ORIGINAL RESEARCH

Patterns of Tobacco Use and its Relation to Oral Precancers and Cancers among Individuals Visiting a Tertiary Hospital in South India

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Abstract

Aim: The aim of this study was to evaluate the use of tobacco and its association with oral precancers and cancers.

Materials and methods: Medical records of 1,007 individuals were assessed for the patterns of tobacco abuse and the presence of tobacco-related oral mucosal alterations.

Results: This study comprised 1,007 individuals (M:F: 95.4%:4.6%). In the cohort, 60.1% had smoking habit and 56.1% had smokeless habit. Of the bidi smokers, 18.2% developed carcinoma, 14.3% developed leukoplakia, which is statistically significant ($p < 0.001$). A logistic regression analysis of the development of oral submucous fibrosis (OSMF) shows that habit of smokeless forms of tobacco has an odds ratio (OR) of 18+ when compared with smoking. Combination of bidi and gutkha had 12.3 times higher risk of developing oral cancer and 4.4 times risk of developing leukoplakia. A total of 33.3% betel quid and gutkha chewers presented with tobacco pouch keratosis, which is statistically significant.

Conclusion: Smoked and smokeless forms of tobacco were equally popular among the study population. The packeted form of smokeless tobacco (gutkha) was more prevalent. Oral submucous fibrosis was more common than leukoplakia, and oral cancer developed more frequently in elderly men smoking bidis.

Clinical significance: This study throws light on the fact that the use of both smoke and smokeless forms of tobacco is still prevalent, and the use of gutkha was most prevalent. These findings will help tobacco cessation and counseling centers to focus their effort in motivating people to stop gutkha chewing habit. This also brings to the forefront the need to create better treatment strategies to manage OSMF.

Keywords: India, Oral cancer, Oral precancers, Prevalence, Tobacco.

The Journal of Contemporary Dental Practice (2020): 10.5005/jp-journals-10024-2791

Introduction

India is considered the oral cancer capital of the world with 80,000 new cases diagnosed annually and 52,000 oral cancer-related deaths registered per year.[1,2] Thirty-eight percent of the malignancies of the oral cavity arise from premalignant lesions such as leukoplakia, erythroplakia, and oral submucous fibrosis (OSMF).[3,4] Tobacco-related cancers are expected to increase the total cancer burden to 30% by 2020.[5]

A number of predisposing factors for the development of oral precancers/cancers have been studied, some of which are region specific. In the western world, cigarette smoking and human papillomavirus are a major concern, whereas in Southeast Asia, various forms of smokeless tobacco (gutkha, paan, misri, mawa, etc.) apart from cigarette and "bidi" (hand-rolled thin cigarettes) are more relevant factors.[1,2,5–8] Gutkha (commercially packeted) consists of a plethora of unknown substances, whereas paan (hand rolled) consists of betel leaf, areca nut, tobacco, and slaked lime. Studies have shown that these substances contain high levels of trace elements such as copper (known to cause fibrosis of the oral mucosa), magnesium, zinc, etc. which may, in turn, lead to the development of oral precancers and carcinoma.[9] The use of smokeless tobacco may appear to be region specific; however, over the past decade, there has been an exponential rise in South Asian immigrants residing in the United Kingdom and Ireland. This has significantly affected the healthcare services, as patients are now entering the hospital with conditions, as well as habits, that are new to the region. A review of literature revealed a higher incidence of oral precancers and cancers amongst the South Asian immigrants in the United Kingdom and United States, when compared with the general population. A large percentage of these lesions are due to the consumption of smokeless tobacco, which have been imported from South Asia.[10,11] Cigarette smoking has decreased over the

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How to cite this article: Khan A, Ongole R, Baptist J, *et al.* Patterns of Tobacco Use and its Relation to Oral Precancers and Cancers among Individuals Visiting a Tertiary Hospital in South India. J Contemp Dent Pract 2020;21(3):304–309.

Source of support: Nil

Conflict of interest: None

past 20 years in contrast to an apparent rise in the consumption of smokeless tobacco products (chewing tobacco and snuff) particularly in the United States. Smokeless tobacco products vary considerably in composition and usage patterns across different regions of the world. Use of smokeless tobacco is found to be higher in rural than urban areas, in regions with small communities and where there is a tradition of smokeless tobacco use. Among the young population, the likelihood of using smokeless tobacco increases with age. Family members and peers are important influences on smokeless tobacco use by children and adolescents.[12]

Areca nut has been commonly used in the Asia Pacific region and is socially acceptable among all sectors of the society, including women, owing to its ceremonial value. Usually incorporated within a betel quid or pan, areca nut is the fourth most common psychoactive substance used in the world.[13] The mouth is the only body site which permits viewing with the naked eye, the ravages caused by smoked and smokeless tobacco use. When compared with other body sites, the mouth offers a unique opportunity for defining biomarkers as it permits repeated, noninvasive examination in longitudinal cases of tobacco-associated acute and chronic diseases.[4] Hence, it is extremely important for dental and medical professionals to be aware of various tobacco-related habits that are not indigenous to Europe/continental America. This awareness can be crucial in early diagnosis, intervention, and better prognosis of patients suffering from related conditions.

With an aim to evaluate the use of tobacco and its association with oral precancers and cancers, we set the following objectives for the study: to assess the prevalence of tobacco use (smoked and smokeless) and the prevalence of oral potentially malignant disorders and carcinoma among them; to evaluate the association between tobacco use and oral precancers; and to assess the association between chewable and non-chewable forms of tobacco with other oral mucosal lesions.

Materials and Methods

After obtaining approval from the Institutional Scientific and Ethics Committee, a retrospective review of the outpatient records of 1,007 individuals (out of a total of 45,000 patient records) with a history of tobacco use in various forms (smoked and smokeless) was performed, for the patterns of tobacco abuse and the presence of related oral mucosal alterations.

The study was conducted at a tertiary hospital in Mangaluru, India. Hospital records between the years 2013 and 2017 were chosen for the study. Individuals without any habit history or with lesions unrelated to tobacco use were excluded from the study. Individuals who consumed alcohol as the only habit without associated tobacco use were also excluded. Permission from the ethics committee of the dental hospital was obtained prior to the study.

Data obtained from the records included the individual's age, gender, type of tobacco use, pattern, frequency and duration, combined habits (if any), and the presence of oral mucosal lesions (leukoplakia, lichen planus, OSMF, and malignancy). The presence of tobacco-related mucosal changes such as smoker's melanosis, smoker's palate, betel chewers' mucosa, and tobacco pouch keratosis was also noted. Smokers were further categorized as those who smoke cigarettes or bidi and those who smoke both. Similarly, in the smokeless form of tobacco use, individuals were categorized based on the form of tobacco used such as gutkha, betel quid, snuff, or a combination of gutkha and betel quid.

Results

This study comprised 1,007 individuals (M:F: 19:1). In the cohort, 60.2% had smoking habit and 56.1% had smokeless habit. Of the 1,007 patient records, 12.6% ($n = 127$) revealed a combination of smoking and smokeless tobacco habit. The oldest patient was 83 years of age and the youngest was 15 years. The mean frequency and duration of habits are summarized in Table 1. The analysis of duration of the habit showed longer duration of 11.3 ± 10.18 years of smoking habit followed by combination (10.68 ± 10.14 years) and least duration with smokeless habit (8.10 ± 7.74 years). The frequency was also higher among the smoking habit (7.73 ± 10.35 units per day) when compared with smokeless habit (4.49 ± 3.8 units per day).

Unsurprisingly, we found that cigarette smoking was the most prevalent habit among the study population (52%). The most commonly used smokeless product was gutkha (26%) followed by betel quid (24%) (Table 2). Betel quid was found to be the most used product among women (77%) (Fig. 1).

A review of oral lesions revealed that tobacco pouch keratosis was the most common lesion among patients with a habit history (7.8%). Patients with a habit history had a 7.2% prevalence in the development of OSMF, of which 13.2% were gutkha chewers. A binary logistic regression analysis with respect to all the habits involved in the development of leukoplakia showed that the two significant factors attending were bidi smoking, with an OR of 4.47, followed by gutkha (OR = 2.5). More than 5% of individuals with a habit history developed oral leukoplakia.

Smokeless habit presence increases the risk of developing OSMF. A total of 99.4% of individuals without habit did not have OSMF when compared with 13.2%, 13.9%, and 14.3% of gutkha, betel quid, and snuff habits showing the lesion (Table 3).

Oral submucous fibrosis caused by smokeless forms of tobacco was most prevalent in the study population. Snuff had an OR of 18.733 for developing OSMF followed by gutkha (OR: 17.704). Leukoplakia was most commonly associated with bidi smoking (OR of 4.469) followed by gutkha (OR of 2.506) (Tables 4 and 5). The majority of patients who only had a smokeless habit were found to have tobacco pouch keratosis (7.8%), whereas patients who chewed only gutkha had a 15.5% prevalence in the development of tobacco pouch keratosis.

Table 1: Mean duration and frequency of smoking, smokeless and combined habits

			Count	*Mean*	*Standard deviation*
Habit	Combination	Duration in years	127	10.6822	10.4105
		Frequency (cigarettes/day)	127	6.70	6.96
	Smokeless habit	Duration in years	398	8.10	7.74
		Frequency (cigarettes/day)	398	4.497	3.8
	Smoking habit	Duration in years	482	11.3280	10.1897
		Frequency (cigarettes/day)	482	7.73	10.35

Table 2: Frequency distribution of the gender, habits and associated mucosal changes of the cohort

	Category	*Count (total n = 1,007)*	*Prevalence*
Gender	Male	961	95.4
	Female	46	4.6
Smoking habit	No smoking habit	401	39.8
	Cigarette	524	52.03575
	Bidi	77	7.646475
	Cigarette and bidi	5	0.496524
Habit of smokeless tobacco	No smokeless habit	482	47.9
	Gutkha	265	26.3
	Betel quid	244	24.2
	Snuff	7	0.7
	Gutkha + betel quid	9	0.9
	Leukoplakia	55	5.5
	OSMF	73	7.2
	Carcinoma	48	4.8
Other tobacco-related mucosal changes	Others	859	85.3
	Smoker's melanosis	42	4.2
	Smoker's palate	25	2.5
	Betel chewers' mucosa	2	0.2
	Tobacco pouch keratosis	79	7.8

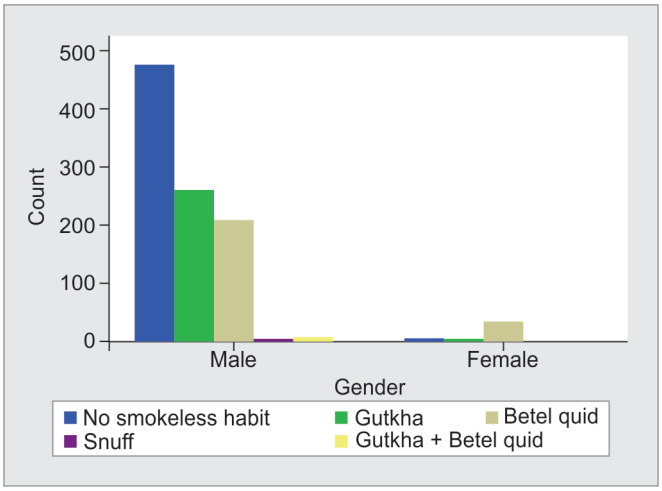

Fig. 1: Association of gender with type of smokeless tobacco use

Individuals with a habit of drinking alcohol, in addition to smoking, had a higher chance of developing smoker's melanosis. Betel quid chewing led to a greater risk (10.3%) of developing carcinoma. Logistic regression for predicting the development of cancer led to correlated odds of multiple habits being present in an individual. The corrected odds of bidi smoking is 12.239 for the development of cancer (Table 6).

Discussion

Tobacco products are causally linked to a variety of cancers, including those of the oral cavity and aerodigestive tract, liver, pancreas, bladder, ureter, kidney, and cervix, and also to the development of myeloid leukemia. More than 60 carcinogens are present in cigarette smoke, and at least 16 in unburned tobacco have been identified.[1] Among these, the most studied are tobacco-specific nitrosamines, such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N-nitrosonornicotine (NNN), polycyclic aromatic hydrocarbons (PAH), such as benzo[*a*]pyrene, and aromatic amines. In particular, NNK, NNN, and PAH have been causally linked to oral cancer.[1] The association between tobacco smoking and oral cancer is dose dependent, with the risk for cancer development proportional to the number of daily smoked cigarettes and the duration of smoking.[2] Tobacco's popularity may be explained by its capacity to counter adverse conditions, which were frequent in the past-hunger, thirst, fatigue, fear, and cold. A widespread use of tobacco among ancient South American populations in the form of "pituri," another nicotine-containing plant, can be attributed to its ability to assuage hunger and fatigue.[1]

According to the Global Adult Tobacco Survey India 2016–2017[14] (a nationally representative household survey of adult smokeless tobacco users, 15 years and older), 32% of the population are current users of tobacco. Of these, 10.6% are smokers, while 21.4% use a smokeless form of tobacco. Chockalingam et al. in their study comprising residents of Chennai, India, found a prevalence of 19.4% tobacco use. Among whom, 12.4% were smokers and 7.0% had a smokeless tobacco habit.[15]

Our study, which only involved individuals with a tobacco habit, showed that 60.2% of the study population were smokers, whereas 56.1% had a smokeless habit. Cigarettes were the most popular among smokers (52%), whereas gutkha was the preferred smokeless tobacco product (26.3%).[16] Mehrotra et al. and Karthik and Mohan have found betel quid chewing to be more popular among females[13,17] followed by reverse smoking.[18] Our study showed similar results *vis-a-vis* betel quid chewing, but we did not find any subjects with a reverse smoking habit.

Association of tobacco smoking and leukoplakia has been established by several studies[19–22] with our study showing concurrent results, where 5.5% chance of developing leukoplakia is associated with a habit history. Tobacco pouch keratosis is the most common oral lesion associated with the use of smokeless tobacco;[13,17,18,23,24] our study estimates its prevalence to be approximately 7.8% of all tobacco-associated oral mucosal lesions. Several studies, have found a near-equal prevalence of OSMF in

Table 3: Logistic regression for precancerous leukoplakia

								95% CI for OR	
		B	*SE*	*Wald*	*df*	*p value*	*OR*	*Upper*	*Lower*
Step 1[a]	No smoking habit			12.029	3	0.007			
	Cigarette	0.198	0.403	0.242	1	0.623	1.219	0.554	2.683
	Bidi	1.497	0.500	8.970	1	0.003	4.469	1.678	11.902
	Cigarette and bidi	−18.077	17793.916	0.000	1	0.999	0.000	0.000	
	No smokeless habit			4.936	4	0.294			
	Gutkha	0.919	0.414	4.912	1	0.027	2.506	1.112	5.645
	Betel quid	0.702	0.454	2.387	1	0.122	2.018	0.828	4.917
	Snuff	−17.554	15185.822	0.000	1	0.999	0.000	0.000	
	Gutkha + betel quid	−18.103	12812.011	0.000	1	0.999	0.000	0.000	
	Alcohol (1)	0.620	0.350	3.142	1	0.076	1.859	0.937	3.690
	Constant	−3.679	0.452	66.132	1	<0.001	0.025		

[a]Variable(s) entered on step 1: smokers, smokeless, and alcohol; SE, standard error; CI, confidence interval

Table 4: Chi square test for testing association between the presence of oral submucous fibrosis (OSMF) and the smokeless tobacco habit

Crosstab					
			OSMF		
			No	*Yes*	*Total*
Smokeless tobacco habit	No smokeless habit	Count	479	3	482
		% within smokeless	99.4	0.6	100.0
	Gutkha	Count	230	35	265
		% within smokeless	86.8	13.2	100.0
	Betel quid	Count	210	34	244
		% within smokeless	86.1	13.9	100.0
	Snuff	Count	6	1	7
		% within smokeless	85.7	14.3	100.0
	Gutkha + betel quid	Count	9	0	9
		% within smokeless	100.0	0.0	100.0
Total		Count	934	73	1,007
		% within smokeless	92.8	7.2	100.0

Chi-square value of 62.910 and *p* value of < 0.001

individuals using smokeless tobacco[12,13,23] although prevalence in rural populations may be as high as 25% as reported by Keluskar and Kale.[25]

Our study found a 12-fold increase in risk of oral cancer in bidi smokers, similar to the study by Madani et al.[26]

This could be a result of higher nicotine content, tar, and particulate matter present in bidis.[27,28] Additionally, most bidis are unfiltered; therefore, a greater amount of these carcinogens may be delivered to the oral cavity during smoking.

In recent times, use of smokeless tobacco has garnered attention among clinicians and researchers alike owing to a vast majority of the population using these products and the occurrence of various associated mucosal lesions, which may be precancerous in nature. The smokeless tobacco products are available in myriad forms and follow no standard packaging or labeling of their contents. This exposes the oral cavity to a plethora of unknown substances which may pose new threats to oral and overall health. Smokeless tobacco products, though banned in a lot of states, continue to be manufactured and sold widely.

Conclusion

Our study revealed that both the forms of tobacco use (smoke and smokeless) are very common. Gutkha use is more prevalent than betel quid use. The study also shows that oral cancer was seen more frequently in elderly men who had the habit of smoking bidis. Leukoplakia was relatively rare when compared with OSMF.

The limitation of our study was that it was retrospective in nature. Hence, larger population studies examining their association with oral lesions prospectively and a longitudinal study may be imperative in acquiring the magnitude of the health concern posed by smokeless tobacco products in the Indian subcontinent.

Table 5: Logistic regression for oral submucous fibrosis

							95% CI for OR	
	B	*SE*	*Wald*	*df*	*p value*	*OR*	*Lower*	*Upper*
No smoking habit			2.574	3	0.462			
Cigarette	−0.322	0.336	0.915	1	0.339	0.725	0.375	1.401
Bidi	−17.746	4184.579	0.000	1	0.997	0.000	0.000	
Cigarette and bidi	1.542	1.293	1.423	1	0.233	4.675	0.371	58.916
No smokeless habit			19.819	4	**0.001**			
Gutkha	2.874	0.660	18.942	1	**<0.001**	17.704	4.853	64.583
Betel quid	2.924	0.669	19.136	1	**<0.001**	18.623	5.024	69.035
Snuff	2.930	1.262	5.391	1	**0.020**	18.733	1.579	222.244
Gutkha + betel quid	−16.352	13177.356	0.000	1	0.999	0.000	0.000	
Alcohol (1)	0.158	0.433	0.134	1	0.715	1.171	0.502	2.735
Constant	−4.680	.669	48.932	1	<0.001	0.009		

SE, standard error; CI, confidence interval; *p* values < 0.05 are considered significant and are marked in bold

Table 6: Logistic regression for oral cancer

		Variables in the equation						
							95% CI for OR	
		B	*SE*	*Wald*	*df*	*p value*	*OR*	*Lower*	*Upper*
Step 1[a]	Smokers			32.177	3	<**0.001**			
	Cigarette smokers	0.182	0.436	0.174	1	0.677	1.199	0.510	2.818
	Bidi smokers	2.505	0.523	22.914	1	<**0.001**	12.239	4.389	34.130
	Cigarette + bidi smokers	−17.085	17919.727	0.000	1	0.999	0.000	0.000	
	Smokeless tobacco			23.136	4	**<0.001**			
	Gutkha	0.459	0.533	0.740	1	0.390	1.582	0.556	4.499
	Betel quid	2.049	0.475	18.630	1	**<0.001**	7.760	3.061	19.678
	Snuff	−16.806	15183.901	0.000	1	0.999	0.000	0.000	
	Gutkha + betel quid	−17.785	12251.049	0.000	1	0.999	0.000	0.000	
	Tobacco + alcohol	0.513	0.389	1.743	1	0.187	1.671	0.780	3.580
	Constant	−4.424	0.510	75.137	1	**<0.001**	0.012		

[a]Variable(s) entered on step 1: smokers, smokeless, and alcohol; SE, standard error; CI, confidence interval; *p* values < 0.05 are considered significant and are marked in bold

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