



Evaluating the Effects of Frequency and Duration of Tobacco Use on Oral Mucosa in Patients Visiting Hamdard University Dental Hospital

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ABSTRACT

Background: Use of tobacco in any form (smoke or smokeless) is one of the most popular habits around the globe that over one billion people routinely consume tobacco products like cigarettes, chalia, pan, niswar. Almost 23.9 million Pakistani adults currently use tobacco in any form like cigarettes smoking, betel nut, betel quid, pan chalia are all well recognized habits in developing oral lesions including precancerous and cancerous lesions like smokers melanosis, submucous fibrosis, lichen planus, leukoplakia, squamous cell carcinoma etc. Location and type of oral mucosal lesions varies with the way tobacco is consumed along with its frequency and duration.

Objectives: Objective of the current study is to assess the effects of frequency and duration of tobacco (smoke and smokeless) use on oral mucosa among patients reported at Hamdard university dental hospital.

Methods: The study designed as case-control and data has been collected from 280 individuals who were tobacco users categorized in groups of smokers, chewers and mixed according to their habits. Half of the subjects were assigned as cases (diagnosed with oral mucosal lesion) and the remaining half assigned as controls (who were lesion free). The study protocol includes questionnaire-based interview along with clinical examination of Oral cavity. Statistical assessment has been performed with SPSS 16.0 software guided with *chi-square* test and association of the variables with the lesions would be assessed through multiple logistic regression analysis.

Results: Eight different types of mucosal lesions noticed in the oral cavity among patients who have habits of smoking (cigrates), chewing (betel nuts) and mixed habits (smoking and chewing). Out of which leukoplakia found to be the commonest lesion within oral cavity following OSF (Oral Submucous Fibrosis) and smoker's melanosis).

Conclusion: Outcomes of this study shows valuable data on association of oral lesions in patients who were involved in the habits of smoking, chewing and both (mixed). Few precancerous and cancerous conditions like oral squamous cell carcinoma were also encountered along with other mucosal lesions.

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Males were more prevalent in these habits than females therefore the majority of the lesions found in men. Moreover, increase in the frequency and duration of habits significantly increases the risk of developing lesions in case population.

Keywords: Tobacco; Habits; Oral mucosal lesions; Case population

INTRODUCTION

Oral health is one of the essential elements that contribute to individual prosperity and personal satisfaction. Diseases that involve oral cavity are so widespread that it affects a large number of the population including any age group or gender. Lining of oral cavity comprises of keratinized and non-keratinized epithelium which provide protection against any insult and also play important functions of protection, secretion and sensation [1]. Compromised oral health puts deleterious effects on general prosperity and balance the healthy life of an individual. Oral wellbeing is influenced by conditions including tooth decay, dental cavities, periodontal disease and tooth loss. In light of the global burden of disease study 2019 estimated that oral diseases affect 3.5 billion individuals worldwide [2]. Abnormalities in oral mucosa may occur either due to infections, local factors like irritation or trauma, systemic illness and increased use of chewing or smoked tobacco, betel nuts, betel quid and alcoholism. Habits of chewing tobacco like betel nuts, areca and pan chalia are essential components of the cultural material in many parts of the world that approximately represent 20% of world population and these components are very common almost in all ages [3]. Cigarettes/cigars has become the most popular mode of smoking and is routinely used by over one billion people in the world. This habit/practice may have begun as early as 5000-3000 BC [4]. Tobacco use stands as the most frequent cause of mortality worldwide that accounts for more than 6 million deaths per year. It is considered as a serious health hazard for numerous medical problems, including chronic diseases like cardiovascular and chronic respiratory diseases, lung cancers and oral lesions [5].

Tobacco induced mucosal lesions usually affect oral cavity and have established association with tobacco intake in any form are leukoplakia, erythroplakia, Oral Submucous Fibrosis (OSF), Smoker's palate, lichen planus are known to have a high risk of developing malignant lesions [6]. Site and type of mucosal lesion vary with the way the tobacco is used in respect to frequency and duration. In Pakistan, chewing tobacco is dominant which include pan masala, gutka, mawa, snuff and main pori and their extensive use in the community lead to oral cancers [7]. Other south Asian countries also have higher rate of consumption of smokeless tobacco and areca nut [8].

Smoke tobacco in any form like cigarettes and smokeless tobacco in any form like gutka or betel nuts contains several potent nitrosamines. These chemicals have deleterious effects on oral mucosa and may promote specific types of precancerous and cancerous lesions [9]. The potential risk of oral cancers rises with age, tobacco usage and alcohol intake

and it poor prognosis primarily due to late reporting and missed diagnosis by the health care providers [10].

A study was conducted in Karachi 2012, Aim to evaluate the relationship between Oral Squamous Cell Carcinoma (OSCC) with different chewing habits and concluded that various forms of tobacco chewing habits lead to OSCC within 5-10 years of exposure time [11]. Another, multicenter cross-sectional study was completed in Karachi 2015, showed an Association of oral submucous fibrosis with frequency and consumption of Areca Nut and its Derivatives in patient's of varying ages. Conclusion reveals that chances of developing Oral submucous fibrosis increased as duration and frequency of areca nut consumption increased especially from early age [12].

After taking all these deleterious effects of chewable and non-chewable tobacco under consideration, this study was conducted to evaluate the effects of frequency and duration of tobacco use on oral mucosa in patients visited outpatient department of Hamdard university dental hospital, Karachi.

MATERIALS AND METHODS

The study designed as a case control study to assess the effects of exposure (tobacco consumption in the form of smoke, smokeless tobacco/betel nuts or mixed form) on oral mucosa in patients who came to hospital for seeking dental treatment and with history of tobacco usage [13]. Sum of 280 patients has been selected to include in the study through Systematic random sampling and data was drawn from Dec 2020 to March 2021. Every participant of the study would be informed, given verbal consent and complete a questionnaire-based interviews.

Inclusion Criteria

Both individuals (male/female) age 18 years or above but not more than 60 years, consent to give detail history and Dental examination. Patients who have practiced tobacco consumption minimum for a period of 1 year and still actively continuing this habit and can undergo biopsy procedure if needed.

Exclusion Criteria

Both individuals (male/female) age below 18 years and above 60 years, not consent to give detail history and examination [14]. Any patient with systemic disease, taking medication and give up habit of tobacco usage in the past 1 year. Also, patients who were refuse to undergo biopsy procedure if needed were excluded.

Confidentiality of respondents were maintained and participation solely voluntary. The study was carried out at Hamdard university dental hospital, Karachi after having a formal ethical approval from the competent authority of Hamdard University. All patients were examined clinically by a specialist examiner in the Department of Oral Medicine. Clinical diagnosis would be made by following criteria available in the epidemiology guide for diagnosing oral mucosal diseases by the world health organization [15].

Sample size calculation of the study had been done by open epi software and half of the study participants were categorized as cases (those diagnosed with oral mucosal lesion and using tobacco) and half of the subjects categorized as controls (those who were lesions free and using tobacco), matched for age, gender, habits and duration. Distribution of sample would be equal *i.e.*, 140 cases and 140 controls [16].

Based on habits, the study group (controls and cases) further divided into smoker's group, chewers group and mixed group (smoking+chewing).

RESULTS

In the current study, a sum of 280 individuals/patients aged between 18-60 years were participated, comprising of 272 (97%) males and 8 (3%) females in both categories (*i.e.* Case and Control group) constituted total study population [17]. Majority of the patients in both categories belonged to 51-60 years of age group (48;34%) had completed secondary education (88,32.5%) (Table 1).

Table 1: Distribution of the study participants by their basic characteristics.

Demographic characteristics	No of respondent's n (%)		p-value*	
	Cases	Controls		
Age groups	18-28 years	23 (16%)	23 (16%)	0.99
	29-39 years	37 (26%)	37 (26%)	
	40-50 years	32 (22.8%)	32 (22.8%)	
	51-60 years	48 (34%)	48 (34%)	
Gender	Male	136 (97%)	136 (97%)	1
	Female	4 (3%)	4 (3%)	
Education	No education	37 (27%)	16 (12%)	0.005
	Primary education	27 (20%)	35 (25%)	
	Secondary education	43 (31.8%)	45 (33%)	
	High school/college	10 (7%)	11(7.8%)	
	Graduation	15 (11%)	30 (22%)	

In our study, smoker's melanosis and smoker's palate (28%, 24%) were identified as most common lesions followed by leucoedema and leukoplakia among smoker's group [18]. Among the group of tobacco chewers, oral sub-mucous fibrosis (38%) was the most widely recognized lesion followed by Leukoplakia (24%) and Carcinoma (14%). Whereas among the mixed group, oral submucous fibrosis and leukoplakia

were found to be the most common lesions. Altogether, the most frequently reported lesions were of leukoplakia (22%) followed by oral submucous fibrosis (19%) and smoker's palate (14%) (Table 2).

Table 2: Distribution of mucosal lesion with respect to particular habits.

Oral mucosal lesions	Habits						Total
	Smokers		Chewer		Mixed		
	n	%	n	%	n	%	
Leukoplakia	10	20.00%	12	24%	10	23%	32 (22%)

Oral submucous fibrosis	1	2%	19	38%	7	17.50%	27 (19%)
Lichen planus	0	0	7	14%	2	5%	9 (6%)
Squamous cell carcinoma	0	0	9	18%	4	10%	13 (9%)
Smoker's melanosis	14	28.00%	0	0	5	12.50%	19 (13%)
Smoker's palate	12	24.00%	0	0	8	20%	20 (14%)
Leucoedema	10	20.00%	0	0	4	10%	14 (10%)
Tobacco pouch Keratosis	3	6%	3	6%	0	0	6 (4%)
Total	50		50		40		140

Weight means \pm standard deviation of frequency and duration of consuming tobacco in any form between control and cases categories was measured [19]. The contrast among the methods seen to be well significant (**Table 3**).

Table 3: Assessment between controls and cases mean of duration and frequency.

Groups	Variable	Weighted mean \pm standard deviation	P-value
Controls	Duration	2.30 \pm 1.08	0.0311*
Cases		2.60 \pm 1.23	
Controls	Frequency	2.09 \pm 0.86	0.0001*
Cases		3.01 \pm 1.19	

Smoker's Group

As the sample size of our study constitutes 97% of those patients who were males and only 3% were females, therefore only males have been taken into consideration for comparison [20].

Observing the length of smoking habits (**Table 4**), displayed significant Odds Ratio (OR) of 53 in those patients having

smoking history for over 30 years with highly significant p value *i.e.*, $p=0.001$, signifying 53 times higher risk of developing lesions in the cases population when contrasted with controls.

Table 4: Estimation of risk in patients with smoking habit and dose response relationship when consider duration of smoking.

Duration	Cases/Controls	Odds ratio (%CI)	p-value
Less than 5 years	0/10	-	0.02
5-10 years	14-May	3.87	0.04
11-20 years	12-Sep	1.38	0.37
21-30 years	18/7	4.25	0.03
>30 years	13/2	53.1	0.001*

Note: *Highly significant, 95% CI=95% Confidence Interval

Considering **Table 5** displays frequencies in smokers who smokes 11 to 15 times and those who smoke more than 15 cigarettes/bidi/huka each day had significant Odds Ratio (OR)

of 4.68 and 22.9 respectively with highly significant p value *i.e.*, $p=0.004$ and $p=0.001$ respectively in each segment.

Table 5: Estimation of risk in smokers and dose response relationship when consider frequency of smoking.

Frequency	Cases/Controls	Odds ratio (95% CI)	p-value
1	0/1	-	0.47
5-Feb	16-Apr	0.13	0.001*
10-Jun	19-Aug	0.23	0.26
15-Nov	10-May	4.68	0.004*
>15	28/6	22.97	0.001*

Note: *Highly significant; 95% CI=95% Confidence Interval

Chewer's Group

Results of **Table 6** reveals significant Odds Ratio (OR) of 4.67 for individuals who had been consuming tobacco in chewable

form for 21-30 years ($p=0.02$) suggesting 4.67 times greater risk of getting a lesion.

Table 6: Estimation of risk in patients with chewing habits and dose response relationship in respect to span of chewing tobacco.

Duration	Cases/Controls	Odds ratio (95% CI)*	p-value
<5 years	11-Feb	0.29	0.06
5-10 years	16-Mar	0.31	0.02
11-20 years	13-Sep	2.1	0.09
21-30 years	3-Jun	4.67	0.03
>30 years	2-Mar	4.31	0.07

Note: *95% CI=95% Confidence Interval

On the other hand, frequency of chewing habit shows significant Odds Ratio (OR) of 8.95 in individuals who uses 11–15 sachets of betel nut/gutka/mawa/pan per day (**Table 7**).

Table 7: Estimation of risk in patients with chewing habits and dose response relationship in respect to frequency of chewing tobacco.

Frequency	Case/Control	Odds ratio (% CI)*	p-values
1	12-Feb	0.2	0.09
5-Feb	24-Oct	0.32	0.02
10-Jun	15/9	5.3	0.001
15-Nov	1-Apr	8.95	0.02

Note: *95% CI=95% confidence interval

Mixed Group

Considering the duration of mixed habits *i.e.*, smoking and chewing, **Table 8** displays substantial risk for individuals who had been chewing along with smoking for over 30 years ($p=0.001$) [21]. On the other hand, **Table 9** shows frequencies

in individuals who smokes and chew tobacco more than 15 times each day had significant odds ratio of 10.4 and $p=0.001$.

Table 8: Estimation of risk in patients with mix of propensities *i.e.*, smoking and chewing and dose response relationship when considering duration.

Duration	Cases/Controls	Odds ratio (%CI) [*]	p-values
<5 years	10-Feb	0.25	0.02
5-10 years	13-Mar	0.37	0.001
11-20 years	10-May	1.24	0.48
21-30 years	4-Jul	2.63	0.1
>30 years	Aug-00		0.001

Note: ^{*}95% CI=95% Confidence Interval

Table 9: Risk estimation in patients with mix of propensities *i.e.*, smoking and chewing and dose-response relationship when considering frequency.

Frequency	Case/Control	Odds ratio (%CI) [*]	p-values
1	0/1	-	0.001
5-Feb	Apr-35	0.12	0.01
10-Jun	9-Jul	0.13	0.02
15-Nov	1-Feb	1.95	0.51
>15	18/6	10.2	0.001

Note: ^{*}95% CI=95% Confidence Interval

DISCUSSION

The current study was carried out with the background that the initiation and progression of oral mucosal lesions was dependent on the frequency and duration of tobacco use. The current study included 280 patients who were tobacco users of which 97% were males and 3% of females. Male dominance in present study was also highlighted in the past study by Behura [22]. This may be due to the reason that there are several professions of males that need enormous physical energy and concentration like those who drive vehicles in odd working hours. This situation can be stressful and may one of the reason of initiation of harmful oral habits [23]. Majority of the patients having oral lesions affected by tobacco belonged to the age group between 50-59 years. These current finding matches with the survey done by the National Health and Nutrition Examination Survey (NHANES) results which concludes that the occurrence of oral lesion increased with age, thus suggesting use of tobacco in elderly age as an important predictor of oral lesion [24].

Smokers Group

Out of 50 lesions found in oral cavity identified in patients who smokes, Smoker's melanosis was the most habitually discovered oral lesion (28%) and is compatible with the results of former studies conducted by Saraswathi and Sujatha. Smoker's palate (24%) and Leukoplakia (20%) was the

second and third most frequently reported lesions. Oral Squamous Cell Carcinoma (OSCC) was the least [25].

Dose-response assessment had done for duration and frequency of smoking tobacco. Results conclude that cigarettes smoking for over 30 years in terms of duration and smokes for over 15 cigarettes each day in terms of frequency suggested sturdiest analyst of threat in case population.

Chewers Group

Chewing habit is more prevalent in males than females and the finding is steady with the previous research done by Saraswathi and Sinha. Among 50 cases of oral mucosal lesions found in chewers, oral submucous fibrosis was the most commonly reported lesions (38%) and consistent with the findings of Yang. Lichen planus is the least reported cases among this group.

Dose-response analysis had done for both regularity and length of chewing tobacco/betel nuts on developing oral mucosa lesions. Tobacco/betel nuts consumed for 21-30 years were period of maximum risk in males. Further, the daily frequency of chewing tobacco had a significant threat in the case population with the maximum risk associated with consuming of 11-15 packets per day.

Mixed Group

Mixed group of study contains those individuals who have both habits (smoking+chewing) and was dominant in males

than females and the outcome was attuned with previous research by Yang [26,27]. Considering 40 oral mucosal lesions found in mixed group, leukoplakia found to be most frequently reported lesion (22%), which is not consistent through the findings of Yang who stated oral submucous fibrosis as most frequent oral lesion. Smoker's palate (20%) found to be second commonest lesion followed by OSMF (17%). Determining dose-response relationship; it was observed that smoking and chewing for over 30 years had notable hazards. Daily consume of cigarettes and betel nuts (mixed habit) showed a significant risk in case population with greatest threat related with smoking and chewing over 15 times per day.

All cases of mucosal lesions in this study were predominantly evident in males and about 28% cases of Smokers melanosis were seen in smokers and the remaining 12.5% reported in individuals consuming both smoking and chewing tobacco. This finding was similar to the observation made by Hedin in the past [28]. The most prevalent type of smoking habit in our study was filtered cigarette.

In our study, 24% cases of leukoplakia were found in chewers group, 22% in mixed group and 20% found in smokers group signifying link with both tobacco smoking and chewing betel quid/areca nuts. These results were consistent with the outcomes of Yang and Rani [29]. Blends of cigarette+gutka and bidi+gutka were main funders of leukoplakia in mixed group while areca nut in chewers group and cigarettes in smoker's group.

Chewers contribute 38% Oral Submucous Fibrosis (OSMF) and the rest 17.5% contribute by patients having mixed habits and findings were compatible with the results of Shah N and Ariyawardana, et al. Another previous study done by Lee, et al. reported that mixed habits have a higher risk of developing OSMF than chewing habit alone. Results of the present study shows higher prevalence in men as studies conducted by Shah N and Sharma PP, Sinor, Ahmed in India proposed male predominance in OSMF cases whereas Yang, have proposed female dominance. Use of Gutka has considered to be the major risk in initiating and progression of oral submucous fibrosis in this research work followed by Mawa and this observation is in covenant with the results of Hazarey.

Chewing habits in the current study are the main risk in the progression of oral squamous cell carcinoma with 18% of cases followed by 10% of cases in mixed group. Previous studies by Thomas, Hirayama, Reichart and Balaram P, reported chewing habit as the main threat for oral squamous cell carcinoma. In our study, patients who are under the age of 50 years, encounter 23% of the lesions and the rest 34% above 50 years. Tobacco pouch keratosis was exclusively seen in chewers groups proposing betel quid/mawa/gutka chewing as the main risk factor. In this study, lesions similar to Oral Lichen Planus seen in 14% of the chewers and remaining 8% in patients with mixed habits proposing habit of chewing tobacco is main risk factor and this was steady with the results of Daftary.

CONCLUSION

In conclusion, the study results provide data on the association of oral mucosal lesions amongst patients who use tobacco as smokers, chewers and mixed habits. There are 8 habits related to oral mucosal lesions highlighted in this study which also include some possibly malignant conditions and squamous cell carcinoma. Customs are more prevalent in men than women thus more lesions were seen in males. Smoking is a chief risk factor in the progression of smoker's melanosis, smoker's palate and leukoedema whereas chewing habit has greater risk of developing oral submucous fibrosis, Leukoplakia, Squamous cell carcinoma and tobacco pouch keratosis. Mixed habits of chewing and smoking tobacco are the main risk in developing lesions like leukoplakia, smoker's palate and oral submucous fibrosis.

LIMITATIONS

The present study has some limitations which include potential information bias, as self-reporting by the participants might have led to under reporting of tobacco use. There might be an introduction of selection bias as some of the patients were doubtful about his/her age or tobacco usage.

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