RESEARCH ARTICLE

Correlation of Habits and Clinical Findings with Histopathological Diagnosis in Oral Submucosal Fibrosis Patients

Syeda Arshiya Ara[1]*, Vini Arora[1], Syed Zakaullah[2], Syed Ahmed Raheel[1], Prakash Rampure[1], Sajna Ashraf[1]

Abstract

Background: Oral submucosal fibrosis (OSMF) is one of the most prevalent premalignant conditions in India which is easy to diagnose but difficult to manage. At present it is considered as irreversible and incurable. It has also been referred to as an epidemic in India. Aims and Objectives: To correlate the frequency and duration of habits with clinical staging, functional staging and histopathological grading and to correlate the clinical and functional staging with histopathological grading. Materials and Methods: The study included a total of 90 subjects, 80 with OSMF in the experimental group and 10 patients in the control group. Patient personal history was recorded with chewing habits, including frequency and duration of chewing. The site of keeping the quid, time duration and whether he/she swallows it or spits it were also noted. Clinical staging was done on the presence of palpable fibrous bands. Functional staging was accomplished by measuring mouth opening. Incisional biopsy was done for all the patients for histopathological examination. Histopathological grading was according to Pindborg and Sirsat. Results: The experimental group comprised 71 males and 9 females, the majority of which were in the age group of 21-30 years. Correlation of habits with clinical staging, functional staging and histopathological grading were significant ($p<0.05$). Clinical and functional staging did not correlate with histopathological grading, but the correlation of clinical and functional staging was highly significant ($p<0.01$). Conclusions: The widespread habit of chewing gutkha is a major risk factor for OSMF, especially in the younger age group. In this study, it was found that with increase in the duration and frequency of the habit the severity of the disease increased.

Keywords: OSMF - habits - frequency - duration - clinical staging - functional staging - histopathological grading

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Introduction

Oral submucosal fibrosis (OSMF) is an insidious, chronic disease affecting any part of oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with a juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy, leading to stiffness of the oral mucosa and causing trismus and inability to eat (Pindborg and Sirsat, 1966). It is one of the most prevalent premalignant condition in India which is easy to diagnose but difficult to manage. At present it is considered as irreversible and incurable. It has also been referred to as an epidemic in India (Gupta et al., 1998).

The chewing of betel nut has been recognized as one of the most important etiological factor for the causation of OSMF (Ravikiran Ongole and Praveen, 2010). There is dose dependence between areca quid chewing habit and the development of this oral mucosal disorder. Areca nuts contain alkaloids, of which arecoline seems to be a primary etiologic factor (Greenberg and Glick, 2003).

Although there are regional variations in the type of areca nut products used in India, the betel quid (BQ) was the most popular and prevalent habit in ancient Indian culture. But in 1980, both areca quid products such as Pan Masala (Areca quid) and Gutkha (AQ+tobacco) were introduced in Indian market as commercial preparations. Since then there has been an increase in the use Pan Masala (Areca quid) and Gutkha (AQ+T) in the younger age groups, which had lead to increased incidence of OSF (Hazarey et al., 2007).

In spite of the fact that the habit of areca nut chewing with or without betel quid is rampant, the correlations between the extent and duration of addictions with clinical, functional and histopathological grading have been reported barely. Thus this study was designed to investigate these issues with the following aims: i) To correlate the frequency and duration of habits with clinical and functional staging; ii) To correlate the frequency and duration of habits with histopathological grading; iii) To correlate the clinical and functional staging with histopathological grading. The objectives were: i) help to assess the prognosis of the disease; ii) In future, it may

*[1]Department of Oral Medicine and Radiology, [2]Department of Oral and Maxillofacial Surgery, Al-Badar Rural Dental College and Hospital, Gulbarga, India *For correspondence: drarshiyazaka@gmail.com*

aid in planning the treatment of OSMF.

Materials and Methods

The study was conducted in the Department of Oral Medicine and Radiology and Oral Pathology and Microbiology of Al-Badar Rural Dental College and Hospital, Gulbarga.

The subjects were from the patients attending the outpatient Department of Oral Medicine and Radiology. The study included a total of 90 subjects, 80 patients with OSMF in the experimental group and, 10 patients in control group.

The study was conducted by strictly adhering to the ethical protocols and written consent was obtained from all the patients to include them in the study.

Inclusion criteria

Patients who have the deleterious habit of using areca nut and areca nut containing products, tobacco mixed with areca nut in different forms, alcohol, are satisfying the clinical criteria as given in Bailoor and Nagesh (2005) and who will be histopathologically confirmed as having OSMF.

Controls were selected after confirming that they are not having any deleterious habits as mentioned above and do not show any signs and symptoms of OSMF.

Exclusion criteria

Oro mucosal disorders with clinical features same as OSMF. Any systemic disorders which can cause similar symptoms. Patients who are under treatment for OSMF. Clinically diagnosed cases of OSMF not ready for incisional biopsy. Clinically diagnosed cases of OSMF without any habits. Patients with medically compromised conditions.

The clinical examination was carried out following the method described by Kerr et al. (1983).

The patient's personal history was recorded with chewing habits, frequency and duration of chewing. The site of keeping the quid, time duration and whether he/she swallows it or spits it were also noted. Symptoms like burning sensation, restricted mouth opening, difficulty in swallowing, speech and hearing and excessive and reduced salivation was noted. Extra orally the patients were examined for flattening of cheeks. Lymph nodes were examined for their location, size in cms, tenderness and for their consistency. Intra orally signs like blanching and marbled appearance of the oral mucosa, hockey stick appearance of uvula, erosions and ulcerations, interincisal mouth opening, tongue protrusion and cheek flexibility were noted. The parameters like mouth opening (interincisal distance), cheek flexibility and tongue protrusion were recorded as mentioned by Ranganathan et al. (2001).

Clinical and functional staging of OSMF was done according to Haider et al. (2000). Clinical staging was done on the presence of palpable fibrous bands and is as follows: STAGE I- faucial bands only, STAGE II- faucial and buccal bands only, STAGE III- faucial, buccal and labial bands.

Functional staging was done by measuring the mouth opening with scale and divider from the mesioincisal angle of upper central incisor to the lower central incisor and is as follows: STAGE A- mouth opening greater than or equal to 20 mm, STAGE B- mouth opening 11-19 mm, STAGE C- mouth opening less than or equal to 10 mm.

Routine haematological examination was done for all the patients in the experimental and control group. This was followed by incisional biopsy for histopathological examination for all the patients. The histopathological grading of OSMF was done according to Pindborg et al. (1966).

Chi square test was utilized to determine association between variables. Correlation coefficient was used to find the relationship between the relative variables. For all tests, a 'p' value of 0.05 or less will be utilized for statistical significance.

Results

The 80 patients were in the age range of 15-65 years with a mean age of 29.25±11.49 years. The maximum subjects 38 (47.5%) were in the age group of 21-30 years.

Out of 80 subjects 9 were females and 71 were males. Thus it shows a male predominance. Of 80 subjects 39 (48.8%) chewed only gutkha, 14 (17.5%) only arecanut, 5 (6.2%) only tobacco, 1 (1.3%) betel quid, 6 (7.5%) gutkha and tobacco, 2 (2.5%) gutkha and bidi, 4 (5%) gutkha and alcohol, 3 (3.7%) gutkha and cigarette, 2 (2.5%) gutkha, bidi and alcohol, 2 (2.5%) gutkha cigarette and alcohol, 2 (2.5%) gutkha, tobacco, cigarette and alcohol. It was noted that the majority of subjects in our study chewed only gutkha (48.8%).

The average mouth opening in the experimental group was 24.48 mm and in the control group was 44.25 mm. The average tongue protrusion in the experimental group was 21.60 mm and in the control group was 23.89 mm. The average cheek flexibility in the experimental group was 7.18 mm and in the control group was 9.17 mm.

Out of 80 OSMF patients, 17 (21.2%) had faucial bands, 47 (58.8%) had buccal and faucial bands, 16 (20%) had buccal, faucial and labial bands and they were staged into stage I, stage II, and stage III respectively.

Functional staging was done according to the mouth opening. The experimental subjects were divided into 3 groups. There were 60 (75%) patients in Stage A, 15 (18.8%) in Stage B and 5 (6.2%) in Stage C.

The experimental subjects were divided into 4 stages, depending upon the histological features. *i*) Very early stage: 22 (27.5%) patients; *ii)* Early stage: 33 (41.3%) patients; *iii*) Moderately advanced stage: 18 (22.5%) patients and; *iv*)Advanced stage: 7 (8.7%) patients.

Comparison of habits with clinical staging

On correlating the clinical findings with the patient's addiction habits, 17 (21.2%) patients were in clinical stage I, of which 9 (52.8%) patients chewed only gutkha, 2 (11.8%) consumed areca nut, 1 (5.9%) consumed tobacco, 2 (11.8%) consumed gutkha and tobacco, 1 (5.9%) consumed both gutkha and bidi, 1 (5.9%) consumed gutkha and alcohol and 1 (5.9%) consumed gutkha and

cigarette.

On correlating the clinical findings with frequency and duration of addiction in OSMF stage I, maximum patients were addicted for at least 3-4 years and used the products 2-3 times per day. Out of 47 (58.8%) patients in clinical stage II, 20 (42.6%) chewed only gutkha, 12 (25.5%) consumed only areca nut, 2 (4.3%) consumed only tobacco, 1 (2.1%) consumed betel nut, 4 (8.5%) consumed both gutkha and tobacco, 1 (2.1%) consumed gutkha and bidi, 3 (6.4%) consumed gutkha and alcohol, 1 (2.1%) consumed gutkha and cigarette, 1 (2.1%) consumed gutkha, cigarette and alcohol and 2 (4.3%) consumed gutkha, cigarette, tobacco and alcohol.

On correlating the clinical findings with frequency and duration of addiction in OSMF stage II, maximum patients were addicted for at least 8-10 years and used the products 5-10 times per day. Out of 16 (20%) patients in clinical stage III, 10 (62.4%) chewed only gutkha, 2 (12.5%) consumed only tobacco, 1 (6.3%) consumed both gutkha and bidi, 2 (12.5%) consumed gutkha and alcohol and 1 (6.3%) consumed gutkha, bidi and alcohol.

On correlating the clinical findings with frequency and duration of addiction in OSMF stage III, maximum patients were addicted for at least 15-20 years and used the products 10-15 times per day.

The clinical staging was correlated with frequency and duration of habits with the help of correlation coefficient and p value. The correlation coefficient(r) was 0.683 and $p<0.05$ for clinical staging and frequency of habits which is statistically significant and signifies that as the frequency of habits increases the clinical staging increases. The correlation coefficient(r) was 0.81 and $p<0.01$ for clinical staging and duration of habits which is statistically significant and signifies that as the duration of habits increases the clinical staging increases.

Comparison of habits with functional staging

On correlating the functional staging with the patient's addiction habits, 60 (75%) had OSMF stage A, of which 21 (35%) were habituated to only gutkha, 13 (21.7%) consumed areca nut, 5 (8.3%) consumed only tobacco, 1 (1.7%) consumed betel nut, 4 (6.7%) consumed gutkha and tobacco, 3 (5%) patients were both gutkha chewer and beedi smoker, 3 (5%) patients consumed both gutkha and alcohol, 2 (3.3%) patients were both gutkha chewer and cigarette smoker, 2 (3.3%) consumed gutkha, cigarette and alcohol, 2 (3.3%) patient consumed gutkha, beedi, alcohol and 4 (6.7%) patients were addicted to gutkha, cigarette, tobacco and alcohol.

On correlating the functional staging with frequency and duration of addiction in OSMF stage A, maximum patients were addicted for at least 8-10 years and used the products 6-8 times per day.

In OSMF stage B, out of 15 (18.8%) patients, 8(53.3%) were habituated to only gutkha, 1 (6.7%) consumed only areca nut, 2 (13.5%) patients were gutkha and tobacco users, 1 (6.7%) patient was both gutkha chewer and beedi smoker, 1 (6.7%) patient consumed gutkha and alcohol, 1 (6.7%) patient consumed gutkha and cigarette and 1 (6.7%) patient was addicted to gutkha, bidi and alcohol. In this group, maximum patients were addicted for 12-15 years and daily consumed the substances 10-12 times per day.

In OSMF stage C, out of 5 (6.2%) patients, 2 (40%) were habituated to only gutkha, 1(20%) was habituated to only tobacco, 1 (20%) patient was both gutkha chewer and beedi smoker and 1 (20%) patient consumed both gutkha and alcohol. Majority of the patients of this group consumed the products for 20 years with a frequency of 15 times per day.

The functional staging was correlated with frequency and duration of habits with the help of correlation coefficient and p value.

The correlation coefficient(r) was 0.693 and $p<0.05$ for functional staging and frequency of habits which is statistically significant and signifies that as the frequency of habits increases the functional staging increases. The correlation coefficient(r) was 0.83 and $p<0.05$ for functional staging and duration of habits which is statistically significant and signifies that as the duration of habits increases the functional staging increases.

Comparison of habits with histopathological grading

On correlating the histopathological findings with the patient's addiction habits, 22 (27.5%) had OSMF grade I, of which 7 (31.9%) were habituated to only gutkha, 5 (22.9%) consumed areca nut, 3 (13.7%) consumed tobacco, 1 (4.5%) consumed betel nut, 1 (4.5%) consumed gutkha and tobacco, 1 (4.5%) patient was both gutkha chewer and beedi smoker, 1 (4.5%) patient consumed both gutkha and alcohol, 1 (4.5%) patient was both gutkha chewer and cigarette smoker, 1 (4.5%) patient consumed gutkha, beedi, alcohol and 1 (4.5%) patient was addicted to gutkha, cigarette, tobacco and alcohol. On correlating the histopathological findings with frequency and duration of addiction in OSMF grade I, maximum patients were addicted for at least 3-5 years and used the products 2-3 times per day.

In OSMF grade II, out of 33 (41.3%) patients, 19 (57.6%) were habituated to only gutkha, 8 (24.3%) were addicted to areca nut, 1 (3%) was habituated to only tobacco, 2 (6%) patients consumed both gutkha and tobacco, 1 (3%) patient was both gutkha chewer and beedi smoker, 1 (3%) patient consumed gutkha, cigarette, alcohol and 1 (3%) patient was addicted to gutkha, cigarette, tobacco and alcohol. In this group, maximum patients were addicted for 5-6 years and daily consumed the substances 6-8 times per day.

In OSMF grade III, out of 18 (22.5%) patients, 9 (50%) were habituated to only gutkha, 1 (5.6%) was addicted to areca nut, 1 (5.6%) was habituated to only tobacco, 1 (5.6%) patient consumed gutkha and tobacco, 1 (5.6%) patient was both gutkha chewer and beedi smoker, 2 (11.1%) patients were used to gutkha and alcohol, 2 (11.1%) consumed gutkha and cigarette and 1 (5.6%) patient was addicted to gutkha, cigarette, tobacco and alcohol. Majority of the patients of this group consumed the products for 20 years with a frequency of 15-17 per day.

In OSMF grade IV, out of 7 (8.7%) patients, 4 were habituated to only gutkha, 2 consumed gutkha and tobacco and 1 consumed gutkha, cigarette and alcohol. The patients

Table 1. Comparison of Functional Staging with Histopathological Grading*

Clinical staging	No. of patients	Histopathological grading			
		I	II	III	IV
I	17 (21.2%)	4	7	4	2
II	47 (58.8%)	13	24	7	3
III	16 (20%)	4	3	7	2

*Chi Square=6.82 and p values>0.05

Table 2. Comparison of Functional Staging with Histopathological Grading*

Clinical staging	No. of patients	Histopathological grading			
		I	II	III	IV
A	60 (75%)	18	26	12	4
B	15 (18.8%)	1	8	3	3
C	5 (6.2%)	2	0	3	0

*Chi Square=4.73 and p values>0.05

Table 3. Comparison of Clinical Staging with Functional Staging*

Staging	Clinical staging	Functional staging
I	17 (21.2%)	60 (75%)
II	47 (58.8%	15 (18.8%)
III	16 (20.0%)	5 (6.2%)

*Chi Square=46.18 and p values<0.001

consumed the products for duration of 20 years with a frequency of 15-20 per day.

The histopathological grading was correlated with frequency and duration of habits with the help of correlation coefficient and p value. The correlation coefficient(r) was 0.74 and p value less than 0.05 for histopathological grading and frequency of habits which is statistically significant and signifies that as the frequency of habits increases the histopathological staging increases. The correlation coefficient(r) was 0.91 and p value less than 0.01 for histopathological grading and duration of habits which signifies that as the duration of habits increases the histopathological grading increases.

On correlating the clinical staging and histopathological grading, the statistical analysis with chi square test was not significant 6.82 with p>0.05 (Table 1). Statistical analysis of functional staging with histopathological grading was not significant with chi square value of 4.73 and p>0.05 (Table 2). On correlating the clinical and functional staging, statistical analysis with chi square test was highly significant (46.18) with p<0.001 (Table 3).

Discussion

In our study, 80 patients were in the age range of 15-65 years with the mean age of 29.25±11.49 years. This is comparable to the mean age of 26.1 years specified by Rao (1962), 32 years reported by Haider et al. (2000) and 26 years as reported by Ceena et al. (2009).

Majority of our cases which were 38 (47.5%) in number were in the age range of 21-30 years. Our study shows that the younger age group is more habituated for chewing arecanut and are susceptible for OSMF. Increase in the chewing habit of the areca nut without any tobacco and the use of various commercial products containing areca nut may explain the decrease in the age of OSMF cases due to various chewing habits.

In our study among 80 OSMF patients, 71 were males and 9 were females, thus showing a male predominance. Similar male predominance was reported by Shiau (1979), Lai (1995), Kumar et al. (2007), Ranganathan (2004), Ceena et al. (2009) and Pandya et al. (2009)

But many other investigations have reported a female predominance, like Rao (1962), Pindborg (1970), Caniff (1986) and Johnson (2000).

This male predominance in our study could be due to the gutkha chewing habit which is mostly practised by younger men in this part of the country.

In general it was found that, of the 80 OSMF subjects, 60 patients chewed either gutkha alone or in combinations. Gutkha is a mixture of arecanut, tobacco, lime, katechu and flavouring compounds which are marketed in small sachets or pouches. The habit-forming process of gutkha chewers is due to tobacco and areca nut, which if consumed for longer duration and frequencies is responsible for causing addiction, leading to OSMF.

It was found that average betel quid (areca nut, tobacco, catechu and lime wrapped in betel leaf) approximately weighing 3.5-4 grams has 70 per cent moisture and dry weight of areca nut and tobacco is only 1.14 grams where as the gutkha sachet weighing 3.5 gram has only 7 per cent moisture and dry weight 3.26 grams (Babu et al., 1996). Since habitual chewers tend to consume more dry weight of areca nut and tobacco when they use gutkha so they probably develop more fibrosis of the oral mucosa, particularly the disorder afflicting quite earlier as well.

Our observations of 60 patients who chewed gutkha is comparable to Sinor et al. (1990). We also noted OSMF in a patient who chewed raw arecanut only which was comparable with Bhonsle (1987), Maher (1994), Van Wyk (1994) and Ranganathan (2004). Hence we presume that arecanut plays an important role in the etiology of OSMF.

We noted that of 80 subjects, 47 had faucial and buccal bands which are comparable to studies of Moos and Madan (1968), Gupta (1978) and Sinor (1990).

In the present study of the 80 subjects, 16 had faucial, buccal and labial bands which are comparable to Gupta (1978), Shiau (1979), Seedat (1988) and Sinor (1990).

The average mouth opening in the experimental group was 24.48 mm and in the control group was 44.25 mm.

The average tongue protrusion in the experimental group was 21.60 mm and in the control group was 23.89 mm.

The average cheek flexibility in the experimental group was 7.18 mm and in the control group was 9.17 mm.

Ranganathan et al. (2001) showed that the mean values of mouth opening, tongue protrusion and cheek flexibility in males were 47.5, 24.9 and 9.7 mm respectively, and in females the mean values were 44.6, 24.8 and 9.0 mm respectively.

Of 80 subjects, 60 had mouth opening ≥20mm, which is comparable to studies of Caniff (1986) and Lai (1995). 15 had mouth opening of 11-19 mm, which is comparable to Seedat (1988). 5 (10%) had mouth opening ≤10 mm which is comparable to Haider et al. (2000).

The correlation of clinical staging with the frequency

and duration of habits was statistically significant. The results of our study are comparable and similar to the study done by Ahmad et al. (2006), Rajendran et al. (2002) and Maher et al. (1994).

Ahmad et al. (2006) found out the relation of severity with socioeconomic status, gutkha and other areca nut products along with its duration, frequency, time of keeping in the mouth and style of chewing. In this study it was found that frequency of addiction, duration of chewing with style of keeping in minutes the gutkha and other products have direct significant relation with the severity of the disorder.

But the studies done by Rajendran et al. (2002) and Maher et al. (1994) reported that frequency of taking areca nut and tobacco quid has a significant relation with the severity of OSMF but duration has no relation even if the patient takes gutkha throughout his life.

The functional staging was correlated with frequency and duration of habits with the help of correlation coefficient and p value which was statistically significant. On contrary, Goel et al. (2010) correlated the habits with mouth opening and histopathological grading and suggested that the daily consumption was more significant than the total duration of the habit and a study done by Modi et al. (2012) showed that significant and direct correlation to the manifestation of OSF was seen with frequency rather than duration of chewing.

The histopathological grading was correlated with frequency and duration of habits with the help of correlation coefficient and p value which was statistically significant. Our study is in concordance with the study done by Pandya et al. (2009) who correlated the addiction habits and histopathological findings found that maximum patients had histopathological grade III OSF and took tobacco products for 8-10 years or more with high frequency (7-10 times per day) followed by histopathological grade II and I. In this study, an increase in histopathological grading was found with severity and duration of addiction habit.

An earlier study from India by Sinor et al. (1990) also reported that both the duration and the frequency of chewing increased the relative risk of developing OSF.

But the studies done by Shah et al. (1998) and Maher et al. (1994) reported that the total duration of the chewing habit was not significantly correlated to OSF. They hypothesized that the exposure to the total burden of various harmful substances in a given period, i.e., daily consumption (frequency) was more significant that the total duration of the habit.

In total contrast to these observations, a study from the UK by Caniff et al. (1986) had earlier observed that there was no demonstrable relationship between the amount of betel nuts chewed and the extent of fibrosis or limitation in mouth opening. Shah et al. (1998) have suggested that smaller sample size (44) in the study by Caniff et al. (1986) could be the reason for this variation.

On correlating clinical staging and histological grading, the statistical analysis with Chi square test was not significant (5.73) with $p>0.05$ which is in concordance with the study done by Ceena et al. (2009) who also found that there is no significant correlation between clinical staging and histopathological grading.

But the study done by Tupkari et al. (2007) in the Marathwada region of Maharashtra found that histopathology was the characteristic of OSMF and was consistent with the clinical grades of the disease.

The correlation of functional staging with histopathological grading was statistically significant. The results of the present study are similar to the studies done by Kiran et al. (2007), Pandya et al. (2009), Goel et al. (2010), Rooban et al. (2005), Tupkari et al. (2007) and Rajendran et al. (1994)

On contrary, Ceena et al. (2009) and Shivakumar et al. (2010) on correlating the severity of disease and degree of mouth opening found statistically significant results. The variations in the result can be due to the dependence on various other factors such as site of involvement, extent of fibrosis, involvement of underlying musculature, duration of the disease and difference in the staging system used.

On correlating clinical and functional staging, the statistical analysis with Chi square test was highly significant (15.38) with $p<0.001$ which is similar to the study done by Haider et al. (2000).

In conclusion, a comparison of clinical, functional and histopathological stages of OSMF was statistically analyzed on 80 OSMF patients. It was found that the comparison of clinical and functional staging with histopathological grading did not provide any valuable information as to the severity of the disease. However, the comparison of clinical and functional staging was more reliable in providing the severity of the disease. It was also observed that the severity of the disease increases with the increase in the duration and frequency of habits. Since the present study was based on a relatively smaller sample size, it would be worthwhile to conduct a similar study with a larger sample size. In future, studies should also compare OSMF cases in different demographic features of ethnicity, geographic localization and socioeconomic status backed with epidemiological and experimental evidences. The uncertainity and flaws in the OSMF management protocol can be dealt with, only if research is focused to characterize the pathogenesis in spite of numerous difficulties encountered.

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