RESEARCH ARTICLE

Effect of Frequency and Duration of Tobacco Use on Oral Mucosal Lesions – A Cross-Sectional Study among Tobacco Users in Hyderabad, India

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Abstract

Purpose: Tobacco use is one of the most important risk factors for the development of oral mucosal lesions including oral pre-cancer and cancer. The type and location of the lesion varies with the type of tobacco used, the way it is used, and the frequency and duration of use. Hence, the present study aimed to determine the effect of frequency and duration of tobacco use on oral mucosal lesions among tobacco users in Hyderabad city. **Materials and Methods:** A cross-sectional study was carried out among 280 tobacco users who were categorized into smokers, chewers and mixed groups according to the habit. One forty subjects diagnosed with Oral Mucosal Lesions, designated as cases and One forty lesion free controls, frequency matched for age, gender, habit and family income were assessed. The study protocol included a visual oral soft tissue examination and a questionnaire-based interview. Statistical analysis was done using Chi square test and t- test. Multiple logistic regression analysis was done to assess the association of the variables with lesions. **Results:** Oral submucous fibrosis (18%) was the most common oral mucosal lesion followed by Leukoplakia (14%) and Smoker's palate (12%). Dose-response relationships were observed for both duration and frequency of habits on the risk of oral mucosal lesions. However, it was significant only for frequency of the habit. A significant positive correlation was observed between occurrence of lesion and those with no education (p=0.005). **Conclusion:** The study revealed that frequency and duration of tobacco use was associated with the risk of oral mucosal lesions.

Keywords: Tobacco- dose-response relationship- habits- oral mucosal lesions

Introduction

Oral health contributes to personal well-being and quality of life. It plays an essential role in the pursuit of health. Oral diseases bother humans of all ages and pragmatically, no individual in the course of their lifetime escapes from dental/oral diseases (Singh et al., 2016).

Oral cavity is prone for a myriad of changes with advancing age and also as a result of numerous environmental and life-style related factors such as unhealthy diet, tobacco use etc. Oral mucosal lesions can arise as a result of infections, local trauma or irritation, systemic diseases and excessive consumption of tobacco, betel quid and alcohol (Sridharan, 2014). Tobacco use is one of the most potential risk factors for the development of oral mucosal changes including oral pre-cancer and cancer (Lodha et al., 2015).

In India, tobacco was introduced by the Portuguese about 400 years ago and it has swiftly become a part of socio-cultural milieu in various communities since then (Sridharan, 2014). Now, India is world's third largest tobacco growing country and second largest consumer of tobacco products in the world (Shaik et al., 2016). According to Global Adult Tobacco Survey (GATS), India 2010, the prevalence of tobacco use among Indian adults is 35%. Smoking tobacco in the form of cigarettes or bidis is a common practice in India and a major chewing form is pan with tobacco. Dry tobacco-areca nut preparations such as paan masala (mixture of betel leaf with lime, areca nut, clove, cardamom, mint and tobacco essence in the form of granules), gutkha(crushed betel nut, tobacco and sweet or savory flavorings) and mawa(thin shavings of areca nut with the addition of some tobacco and slaked lime wrapped in a cellophane paper) are also popular and extremely addictive. Thousands of chemical compounds are detected in both smoked as well as smokeless form of tobacco which act not only as irritants and toxins, but also are deadly carcinogens. Nicotine, an alkaloid, is mainly accountable for addiction, which along with tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons, and many others act as potent carcinogens (Kumar et al., 2016).

Smoking and tobacco chewing have been positively associated with oral lesions such as leukoplakia, oral

submucous fibrosis and oral lichen planus, which have the potential for malignant transformation. (Yen et al., 2007). The type and location of the lesion varies with the type of tobacco used, the way it is used, and the frequency and duration of use (Behura et al., 2015). Though few studies (Chandra and Govindraju, 2012; Garcia-Pola Vallejo et al., 2002; Kaugers et al., 1992; Narasannavar et al., 2014) have attempted to assess the prevalence of oral mucosal lesions; a search of literature revealed scarcity of studies to assess the dose-response relationship in terms of duration and frequency of habits associated with oral mucosal lesions in Hyderabad city.

Henceforth, the present study is an attempt to assess the effect of frequency and duration of tobacco use on Oral mucosal lesions among tobacco users in Hyderabad city, Telangana.

Materials and Methods

A cross-sectional study was carried out to determine the association of oral mucosal lesions in a cohort of dental patients with smoking and/or chewing habits. Ethical approval was obtained from the Institutional Review Board of Panineeya Institute of Dental Sciences and Research Centre (PMVIDS and RC/IEC/PHD/ PR/0068). All the patients were informed regarding the study and written consent in the local language was obtained. Anonymity and confidentiality of respondents was maintained and participation was voluntary. The study conforms to the STROBE guidelines for observational study design (Elm et al., 2007).

Subjects aged 18 years or more with smoking and/ or chewing habits attending the Out Patient Department, Department of Oral Medicine and Radiology of Panineeya Institute of Dental Sciences were included in the study. The study was carried out for a period of 4 months from February 2015 to May 2015. Smokers were defined as daily or almost daily smokers, who had smoked at least 100 pieces of cigarettes in their lifetime as elucidated in the tobacco glossary by the Centers for Disease Control and Prevention (CDC). Tobacco/betel nut/betel quid chewers were defined as daily or almost daily chewers, who had the habit for at least six months. People not willing to participate, those with the habit of alcohol and those with infections, local trauma/irritation or systemic diseases that cause oral lesions were excluded from the study. Based on the habits, the study group was categorized into smokers, chewers and mixed (smoking + chewing).

The study protocol included a visual oral soft tissue examination and a questionnaire-based interview. The questionnaire included demographic details like age, gender, educational status and monthly income. Details of the habits such as duration in years and frequency were recorded.

Clinical Oral Examination

All the subjects were clinically examined by a single examiner who was trained in the Department of Oral Medicine for 4 weeks. The clinical diagnosis was established based on the criteria as provided by the epidemiology guide for the diagnosis of oral mucosal

diseases by the World Health Organization (Kramer et al., 1980). Digital palpation using necessary precautions was done to gain an idea of the texture of the tissues of particular lesions. Additionally, scalpel biopsies were performed for those requiring further diagnosis to establish a definitive histopathological diagnosis.

A total of 280 subjects constituted the study population as obtained by convenience sampling. One hundred and forty subjects diagnosed with oral mucosal lesions designated as "cases" and 140 lesion-free "controls", matched for age, gender, habit and family income were assessed during the study. The 140 "cases" and 140 "controls" were distributed as follows:

Smokers group had 50 "cases" and 50 "controls"
Chewers group had 50 "cases" and 50 "controls"
Mixed group has 40 "cases" and 40 "controls".

Statistical Analysis: Statistical analysis was done utilizing Statistical Package for Social Sciences Software (SPSS Version 20.0). Comparison of cases and controls was done using t-test. Association between frequency and duration of habits in cases and controls was estimated using Chi square test. Simple and multiple logistic regression analysis was carried out to study the effect of variables on the probability of developing lesions. The level of significance was set at 0.05.

Results

A total of 280 subjects comprising of 272 (97%) males and 8 (3%) females, aged between 20-65 years constituted the study population. The majority of the cases belonged to 50-59 year age group (40; 28.5%), finished secondary education (43; 31%) and had a monthly income of Rs.5001-10,000/- (69; 49%). (Table-1)

The mean ± standard deviation was calculated and compared for cases and controls and the difference was found to be statistically significant both for duration (p=0.05*) and frequency of tobacco use. (p=0.0001*). (Table-2)

Among smokers, smokers melanosis and smokers palate (18%) were found to be most common followed by Leucoedema and Leukoplakia (10%). Whereas, Oral sub-mucous fibrosis (30%) was most common among chewers followed by Leukoplakia (18%) and Carcinoma (14%). Among the mixed group, most common lesions were sub-mucous fibrosis and Leukoplakia. Overall, most of the cases were affected with oral sub-mucous fibrosis (18%) followed by Leukoplakia (14%) and smokers palate (12%) (Table-3).

It was observed that 18% of the cases smoked more than 15 cigarettes / day compared to only 4% of the controls. A significant association was observed between frequency of smoking and the occurrence of oral mucosal lesions among cases (p= 0.003*). Among the chewers group, none of the cases had limited chewing tobacco to one time / day. Moreover, 22% of the cases chewed more than 15 times / day compared to only 2% of the controls. Therefore, it was found that the association between frequency of smokeless tobacco usage and the presence of oral mucosal lesions was highly significant (p= 0.0002*). Even though it was noticed that none of the controls had

Effect of Tobacco on Oral Mucosal Lesions

Table 1. Demographic Distribution of the Entire Study Subjects

Characteristics	No of respondents n (%)		p-value
	Cases	Controls	
Age groups			
20-29 yrs	18 (12.8)	18 (12.8)	0.99
30-39 yrs	37 (26.4)	37 (26.4)	
40-49 yrs	32 (22.8)	32 (22.8)	
50-59 yrs	40 (28.5)	40 (28.5)	
+ 60 yrs	13 (9.2)	13 (9.2)	
Gender			
Male	136 (97.1)	136 (97.1)	1
Female	4 (2.9)	4 (2.8)	
Education			
No Education	39 (27.8)	17 (12.1)	0.005*
Primary Education	29 (20.7)	35 (25.0)	
Secondary Education	43 (30.7)	45 (32.1)	
High School	13 (9.2)	11 (7.8)	
Graduation	16 (11.4)	32 (22.8)	
Monthly Income			
<5,000	29 (20.7)	29 (20.7)	1
5,001-10,000	69 (49.2)	69 (49.2)	
>10,000	42 (30.0)	42 (30.0)	

*p≤0.05 Statistically significant.

the habit of smoking / chewing more than 15 times / day, more controls (60%) smoked / chewed 2-5 times / day when compared to cases (47.5%). But there was no significant association found among frequency of mixed habits and oral mucosal lesions (Table 4)

While majority of the cases (14; 28%) had been smoking for duration of 11-20 years, 36% of the controls smoked for duration of less than 5 years. It was observed that equal number (20; 40%) of cases and controls among chewers group had the habit for duration of 5-10 years. Whereas, 8 (16%) of the cases chewed for more than 30 years when compared to only 1 (2%) among the controls. Among mixed group, both cases and controls reported to smoke and chew for comparable durations. Surprisingly, no significant association was found between duration of smoking, smokeless and mixed habits and the presence of oral mucosal lesions (Table 5).

Simple logistic regression analysis showed no significant association between age and the presence of lesions. Whereas a highly significant association was found for subjects with no education (p= 0.0001*) and the occurrence of lesions with a risk of 4.6 times (Odds Ratio, OR=4.59) than those who finished graduation.

Table 2. Comparison of Controls and Cases with Mean of Duration and Frequency

Variable	Groups	Mean± SD	P-value
Duration	Controls	2.30±1.08	0.0311*
	Cases	2.60±1.23	
Frequency	Controls	2.09±0.86	0.0001*
	Cases	3.01±1.19	

*p≤0.05 Statistically significant.

Table 3. Distribution of Oral Mucosal Lesions Based on Habits

Oral Mucosal Lesions	Habit			Total
	No of respondents n (%)			
	Smoking	Smokeless	Mixed	
Carcinoma	1 (2.0)	7 (14.0)	4 (10.0)	12 (8.5)
Leukoplakia	5 (10.0)	9 (18.0)	6 (15.0)	20 (14.2)
Lichen Planus	1 (2.0)	2 (4.0)	1 (2.5)	4 (2.8)
Submucous fibrosis	4 (8.0)	15 (30.0)	6 (15.0)	25 (17.8)
Candidiasis	3 (6.0)	5 (10.0)	1 (2.5)	9 (6.4)
Smokers melanosis	9 (18.0)	1 (2.0)	5 (12.5)	15 (10.7)
Smokers palate	9 (18.0)	0	8 (20.0)	17 (12.1)
Tobacco pouch Keratosis	0	4 (8.0)	0	4 (2.9)
Pan chewers lesion	0	1 (2.0)	0	1 (0.7)
Leukoedema	6 (12.0)	0	5 (12.5)	11 (7.9)
Others	12 (24.0)	6 (12.0)	4 (10)	22 (15.7)
Total	50	50	40	140

Subjects who had the habit for a duration of >30 years were reported to be at a risk of more than 3 times (OR=3.05) as compared to those who smoked / chewed for < 5 years. This finding was statistically significant (p=0.03*). Based on frequency, increased risk of lesions was reported with increased frequency. Though higher risk was observed for habit frequency of > 15 times/day (OR= 0.42), significant difference was reported only for the lesser frequency domains i.e., 2-5times/day (p=0.0001*), 6-10times/day (p=0.0001*) and 11-15times/day (p=0.02*).

Multiple logistic regression analysis for all the habits as a whole for age groups revealed that subjects aged 30-39 years were at a higher risk (OR= 0.69) and 50-59 years age group at a lower risk (OR= 0.31) of developing lesions.

Table 4. Association between Frequency of Smoking, Smokeless and Mixed Habits in Controls and Cases

Habits	Frequency	Controls	Cases	P-value
Smoking	1	12 (24.0)	4 (8.0)	0.0036*
	2-5	30 (60.0)	17 (34.0)	
	6-10	5 (10.0)	11 (22.0)	
	11-15	1 (2.0)	9 (18.0)	
	>15	2 (4.0)	9 (18.0)	
	Total	50	50	
Smokeless	1	9 (18.0)	-	0.0002*
	2-5	25 (50.0)	13 (26.0)	
	6-10	13 (26.0)	16 (32.0)	
	11-15	2 (4.0)	10 (20.0)	
	>15	1 (2.0)	11 (22.0)	
	Total	50	50	
Mixed	1	9 (22.5)	5 (12.5)	0.1884
	2-5	24 (60.0)	19 (47.5)	
	6-10	4 (10.0)	9 (22.5)	
	11-15	3 (7.5)	5 (12.5)	
	>15	-	2 (5.0)	
	Total	40	40	

*p≤0.05 Statistically significant.

Table 5. Association between Duration of Smoking, Smokeless and Mixed Habits in Controls and Cases

Habits	Duration	Controls	Cases	P-value
Smoking	<5 years	18 (36.0)	12 (24.0)	0.3276
	5-10 years	17 (34.0)	13 (26.0)	
	11-20 years	9 (18.0)	14 (28.0)	
	21-30 years	3 (6.0)	7 (14.0)	
	>30 years	3 (6.0)	4 (8.0)	
	Total	50	50	
Smokeless	<5 years	10 (20.0)	7 (14.0)	0.1352
	5-10 years	20 (40.0)	20 (40.0)	
	11-20 years	13 (26.0)	12 (24.0)	
	21-30 years	6 (12.0)	3 (6.0)	
	>30 years	1 (2.0)	8 (16.0)	
	Total	50	50 ()	
Mixed	<5 years	8 (20.0)	8 (20.0)	0.7733
	5-10 years	13 (32.5)	14 (35.0)	
	11-20 years	15 (37.5)	11 (27.5)	
	21-30 years	1 (2.5)	3 (7.5)	
	>30 years	3 (7.5)	4 (10.0)	
	Total	40	40	

*p≤0.05 Statistically significant.

However, only the latter was found to be significant. Based on education, increased risk of lesions was seen among those with no education. But this difference was not significant. When comparison was done based on duration, higher risk was observed among those who had the habit for 5-10 years but this finding was not significant. Based on frequency, significant findings were noticed for all the domains with subjects with habit frequency of >15 times/day at the highest risk of developing lesions (OR= 65.91) (Table 6).

When comparison was done individually for each habit, with regard to age groups, increased risk of lesions was observed for 30-39 years age group among smoking and mixed habits (OR= 0.64 and 0.41 respectively). On the other hand, 40-49 years age group was at higher risk (OR= 1.69) among smokeless habit. However, these findings were not significant based on age groups. Based on education, subjects with no education were at higher risk among smoking and mixed habits (OR= 12.19 and 56.27 respectively) but this difference was significant only for mixed habits. Moreover, significant association was found for secondary education and high school domains among smoking habit and for graduation domain among mixed habits group with the least risk of lesions. For smoking and smokeless habits, higher odds ratio (OR= 0.78 and 0.62 respectively) was reported for

Table 6. Simple Logistic Regression Analysis by Different Variables as a Whole

Characteristics	OR	p-value
Age groups		
20-29 yrs	Ref.	
30-39 yrs	0.92	0.84
40-49 yrs	0.95	0.896
50-59 yrs	0.95	0.892
+ 60 yrs	0.95	0.916
Education		
No Education	4.59	0.0001*
Primary Education	1.66	0.202
Secondary Education	1.91	0.083
High School	2.36	0.093
Graduation	Ref.	
Alcohol (No vs Yes)	1.26	0.339
Duration		
<5 years	Ref.	
5-10 years	1.25	0.488
11-20 years	1.33	0.404
21-30 years	1.73	0.263
>30 years	3.05	0.0320*
Frequency		
1	Ref.	
2-5	0.04	0.0001*
6-10	0.09	0.0001*
11-15	0.22	0.0260*
>15	0.55	0.429

*p≤0.05 Statistically significant.

Table 7. Multiple Logistic Regression Analysis by Different Variables as a Whole

Characteristics	p-value	OR
Age groups		
20-29 yrs		Ref.
30-39 yrs	0.464	0.69
40-49 yrs	0.316	0.57
50-59 yrs	0.0500*	0.31
60+ yrs	0.194	0.35
Education		
No Education	0.846	0.92
Primary Education	0.371	0.62
Secondary Education	0.184	0.37
High School	0.357	0.49
Graduation		Ref.
Alcohol (No vs Yes)	0.898	0.96
Duration		
<5 years		Ref.
5-10 years	0.846	0.92
11-20 years	0.371	0.62
21-30 years	0.184	0.37
>30 years	0.357	0.49
Frequency		
1		Ref.
2-5	0.0340*	2.62
6-10	0.0001*	8.66
11-15	0.0001*	27.62
>15	0.0001*	65.91

*p≤0.05 Statistically significant.

habit duration of 5-10 years. Whereas for mixed habits, it was observed to be higher for those with habit duration of 21-30 years (OR= 5.95). However, none of these findings were significant. When comparison was done based on frequency, highest risk was reported for habit frequency of >15times/day for both smoking and mixed habits (OR= 106.73 and 12.71 respectively). Among smokers, a highly significant association was seen for all the domains except for frequency of 2-5/day. Whereas for mixed habits, it was significant only for the frequency domain >15 times/day (Table 7).

Discussion

The tobacco epidemic is expanding especially in developing and less developed countries adding significantly to their burden of disease and poverty. India is in the second phase of tobacco epidemic with nearly one million persons dying due to a very high prevalence of chewing and smokeless tobacco use in the country. Tobacco harms economy and sustainable development as the tobacco use prevalence is high among the lower income groups (GATS India, 2009-10).

A variety of oral mucosal lesions and conditions are associated with the habit of smoking and chewing tobacco, and many of these carry a potential risk for the development of cancer. Studies (Al-Maweri et al., 2014; Aruna et al., 2011; Yen et al., 2007) highlighted that the initiation and progression of oral lesions was dependent on the type of tobacco product, duration and the frequency of tobacco use. With this background, the present study was conducted to find the effect of frequency and duration of tobacco use on oral mucosal lesions.

The present study comprised of 280 tobacco users of which 97% were males and 3% were females. Male predominance was also reported in studies by Saraswathi et al., (2006) and Behura et al., (2015). This might be due to the fact that several occupations of men require a substantial amount of physical energy and a high level of concentration like in case of drivers with odd working hours. This can be stressful, which in conjunction with peer pressure can lead to the initiation of deleterious oral habits (Sujatha et al., 2012). Majority of the lesion affected tobacco users belonged to 50-59 year age group. This finding matches with the analysis of the National Health and Nutrition Examination Survey (NHANES) database which emphasized that the chance of a lesion being present increased with age, thus suggesting tobacco use in older age as a significant predictor of oral lesions (Rani et al., 2003).

Among the 50 oral mucosal lesions found in smokers, Smoker's melanosis and smoker's palate were the most frequently encountered lesions (18%) and this finding was compatible with that of previous studies by Saraswathi et al., (2006), Hedin et al., (1993) and Sujatha et al., (2012). Among chewers, Oral Submucous Fibrosis was found to be most common, followed by Leukoplakia. Similar finding was observed by Gupta et al (2014) and Reddy et al., (2015). Irrespective of the type of habit, Oral Submucous Fibrosis followed by Leukoplakia were the most commonly encountered lesions among cases. This

was consistent with the findings of Patil et al., (2013) and Sujatha et al., (2012).

According to a study by the World Health Organization (WHO), a majority of those dying due to smoking are illiterates. By the same token, a highly significant association was found for subjects with no education. It is likely that less educated people are less aware of the health hazards of tobacco consumption and often find themselves in conditions predisposing them to initiation of smoking and chewing of tobacco. Therefore, they are more likely to have higher degree of fatalism or higher overall risk taking behavior (Bobak et al., 2000; Rani et al., 2003).

With regard to duration of the tobacco habit among cases and controls, it was noticed that majority of the cases had the habit for longer duration when compared to controls showing that duration of tobacco use has an effect on oral mucosal lesions. But, to our surprise, this finding was not found to be significant in our study. This was in agreement with a study done by Reddy et al., (2015) which stated that the frequency, rather than the total duration of the habit is directly related to oral lesions. However, few studies (Behura et al., 2015; Sujatha et al., 2012) remarked a significant association between duration of tobacco use and oral lesions.

A significant association was observed between frequency of tobacco use and the occurrence of oral mucosal lesions with majority of the cases using tobacco for more than 15 times per day. The possible rationale behind this is that, long term contact of tobacco with the oral mucosa induces variety of changes which could be due to prolonged exposure to the carcinogen itself or as a protective mechanism of the oral cavity.

The study has certain limitations which include potential information bias, as self-reporting by the patients might have led to underreporting of tobacco use. Another flaw could be detection bias, as the researcher was aware of the habit history of the subjects prior to oral examination.

In conclusion, the present study findings provide information on the association of Oral Mucosal lesions among tobacco users. Dose-response relationships were observed both for duration and frequency of habits on the risk of oral mucosal lesions, and higher frequency, in particular, as a significant predictor of risk in the case population. The study highlighted lack of education as a significant risk indicator of developing habits predisposing themselves to fatal lesions. Therefore, awareness campaigns to educate vulnerable population and necessary interventions to eliminate the use of tobacco preparations are highly recommended.

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