Journal of Current Research in Oral Surgery 2021, Volume 1, Page No: 1-7 Copyright CC BY-NC-SA 4.0 Available online at: <u>www.tsdp.net</u>



Original Article

Clinicopathological Features of Oral Submucous Fibrosis, A Retrospective Analysis from a Single Institution

Xinjia Cai¹, Junhui Huang^{2*}

¹Department of Oral Pathology, Peking University School and Hospital of Stomatology & National Center of Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Research Center of Oral Biomaterials and Digital Medical Devices, Beijing, China. ²Hunan Key Laboratory of Oral Health Research & Xiangya Stomatological Hospital & Xiangya School of Stomatology, Central South University, Changsha, Hunan, China.

*E-mail 🖂 808003@csu.edu.cn

Received: 06 June 2021; Revised: 03 August 2021; Accepted: 06August 2021

ABSTRACT

A fibrotic and possibly cancerous condition of the oral cavity is called oral submucous fibrosis (OSMF). The areca nut's function in the pathophysiology of OSMF and its prevalence in the Southeast Asian population is well established. However, research into the risk factors and demographics of those afflicted is required to comprehend the pathogenesis of the illness. Therefore, the current retrospective study aimed to evaluate the clinicopathological characteristics of OSMF. The current analysis included OSMF cases that were clinically and histologically identified and reported between 1998 and 2018. Criteria for clinicopathological included gender, age, stage, grade, and history of habits. The chi-square test was used to examine the relationship. The male-to-female ratio of OSMF cases was 10.7:1, indicating a male predominance. A wide age range was seen from 14 to 84 years old. There was a strong correlation (P < 0.05) between the histological grade of OSMF and the clinical stage. Most of the patients (63 out of 141) had advanced OSMF grades. There was a significant association between history of habit, gender, age, and OSMF grade (P < 0.05). The current study showed that there is a strong association between tobacco and betel nut usage in the younger age group and the grade and stage of OSMF progress. The study emphasizes the necessity of educating patients about substance use and its detrimental effects on the course of their disease and their quality of life.

Keywords: Tobacco, Areca nut, Carcinoma, Oral submucous fibrosis

How to Cite This Article: Cai X, Huang J. Clinicopathological Features of Oral Submucous Fibrosis, A Retrospective Analysis from a Single Institution. J Curr Res Oral Surg. 2021;1:1-7. https://doi.org/10.51847/ETA8y0DM3n

Introduction

The majority of people with OSMF (oral submucous fibrosis), a fibrotic problem of the oral cavity, are from South-East Asia [1]. Because of the growing fibrosis of the affected tissues, it is also referred to as a potentially malignant illness and results in debilitation [2]. Numerous clinical and histological characteristics are present in OSMF [1, 2]. Despite being multifactorial, the sustained utilization of areca or betel nut is thought to be the main component causing these changes [2, 3]. Commercially accessible areca nut products, such as gutkha, have been linked to OSMF's early onset and

progression [2, 4, 5]. According to reports, eating pan and gutkha is frequently linked to OSMF in northern India [6]. Despite the ban on gutkha, the increasing OSMF prevalence, its invariable nature, and its malignant metamorphosis demand that clinicopathological parameters such as patient age, gender, habits, stage, and OSMF grades be studied. To assess the histological and clinical characteristics of reported OSMF cases in a single institution, the current retrospective analysis was conducted.

Materials and Methods

After obtaining Institutional ethical clearance, the present retrospective study was undertaken. A total of 141 clinically and histologically diagnosed cases of OSMF reported from 1998 to 2018 were included in the study. Clinical data consisting of age, gender, clinical signs and symptoms, stage, and habits were retrieved. Habits documented were grouped as 0. no documentation of history on patient record; 1. Betel leaf with or without lime; 2. Betel nut alone; 3. Gutkha; 4. Tobacco; 5. The combination of two or more, and 6. No habit of addictive substance consumption. Clinical signs and symptoms as available from patient records were grouped into 0. Presenting with a sharp tooth, denture trauma, and others; 1. Burning sensation and blanching of mucosa with or without blisters; 2. Palpable bands in the buccal mucosa and/or circumoral mucosa with or without blistering and burning sensation, difficulty in mouth opening (26-35 mm); 3. Palpable bands extending to raphe, uvula, tongue, and difficult mouth opening (15-25 mm) or one finger opening, erythematous areas; 4. Difficulty in mouth opening (less than 15 mm) with ulcers/white lesions; 5. Difficulty in mouth opening and associated with carcinomatous growth. For grading of OSMF, we used modified Pindborg and Sirsat classification and added categories of OSMF with dysplasia and OSMF with carcinoma [1]. The available clinical stage as mentioned on the patient record as per Khanna JN and Andrade criteria was also included for comparison [7]. All the cases included were histologically evaluated by two trained pathologists of similar experience in diagnosing head and neck pathologies for confirmation of the histological grade of OSMF. The data was tabulated and Chi-Square analysis was performed to test the difference between the clinical and histopathological parameters (P < 0.05).

Results and Discussion

Age and gender

A masculine propensity was indicated by the gender distribution's ratio of male-to-female of 10.7:1. Most females (78.6%) were in the over-40 age group, while most males (97%), on the other hand, were in the younger age range of 40 and under. The cases' ages ranged from 14 to 84 years old. The age group under 40 years old accounted for 70% of the cases (99 out of 141 total) (Table 1).

Table 1. OSMF distribution based on the age and gender groups

Gender	Age ≤ 40 years (N (%))	Age > 40 years (N (%))	Total no. (N (%))
Male	96 (97%)	33 (78.6%)	129 (91.5%)
Female	3 (3%)	9 (21.4%)	12 (8.5%)
Total	99 (100%)	42 (100%)	141 (100%)

Grade and habits

Most individuals (63 out of 141) had moderately advanced OSMF at presentation (**Table 2**). Five cases, one of which was linked to denture damage, had no habit history provided by the patient, while 116

patients provided a history of habits. For 20 patients, no habit history was recorded. The majority of cases had a history of chewing gutkha or combining two or more behaviors (**Table 3**).

Table 2. OSMF distribution base	d on the histopathological grade
stanethological grade	Participants no. (N (%))

Histopathological grade	Participants no. (N (%))
Very early OSMF	10 (7.1%)
Early OSMF	34 (24.1%)
Moderately advanced OSMF	63 (44.7%)
Advanced OSMF	22 (15.6%)
OSMF with dysplasia	6 (4.3%)
OSMF with Carcinoma	6 (4.3%)

Table 3. OSMF distribution based on the habits	Table 3.	OSMF	distribution	based	on the	e habits	
--	----------	------	--------------	-------	--------	----------	--

Habits (Score assigned)	Participants no. (N (%))
0: No history documented	20 (14.2%)
1: Betal leaf with or without lime	2 (1.4%)

26 (18.4%)
32 (22.7%)
24 (17.0%)
32 (22.7%)
5 (3.5%)

Grade and gender

Males accounted for over 50% of cases with moderately advanced OSMF, whereas females exhibited the majority of early-grade cases. Male patients accounted for the bulk of the 12 instances that showed OSMF with cancer (6 cases) and OSMF with dysplasia (6 cases) (11 out of 12 cases).

Association between age, grade, habits, and gender There was a notable relation between habit and gender

T.LL 4 C

(P = 0.046), with approximately 50% of females exhibiting a betel nut use habit history and all gutkha chewers being male (Table 4). Among Gutkha chewers, moderately advanced OSMF was present in 50% of cases, followed by advanced OSMF (28.1%). The OSMF grades and habit history were significantly correlated (P = 0.048) (Table 5), and the histological score and patient age were significantly correlated (P = 0.001) (Table 6).

	1	able 4. Con	nparison	of the res		ion and g	gender			
Gender				I	Iabit				- Total	D . I .
Genuer	-	0	1	2	3	4	5	6	Total	P-value
Female -	Count	0	0	6	0	3	2	1	12	
Female	Within gender (%)	0.0	0.0	50.0	0.0	25.0	16.7	8.3	100.0	•
Male -	Count	20	2	20	32	21	30	4	129	- 0.046*
Male -	Within gender (%)	15.5	1.6	15.5	24.8	16.3	23.3	3	100.0	- 0.040
T-4-1	Count	20	2	26	32	24	32	5	141	_
Total -	Within gender (%)	14.2	1.4	18.4	22.7	17.0	22.7	3.6	100.0	_

C 41

14

C1 1 14

Chi-square test; * shows a significant difference at $P \le 0.05$.

Habits: (0) No history is reported; (1) leaf of betel, lime or not; (2) betel nut; (3) gutkha; (4) tobacco; (5) the fusion of two or more; and (6) No habit of consuming addictive substances.

Histopathological				Habit				T (1	D 1
Grade	0	1	2	3	4	5	6	– Total	P-value
Very early OSMF	1 (5%)	0	4 (15.4%)	3 (9.4%)	1 (4.2%)	1 (3.1%)	0	10 (7.1%)	
Early OSMF	6 (30%)	0	10 (38.5%)	3 (9.4%)	9 (37.5%)	4 (12.5%)	2 (40%)	34 (24.1%)	
Moderately advanced OSMF	l 9 (45%)	2 (100%)	11 (42.3%)	16 (50%)	11 (45.8%)	12 (37.5%)	2 (40%)	63 (44.7%)	
Advanced OSMF	2 (10%)	0	1 (3.8%)	9 (28.1%)	2 (8.3%)	7 (21.9%)	1 (20%)	22 (15.6%)	0.048*
OSMF with dysplasia	2 (10%)	0	0	0	1 (4.2%)	3 (9.4%)	0	6 (4.3%)	
OSMF with Carcinoma	0	0	0	1 (3.1%)	0	5 (15.6%)	0	6 (4.3%)	
Total	20 (100%)	2 (100%)	26 (100%)	32 (10%)	24 (100%)	32 (100%)	5 (100%)	141 (100%)	

Table 5. Correlation of histopathological scores with habits

Chi-square test; * shows a significant difference at $P \le 0.05$.

Habits: (0) no history is recorded; (1) betel leaf without or with lime; (2) betel nut; (3) gutkha; (4) tobacco; (5) any combination of two or more; and (6) No habit of using addictive substances.

	Α	ge group	Tetal	N 1
Histopathological grade	≤ 40	— Total	P-value	
Very early OSMF	6 (5.9%)	4 (10%)	10 (7.1%)	
Early OSMF	19 (18.8%)	15 (37.5%)	34 (24.1%)	-
Moderately advanced OSMF	56 (55.4%)	7 (17.5%)	63 (44.7%)	-
Advanced OSMF	15 (14.9%)	7 (17.5%)	22 (15.6%)	0.001*
OSMF with dysplasia	1 (1%)	5 (12.5%)	6 (4.3%)	-
OSMF with Carcinoma	4 (4%)	2 (5%)	6 (4.3%)	_
Total	101 (100%)	40 (100%)	141 (100%)	-

 Table 6. Correlation of OSMF histopathological grade with age groups

Chi-square test; * shows a significant difference at $P \leq 0.05$

OSMF stage, grade, and clinical presentation

Based on the staging criteria, 11 out of 141 instances had Stage 4 OSMF (7.8%), while 79 out of 141 participants overall had Stage 2 OSMF (56%) (**Table**

7). Clinically, 53 out of 141 individuals had palpable bands involving the tongue, uvula, and raphe, a smaller mouth opening, and a few erythematous spots (**Table 8**).

Table 7.	Table 7. OSMF Distribution based on the clinical stage						
Stage	No. of participants (N (%))						
1	30 (21.3%)						
2	79 (56.0%)						
3	21 (14.9%)						
4	11 (7.8%)						

Fable 7. OSMF Distribution based on the clinical stage

Table 8	. Distribution	of OSMF	cases	based	on the	clinical	presentation
---------	----------------	---------	-------	-------	--------	----------	--------------

Clinical symptoms and signs (Score)	No. of participants (N (%))
Not relevant to OSMF/other signs such as denture irritation, sharp tooth, etc. (0)	6 (4.3%)
Blistering, mucosa blanching, and burning sensation (1)	14 (9.9%)
Palpable bands in circumoral and/or BM, hardness in mouth opening [26-35 mm], burning sensation, and blistering (2)	47 (33.3%)
Palpable bands expanding to the tongue, uvula, raphe, and problem mouth opening [15-25 mm] or one finger opening, erythematous areas (3)	53 (37.6%)
Limited mouth opening [< 15 mm] with Ulcers/white lesions (4)	15 (10.6%)
Limited mouth opening and related cancer [5]	6 (4.3%)

Association between stage, grade, and clinical symptoms – signs

The histopathological grade of OSMF was significantly correlated with clinical signs and symptoms and clinical stage (P = 0.001) (**Tables 9 and 10**). Most patients reported stage 2 OSMF, however,

70% of these cases had a histology grade of moderately advanced OSMF. 50% of stage 1 OSMF cases had the early OSMF histological features, whereas stage 3 and 4 OSMF cases either had progressed dysplasia or OSMF and cancer with OSMF (**Table 10**).

Table 9. Correlation	of histopathologica	al scores with clinical	symptoms and signs
	1 0		

Histopathological grada	Clinical signs and symptoms						– Total	P-value
Histopathological grade	0	1	2	3	4	5	- Totai	r-value
Very early OSMF	1 (16.7%)	4 (28.6%)	5 (10.6%)	0	0	0	10 (7.1%)	- 0.001*
Early OSMF	5 (83.3%)	4 (28.6%)	18 (38.3%)	3 (5.7%)	4 (26.7%)	0	34 (24.1%)	- 0.001

Cai and Huang, Clinicopathological Features of Oral Submucous Fibrosis, A Retrospective Analysis from a Single Institution

Moderately advanced OSMF	0	6 (42.9%)	23 (48.9%)	28 (52.8%)	6 (40%)	0	63 (44.7%)
Advanced OSMF	0	0	1 (2.1%)	21 (39.6%)	0	0	22 (15.6%)
OSMF with dysplasia	0	0	0	1 (1.9%)	5 (33.5%)	0	6 (4.3%)
OSMF with Carcinoma	0	0	0	0	0	6 (100%)	6 (4.3%)
Total	6 (100%)	14 (100%)	47 (100%)	53 (100%)	15 (100%)	6 (100%)	141 (100%)

Chi-square test; * shows a significant difference at $P \le 0.05$.

Clinical Signs and Symptoms: 0. Trauma to the denture, sharp teeth, and others; 1. A burning feeling and mucosal blanching, whether blisters are present or not; 2. Painful bands in the circumoral and/or buccal mucosa, with or without burning and blistering, and trouble opening the mouth (26–35 mm); 3. The tongue,

uvula, raphe, and difficulty mouth opening (15–25 mm) or one finger opening, as well as erythematous patches, are palpable bands; 4. Difficulty opening the mouth (less than 15 mm) due to white lesions or ulcers; and 5. Having trouble opening your mouth and having cancerous growth.

Table 10.	Correlation of	f histopathological	scores with OSMF stages
-----------	----------------	---------------------	-------------------------

Historathelegical grade		St	- Total	P-value		
Histopathological grade	Stage 1	Stage 2	Stage 3	Stage 4	- Totai	r-value
Very early OSMF	8 (26.7%)	2 (2.5%)	0	0	10 (7.1%)	
Early OSMF	15 (50%)	16 (20.3%)	3 (14.3%)	0	34 (24.1%)	
Moderately advanced OSMF	7 (23.3%)	56 (70.9%)	0	0	63 (44.7%)	
Advanced OSMF	0	5 (6.3%)	16 (76.2%)	1 (9.1%)	22 (15.6%)	0.001*
OSMF with dysplasia	0	0	2 (9.5%)	4 (36.4%)	6 (4.3%)	
OSMF with carcinoma	0	0	0	6 (54.5%)	6 (4.3%)	
Total	30 (100%)	79 (100%)	21 (100%)	11 (100%)	141 (100%)	

Chi-square test; * shows a significant difference at $P \le 0.0$

OSMF is thought to have a complex pathophysiology. Nonetheless, the primary etiological agent for OSMF is thought to be the areca nut [2, 3, 5]. Consuming betel leaves and areca nuts is a common practice in India. There has been a recent increase in the use of different commercially available areca nut preparations, either by themselves or in combination with other substances including tobacco and lime [6, 8]. The relation between the use of products of areca nut and the analysis of the specifications of the OSMF-affected population must be evaluated in light of the alteration in the accessibility and forms of these substances.

Prior studies showed that OSMF primarily affected women, although more cases of OSMF have lately been stated in male people [6]. Hazarey *et al.* [6] stated this could be related to ease of access to commercially existing areca nut products. The male-to-female ratio in our cases was 10.7:1, indicating a male predilection. A male majority in OSMF cases was also identified by More *et al.* [5], Biradar *et al.* [9], Srivastava *et al.* [10], Angadi *et al.* [11], Cai *et al.* [12], and Yang *et al.* [13]. The OSMF age distribution in our current study ranged from 14-84 years old. According to recent research, OSMF typically affects people in the younger age range [6, 14]. A small number of Chinese and Indian investigations have documented OSMF in young patients and youngsters between the ages of 9 and 16 [12, 14-16]. Similar findings from our study indicated that the age group under 40 years old had the highest number of instances. Additionally, the age-wise distribution revealed that patients in the younger age group were primarily male and had moderate to advanced OSMF clinical grade and stage. The findings of Angadi et al. [11] and Cai et al. [12], who observed a comparable correlation between gender, age, and clinicopathological characteristics, were consistent with this. Additionally, it has been noted that younger age groups are more likely to have OSMF with cancer [15].

The most frequent clinical manifestation observed in our study was a limited mouth opening (between 15 and 25 mm) accompanied by palpable bands and a burning feeling. In OSMF patients, mouth opening was likewise observed to be most influenced by Angadi *et*

al. [11].

Only half of the female patients in the current study had a history of consuming areca nuts, and the majority of the female patients came with an early OSMF grade. On the other hand, every gutkha chewer was a man and had an advanced OSMF grade. In their research, More et al. [5] and Hazarey et al. [6] also discovered a comparable habit-gender relationship. Advanced grades of OSMF have been associated with the intake of commercial areca nut products, such as gutkha [5, 17]. As a potentially cancerous condition, OSMF may manifest as dysplasia or change into carcinoma. In our investigation, we discovered 4.2% of instances in both the OSMF with cancer and OSMF with dysplasia groups. It's interesting to note that all OSMF instances with cancer had a history of consuming two or more substances for more than ten years, such as tobacco, gutkha, and/or betel nut. In contrast, 78.1% of the 32 gutkha chewers had moderately progressive to advanced OSMF, and 75% of these individuals had consumed gutkha for fewer than ten years. The results of Hazarey et al. [6], Angadi et al. [11], and Avinash Tejasvi et al. [18] are supported by our investigation. Commercial items containing significant amounts of arecoline and tobacco, or the combination of two or more of these substances, may cause OSMF to advance prematurely, cause mechanical irritation, persistent chemicals, and perhaps develop into malignant transformation.

The easy access to tobacco, products of areca nut, and other addictive substances, despite the prohibition of Gutkha [19], emphasizes the necessity of regular youth awareness programs about the link between these behaviors and potentially harmful conditions like OSMF [6, 15]. It is necessary to address the potential malignant evolution of OSMF, its influence on life quality, and the financial burden of treatment requirements [20–23]. All across the nation, stringent regulations must be put in place to control the supply of these commercial and natural betel nut/tobacco products.

Factors such as dietary status, overall health, habit frequency for all patients, and socioeconomic level were unavailable because this study is retrospective. Because it was a single institute study, fewer incidences of malignant and dysplastic changes in OSMF were found. More multicentric research should be done to examine the relationships and help identify the pathophysiology of OSMF.

Conclusion

The current retrospective analysis identifies the important correlations seen in these individuals and

examines the different clinicopathological characteristics of OSMF. Histologically, OSMF advanced grades were seen in male patients under 40 years of age, although clinically, limited mouth opening was the most typical presentation of OSMF. Individuals with advanced OSMF instances that were connected with dysplasia and cancer had a history of consuming gutkha or more than two substances, such as tobacco and betel nut.

Acknowledgments: The authors would like to thank Dr Mahesh Khairnar for the statistical help in data analysis.

Conflict of Interest: None

Financial Support: None

Ethics Statement: The ethics review board authorized the waiver of written informed consent because the study is retrospective.

References

- Pindborg JJ, Sirasat SM. Oral submucous fibrosis. Oral Surg Oral Med Oral Pathol. 1966;22(6):764-79.
- More CB, Rao NR. Proposed clinical definition for oral submucous fibrosis. J Oral Biol Craniofac Res. 2019;9(4):311-4. doi:10.1016/j.jobcr.2019.06.016
- 3. Rao NR, Villa A, More CB, Jayasinghe RD, Kerr AR, Johnson NW. Oral submucous fibrosis: a contemporary narrative review with a proposed inter-professional approach for an early diagnosis and clinical management. J Otolaryngol Head Neck Surg. 2020;49(1):3. doi:10.1186/s40463-020-0399-7
- Hande AH, Chaudhary MS, Gawande MN, Gadbail AR, Zade PR, Bajaj S, et al. Oral submucous fibrosis: an enigmatic morpho-insight. J Cancer Res Ther. 2019;15(3):463-9. doi:10.4103/jcrt.JCRT_522_17
- More CB, Rao NR, More S, Johnson NW. Reasons for initiation of areca nut and related products in patients with oral submucous fibrosis within an endemic area in Gujarat, India. Subst Use Misuse. 2020;55(9):1413-21.

doi:10.1080/10826084.2019.1660678

 Hazarey VK, Erlewad DM, Mundhe KA, Ughade SN. Oral submucous fibrosis: study of 1000 cases from central India. J Oral Pathol Med. 2007;36(1):12-7.

- Khanna JN, Andrade NN. Oral submucous fibrosis: a new concept in surgical management. Report of 100 cases. Int J Oral Maxillofac Surg. 1995;24(6):433-9.
- Jha VK, Kandula S, Ningappa Chinnannavar S, Rout P, Mishra S, Bajoria AA. Oral submucous fibrosis: correlation of clinical grading to various habit factors. J Int Soc Prev Community Dent. 2019;9(4):363-71.
 - doi:10.4103/jispcd.JISPCD_92_19
- Biradar SB, Munde AD, Biradar BC, Shaik SS, Mishra S. Oral submucous fibrosis: a clinicohistopathological correlational study. J Can Res Ther. 2018;14(3):597-603.
- Srivastava R, Jyoti B, Pradhan D, Siddiqui Z. Prevalence of oral submucous fibrosis in patients visiting dental OPD of a dental college in Kanpur: a demographic study. J Family Med Prim Care. 2019;8(8):2612-7.

doi:10.4103/jfmpc.jfmpc_465_19

- Angadi PV, Rekha KP. Oral submucous fibrosis: a clinicopathologic review of 205 cases in Indians. Oral Maxillofac Surg. 2011;15(1):15-9.
- Cai X, Yao Z, Liu G, Cui L, Li H, Huang J. Oral submucous fibrosis: a clinicopathological study of 674 cases in China. J Oral Pathol Med. 2019;48(4):321-5.
- Yang SF, Wang YH, Su NY, Yu HC, Wei CY, Yu CH, et al. Changes in prevalence of precancerous oral submucous fibrosis from 1996 to 2013 in Taiwan: a nationwide population-based retrospective study. J Formos Med Assoc. 2018;117(2):147-52.

doi:10.1016/j.jfma.2017.01.012

- More CB, Rao NR, Hegde R, Brahmbhatt RM, Shrestha A, Kumar G. Oral submucous fibrosis in children and adolescents: analysis of 36 cases. J Indian Soc Pedod Prev Dent. 2020;38(2):190-9. doi:10.4103/JISPPD_JISPPD_173_20
- 15. Chaturvedi P, Vaishampayan SS, Nair S, Nair D, Agarwal JP, Kane SV, et al. Oral squamous cell carcinoma arising in background of oral

submucous fibrosis: a clinicopathologically distinct disease. Head Neck. 2013;35(10):1404-9.

- Jain A, Taneja S. Oral submucous fibrosis in pediatric patients: a systematic review and protocol for management. Int J Surg Oncol. 2019;2019(1):3497136. doi:10.1155/2019/3497136
- Ali FM, Aher V, Prasant MC, Bhushan P, Mudhol A, Suryavanshi H. Oral submucous fibrosis: comparing clinical grading with duration and frequency of habit among areca nut and its products chewers. J Cancer Res Ther. 2013;9(3):471-6.
- Avinash Tejasvi ML, Anulekha CK, Afroze MM, Shenai KP, Chatra L, Bhayya H. A correlation between oral mucosal lesions and various quidchewing habit patterns: a cross-sectional study. J Cancer Res Ther. 2019;15(3):620-4. doi:10.4103/jcrt.JCRT_620_14
- 19. Pai SA. Gutkha banned in Indian states. Lancet Oncol. 2002;3(9):521.
- Yang PY, Chen YT, Wang YH, Su NY, Yu HC, Chang YC. Malignant transformation of oral submucous fibrosis in Taiwan: a nationwide population-based retrospective cohort study. J Oral Pathol Med. 2017;46(10):1040-5.
- Speight PM, Khurram SA, Kujan O. Oral potentially malignant disorders: risk of progression to malignancy. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018;125(6):612-27.
- 22. Acharya S, Rahman S, Hallikeri K. A retrospective study of clinicopathological features of oral squamous cell carcinoma with oral submucous fibrosis. J Oral Maxillofac Pathol. 2019;23(1):162.

doi:10.4103/jomfp.JOMFP_275_17

Chaudhry K, Bali R, Patnana AK, Chattopadhyay C, Sharma PP, Khatana S. Impact of oral submucous fibrosis on quality of life: a multifactorial assessment. J Maxillofac Oral Surg. 2020;19(2):251-6. doi:10.1007/s12663-019-01190-4