSMF**

The clinical diagnosis and functional staging of the OSMF cases was made using the *Haider et al 2000* clinical and functional staging criteria wherein the inter-incisal mouth opening is more than 20 mm in stage I; in stage II, the inter-incisal mouth opening is 10–20 mm; and in stage III, the inter-incisal mouth opening is <10 mm.<sup>[5]</sup> The patients were examined while sitting on the dental chair under artificial light. Mouth opening was measured and the palpable fibrous bands were noticed in cases of OSMF. The diagnosed cases of OSMF were categorized into mild, moderate and severe cases based on the mouth opening and palpable fibrous bands location. The observations were tabulated and analysed using Chi square/Fisher exact test through software **R version 3.6.3 (2020-02-29)**. All the p values less than 0.05 were considered to be statistically significant.

#### **RESULTS**

A total of 152 cases of OSMF were included in the study out of which 129 were males and 23 were females. (Figure 1) The 69.1% of the patients were in the age range of 21-40, 24.3% in 41-60 and 5.3% in <20 age groups respectively. (Figure 2) The mean age of the study participant was 33.16±0.90. 81.6% worked as a labourer among the study participants. 69.1% of the participants used the smokeless form of tobacco in the form of Zarda or Khaini along with guthka/supari while

30.9% of the participants used the smoke form of tobacco in the form of bidi or cigarette. The frequency of tobacco consumption per day >15 times in 37.1%, 5-10 times in 32.2 %, 10-15 times in 21.1% and <5 times in 9.2% of the participants respectively. The duration of tobacco consumption >15 years in 30.9%, 6-10 years or 11-15 years in 26.3 %, and <5 years in 16.4% of the participants respectively. Fifty one patients had mild or Stage I, 79 had moderate or stage II and 22 had severe or stage III OSMF. 53.9% of the participants had mouth opening of 10-20 mm, 9.9% had <10 mm and 36.2% had >20 mm respectively. Fibrous bands and burning sensation were present in 100% the cases of the OSMF. Stage III clinical staging i.e. fibrous bands present in the faucial, buccal and labial surfaces were found in 65.1% of the cases of OSMF followed by 31.6% in the faucial and buccal surfaces. (Table 1)

The most common age group affected with the OSMF was 21-40 years followed by 40-60 years and the males were the majority affected. There was no significant deviation was observed in the distribution of the participants according to age and gender based on the OSMF grading. (p=0.228; p=0.091) (Table 2 & 3)

The duration of the tobacco/supari/guthka consumption was found to be associated with the severity grades of the OSMF. (p=0.042) (Table 4) The frequency of the tobacco/supari/guthka consumption per day was significantly associated with the severity grades of the OSMF. (p=0.001) (Table 5) Majority of the OSMF cases had consumed guthka/supari with tobacco product however only 20 cases of OSMF had consumed guthka/supari without tobacco. The consumption of guthka/supari with tobacco was found to be associated with the severity of the OSMF. (p=0.025) (Table 6)

Mouth opening was decreased as the severity of the OSMF increases. The decrease in the mouth opening was found to be significantly correlated with the severity of OSMF. (p=0.00) (Table 7)

#### **DISCUSSION**

In the present study, of the 152 participants, we observed that 129 were males and 23 were females. Male predominance was observed, which was in accordance with the study conducted by Reddy *et al* and Chatuvedi *et al.*<sup>[6,7]</sup> Sinor *et al* also reported male predominance affected with OSMF with guthka/ supari chewing habits. This could be due to the reasons that usually males have long daytime-based work such as rikshaw drivers, day laborers and easy availability of the guthka/supari/tobacco products in the market. High physical activity among the day laborers are more likely prompt these subjects to tobacco-related bad chewing habits.<sup>[8,9]</sup> The most common age group affected with OSMF in the present study was 21-40 years which was in accordance with the study conducted by *Pandya S et al* where they found increased severity in the younger age group.<sup>[10]</sup>

The consumption of gutkha/supari and other areca nut products are the main etiological factor of the OSMF. Tobacco and other products like pan masala, mawa also play a role in the etiology of this condition. In the present study, gutkha/supari and other areca nut product users, such as addition of tobacco showed a significant increase in the occurrence and severity of the OSMF cases. The role of chewing tobacco along with gutkha/supari was found to be significant in this study. The studies have shown that tobacco chewing had shown to cause oral leukoplakia and carcinoma in cases with longer duration. Long-term follow-up is required to ascertain whether malignant change occurs more frequently in cases of gutkha/supari/betel nut with tobacco compared with those who chew it without tobacco.<sup>[11]</sup> A study by *Mathew et al* reported that subjects chewing betel quid with tobacco were highest followed by gutkha chewers and betel quid with areca nut.<sup>[12]</sup>

In this study, as the duration of consuming areca nut products like gutkha/supari with or without tobacco exceeded more than 5 years, the severity of the OSMF also increased. Stage II OSMF cases were observed in the majority followed by stage I and stage III respectively. As the frequency of habit of consuming areca nut products like gutkha/supari with or without tobacco increased for more than 5-10 times per day, the severity of OSMF also increased. The duration and frequency of consuming gutkha/supari with tobacco products had significant correlation with the severity grades of the OSMF in the form of clinical and functional grading. Thus, if the parameters like duration and frequency of the bad chewing habits increases the severity outcome of the OSMF increases. These results are in accordance with the study done by (Ray G et al, 2019) which found the same correlation with the clinical severity of the OSMF.<sup>[13]</sup>

Limited mouth opening or decreased ability to open the mouth completely and presence of fibrous bands/blanching was one of the most common clinical/functional sign of the OSMF in 93.4 % and 100 % of the cases respectively. The limited mouth opening was found to be consistent with a study conducted by *Marathe et al.*<sup>[14]</sup> Another study by *Kiran Kumar et al.* also revealed that as the severity of the OSMF increases the mouth opening decreases.<sup>[15]</sup> This could be due to the fact that the most of the patients were reported only after the onset of restricted mouth opening and tongue movements.

The presence of fibrous bands on the buccal mucosa was present in all the cases. The similar pattern was observed by *Raina et al* in their study.<sup>[16]</sup> It was also observed that more than half of the patients (52 %) had stage II OSMF followed by stage I OSMF (33.5%). In a study conducted by *Phatak et al* they have found a similar distribution.<sup>[1]</sup> The alkaloids present in betel nut, arecaine and arecoline are responsible for the differentiation of fibroblasts into phenotypes which produces collagen.

Arecoline gets converted in to arecaine which is the active metabolite. Betel nut also contains tannin which has ability to stabilize collagen by cross-linking it by forming a more stable collagen structure hence reduced degradation of collagen.

In the present study buccal mucosa, retromolar area, and soft palate was predominantly affected, which was similar with a previous study by *Das M et al*, but in a study by *Bhonsle RB et al* labial mucosa was found to be significantly affected, which could be due to regional variation with respect to various chewing habits practiced in different parts of India.<sup>[17,18]</sup>

In this study, the parameters in the form of duration and frequency had a significant correlation with the severity of the disease in the form of clinical and functional grading. This is in accordance with the literature, which explains that high alkaloid content of arecoline and tobacco ingredients, such as nitrosamine, are absorbed more in the patients who are chronic habitual of these products.

**Table 1: Socio-demographic Characteristics and Clinical parameters of the study participants included in the study.**

Background Characteristics	Frequency N=152	Percent
<b>Age Group</b>		
<20 year	8	5.3
21-40 years	105	69.1
41-60 years	37	24.3
>60 years	2	1.3
<b>Sex</b>		
Male	129	84.9
Female	23	15.1
<b>Occupation</b>		
Labourer	124	81.6
Others	28	18.4
<b>Type of Tobacco consumption</b>		
Smokeless (guthka, supari, zarda, khaini)	105	69.1
Smoke (bidi, cigarette)	47	30.9
<b>Duration</b>		
<5 year	25	16.4
6-10 years	40	26.3
11-15 years	40	26.3
>15 years	47	30.9
<b>Frequency per day</b>		
<5times	14	9.2
5-10 times	49	32.2
10-15 times	32	21.1
>15times	57	37.5
<b>Mouth Opening</b>		
<10mm	15	9.9
10-20mm	82	53.9
>20mm	55	36.2
<b>Location of fibrous bands</b>		
Faucials	5	3.3
Faucials, Buccal	48	31.6
Faucial, Buccal and labial	99	65.1
<b>Burning sensation</b>		
Present	152	100
Absent	0	0

**Table 2: Age wise association with the OSMF severity of the study participants included in the study.**

Age Group	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	p value
	n=51	n =79	n=22	N=152		
<20	6 (11.8)	2 (2.5)	0(0.0)	8 (5.3)	9.35	0.228
21-40	31 (60.8)	57 (72.2)	17 (77.3)	105 (69.1)		
41-60	14 (27.5)	18 (22.8)	5 (22.7)	37 (24.3)		
>60	0(0.0)	2 (2.5)	0 (0.0)	2 (1.3)		

**Table 3: Gender wise association with the OSMF severity of the study participants included in the study.**

Sex	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	p value
	n=51	n =79	n=22	N=152		
Male	45 (88.2)	69 (87.3)	15(68.2)	129 (84.9)	5.59	0.091
Female	6 (11.8)	10 (12.7)	7 (31.8)	23 (15.1)		

**Table 4: Association of the duration of chewing habits with the OSMF severity of the study participants included in the study.**

Duration (years)	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	p value
	n=51	n =79	n=22	N=152		
<5 year	8 (15.7)	11 (13.9)	6 (27.3)	25 (16.4)	9.98	0.042*
6-10 year	15 (29.4)	25 (31.6)	0 (0.0)	40 (26.3)		
11-15 year	13 (25.5)	19 (24.1)	8 (36.4)	40 (26.3)		
>15 year	15 (29.4)	24 (30.4)	8 (36.4)	47 (30.9)		

**Table 5: Association of the frequency of chewing habits with the OSMF severity of the study participants included in the study.**

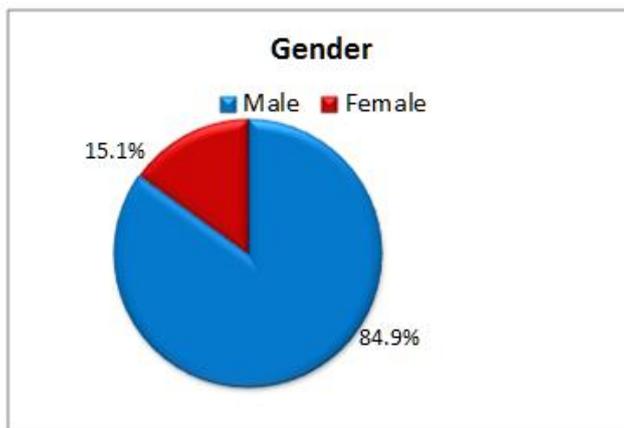
Frequency of Tabcoo consumption per day	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	p value
	n=51	n =79	n=22	N=152		
<5	6 (11.8)	8 (10.1)	0 (0.0)	14 (9.2)	22.092	0.001*
5-10	7(13.7)	32 (40.5)	10 (45.5)	49 (32.2)		
11-15	8 (15.7)	17 (21.5)	7 (31.8)	32 (21.1)		
>15	30 (58.8)	22 (27.8)	5 (22.7)	57 (37.5)		

**Table 6: Association between the types of tobacco products consumption with the OSMF severity of the study participants included in the study.**

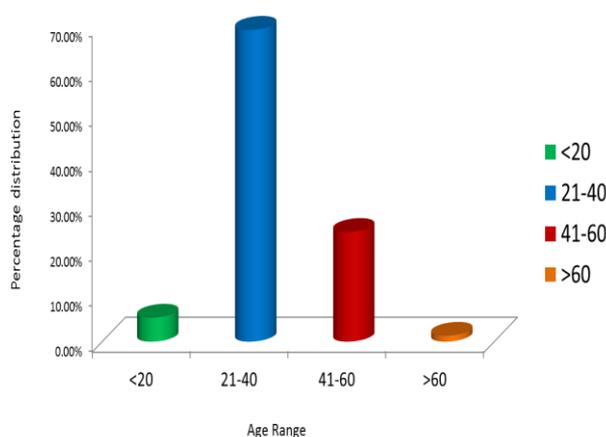
Type of tabcoo consumption	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	P value
	n=51	n =79	n=22	N=152		
Paan/supari without tabcoo	2 (3.9)	13 (16.5)	5 (22.7)	20 (13.2)	6.32	0.025*
Paan + gutkha + tabcoo	49 (96.1)	66 (83.5)	17 (77.3)	132 (86.8)		

**Table 7: Association between the mouth opening with the OSMF severity of the study participants included in the study.**

Mouth opening	Stage I n(%)	Stage II n(%)	Stage III n(%)	Total N(%)	Chi sq.	P value
	n=51	n =79	n=22	N=152		
<15	0(0.0)	0(0.0)	15 (68.2)	15 (9.9)	212.317	0.000*
16-35	2 (3.9)	73 (92.4)	7 (31.8)	82 (53.9)		
>35	49 (96.1)	6 (7.6)	0(0.0)	55 (36.2)		



**Figure 1: Gender wise percentage distribution of the study participants included in the study.**



**Figure 2: Age wise percentage distribution of the study participants included in the study.**

## CONCLUSION

As we all know betel nut containing products like guthka/supari and tobacco chewing is common amongst the labourer rural population. This survey showed that more than half of the total cases of OSMF were in the younger age group. The studies with large sample size should be planned to find more risk factors associated with OSMF. The susceptible populations should be aware of the high risk of malignant transformation of long standing OSMF's cases and poor prognosis leading to death or disability in majority of the cases. Based on the study results the authors recommended that community based education programs on oral health awareness and ill effects of guthka/supari/tobacco be developed to emphasize the adolescence at younger age. A primordial mode of prevention like changing of life style should be adopted. There are studies available in the literature related to the treatment of moderate or severe cases of OSMF which can be used as a motivational tool to aware the general population.

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## Conflicts of interest

The authors have no conflicts of interest.

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