Original Article

Assessment and correlation between functional and histological staging of oral submucous fibrosis: A clinicohistopathologic study

ABSTRACT

Background and Objective: Oral submucous fibrosis (OSMF) is a precancerous condition. It is widespread in the Asian subcontinent, with India bearing most of the burden. It is characterized by mucosal rigidity of varying intensity due to the fibroelastic changes of the juxta epithelial layer, resulting in a progressive inability to open the mouth. Early recognition with accurate staging of the disease and appropriate treatment planning is of utmost importance to prevent the malignant transformation and to improve the quality of life of the patient. In the present study, an attempt is made to clinically evaluate the condition and correlate it with the histopathological findings according to standard criteria.

Materials and Methods: A hospital-based study was conducted on sixty OSMF patients. Detailed history was recorded, and functional staging was given depending on mouth opening. Punch biopsy was performed, and histological stages were given based on standard criteria. The data so received were mathematically evaluated to determine whether any correlation exists between the stages using Chi-square test.

Results: The sixty patients were in the age range of 16–50 years. Male-to-female ratio was that of 97:3. The statistical analysis using Chi-square test showed statistically significant association ($P < 0.001$) between the functional and histologic stages.

Conclusion: There is a definite correlation between functional and histological stages of OSMF which suggests that clinically advanced OSMF has extensive fibrosis histologically.

Keywords: Functional staging, histological staging, oral submucous fibrosis

INTRODUCTION

Oral submucous fibrosis (OSMF) is an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria with epithelial atrophy, leading to stiffness of mucosa and causing trismus and inability to eat.[1] It occurs predominantly in Indians and South-East Asians. Its prevalence in Indian population is 0.2%–0.5%, with chances of malignant transformation in 3%–7.6% of cases.[2] OSMF is a multifactorial condition which includes factors such as areca nut consumption, ingestion of chillies, genetic and immunologic processes, nutritional deficiency in the form of B complex, iron deficiency, and

Access this article online	
Website: www.njms.in	Quick Response Code
DOI: 10.4103/njms.NJMS_15_18	

Pooja Bhatt, M. Manjunath[1], Deepak Khakhla[2], Priyanka Gubrellay[3], Rahul Bhargava[4], L. Guruprasad[5]

Departments of Oral Medicine and Radiology and [3]Prosthodontics and Implantology, RR Dental College and Hospital, Umarda, [4]Department of Conservative Dentistry and Endodontics, Darshan Dental College and Hospital, Udaipur, Rajasthan, [1]Department of Oral Medicine and Radiology, VS Dental College and Hospital, [5]Department of Dentistry, East Point College of Medical Science and Research Centre, Bengaluru, Karnataka, [2]Department of Oral and Maxillofacial Surgery, AIIMS, New Delhi, India

Address for correspondence: Dr. Deepak Khakhla, Department of Oral and Maxillofacial Surgery, Centre of Dental Education and Research, AIIMS, New Delhi, India.
E-mail: drdeepak4987@gmail.com

Received: 17-02-2018, **Revised:** 05-04-2018, **Accepted:** 28-06-2018

How to cite this article: Bhatt P, Manjunath M, Khakhla D, Gubrellay P, Bhargava R, Guruprasad L. Assessment and correlation between functional and histological staging of oral submucous fibrosis: A clinicohistopathologic study. Natl J Maxillofac Surg 2019;10:27-32.

malnutrition, which derange the repair of the inflamed oral mucosa, leading to defective healing and resultant scarring.[3,4] The main risk factor in OSMF includes consumption of areca nut and its products.[5] Chewing areca nut is a practice dating to centuries back in many parts of Asia such as India, Pakistan, Bangladesh, Sri Lanka, and Papua New Guinea, and its use is also reported from parts of Indonesia, Myanmar (Burma), Cambodia, Vietnam, the Philippines, Taiwan, South China, and several islands in the Pacific Ocean. It has always been a part of religious, social, and cultural rituals and of everyday life and the practice enjoys complete social acceptance, even today.[6] There is ample clinical, statistical, and epidemiological evidence to prove the direct involvement of areca nut in the pathogenesis of OSMF. Betel quid is a potent mix of carcinogens and carcinogen-aiding compounds. Areca nut contains at least three carcinogenic compounds, namely arecoline, arecaidine, and safrole. The most frequently affected sites of OSMF occurring in the oral cavity are the buccal mucosa, retromolar area, followed by the soft palate, palatal fauces, uvula, tongue, and labial mucosa.[7] The clinical symptoms begin with burning sensation of mucosa with hot and spicy food. Excessive salivation, blisters, ulceration, and altered gustatory sensations follow soon. This gradually worsens to inability of opening mouth and feeling of stiffness spreading to the tongue, floor of mouth, and pharynx.[8]

Over years, a number of studies have been done to report different aspects of OSMF. Different clinical stages are proposed depending on interincisal opening, symptoms, and presence of palpable fibrous bands. Depending on histological features ranging from early epithelial hyperplasia to advanced atrophy associated with juxta-epithelial inflammatory reaction and fibroblastic changes in lamina propria, OSMF is again divided into a number of stages. Yet, there is a paucity of studies, which correlates the clinical features to the various histopathological changes of OSMF. Therefore, an attempt has been made to correlate the functional and histological parameters that could help arrive at a comprehensive staging and formulate a definite treatment plan.

MATERIALS AND METHODS

Sixty OSMF patients were selected from the Department of Oral Medicine and Radiology, V.S Dental College and Hospital, Bengaluru, Karnataka. Ethical approval for the study was obtained from the Ethical Committee of the institute and informed consent was obtained from patients prior to the procedure. Participants included were individuals with classic features of OSMF such as mucosal blanching, burning sensation, hardening of mucosa, presence of fibrous bands, and inability to open mouth completely. Patients undergoing treatment for OSMF, immunocompromised/debilitated patients, and those with temporomandibular joint problems were excluded from the study.

Mouth opening was determined by measuring the interincisor distance, i.e., distance from mesioincisal angle of upper central incisor to mesioincisal angle of lower incisor with the help of a metal scale and divider [Figure 1]. Based on interincisor distance, the patients were divided into four functional categories according to Khanna and Andrade[8] [Table 1]. Necessary blood investigations and punch biopsy were then performed from the site of fibrous bands. The specimens were preserved in 10% formalin for histopathological examination. Histologically, participants were divided into four groups according to Khanna and Andrade[8] [Table 2 and Figures 2-5]. The clinical and histological data were collected, and Pearson's Chi-square test was used to determine association between variables.

RESULTS

The sixty participants were in the age range of 16–50 years, with a mean of 31.60 years and most of the patients belonging to male gender [Tables 3 and 4]. Most of the patients (16 [27%]) were in the age range of 26–30 years. In the present study, the minimum mouth opening was 12 mm and the maximum was 47 mm.

Figure 1: Measurement of mouth opening (original)

Table 1: Functional staging of oral submucous fibrosis

Functional group	Clinical features
Group I	Very early case - mouth opening >36 mm
Group II	Early case - mouth opening 26-35 mm
Group III	Moderately advanced cases - mouth opening 15-25 mm
Group Iva	Advanced cases - mouth opening 2-15
Group IVb	Advanced cases with premalignant changes and malignant transformation

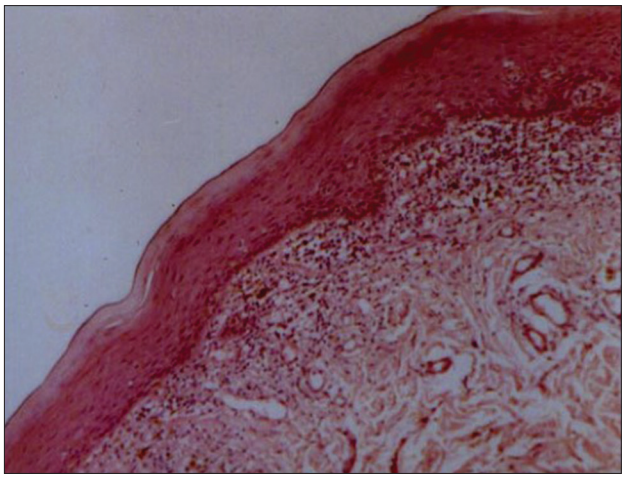

Figure 2: Very early oral submucous fibrosis (original)

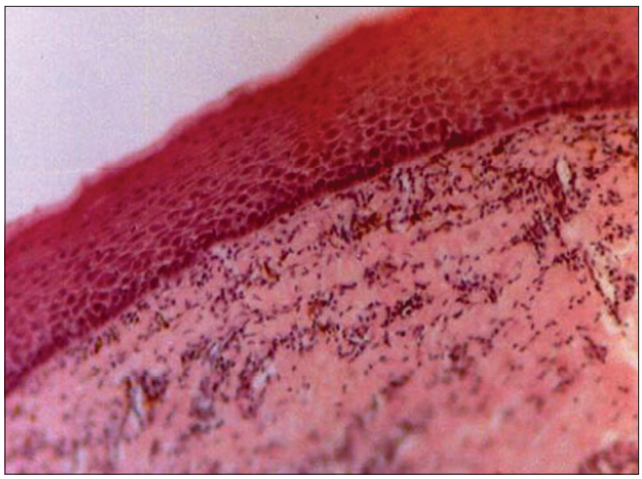

Figure 3: Early stage of oral submucous fibrosis (original)

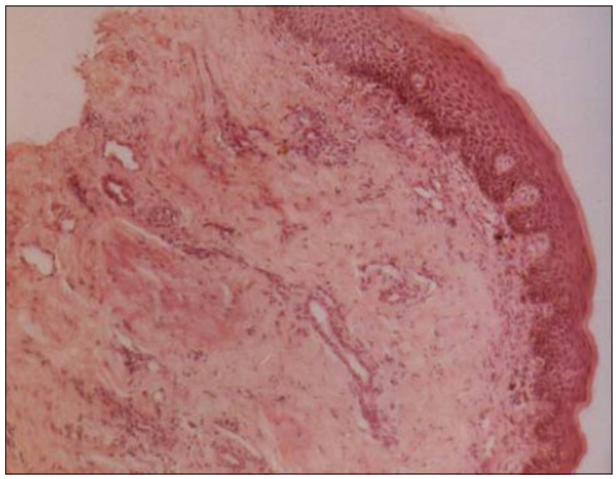

Figure 4: Moderately advanced oral submucous fibrosis (original)

Table 2: Histological staging of oral submucous fibrosis

Group	Histological features
Group I - very early	Fine fibrillar collagen network interspersed with marked edema, blood vessels dilated and congested, large aggregate of plump fibroblasts with abundant cytoplasm, inflammatory cells mainly PMN with few eosinophils. Epithelium normal, with occasional hyperplasia
Group II - early	Juxta-epithelial hyalinization with collagen present as thickened but separate bundles, blood vessels dilated and congested, moderate number of young fibroblasts, inflammatory cells mainly PMN, eosinophils, and occasional plasma cells. Epithelium shows flattening/shortening of rete pegs with varying degree of keratinization
Group III - moderately advanced	Juxta-epithelial hyalinization is present. Faintly discernible collagen bundles separated by very slight, residual edema. Muscle fibers interspersed within collagen fibers reveal the beginning of degeneration and irregularity of striae. Blood vessels constricted, mature fibrocytes with scanty cytoplasm, and spindle-shaped nuclei. Inflammatory cells, mainly lymphocytes and plasma cells. Epithelium markedly atrophic with total loss of rete pegs
Group IV - advanced	Collagen hyalinized as a smooth sheet eliminating all evidences of individual bundles. Extensive fibrosis obliterating the mucosal blood vessels and eliminating melanocytes. Fibroblasts markedly absent within hyalinized zones. Extensive degeneration of muscle fibers. Total loss of rete pegs with mild-to-moderate atypia

PMN: Polymorphonuclear

Table 3: Gender distribution

Gender	*n* (%)
Male	58 (97)
Female	2 (3)
Total	60 (100)

Table 4: Sample distribution according to age group and gender

Age group (years)	Male, *n* (%)	Female, *n* (%)
16-25	14 (24)	0
26-30	16 (28)	0
31-35	12 (21)	0
36-40	8 (14)	2 (100)
41-50	8 (14)	0
Total	58 (100)	2 (100)

In the functional staging, the participants were classified into four groups. In the first group with mouth opening of >36 mm, there were 6 (10%) participants; in Group II with mouth opening of 35–26 mm, there were 30 (50%) participants; in Group III with mouth opening of 25–16 mm, there were 14 (23%) participants; 8 (14%) participants were in Group IV (A) and 2 (3%) participants were in Group IV (B) with mouth opening <15 mm [Table 5].

In the histological staging, the sixty OSMF tissue specimens were divided into four groups depending on various histological features as follows; Group I: 6 (10%) participants, Group II: 12 (20%) participants, Group III: 36 (60%) participants,

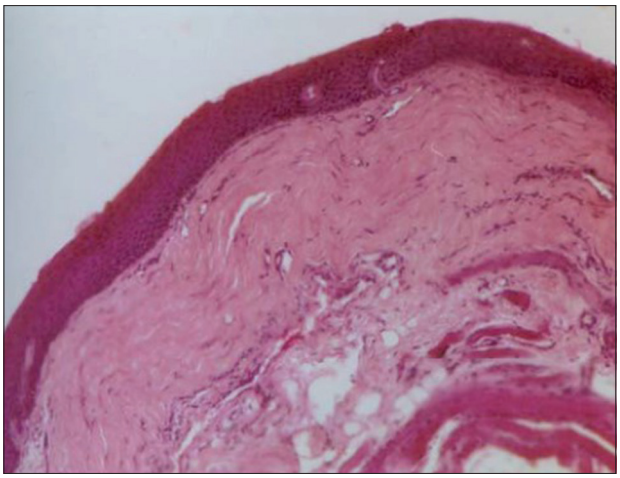

Figure 5: Advanced oral submucous fibrosis (original)

and Group IV: 6 (10%) participants. Out of which, 2 had well-differentiated squamous cell carcinoma [Table 6].

While correlating the functional and histological staging, the six participants in functional Stage I belonged to histological Group I; of thirty participants in functional Stage II, 8 belonged to histologic Stage II; and 22 were in Group III of histological stage; out of 14 participants in functional Stage III, 4 and 10 were in histological Groups II and III, respectively; of ten participants in functional Stage IV (A and B), four and six participants were in histological Groups III and IV, respectively [Table 7].

Statistical analysis with Chi-square test showed highly statistically significant relation with $P < 0.001$.

DISCUSSION

The oral mucous membrane is a unique tissue which is continuously exposed to various stresses such as heat, cold, microorganisms, chemicals, and mechanical irritants in the process of food intake. In response to these stresses, both epithelium and connective tissue layers of the oral mucosa also exhibit acute and chronic reactive changes.[3,9]

OSMF is a chronic debilitating disease and a well-recognized potentially malignant condition of the oral cavity associated with betel nut chewing. It is characterized by a generalized submucosal fibrosis of the oral soft tissue, resulting in marked rigidity and progressive inability to open the mouth.

In the present study, the sixty participants were in the age range of 16–50 years with a mean age of 31.60 years. This is comparable to the mean age of 32 years reported by Haider *et al*.[10] Most participants were in the second and

Table 5: Sample distribution according to functional stage

Functional stage	*n* (%)
I	6 (10)
II	30 (50)
III	14 (23)
IVa	8 (14)
IVb	2 (3)
Total	60 (100)

Table 6: Sample distribution according to histological stage

Histological stage	*n* (%)
I	6 (10)
II	12 (20)
III	36 (60)
IV	6 (10)
Total	60 (100)

Table 7: Association between functional stage a histological stage

Functional stage	Histological stage				χ^2	*P*
	I	II	III	IV		
I	6	0	0	0	49.254	<0.001*
II	0	8	22	0		
III	0	4	10	0		
IVa	0	0	4	4		
IVb	0	0	0	2		
Total	6	12	36	6		

*Denotes significant association

third decades of life. This changing trend of the disease toward involvement of more number from younger age group could be because of increased social encounters and economic liberty they get at this age in a rapidly developing nation like India. Therefore, during this age, they indulge in various chewing habits with betel nut, betel quid, and pan masala, etc., either to relieve stress or as a fashion. Recently, all areca nut products are associated with OSMF, with the risk being greatest for pan masala, which is having addictive and psychoactive property.[11-14] Of the sixty cases of OSMF studied, 58 cases were male and 2 cases were female [Table 4]. A literature survey shows a wide variation in age and sex distribution of OSMF. Some of the epidemiological surveys in India have shown a female predominance in the occurrence of this entity. We observed a male predominance similar to observation by multiple studies in India.[12-14]

It is well documented that in OSMF, there is a progressive inability to open the mouth and tongue movement gets restricted to varying degrees depending on the severity of the disease process. In a study of 800 normal patients in South India conducted by Ranganathan *et al*.,[11] it was reported that the average size of the mouth opening was 47.5 and 44.6 mm in males and females, respectively. Most of

the patients (50%) in the present study belong to functional Group II (mouth opening 26–35 mm).

OSMF is a disease of altered collagen metabolism. The lesion is characterized by increased collagen fiber formation in the initial stages followed by formation of dense collagen fiber bundles and different degrees of hyalinization. This alters the flexibility of the mucosal tissue leading to restriction in the ability to open one's mouth.[12] The distribution of patients in the histological Group I (10%) is comparable to that of Shivakumar and Sahana[7] where 12% were in Group I. However, a wide variation is seen when other groups were compared such as Group II in the present study constitutes 20% of the participants in contrast to that by Shivakumar and Sahana[7] where it accounts for 44%.

Haider *et al*.[10] studied the clinical and functional grading of 228 OSF patients and concluded that the bands formed initially in the fauces, followed by the buccal and labial areas. This is accompanied by an increase in the severity of the disease as measured by restriction in the ability to open the mouth. In the present study, the site of biopsy chosen was most characteristic of the condition, showed presence of vertical fibrous palpable bands and in most cases was the posterior buccal mucosa. This seems to be the reason for the shift of some of the patients in clinical Stage II to histopathological Grade III. When the correlation of functional staging with histopathological staging was done, a significant correlation was observed between them. Similar findings have been observed in the study by Khanna and Andrade[8] and Shivakumar and Sahana.[7] Studies on qualitative analysis of collagen distribution in different stages of OSMF using Picrosirius red stain under polarized microscopy by Ceena *et al*.,[15] Modak *et al*.,[16] and Radhika *et al*.[17] found that tight packing of collagen fibers in OSMF progressively increased as the disease progressed from early to advanced stages, and it was observed that comparison of functional and histological stages was a reliable indicator of the severity of the disease than clinical staging. However, Rooban *et al*.,[18] Kiran Kumar *et al*.,[12] Goel *et al*.,[19] and Gajendra *et al*.[20] in their studies did not find significant correlation between clinical staging of mouth opening and histological grading of fibrosis. The possibility of a difference in the severity and extent of fibrosis in different regions of the oral mucosa and involved muscles was considered as contributory factors for this variation. Use of different staging systems, exclusion criteria, and biopsy technique could be a reason for the different results. However, a lack of uniform classification regarding clinical, functional, and histological changes of the condition cannot be overemphasized.

CONCLUSION

OSMF is a potentially malignant condition; early recognition with accurate staging of the disease and appropriate treatment planning is of utmost importance to prevent the malignant transformation and to improve the quality of life of the patient. Statistically highly significant ($P < 0.001$) correlation between functional and histological staging suggests that individuals with clinically advanced OSMF had extensive fibrosis histologically, which can be used as a reliable criterion in determining the diagnosis, prognosis, and severity of the disease.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. Oral Surg Oral Med Oral Pathol 1966;22:764-79.
2. Shafer WG, Hine MK, Levy BM. Benign and malignant tumour of the oral cavity. In: A Textbook of Oral Pathology. 4th ed., Ch. 2. Philadelphia: W.B. Saunders Company; 1983. p. 109.
3. Cox SC, Walker DM. Oral submucous fibrosis. A review. Aust Dent J 1996;41:294-9.
4. Pindborg JJ, Bhonsle RB, Murti PR, Gupta PC, Daftary DK, Mehta FS, *et al.* Incidence and early forms of oral submucous fibrosis. Oral Surg Oral Med Oral Pathol 1980;50:40-4.
5. Murti PR, Bhonsle RB, Gupta PC, Daftary DK, Pindborg JJ, Mehta FS. Etiology of oral submucous fibrosis with special reference to the role of arecanut chewing. J Oral Pathol Med 1995; 24:145-52.
6. Gupta PC. Smokeless tobacco use in India Ch 1. In: Smoking and Tobacco Control Monograph 2. Bethesda, MD: National Institutes of Health; 1992. p. 19-25.
7. Shivakumar GC, Sahana S. Correlation between functional and histological staging of oral submucous fibrosis. J Indian Acad Oral Med Radiol 2010;22:133-5.
8. Khanna JN, Andrade NN. Oral submucous fibrosis: A new concept in surgical management. Report of 100 cases. Int J Oral Maxillofac Surg 1995;24:433-9.
9. Gupta SC, Yadav YC. MISI an etiologic factor in oral submucous fibrosis. Indian J Otolaryngol 1978;30:5-6.
10. Haider SM, Merchant AT, Firkee FF, Rahbar MH. Clinical and functional staging of OSF. Br J Oral Maxillofac Surg 2000;38:12-5.
11. Ranganathan K, Devi MU, Joshua E, Kirankumar K, Saraswathi TR. Oral submucous fibrosis: A case-control study in Chennai, South India. J Oral Pathol Med 2004;33:274-7.
12. Kiran Kumar K, Saraswathi TR, Ranganathan K, Uma Devi M, Elizabeth J. Oral submucous fibrosis: A clinico-histopathological study in Chennai. Indian J Dent Res 2007;18:106-11.
13. Pandya S, Chaudhary AK, Singh M, Singh M, Mehrotra R. Correlation of histopathological diagnosis with habits and clinical findings in oral submucous fibrosis. Head Neck Oncol 2009;1:10.
14. Sharma R, Raj SS, Miahra G, Reddy YG, Shenava S, Narang P. Prevalence of oral submucous fibrosis in patients visiting dental college in rural area of Jaipur, Rajasthan. J Indian Acad Oral Med Radiol

2012;24:1-4.
15. Ceena DE, Bastian TS, Ashok L, Annigeri RG. Comparative study of clinicofunctional staging of oral submucous fibrosis with qualitative analysis of collagen fibers under Polarising microscopy. Indian J dent Res 2009; 20:271-76.
16. Modak N, Tamgadge S, Tamgadge A, Bhalerao S. Comparative study of clinical staging of oral submucous fibrosis with qualitative analysis of collagen fibers under polarized microscopy. Iran J Pathol 2015;10:111-9.
17. Radhika T, Sekaran P, Narasimhan M. Qualitative analysis of collagen fibers in oral submucous fibrosis using Picrosirius red stain and polarising microscope. J Clin Diagn Res 2016;10:ZC04-7.
18. Rooban T, Saraswathi TR, Al Zainab FH, Devi U, Eligabeth J, Ranganathan K, *et al.* A light microscopic study of fibrosis involving muscle in oral submucous fibrosis. Indian J Dent Res 2005;16:131-4.
19. Goel S, Ahmed J, Singh MP, Nahar P. Oral submucous fibrosis: A clinico-histopathological comparative study in population of Southern Rajasthan. J Carcinogene Mutagene 2010;1:108-4.
20. Gajendra D, Arora S, Ahmed Mujib B. A clinico-histopathological study of association between fibrosis and mouth opening in oral submucous fibrosis. J Oral Biosci 2009;51:23-30.