

ORAL SUBMUCOUS FIBROSIS – A CLINICOPATHOLOGICAL CORRELATION

Running title: *Clinicopathological correlation of OSMF*

ABSTRACT:

Objective: Oral Submucous Fibrosis (OSMF) is a potentially malignant disorder of the oral mucosa and collagen metabolic disorder caused by betel nut use. Diagnosis of this condition can be made clinically, but ascertaining its malignant transformation histopathology is mandatory. So, the correlation between the clinical and histopathology was conducted.

Materials and Methods: The correlation study was conducted on 20 OSMF patients. Clinical diagnosis with histopathological confirmation was based on the standard approach. Study structure included gender, duration, frequency, and quid placement correlated with clinical and histopathological staging.

Results: The current study has included most of the subjects being males and was below 25 years. Habit duration, frequency, and quid placement were correlated with clinical and histopathological staging and were directly related. Six subjects of (30%) Group 1 cases associated with 3 (42.9%) in the histologically early stage of the disease. Further, 14 (70%) cases in Group 2 clinical staging correlated with 8 (88.9%) cases in moderately advanced histological staging.

Conclusion: The clinical and histopathological correlation was not obtained in the present study. The negative p-value could be because of certain factors like biopsy site selection and decreased study subjects. However, factors like frequency and quid keeping had a positive histopathological correlation.

KEYWORDS:

Oral submucous fibrosis (OSMF), Trismus, Areca, Demography

INTRODUCTION:

Oral submucous fibrosis (OSMF) is a chronic, potentially malignant disorder of the oral mucosa, first described by Schwartz in 1952.

Worldwide estimates of OSMF show confinement to Indians and Southeast Asians, with an overall prevalence rate of about 0.2% to 0.5 % in India and gender prevalence of 0.2-2.3% in males and 1.2-4.57% in females. In addition, the age range of patients with OSMF ranges between 20 and 40 years of age (Reddy V et al.,2011).

It is accepted that the areca nut is the major etiology for the causation of OSMF. The disease occurs mainly in Asia, but cases have been reported worldwide in Kenya, China, the UK, Saudi Arabia, and the other part of the world where Asians are migrating(Ahmad MS et al.,2006).It is considered to be the fourth most abused drug after nicotine, ethanol and caffeine (Sahu RK et al.,2021).

It has been estimated that worldwide, 600 million people chew areca nuts. A causal association between tobacco and betel quid (BQ) chewing habits and oral mucosal diseases such as Leukoplakia, Oral Submucous Fibrosis, and Oral Cancer has been established, and heavy users have significantly increased mortality rate (Nair U, Bartsch H, Nair J 2004).

The dental researchers reported OSMF as simple case reports, population-based studies, or hospital-based case-control studies. In addition, animal experiments and in vitro human fibroblast culture studies were carried out to analyze the etiopathogenesis of OSMF.

Histopathological studies with light microscopy and scanning electron microscopy were also performed. Even then, a dearth of research correlates the clinical features to the various histopathological changes of OSMF (Kiran Kumar K.,2004 & Ray JG et al., 2013). So this study is a novel attempt to correlate the habits, clinical staging, and histopathological staging.

MATERIALS AND METHODS:

The present epidemiological study comprised 20 OSMF patients. The study was approved by the institutional review board. The diagnosis was made based on history and clinical features and confirmed histopathologically.(Figure 1).

Criteria for patient selection:

Inclusion Criteria:

1. Only those patients, who gave signed informed consent on an institutionally approved document, participated in the study.
2. Clinical and histopathological diagnosed cases as per the criteria laid down by Pindborg JJ and Sirsat SM

Exclusion Criteria:

1. Any significant medical history
2. Other associated oral disorders

Method of collecting data:

Clinical Examination and Study parameters

Study subjects' habit history, like areca nut usage (raw or processed), pan chewing (with or without tobacco), and gutkha chewing, was recorded. Additional details like age, gender, duration of chewing, frequency of chewing per day, and time taken to chew are also noted. History of other adverse habits like alcoholism or smoking was also obtained.

3. The procedures were explained, and consent was taken. Local anesthesia was given, and an incisional biopsy was performed from the buccal mucosa where fibrous bands were palpable.

The staging was made as per the criteria laid down by Pindborg JJ and Sirsat SM (1966) (SM Mishra G, Ranganathan K.,2006).

The following distribution was seen in varying stages.

1. Very early stage
2. Early stage
3. Moderately advanced stage
4. Advanced stage

Based on the mouth opening of the patients, clinically, the patients were categorized into two groups

1. Group 1 cases in whom mouth opening is above 30 mm
2. Group 2 cases in whom mouth opening is below 30 mm

The p-value less than 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION:

The age range of patients with OSMF ranges between 20 and 40 years of age. A study conducted in 860 patients showed that peak incidence was seen in 30-40 years of age (Rahul S et al.,2019) Our study depicted that 11 out of 20 were above 25 years, and 9 were below. Our study patients had OSMF solely because of gutka chewing in males and areca chewing habits in females. Similar results have noted a study in which the male to female ratio was 23.6:1(Ali FM et al.,2013).

Arecoline can stimulate fibroblast to increase collagen production by 150% (Canniff JP, Harvey W.,1981). The findings of Babu et al. in OSMF cases depicted that patients reported more addiction to gutkha than other addictive habits. It was also demonstrated that in gutkha induced OSMF, the disease occurred much earlier compared to areca nut induced OSMF. Similar research activity was conducted by Shah and Sharma, who observed that gutkha chewing produced OSMF in advance compared to other products (Ahmad MS et al.,2006). This could be demonstrated by our male to female ratio of 17:3 and their habits as female patients consumed areca nut with betel leaf with their age being slightly more. Further, another cause for delay in the occurrence of OSMF could be due to the protective effect of betel leaf in the oral mucosa because it is known to be rich in beta-carotene and hydroxychavicol quench free radicals (Ahmad MS et al.,2006). The number of patients in the Group 1 cases was 6 (30%), and Group 2 cases were 14 (70%). Duration, frequency, and quid placement were correlated with the clinical staging. (Table 1, 2, 3) Out of 20 cases, 30% were in the Group 1 stage of the disease in which 83.3% cases had a habit duration of fewer than 2 years, and the remaining 70% cases in a Group 2 group had 64.3% patients with more than 2 years of habit duration, 57.1% of subjects had frequency of chewing more than 5 times daily and 64.3% cases used to place the quid for more than 5 minutes. As the habit duration, frequency, and quid placement increase, the mouth opening decreases.

The study subjects were divided into four categories depending upon the histological staging. The staging was done as per the criteria laid down by Pindborg JJ and Sirsat SM (1966) (SM Mishra G, Ranganathan K.,2006). The distribution of subjects among these stages was two subjects in the very early stage, 7 subjects in the early stage, 9 subjects in the moderately advanced stage, and 2 subjects in the advanced stage.

Duration, frequency, and quid placement were correlated with the histopathological staging. (Table 4, 5, 6) The relationship is almost directly proportional as habit duration and quid placement increase, histopathological staging progresses. Out of 45% of cases who chew gutka for more than 5 minutes included 77.8% of cases in the moderately advanced stage. Further, 55% of the subjects who placed the quid more than 5 minutes in the oral cavity had 77.8% of cases in the moderately advanced stage. A similar finding was presented as increase in frequency and duration also increases severity of OSMF (Jha VK.,2019, Rahul S et al.,2019)

Correlation of clinical staging with histopathological staging showed that out of 6 (30%) Group 1 cases, 3 (42.9%) were in the histologically early stage of the disease. Further, 14 (70%) cases in Group 2 clinical staging correlated with 8 (88.9%) cases in moderately advanced histological staging. This correlation shows that histopathological staging gradually increases towards severity as trismus (clinical staging) progresses. (Table 7) Kumar et al. suggested a direct relationship between the frequency of chewing and the occurrence of OSMF in the patients who used paan masala. Literature reviews suggested that duration and frequency of arecanut usage increase the risk of oral cancer as a dose-response relationship. Shah et al. accounted that the duration of the chewing habit did not significantly correlate with the occurrence of OSMF, which was related to histopathological staging also (Pandya S et al., 2009). Maher et al. stated that the daily frequency of habit is more susceptible to risk than the duration of the habit (Kiran Kumar K.,2004). Few patients with Group 2 OSMF may have a shorter habit duration history than other subjects this could be attributed to genetic polymorphism in collagen due to habit (R S, Pai A, Yaji A.,2019). The study was conducted in 2009, in which clinical and histopathological staging was assessed. Stage 1 of that study (subjects with more than 30 mm mouth opening) correlated with our Group 1, and stage 2 (subjects with 20 to 30 mm mouth opening) correlated with our Group 2

. The histopathological staging was also similar to our study. Patients who had clinical staging 1, 3 patients, had grade 1, 5 patients had grade 2. In the stage 2 group, 11 had grade 1, and 17 had grade 2, and 23 had grade 3. (Pandya S et al., 2009)

The results dictate a correlation between these confounding factors in the causation of OSMF. So, counseling and complete elimination of the habit can eradicate this disease. Further, long-term studies with an increased number of cases are required to prove the malignant transformation rate and the pathway involved.

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FIGURES

Figure 1: Clinical finding with characteristic blanching seen over the buccal mucosa



TABLES

Table 1: Habit duration and clinical staging:

Habits duration (years)	Clinical staging				Total	
	Group 1		Group 2			
	N	%	N	%	N	%
1 - 2 yrs	5	83.3	5	35.7	10	50.0
> 2 yrs	1	16.7	9	64.3	10	50.0
Total	6	100.0	14	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.141

Table 2: Frequency and clinical staging:

Frequency (times/day)	Clinical staging				Total	
	Group 1		Group 2			
	N	%	N	%	N	%
1 - 5	5	83.3	6	42.9	11	55.0
> 5	1	16.7	8	57.1	9	45.0
Total	6	100.0	14	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.157

Table 3: Quid keeping and clinical staging:

Quid keeping (minutes)	Clinical staging				Total	
	Group 1		Group 2			
	N	%	N	%	N	%
1 - 5 mins	4	66.7	5	35.7	9	45.0
> 5 mins	2	33.3	9	64.3	11	55.0
Total	6	100.0	14	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.336

Table 4: Habit duration and histopathological staging:

Habits duration (years)	Histopathological staging								Total	
	Very early		Early		Moderately advanced		Advanced			
	N	%	N	%	N	%	N	%	N	%
1 - 2 yrs	0	0.0	3	42.9	5	55.6	2	100.0	10	50.0

> 2 yrs	2	100.0	4	57.1	4	44.4	0	0.0	10	50.0
Total	2	100.0	7	100.0	9	100.0	2	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.300

Table 5: Frequency and histopathological staging:

Frequency (times/day)	Histopathological staging								Total	
	Very early		Early		Moderately advanced		Advanced			
	N	%	N	%	N	%	N	%	N	%
1 – 5	2	100.0	5	71.4	2	22.2	2	100.0	11	55.0
> 5	0	0.0	2	28.6	7	77.8	0	0.0	9	45.0
Total	2	100.0	7	100.0	9	100.0	2	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.047

Table 6: Quid keeping and histopathological staging:

Quid keeping (minutes)	Histopathological staging								Total	
	Very early		Early		Moderately advanced		Advanced			
	N	%	N	%	N	%	N	%	N	%
1 - 5 mins	0	0.0	6	85.7	2	22.2	1	50.0	9	45.0
> 5 mins	2	100.0	1	14.3	7	77.8	1	50.0	11	55.0
Total	2	100.0	7	100.0	9	100.0	2	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.026

Table 7: Clinical and histopathological staging:

Clinical staging	Histopathological staging	Total
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	Very early		Early		Moderately advanced		Advanced			
	N	%	N	%	N	%	N	%	N	%
Group 1	0	0.0	3	42.9	1	11.1	2	100.0	6	30.0
Group 2	2	100.0	4	57.1	8	88.9	0	0.0	14	70.0
Total	2	100.0	7	100.0	9	100.0	2	100.0	20	100.0

Chi-Square Test	P-Value
Fisher's Exact Test	0.066

