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Prevalence and management of oral submucous fibrosis and its implications on prosthodontic treatment: A retrospective study

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ABSTRACT

Oral submucous fibrosis is a chronic, premalignant condition that is prevalent in Asian countries like India, Pakistan and Srilanka. Oral cancer accounts for around 30% of the cancer cases in India. It is important to understand the prevalence of the disease for its effective management. The aim of the study was to understand the prevalence of the condition and the popularity of various treatment modalities used in its management, along with the prevalence of OSMF patients requiring prosthetic rehabilitation. Case sheets of around 23,000 patients were reviewed from March 2019 to June 2020 out of which 100 patients were affected by oral submucous fibrosis. To eliminate bias, all patients affected by the disease were included in the study. Epidemiological data of the patient along with their ongoing treatment, was collected and tabulated in MS Excel sheet. The data was then analyzed using IBM SPSS software version 23: The prevalence of OSMF in males was 92% while in females, it was 8%. The age group of 31-40 years was found to be most commonly affected, and pan chewing was observed to be the most common abusive habit amongst OSMF patients. The most common treatment modality used was non-invasive methods within which antioxidant therapy was the most popularly used modality. The increasing prevalence of OSMF amongst the younger population is a matter of great concern. The present study shows the prevalence of OSMF in males, especially in the young and middle-aged population. Thus it is important to increase awareness amongst the youth regarding the condition and to increase awareness amongst the dentists regarding the various treatment modalities to effectively prevent and clinically manage such conditions.

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INTRODUCTION

Oral submucous fibrosis is a premalignant condition which is most popularly defined as, “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 fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat (Pindborg, 1966). Although it was established in the Indian lit-

erature as Vidari since the time of "Sushruta" (Gupta and Sharma, 1988), it was first reported among 5 East African women of Indian origin by Schwartz under the term, atrophia Idiopathica (Schwartz J: Arophica, idiopathica Tropica mucosa oris. London, England, one lth International Dental Congress, 1952).

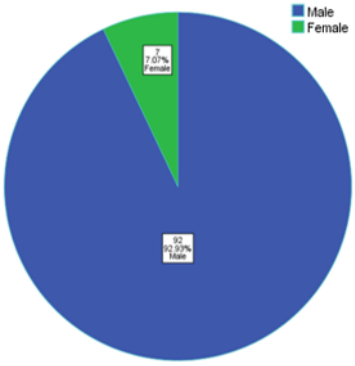

Figure 1: Pie chart showing the prevalence of OSMF is greater in males compared to females.

OSMF is usually found among Indians, Pakistanis, and Srilankans. It commonly affects the oral mucosa, the oropharynx, and, rarely, the larynx. The disease affects people across all genders and ages but is commonly found in the age group 20-40 years with a female predilection of 3:1 (Pindborg, 1965). When it affects patients with partial or complete edentulism, the task of restoring function becomes quite challenging. The condition is thought to be multi factorial in origin with a high incidence in people who chew areca-nut (Pindborg, 1965; Angadi and Rao, 2010).

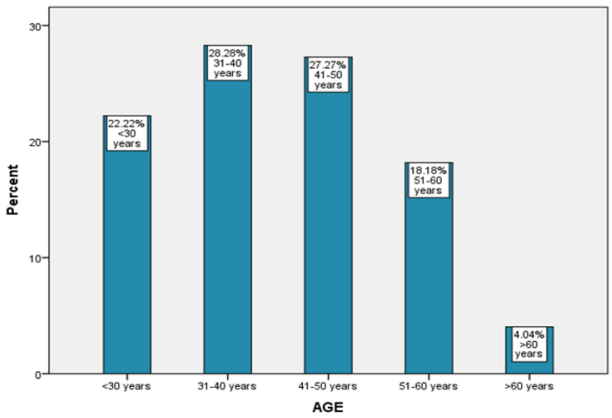

Figure 2: Bar graph depicting the prevalence of OSMF in various age groups.

Other etiological factors playing a role in the disease are tobacco chewing, smoking, alcohol consumption, capsaicin in chillies, and deficiency of iron (Bhattacharya *et al.*, 2016; Ariga *et al.*, 2018), zinc and multivitamins hypersensitivity, autoimmunity, genetic predisposition (HLA-A1 10, HLA-DR3, HLA-DR7 and haplotypes AIO/DR3, BS/DR3, and AlO/B8) (Canniff *et al.*, 1986; Jyothi *et al.*, 2017). The disease is characterized by blanching, stiffness and burning sensation of the oral mucosa. Eventually, fibrotic bands appear, involving buccal mucosa, soft palate, lips and tongue, leading to trismus (Pindborg, 1966). Hypomobility of the soft palate and tongue, loss of gustatory sensation, and occasionally, mild hearing impairment (Aziz, 2008) are the ancillary findings. The disease can be classified clinically into two phases:

- An eruptive phase which is characterized by the formation of vesicles, erythema, and a burning sensation.
- The fibrosis induction phase which is characterized by the disappearance of the vesicles, healing of the ulcers, decreased burning sensation, and blanching and stiffness of the oral and oropharyngeal mucosa. These two phrases appear in a cyclic manner. Any irritation of the oral mucosa leads to exacerbation of the disease, giving rise to an eruptive phase that leads to further fibrosis.

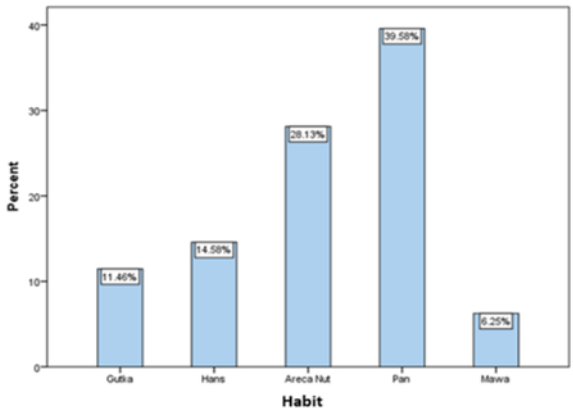

Figure 3: Bar graph depicting the prevalence of various habits in OSMF patients.

The hallmark of diagnosing OSF is clinical and histological. Clinically, one or more of the following symptoms should be present (Wollina *et al.*, 2015; Duraisamy *et al.*, 2019).

- Blanching (Morawetz *et al.*, 1987; Aziz, 2008; Selvan and Ganapathy, 2016) of oral mucosa defined as a persistent, white, marble-like appearance of the oral mucosa, which may be localized, diffuse or reticular.
- The tough, leathery texture of the mucosa.
- Palpable, whitish, fibrous bands.

Oral submucous fibrosis has a high prevalence. In general, life expectancy has increased. Hence, there is a higher percentage of individuals reaching old age with OSMF at different grades of intensity. A well-fitted prosthesis helps OSMF patients with better esthetics, function and overall well-being; hence oral rehabilitation of OSMF patients is difficult but rewarding. A combination of effective treatment of the premalignant condition along with the use of newer technologies in prosthetic rehabilitation should be used for prosthetic management of OSMF patients.

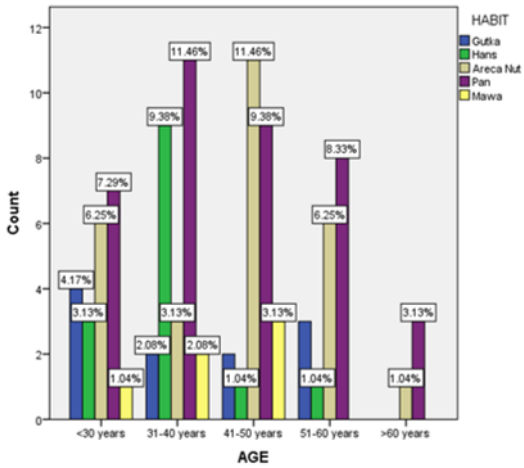

Figure 4: Bar graph depicting the between age and habit of the patient.

A wide range of treatments, such as local injections of steroids, hyaluronidase, human placental extracts, antioxidant therapy, multivitamin therapy (Maher *et al.*, 1997; Ganapathy, 2016), and physiotherapy, have been proposed for treatment of OSMF. Magnetic attachments and modifications of conventional denture designs using silicone liners along with sectional impression techniques can be used for easier prosthetic rehabilitation of patients (Arora *et al.*, 2013; Subasree *et al.*, 2016). The aim of the study was to understand the prevalence of the condition and the popularity of various treatment modalities used in its management, along with the prevalence of OSMF patients requiring prosthetic rehabilitation. This will enable clinicians to manage such patients better and will result in greater clinician as well as patient satisfaction.

MATERIALS AND METHODS

This study was carried out in a university setting at Saveetha Dental College and hospital, Chennai, India by the Department of Prosthodontics and Implantology. The study consisted of a data collector and 1 data reviewer. The disadvantage of the study was its geographical limitation. This study was approved by the institutional ethical board committee.

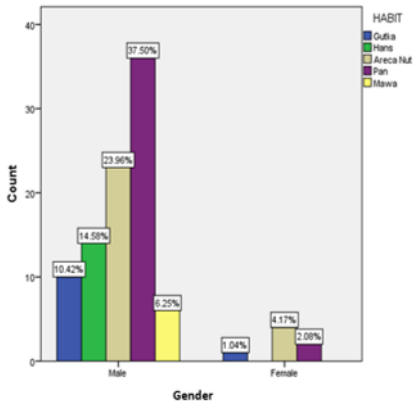

Figure 5: Bar graph depicting the association between gender and habit of the patient.

Data of patients visiting the Saveetha Oral Medicine Department from June 2019–March 2020 was collected by the method of simple random sampling. A total of 376 case sheets were reviewed. Cross verification of error in data was done via telephonic conversation. Measure taken to minimize the sampling bias was that all case sheets of patients undergoing treatment for oral submucous fibrosis at the oral medicine department of Saveetha Dental College, Chennai were included. External validity is that it is applicable to the South Indian population.

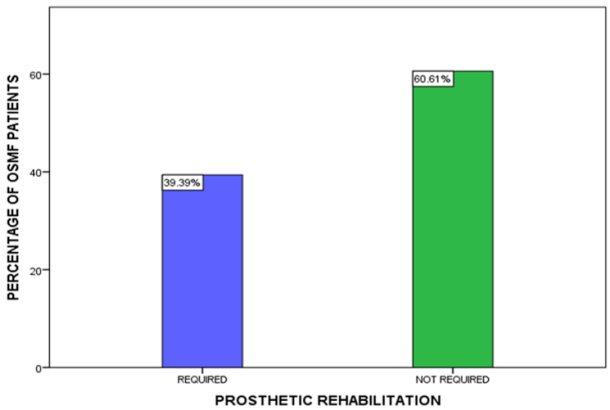

Figure 6: Bar graph depicting the percentage of OSMF patients requiring prosthetic rehabilitation.

The data collected was entered in MS Excel spreadsheet and tabulated. The data was imported in spss software version 23 and variables were defined. Statistical analysis of data was carried out using chi-square test analysis. Independent variable was oral submucous fibrosis while the dependent variables were age, gender, areca nut habit, tobacco/smoking habit, alcohol habit. Data transfer was done using spss software version 23.

Table 1: Various treatment modalities used and their popularity.

S.No	Treatment modality	Percentage
A	Habit Cessation	100%
B	Antioxidant Therapy	
	SM Fibro	82%
	Antoxid	4%
	Lycopene	3%
C	Nutritional Supplements	
	Iron	9%
	Vitamin B12	13%
D	Intralesional Injection	
	Corticosteroid+Hyaluronidase	15%
	Corticosteroid	8%
E	Mouth Exercise	
	Balloon Exercise	3%
	Icecream Sticks	10%

RESULTS AND DISCUSSION

A total of 23,000 case sheets were reviewed out of which 103 were found to be suffering from OSMF. Three patients were not included in the study as their treatment was ongoing and wasn't complete. In the present study, it is observed that out of the 99 subjects, 92 (92.93%) were male, and 7 (7.07%) were female. This shows a strong correlation between the disease and gender of the individual (Figure 1). In the present study, it is observed that the most commonly affected age group was 31-40 years, while the least affected was the age group of individuals above 60 years of age. Hence, it was observed that young to middle age people were more commonly affected, while the older population was least affected (Figure 2).

In the present study, it was observed that out of 99 patients, around 40% were in the habit of taking pan, 29% were in the habit of taking areca nut, 14% were in the habit of taking Hans, 11% were in the habit of taking Gutka, and 6% were in the habit of taking Mawa (Figure 3). It was also observed that the most popularly used treatment modality was Habit cessation and pharmaceutically the most popularly used modality was Antioxidant therapy. The second most popular treatment modality was the use of intralesional injections and nutritional supplement (Table 1). In the present study, it was observed that the most common habit in the age group 31-40 years was panned consumption while in 41-50 year was areca nut consumptionFigure 4Table 2. Although no significant association was found between gender, age and habit of the patients it was observed that consumption of pan was the most common habit amongst men while consumption of areca nut was the most common habit amongst women (Figure 5). In the present study, it is observed that 39.3% of OSMF patients required prosthetic rehabilitation while 60.61% patients didn't (Figure 6), amongst which patients of age 41-50 years required it more frequently than others (Figure 7).

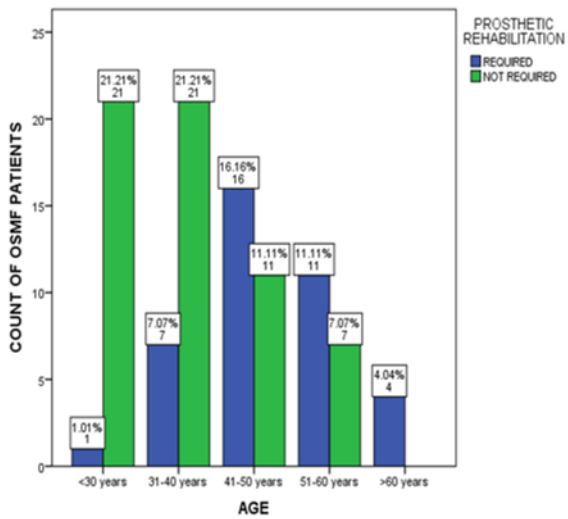

Figure 7: Bar graph depicting the association between age of the OSMF patient and their requirement of prosthetic rehabilitation.

Yang assessed the prevalence, gender and age distribution of OSMF patients in Taiwan between January 1, 1996, and December 31, 2013. It showed that the prevalence of OSMF increased significantly from 8.3 (per 10,000) in 1996 to 16.2 (per 10,000) in 2013 ($P < 0.0001$). Men had shown a significantly higher OSMF prevalence than women (Yang *et al.*, 2018; Ranganathan *et al.*, 2017).

Table 2: Association between Gender and Age of the patient and habits.

Age (Yrs)	Habit (Frequency)					Statistical Analysis	
	Gutka	Hans	Areca Nut	Pan	Mawa	Pearson Chi-Square	P-Value
<30 yrs	4	3	6	7	1		
31-40 yrs	2	9	3	11	2		
41-50 yrs	2	1	11	9	3	22.05	0.141
51-60 yrs	3	1	6	8	0		
>60 yrs	0	0	1	3	0		
Gender							
Male	10	14	23	36	6	4.11	0.39
Female	1	0	4	2	0		

A similar study was conducted in India by Sinor *et al.* (1990); Vijayalakshmi and Ganapathy (2016), which too displayed a greater prevalence of OSMF in males than in females. Male predominance in our study can be attributed to the easy accessibility of areca nuts and its products for males in comparison to females along with the changing lifestyles of youngsters in society. Similar results were also found in several other studies conducted within the Indian subcontinent (Hazarey *et al.*, 2006; Pandya *et al.*, 2009). In this study, the peak incidence was at 31-40 years (31%), followed by >30 years (27%). The observation of present study was similar to study conducted by Nigam, who reported the maximum number of OSMF cases were in the age group of 36-40 years (Nigam *et al.*, 2014; Ganapathy *et al.*, 2017).

This could be because of increased social encounters and economic liberty at that age in a rapidly developing nation like India. Therefore, during that age, there is an increase in indulgence in various habits like consumption of gutka and pan masala, smoking, alcohol, etc., either to relieve stress, as a fashion or due to peer pressure. In the present study consumption of pan (a commercial preparation of areca nuts, lime, catechu and undisclosed coloring, flavoring, and sweetening agents) was found to be the most common habit amongst OSMF patients. Similar results were found in a study conducted by Shah and Sharma (2007); Ashok and Suvitha (2016). Similar results were also observed in a study conducted by Ali *et al.* (2013); Ashok *et al.* (2014) who had found that consumption of pan had more deleterious effects on the oral mucosa than other tobacco products. This could also be due to the use of slaked lime in the preparation of the pan, which increases the reactive oxygen species hence producing a greater deleterious effect than tobacco products consumed without slaked lime.

The most popularly used line of treatment was habit cessation counseling and the use of antioxidant therapy. A study conducted by Singh (2004); Venugopalan *et al.* (2014) had proved that this method is the best line of treatment as the antioxidants help eliminate the free radicals which are responsible for causing genotype and phenotype mutation that cause neoplasms. This therapy also has high patient acceptance as it is a non-invasive and conservative form of treatment. As a secondary line of treatment and for a more holistic approach, it is essential to give the patients nutritional supplements like vitamin B12 and iron. A study conducted by Ramanathan (1981); Kannan and Venugopalan (2018) had observed that around 63% of the OSMF patients reporting had depressed serum iron levels while 50% of them had a vitamin B12 deficiency. Similar results were found in a study conducted by Wang *et al.* (2015). The deficiency of these essential vitamins and minerals could be due to inability to eat well because of the condition. Hence, consumption of nutritional supplements by OSMF patients is highly recommended.

Physiotherapy such as mouth opening exercises is also advised by some clinicians for the management of OSMF. A study by Nidhi *et al.* (2019); Basha *et al.* (2018) observed that OSMF patients, when managed with supplemental therapy along with physiotherapy, showed great improvement in mouth opening when compared to patients who weren't advised physiotherapy. However, some clinicians state that physiotherapy helps only in cases which have undergone surgery, while some even argue that physiotherapy if done without surgery, can cause further fibrosis of the tissues and worsen the situation. Some clinicians also advise the use of intralesional injections with steroids to improve mouth opening of the patient. In a study conducted by Ameer and Shukla (2012); Ajay *et al.* (2017) it was observed that intralesional injections with triamcinolone in OSMF patients by giving biweekly submucosal injections of 40 mg triamcinolone for

12 weeks, patients subjectively showed improvement in symptoms and objectively increase in mouth opening was observed. However, such modalities have drawbacks too. There will be less patient acceptance, increased chances of infections, and they may prove to be more hazardous than conservative methods of treatment. Borle and Borle (1991) had also stated that intralesional injections of various drugs leads to aggravated fibrosis and pronounced trismus (Pindborg *et al.*, 1968). The resultant worsening of this condition with submucosal injections was also attributable (Shah, 2016) to repeated needle stick injury to the soft tissues at multiple sites, clinical irritation from drugs being injected, and to the progressive nature of the disease. Hence, in the present study also we observe that though some patients are advised intralesional injections with corticosteroids, the majority of the patients are treated in a conservative manner with counseling, pharmaceutical therapy and nutritional support.

The management of a patient of OSMF is quite difficult, but complete or partial edentulousness further complicates the situation as it is difficult to carry out the clinical procedure needed in the construction of the prosthesis. In the present study, it was observed that about a third of the OSMF patients require some form of prosthetic rehabilitation. Preliminary management of the patient is essential before carrying out the procedures. Patients can be advised to use salivary substitute to overcome the xerostomia. Impression can be taken using flexible trays or sectional trays using elastomeric impression materials (Fernandes *et al.*, 2009). In the case of sectional trays where the strength of the connecting mid line joint is inadequate, the impressions taken can become deformed. Polyether and polyvinyl siloxane are elastic impression materials that are self-adherent and advised in such cases (Patil *et al.*, 2017). In case of completely edentuless patients, complete sectional dentures with magnetic attachments can be fabricated too. Newer technologies like intraoral scanners can be explored for prosthetic management of OSMF patients; however, it is essential to understand the importance of holistic management of the patient, to achieve better patient satisfaction.

The limitations of this study were that it was geographically limited. The sample size was also less. Hence, studies with larger sample size and longer duration of follow up are required to achieve conclusive data. The management of OSMF patients has been an enigma until now. Effective management is essential for patient survival and for a better quality of life. Hence, this study was important to understand the prevalence of the disorder, to help tackle it at the grass-root level by increasing awareness amongst the youth. The present study also helps us understand the effectiveness and drawbacks of several treatment modalities, thus helping clinicians in the more effective management of OSMF patients. The current study also explains the various technologies and materials available to carry out various clinical procedures in OSMF patients, thus allowing better dental treatment and increasing patient as well as clinician satisfaction.

CONCLUSION

Within the limitations of the present study, the occurrence of OSMF in pan chewers was greater compared to patients with other habits. High prevalence of OSMF, especially amongst men of middle age (31-40 years), was found. Conservative methods such as habit cessation and the use of antioxidants are most popularly used in its management. Since around one-third of OSMF patients require prosthetic rehabilitation, prosthodontists should focus on newer techniques and technologies to allow easy prosthetic rehabilitation of such patients.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

Ajay, R., Suma, K., Ali, S., Sivakumar, J. K., Rakshagan, V., Devaki, V., Divya, K. 2017. Effect of surface modifications on the retention of cement-retained implant crowns under fatigue loads: An In vitro study. *Journal of Pharmacy And Bioallied Sciences*, 9(5):154.

Ali, F. M., Aher, V., Prasant, M. C., Bhushan, P., Mudhol, A., Suryavanshi, H. 2013. Oral submucous fibrosis: Comparing clinical grading with duration and frequency of habit among areca nut and its products chewers. *Journal of Cancer Research and Therapeutics*, 9(3):471.

Ameer, N. T., Shukla, R. K. 2012. A Cross Sectional Study of Oral Submucous Fibrosis in Central India and the Effect of Local Triamcinolone Therapy. *Indian Journal of Otolaryngology and Head and Neck Surgery*, 64(3):240–243.

Angadi, P. V., Rao, S. 2010. Management of oral submucous fibrosis: an overview. *Oral and Maxillofacial Surgery*, 14(3):133–142.

Ariga, P., Nallaswamy, D., Jain, A. R., Ganapathy, D. M. 2018. Determination of Correlation of Width of Maxillary Anterior Teeth using Extraoral and Intraoral Factors in Indian Population: A Systematic Review. *World Journal of Dentistry*, 9(1):68–75.

Arora, P., Wazir, S. S., Sharma, A. 2013. Hinged and sectional complete dentures for restricted mouth opening: A case report and review. *Contemporary Clinical Dentistry*, 4(1):74.

Ashok, V., Nallaswamy, D., Begum, S. B., Nesappan, T. 2014. Lip Bumper Prosthesis for an Acromegaly Patient: A Clinical Report. *The Journal of Indian Prosthodontic Society*, 14(S1):279–282.

Ashok, V., Suvitha, S. 2016. Awareness of all ceramic restoration in rural population. *Research Journal of Pharmacy and Technology*, 9(10):1691.

Aziz, S. R. 2008. Oral Submucous Fibrosis: Case Report and Review of Diagnosis and Treatment. *Journal of Oral and Maxillofacial Surgery*, 66(11):2386–2389.

Basha, F. Y. S., Ganapathy, D., Venugopalan, S. 2018. Oral Hygiene Status among Pregnant Women. *Research Journal of Pharmacy and Technology*, 11(7):3099.

Bhattacharya, P. T., Khaitan, T., Sarkar, S. B., Sinha, R. 2016. Oral submucous fibrosis secondary to iron deficiency anemia: A case report, etiopathogenesis and management. *The journal of nutrition, health & aging*, 20(2):205–208.

Borle, R. M., Borle, S. R. 1991. Management of oral submucous fibrosis: A conservative approach. *Journal of Oral and Maxillofacial Surgery*, 49(8):788–791.

Canniff, J. P., Harvey, W., Harris, M. 1986. Oral submucous fibrosis: its pathogenesis and management. *British Dental Journal*, 160(12):429–434.

Duraisamy, R., Krishnan, C. S., Ramasubramanian, H., Sampathkumar, J., Mariappan, S., Sivaprakasam, A. N. 2019. Compatibility of Nonoriginal Abutments With Implants. *Implant Dentistry*, 28(3):289–295.

Fernandes, A. S., Mascarenhas, K., Aras, M. A. 2009. Custom sectional impression trays with interlocking type handle for microstomia patients. *Indian Journal of Dental Research*, 20(3):370.

Ganapathy, D. 2016. Effect of Resin Bonded Luting Agents Influencing Marginal Discrepancy in All-Ceramic Complete Veneer Crowns. *Journal of clinical and diagnostic research*, 10(12):67–70.

Ganapathy, D. M., Kannan, A., Venugopalan, S. 2017. Effect of Coated Surfaces influencing Screw Loosening in Implants: A Systematic Review and Meta-analysis. *World Journal of Dentistry*, 8(6):496–502.

Gupta, D., Sharma, S. C. 1988. Oral submucous fibrosis—A new treatment regimen. *Journal of Oral and Maxillofacial Surgery*, 46(10):830–833.

Hazarey, V. K., Erlewad, D. M., Mundhe, K. A., Ughade, S. N. 2006. Oral submucous fibrosis: study of 1000 cases from central India. *Journal of Oral Pathology and Medicine*, 36(1):12–17.

Jyothi, S., Robin, P. K., Ganapathy, D., Anandiselvaraj 2017. Periodontal Health Status of Three Different Groups Wearing Temporary Partial Denture. *Research Journal of Pharmacy and Technology*, 10(12):4339.

Kannan, A., Venugopalan, S. 2018. A systematic review on the effect of use of impregnated retraction cords on gingiva. *Research Journal of Pharmacy and Technology*, 11(5):2121.

Maher, R., Aga, P., Johnson, N. W., Sankaranarayanan, R., Warnakulasuriya, S. 1997. Evaluation of multiple micronutrient supplementation in the management of oral submucous fibrosis in Karachi, Pakistan. *Nutrition and Cancer*, 27(1):41–47.

Morawetz, G., Katsikeris, N., Weinberg, S., Listrom, R. 1987. Oral submucous fibrosis. *International Journal of Oral and Maxillofacial Surgery*, 16(5):609–614.

Nidhi, N., Srikrishna, K., Kumar, V. 2019. Role of Physiotherapy in the Management of Oral Submucous Fibrosis: A Case Control Study. *International Journal of Contemporary Medical Research [IJCMR]*, 6(1).

Nigam, N. K., Aravinda, K., Dhillon, M., Gupta, S., Reddy, S., Raju, M. S. 2014. Prevalence of oral submucous fibrosis among habitual gutkha and areca nut chewers in Moradabad district. *Journal of Oral Biology and Craniofacial Research*, 4(1):8–13.

Pandya, S., Chaudhary, A., Singh, M., Singh, M., Mehrotra, R. 2009. Correlation of histopathological diagnosis with habits and clinical findings in oral submucous fibrosis. *Head & Neck Oncology*, 1(1):10.

Patil, S., Sarode, S. C., Sarode, G. S., Bhandi, S., Awan, K. H., Ferrari, M. 2017. Prosthetic rehabilitation of oral submucous fibrosis patients: A systematic review of published case reports and case series. *PLOS ONE*, 12(9):e0184041.

Pindborg, J. 1965. Oral Precancerous Conditions in South East Asia. *International Dental Journal*, 15:190–199.

Pindborg, J. J. 1966. Oral Submucous Fibrosis as a Precancerous Condition. *Journal of Dental*

Research, 45(3):546–553.

Pindborg, J. J., Mehta, F. S., Gupta, P. C., Daftary, D. K. 1968. Prevalence of oral submucous fibrosis among 50,915 Indian villagers. *British Journal of Cancer*, 22(4):646–654.

Ramanathan, K. 1981. Oral submucous fibrosis–an alternative hypothesis as to its causes. *The Medical Journal of Malaysia*, 36(4):243–245.

Ranganathan, H., Ganapathy, D., Jain, A. 2017. The cervical and incisal marginal discrepancy in ceramic laminate veneering materials: A SEM analysis. *Contemporary Clinical Dentistry*, 8(2):272.

Selvan, S. R., Ganapathy, D. 2016. Efficacy of fifth generation cephalosporins against methicillin-resistant Staphylococcus aureus-A review. *Research Journal of Pharmacy and Technology*, 9(10):1815.

Shah, N., Sharma, P. P. 2007. Role of chewing and smoking habits in the etiology of oral submucous fibrosis (OSF): a case-control study. *Journal of Oral Pathology & Medicine*, 27(10):475–479.

Shah, P. H. 2016. Comparison of Therapeutic Efficacy of Placental Extract with Dexamethasone and Hyaluronic Acid with Dexamethasone for Oral Submucous Fibrosis - A Retrospective Analysis. *Journal of clinical and diagnostic research*, 10.

Singh, M. 2004. Efficacy of oral lycopene in the treatment of oral leukoplakia. *Oral Oncology*, 40(6):591–596.

Sinor, P. N., Gupta, P. C., Murti, P. R., Bhonsle, R. B., Daftary, D. K., Mehta, F. S., Pindborg, J. J. 1990. A case-control study of oral submucous fibrosis with special reference to the etiologic role of areca nut. *Journal of Oral Pathology and Medicine*, 19(2):94–98.

Subasree, S., Murthykumar, K., Dhanraj 2016. Effect of Aloe Vera in Oral Health-A Review. *Research Journal of Pharmacy and Technology*, 9(5):609.

Venugopalan, S., Ariga, P., Aggarwal, P., Viswanath, A. 2014. Magnetically retained silicone facial prosthesis. *Nigerian Journal of Clinical Practice*, 17(2):260.

Vijayalakshmi, B., Ganapathy, D. 2016. Medical management of cellulitis. *Research Journal of Pharmacy and Technology*, 9(11):2067.

Wang, Y. P., Wu, Y. C., Cheng, S. J., Chen, H. M., Sun, A., Chang, J. Y. 2015. High frequencies of vitamin B12 and folic acid deficiencies and gastric parietal cell antibody positivity in oral submucous fibrosis patients. *Journal of the Formosan Medical Association*, 114(9):813–819.

Wollina, U., Verma, S. B., Faridi, M., Patil, K. 2015. Oral submucous fibrosis: an update. *Clinical, Cosmetic and Investigational Dermatology*, 8.

Yang, S. F., Wang, Y. H., *et al.* 2018. Changes in prevalence of precancerous oral submucous fibrosis from 1996 to 2013 in Taiwan: A nationwide population-based retrospective study. *Journal of the Formosan Medical Association*, 117(2):147–152.