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Association of habits with clinical symptoms in oral submucous fibrosis patients - a retrospective study

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Abstract: Oral Submucous Fibrosis (OSMF) is a potentially malignant disorder and its early diagnosis is essential to reduce malignant transformation into oral squamous cell carcinoma (OSCC) and thereby reduce morbidity and mortality. This study assessed the chewing habits of the patients visiting Saveetha Dental College and Hospitals with regard to consumption of areca nut and its products, frequency and duration of habits as well as clinical symptoms and signs in OSMF. The aim of this study was to associate the habits with clinicopathological findings in OSMF patients. An institutional based retrospective study was conducted among 64 cases clinically diagnosed with OSMF. A detailed habit history and clinical signs and symptoms were recorded and appropriate statistical analysis was done. The study included 62 OSMF cases of both the gender groups; males (87.5%) and females (12.5%) of age group between 22 to 65 years. In this study, the most common habit was noted to be pan chewing and the commonest clinical symptoms was found to be restricted mouth opening (39%) and associated pain symptoms (28%). A very common clinical site for this lesion was found to be the buccal mucosa bilaterally (79.69%). The habit patterns and clinical features of OSMF are important to facilitate prompt diagnosis and management in order to monitor its clinical severity and progression to OSCC.

Keywords: Oral submucous fibrosis; Potentially malignant; Clinical symptoms; Restricted mouth opening; Pan chewing; Areca nut innovative technique

INTRODUCTION

Oral submucous fibrosis (OSMF), is a chronic, progressive, irreversible, scarring disease of the oral cavity and extending up to the pharynx. (Ali *et al.*, 2013) ; (Haider *et al.*, 2000) It has been given the term 'atrophic idiopathic mucosae oris'; coined by Sir Schwartz in 1952. (Nanavati, Nanavati and Nanavati, 2015) ; (Ahmad *et al.*, 2006) It is a common oral potentially malignant disorder (OPMD) among the South East Asian population with a malignant transformation rate between 7 to 13%. ((Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)) OSMF is found to be the most common among the population of the Indian sub-continent with a prevalence rate of 0.2 to 0.5% consisting of over 2.5 to 10 million cases since 2015. (Sridhar *et al.*, 2016) ; (Ali *et al.*, 2014) (Singh, Gaikwad and Sapra, 2015) ; (Saraswathi *et al.*, 2006) ; (G. Jayaraj *et al.*, 2015) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and

Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)) It commonly affects both the genders, the male to female ratio being 1:3 with a male predominance occuring between the third to fifth decade of life. (Saraswathi *et al.*, 2006) ; (G. Jayaraj *et al.*, 2015) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019))

OSMF is multifactorial in etiology, found to be associated with habits such as areca nut or betel-quid chewing, containing high levels of chemical constituents like alkaloids and flavonoids that interfere with the molecular processes of deposition and degradation of extracellular matrix molecules like collagen. ((Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)) TGF beta is known to play a significant role where its synthesis takes place at the site of inflammation. (Wollina *et al.*, 2015) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)) The hallmark of this lesion being it preceded by vesicle formation, associated with juxta-epithelial inflammatory reaction followed by fibro-elastic changes of lamina propria such as blanching of the mucosa along with epithelial atrophy leading to stiffness of oral mucosa, causing trismus and inability to eat. (Ali *et al.*, 2014) ; (Singh, Gaikwad and Sapra, 2015) ; (Ranganathan *et al.*, 2001) ; (Reddy *et al.*, 2011); (Hazarey *et al.*, 2007) ; (Cai *et al.*, 2019) ; (Angadi and Rekha, 2011) ; (Wollina *et al.*, 2015) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)) The lesion is known to have multiple site involvement including the bilateral involvement of buccal mucosa, the lip mucosa, palatal mucosa, faucial pillars and the mucosa of the floor of the mouth. (Niessen *et al.*, no date) ; (Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019))

Several literatures have been published to correlate the clinical features with the habits including the signs and symptoms of OSMF which have found evidence of the oral lesion to have potential to transform into malignancy such as OSCC, if untreated or inadequately treated. ((Gifrina Jayaraj, Ramani, *et al.*, 2015; Gifrina Jayaraj, Sherlin, *et al.*, 2015; G. Jayaraj *et al.*, 2015; Jangid *et al.*, 2015; Sherlin *et al.*, 2015; Sivaramakrishnan and Ramani, 2015; Swathy, Gheena and Varsha, 2015; Gupta and Ramani, 2016; Thangaraj *et al.*, 2016; Viveka *et al.*, 2016; Sridharan, Ramani and Patankar, 2017; Hannah *et al.*, 2018; Gheena and Ezhilarasan, 2019; Hema Shree *et al.*, 2019; Sridharan *et al.*, 2019)). Therefore,

Our department is passionate about research we have published numerous high quality articles in this domain over the past years (Abraham *et al.*, 2005; Devaki, Sathivel and BalajiRaghavendran, 2009; Neelakantan *et al.*, 2010, 2015; Arja *et al.*, 2013; Ramshankar *et al.*, 2014; Sumathi *et al.*, 2014; Surapaneni and Jainu, 2014; Surapaneni, Priya and Mallika, 2014; Ramamoorthi, Nivedhitha and Divyanand, 2015; Manivannan *et al.*, 2017; Ezhilarasan, 2018; Ezhilarasan, Sokal and Najimi, 2018; J *et al.*, 2018; Ravindiran and Praveenkumar, 2018; Malli Sureshbabu *et al.*, 2019; Mehta *et al.*, 2019; Krishnaswamy *et al.*, 2020; Samuel, Acharya and Rao, 2020; Sathish and Karthick, 2020)

this study aims to associate habit with clinical symptoms and severity in oral submucous fibrosis patients.

MATERIALS AND METHODS

Study design and study setting: This retrospective study was conducted by the department of oral and maxillofacial pathology in Saveetha dental college and hospital, Chennai, to evaluate the habits and clinical

symptoms of oral submucous fibrosis patients from June 2019 to March 2020. The study was initiated after approval from the institutional Scientific review board.

Study population and sampling: After assessment in the university patient data registry, case records of 62 patients with clinically diagnosed oral submucous fibrosis were included in the study and evaluated. The inclusion criteria for the study were patients with clinically diagnosed OSMF; patients with complaints of burning sensation and restricted or limited mouth opening; patients with a history of areca nut chewing habit. The exclusion criteria of the study was patients with other oral lesions excluding OSMF such as oral squamous cell carcinoma and other oral potentially malignant disorders. Cross verification of data for errors was done with the help of an external examiner.

Data collection: A single calibrated examiner evaluated the digital case records of the 62 oral submucous fibrosis patients from June 2019 to March 2020. Demographic details like age, gender along with habit history, site of the lesion and clinical symptoms were also recorded. All consecutive case records of patients with oral submucous fibrosis were included in the study and their data retrieved.

Statistical Analysis: The collected data was validated, tabulated and analysed with Statistical Package for Social Sciences for Windows, version 20.0 (SPSS Inc., Chicago, IL, USA) and results were obtained. Categorical variables were expressed in frequency and percentage. Chi-square test was used to test associations between categorical variables. P value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The study group included both male (87.5%) and female (12.5%) OSMF participants (figure.1) between the age group 22 to 65 years . The most common age group was 31-40 years followed by 21 to 30 years (Figure 2). The habits prevalent among oral submucous fibrosis patients were areca nut (32.81%); mawa (7.8%); Hans (15.6%); pan (39%); Gutkha (4.7%) (Figure 3). Among the participants, the duration of habit ranged between 10 months to 23 years where a majority of cases had 2 years of habit ranged between 10-15% in this study.

The clinical symptoms such as restricted mouth opening were found to be present in 39% of cases followed by associated pain symptoms in among 28 % of cases. The burning sensation was seen in upto 17% of cases. OSMF was an accidental finding in 12% of cases who complained of other symptoms such as swelling, missing teeth and stains on teeth (Figure 4).

The most common site in the oral cavity for its clinical presentation was the buccal mucosa bilaterally (80%) (Figure 5). The most common clinical finding was found to be the blanching of the mucosa and palpable fibrotic bands. It was found that the duration of clinical symptoms vary common during 1 year in 25% of cases and 1 week in less than 15% of cases; 10 years in less than 10% of cases; more than 5% cases showed clinical symptoms for a duration of 3 days, 4 days, 3 weeks, 2 months, 3 months and 6 months. Less than 5% cases had clinical symptoms for 5 days, 10 days, 1 month, 2 years and 5 years.

A statistical chi-square test was done to find the association between OSMF habits and its clinical symptoms. (Figure 6) A positive association was found between panchewing and associated pain symptoms(61%) and Burning sensation and restricted mouth opening being more common among those with areca nut habit. The P value was 0.002 ($p<0.05$) showing statistical significance (Figure 6). Age and clinical symptoms also showed statistical significance with all symptoms being more prevalent among 31-40 years of age(Figure 7).

The areca nut products like pan (fig. 3) are found to have a significant correlation with the clinical site of the lesion which revealed the buccal mucosa bilaterally. (fig.5) This occurrence of the oral lesion particularly the buccal mucosa bilaterally implicates a greater frequency of OSMF patients with the usage of areca nut products like pan habitually placed in the cheek region of the mouth. ((Nanavati, Nanavati and Nanavati, 2015))

Pan chewing showed significant correlation with associated pain symptoms proving evidence that the clinical severity such as trismus and burning sensation including associated pain is having a link with the site and extent of the lesion in OSMF patients. This finding is similar to the study by Reddy V *et al* and Ali *et al. (Ali et al., 2013)* (Reddy *et al.*, 2011) The probability of the associated pain symptoms would have risen as a result of chemical constituents present in the pan which could induce ulceration and accompanied pain sensation.

In this study and also in most other studies, the very common clinical symptoms was restricted mouth opening followed by pain. ((Nanavati, Nanavati and Nanavati, 2015)) This is also in consensus with the results of study by (Angadi and Rekha, 2011)*et al,* where it was found that restricted mouth opening was a more common clinical feature followed by burning sensation (Angadi and Rekha, 2011)Although pain and burning sensation are the initial clinical symptoms, patient do not report to the hospital until they develop difficulty in opening the mouth. This finding just implies that most of the patients are not aware of the presence of the disease until they are told about OSMF and its consequences. Presence of palpable fibrous bands and blanching were the principal clinical findings evident in most cases of OSMF and is also a relevant diagnostic criteria.

As this study was restricted to an institutional study, the samples analysed are from a particular regional data and the sample size of this study is limited owing to its limitations. Probably a larger sample size would have helped to yield a much significant result. The study may guide to establish a better clinical approach in relation with its associated habits.

CONCLUSION

Within the limits of this study, the habits and its clinical symptoms show significant association, with Pain being more common among those with the habit of pan chewing and restricted mouth opening among the areca nut users. This will help in understanding the pathogenesis of OSMF better and in turn help in preventing its malignant transformation.

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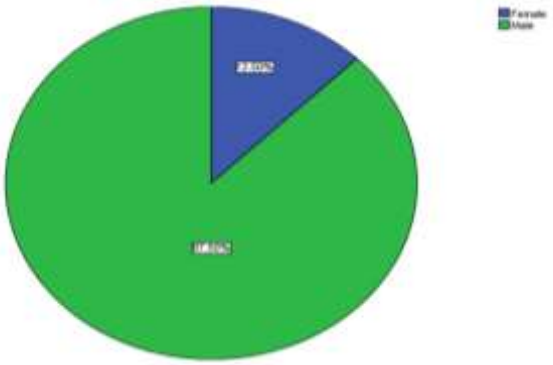

Fig.1: Pie chart depicting the gender distribution of oral submucous fibrosis patients. 87.5% of the participants were males (green) and 12.5% were females (blue).

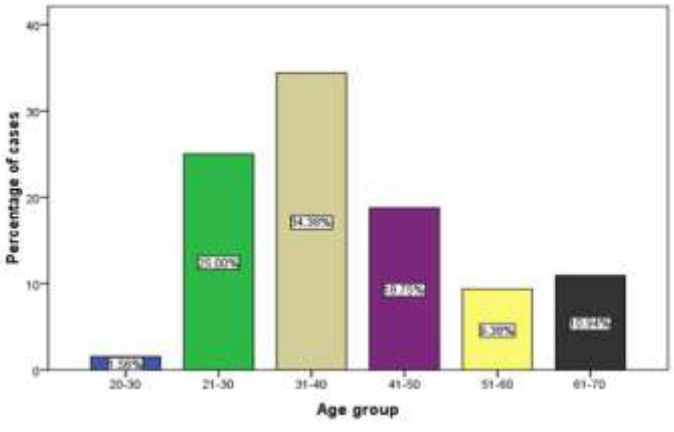

Fig.2: Bar chart representing the age distribution of the oral submucous fibrosis patients. X axis represents the age groups and Y axis represents the percentage of cases. Maximum of the study participants belonged to 31 - 40 years of age(grey) followed by 25% belonging to 21 - 30 years of age(green).

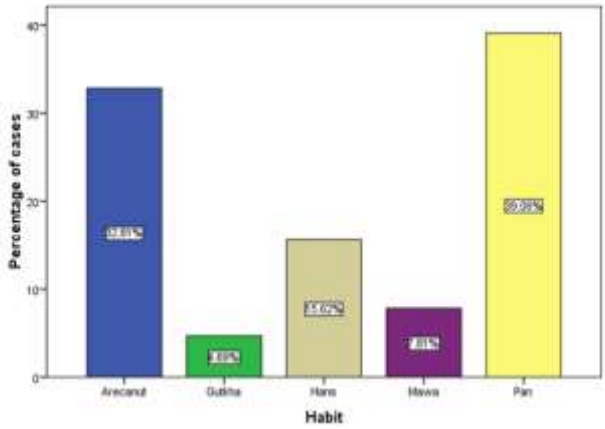

Fig.3: Bar graph representing the frequency distribution of habits among oral submucous fibrosis patients. X axis depicts the habits and Y axis the percentage of cases. The most prevalent habit was pan chewing 39.06% (yellow), followed by areca nut 32.61% (blue), Hans 15.62% (grey), mawa 7.8%(peuple) and Ghutkha 4.69%(green).

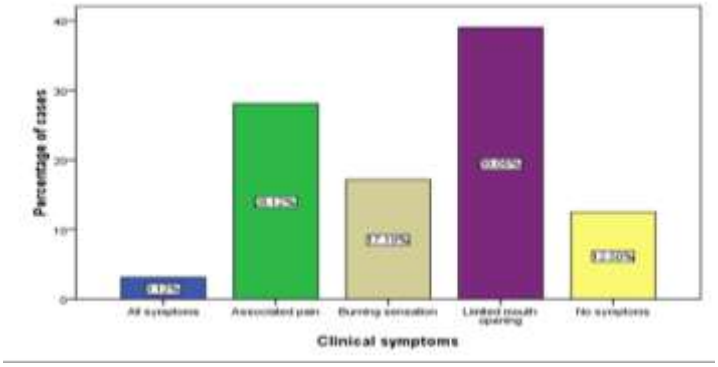

Fig.4: Bar graph representing the frequency distribution of clinical symptoms among oral submucous fibrosis patients. X axis represents the clinical symptoms and Y axis the percentage of cases. The most common symptom being limited mouth opening among 39% (purple), followed by associated pain 28.12%, Burning sensation 17.2% and no clinical symptoms was seen in 12.5% of the cases.

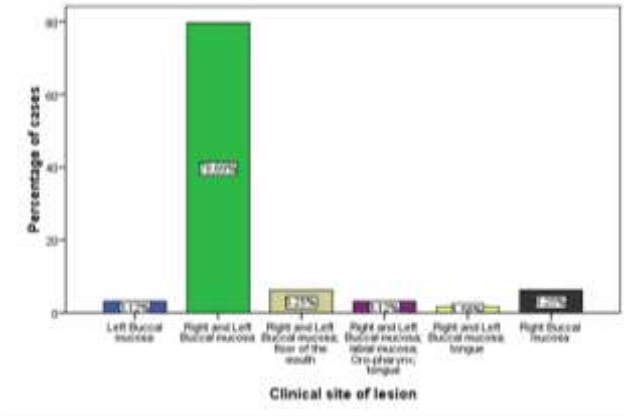

Fig.5: Bar graph representing the frequency distribution of clinical site of occurrence of oral submucous fibrosis. X axis represents the clinical site of the lesion and Y axis represents the percentage of cases. 79.7% of the cases were found bilaterally in both the right and left buccal mucosa(green), 6.2% were found only in the right buccal mucosa(black) and another 6.2% had involvement of the floor of the mouth (grey).

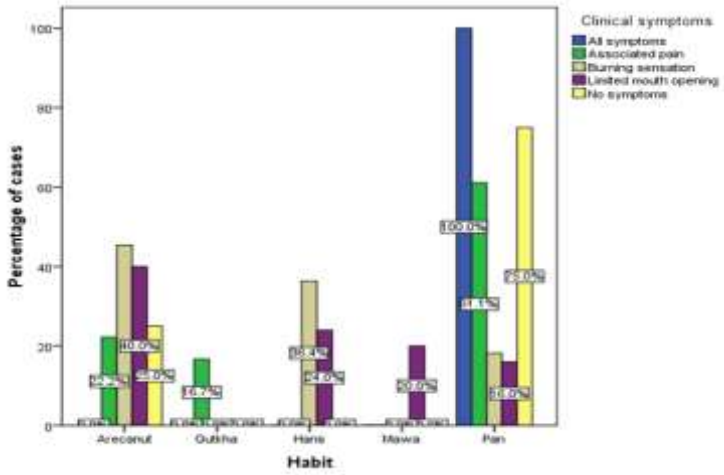

Fig.6: Bar graph representing the association of habits with clinical symptoms among oral submucous fibrosis patients. X axis represents the habits and Y axis the percentage of cases. Chi square analysis showed statistical significance with (Chi square value 37.760) p=0.002 (p<0.05), indicating a significant increase in all symptoms and symptoms of pain among those with habit of pan chewing. Limited mouth opening and burning sensation was more common among areca nut users.

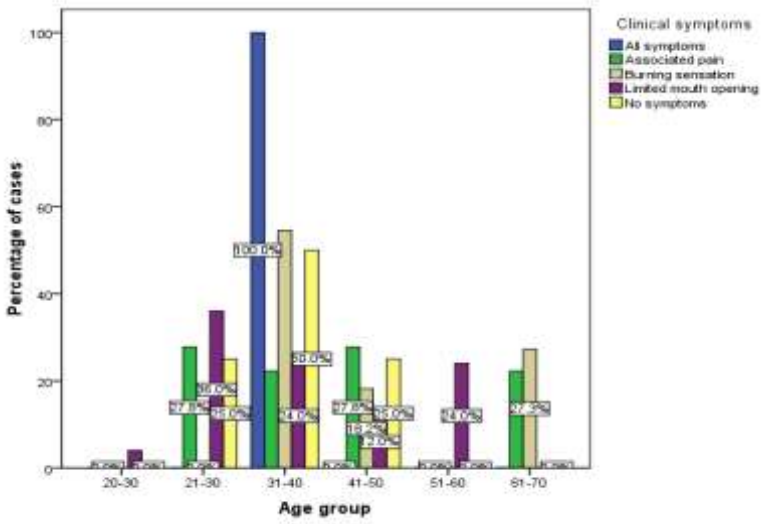

Fig.7: Bar graph representing the association of age groups with clinical symptoms among oral submucous fibrosis patients. X axis represents the age groups and Y axis the percentage of cases. Overall symptoms were more prevalent among the 31-40 age group. Chi square analysis showed statistical significance with (Chi square value 31.909) p=0.044 (p<0.05), indicating a significant increase in all symptoms and burning sensation among those belonging to 31-40 years of age.