ORIGINAL RESEARCH

Clinicopathological Evaluation of Tobacco-related Oral Mucosal Lesions

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Abstract

Aim: To clinically evaluate the nature of precancerous and cancerous lesions associated with tobacco consumption habit and to correlate clinical profile with the histopathological findings of clinically suspected precancerous and cancerous lesions.

Materials and methods: These included the examination of patients who visited the outpatient department (OPD) of the institute that includes 1,500 patients who had tobacco chewing habits were classified into the following two groups according to their characteristics. The study group comprised 270 patients, of which 170 gave consent for biopsy and 100 patients who not gave consent were counseled for tobacco cessation.

Results: Among 270 patients, the highest number of patients, 146 (54.07%) patients, were found to be smokeless tobacco consumers followed by 65 (24.07%) patients who were smoked tobacco consumers while 59 (21.85%) patients were found to have both the habits. Wide variation was noted in duration and frequency of habit. Most prevalent site was the buccal mucosa affected in 138 (51.11%) patients who consumed both smoked as well as smokeless tobacco. And on clinical examination, 138 (51%) patients had leukoplakia followed by 54 (20%) patients with oral squamous cell carcinoma and 40 (15%) patients with oral submucous fibrosis (OSMF). Other patients were tobacco pouch keratosis 17 (6%), smoker's melanosis 8 (3%), smoker's palate 7 (3%), and erythroplakia 6 (2%). The patients who gave consent (170 patients) were evaluated histopathologically to correlate with clinical findings.

Conclusion: Tobacco-related oral lesions are also high, which brings an alarming signal toward the development of cancer. Our contribution as healthcare providers can be made by conducting more oral health education programs and educating the general population about the adverse effects of tobacco. The appropriate clinical assessment and categorization of all these lesions aided us in motivating patients to undergo necessary treatments and also to discontinue their habits in order to prevent deterioration of their conditions.

Clinical significance: Set up de-addiction centers in dental colleges and help tobacco users in discontinuing their habits. Interestingly, this study also served as a mirror for those patients who were unaware of the lesions they were giving abode to in their oral cavities.

Keywords: Oral squamous cell carcinoma, Precancerous and cancerous lesions, Tobacco, Tobacco chewing habit, Tobacco-related lesion.

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Introduction

Tobacco is addictive; the prevalence of oral lesions after consumption of tobacco products ranges from 9.5 to 58.9%.[1] Both smoked and smokeless tobacco contain the alkaloid, nicotine, which is the main addictive agent. The most potent carcinogens in tobacco are the tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons, and many others.[2] Smoking, drinking, chewing tobacco, and areca nut have been positively associated with oral lesions, such as OSMF and leukoplakia that has the potential for malignant transformation. The prevalence of OSMF in India varies between 0.03 and 3.2% according to various studies.[3] The prevalence of leukoplakia in India varies from 0.2 to 5.2%.[2,4] Most authorities regard leukoplakia to be a dynamic rather than a static process, but this is usually in terms of its progression and development of malignancy. There is a wide range in the malignant transformation rate of leukoplakia varying from 0.13 to 2.2%.[5]

Depending on different habits of tobacco consumption, various oral mucosal lesions occur in the oral cavity. The lesions predominantly associated with smoking include leukoedema, leukokeratosis nicotinapalati, palatal erythema, and central papillary atrophy of the tongue. The lesions predominantly associated with tobacco chewing include pan chewers lesion and oral lichen planus-like lesion. The lesions associated with smoking and chewing tobacco that is with a mixed habit include leukoplakia and oral squamous cell carcinomas (OSCC). These lesions are histological continuum between the normal mucosa at one end and high-grade dysplasia/carcinoma *in situ*, at the other, establishing a model of neoplastic progression.[4]

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So, the present study was conducted with the aim to clinically evaluate the nature of precancerous and cancerous lesions associated with tobacco consumption habit and to correlate clinical profile with the histopathological findings of clinically suspected precancerous and cancerous lesions.

Identifying the degree of dysplasia at early stages will help to identify the potential of oral cancer patients in terms of prevention. Given the relatively poor survival rates of oral cancer patients, cessation of tobacco habit remains the key element in oral cancer prevention and control.

Materials and Methods

The present study was conducted in MGV Dental College Nashik, Maharashtra, India, and included the examination of patients who visited the OPD of the institute from January 2009 to December 2009. During the study period, 7,000 patients were scrutinized based on evaluating case paper and clinical examination and 1,500 patients were observed to have tobacco chewing habits and were classified into two groups according to their characteristics. Population below 10 years of age, pregnant females, and if on any form of chemotherapy, radiotherapy, and those who not gave consent were excluded from the study.

The study group comprised 270 patients (237 were males and 33 females) of which 170 gave consent for biopsy and 100 patients who not gave consent were counseled for tobacco cessation. The case history proforma was duly filled with the habit of tobacco type, duration, and frequency, and an informed and written consent was obtained from the patients. Population with tobacco-related lesions associated with the habit of smoked tobacco, smokeless tobacco, and also with mixed habit was biopsied.

All the 270 tobacco-related lesions were classified based on their clinical diagnosis in the form of leukoplakia, erythroplakia, tobacco pouch keratosis, smoker's melanosis, smoker's palate, OSMF, and OSCC. Among 270 patients, 170 patients gave consent for biopsy and all 170 patients' clinical diagnosis was correlated with histopathological findings. Clinical assessment of leukoplakia was done on the criteria provided by Axell et al.[6] which classified leukoplakia as homogeneous and nonhomogeneous. Again homogeneous leukoplakia (Fig. 1A) is divided into thick and thin leukoplakia whereas nonhomogeneous leukoplakia (Fig. 1B) is divided into verrucous, granular, and speckled forms of leukoplakia.

Histopathological assessment of these leukoplakic lesions was done for the degree of epithelial dysplasia according to World Health Organization (WHO) 2005 classification scheme.[7] Histopathological assessment of lesions in patients who were clinically diagnosed with erythroplakia, tobacco pouch keratosis, smoker's melanosis, and smoker's palate was also done for the degree of epithelial dysplasia (Fig. 2) according to WHO 2005 classification scheme.[7] Lesions that were clinically diagnosed as squamous cell carcinoma (Fig. 3) were categorized by TNM staging[8] while histopathological evaluation of the tumor was done with the Bryne's grading system.[9] OSMF lesions were clinically classified according to the Lai classification system.[10] This system is based on mouth opening which was measured by vernier calipers (Fig. 4). Histopathological assessment was done according to Pindborg and Sirsat classification system.[11]

Statistical Analysis

The data were classified according to various rating scales and percentage method, and Chi-square test at 95% confidence interval with relevant degrees of freedom was used to compare clinical profile with histopathological findings to find whether there exists any relationship between them.

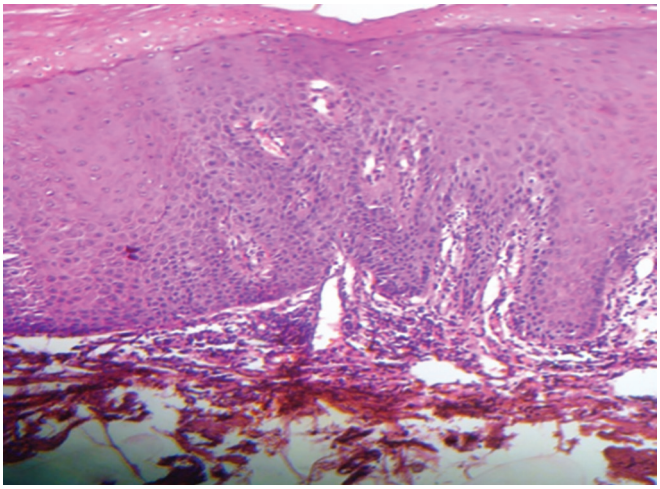
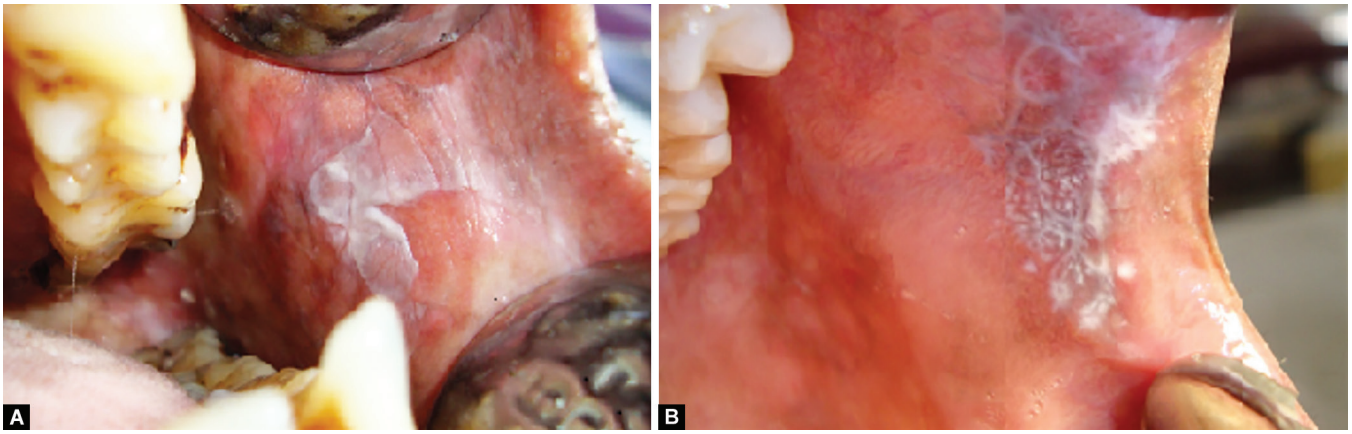


Fig. 2: Leukoplakic lesion showing moderate dysplasia (H&E, ×100)



Figs 1A and B: (A) Buccal mucosa on the left side showing thick homogeneous leukoplakia; (B) Buccal mucosa on the left side showing nonhomogeneous granular leukoplakia

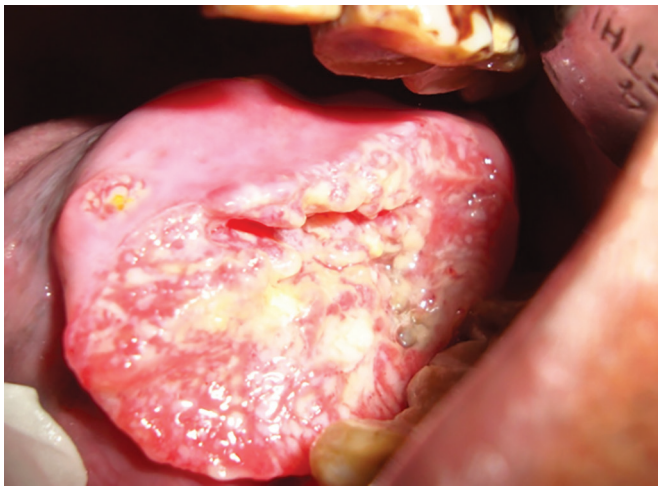


Fig. 3: Lateral border of the tongue on left side showing oral squamous cell carcinoma

Fig. 4: Clinical pictures of OSMF showing 20 mm mouth opening with vernier caliper

Results

The results were analyzed and interpreted as follows. Wide variation was noted among 270 patients in the age, ranging from 11 to 70 years. Most of the patients [93 patients (34.44%)] were in the age-group of 21–30 years.

In all 270 patients, the highest number of patients [146 (54.07%) patients] was found to be smokeless tobacco consumers followed by 65 (24.07%) patients who were smoked tobacco consumers while 59 (21.85%) patients were found to have both the habits. There were many patients who were using different forms of tobacco among them 63 (23.33%) patients used tobacco + lime followed by cigarette smokers of 53 patients (19.62%), followed by 46 patients (17.03%) who were gutkha chewers, then gutkha + cigarette were consumed by 25 patients (9.25%) and plain tobacco in 23 (8.51%) patients. Wide variation was noted in duration and frequency of habit. Fifty-three (19.62%) patients had the habit of tobacco consumption for 6–10 years, followed by 48 (17.77%) patients for 1–5 years (Table 1). While 107 (39.62%) patients consumed tobacco 12–14 times/day followed by 35 patients (12.96%) who consumed for 6–8 times/day. Most prevalent site was the buccal mucosa affected in 138 (51.11%) patients who consumed both smoked as well as smokeless tobacco.

The prevalence of tobacco consumption in the patients who visited the college OPD was 21.42% of which the prevalence of patients who had tobacco-related lesions was 18%. Tobacco-related oral mucosal lesions (Table 2) showed that among 270 patients, 138 (51%) patients had leukoplakia followed by 54 (20%) patients with OSCC and 40 (15%) patients with OSMF. Other patients were tobacco pouch keratosis 17 (6%), smoker's melanosis 8 (3%), smoker's palate 7 (3%), and erythroplakia 6 (2%). In the present study, leukoplakia patients were of maximum numbers as compared to the other lesions; hence Chi-square test was applied at 95% confidence level with relative degree of freedom to the group of leukoplakia. This was done to find out the association of leukoplakia with the type of tobacco consumed and to correlate leukoplakia. The Chi-square value obtained was 0.001 with *p* value of 0.969, which was statistically insignificant, while all the other lesions were analyzed by the percentage method.

In 170 patients (who gave consent), classified based on clinical diagnosis, 71 (44%) patients were of leukoplakia, followed by 46 (27%) patients with OSCC and 35 (21%) patients had OSMF. Tobacco pouch keratosis—seven (4%), smoker's melanosis—four (2%), erythroplakia—four (2%), and smoker's palate—three (2%) cases, respectively, were biopsied and evaluated for dysplasia histopathologically.

Among 71 cases of leukoplakia, histopathologically found, homogeneous leukoplakia was 54 cases and nonhomogeneous leukoplakia was 17 cases. In 54 homogeneous cases, 16 cases

Table 1: Distribution of individuals according to type of tobacco

Type of tobacco	*Number of patients*
Tobacco	26
Tobacco + Lime	80
Kharra	3
Panmasala	8
Gutkha	38
Cigarette	50
Bidi	13
Tobacco + Cigarette	2
Tobacco + Bidi	3
Tobacco, lime + Cigarette	7
Tobacco, lime + Bidi	11
Kharra + Cigarette	2
Kharra + Bidi	2
Panmasala + Cigarette	2
Panmasala + Bidi	1
Gutkha + Cigarette	18
Gutkha + Bidi	4

Table 2: Distribution of individuals according to tobacco-related oral mucosal lesions

Tobacco-related oral mucosal lesions	*Number of patients*
Leukoplakia	138
Erythroplakia	6
Oral squamous cell carcinoma	54
Oral submucous fibrosis	40
Smokers palate	7
Tobacco pouch keratosis	17
Smokers melanosis	8

were thin form and 38 cases were thick form of leukoplakia. Histopathologically, in 16 thin homogeneous leukoplakia cases, 13 cases showed no evidence of dysplasia and 3 cases showed mild dysplasia. While in 38 cases who have diagnosed with thick homogeneous leukoplakia, histopathologically no dysplasia in 19 cases, mild dysplasia in 16 cases, and moderate dysplasia in 3 cases were found. No one of thin and thick leukoplakic cases had histopathologically shown severe dysplasia and carcinoma *in situ*.

In 17 nonhomogeneous cases, we found that 6 were granular, 5 were verrucous, and 6 were speckled nonhomogeneous leukoplakia cases. In six granular cases, three cases showed moderate dysplasia while two cases showed no dysplasia and only one case showed mild dysplasia. In five verrucous cases, two cases were diagnosed as no dysplasia, two were mild dysplasia, and one case had moderate dysplasia. In six speckled cases, four of them showed moderate dysplasia while equal of one in each case showed no dysplasia and mild dysplasia, respectively. While four erythroplakia patients showed moderate dysplasia in two cases while severe dysplasia and carcinoma *in situ* in one case, respectively (Table 3).

In the study group, all patients with OSMF (n = 35) who had shown very early stage (n = 4) clinically had shown early stage 4 (100%) histopathologically. In case of OSMF patients who clinically showed early stage, (n = 14) equal of 35.71% had shown early and moderately advanced stage while again equal to 14.29% showed very early and advanced stage histopathologically. Of the patients who showed moderately advanced stage, (n = 17) clinically maximum of 52.94% showed moderately advanced stage histopathologically also while 47.06% showed early stage (Table 4).

Chi-square test was applied to check whether the clinical diagnosis of leukoplakia was associated with histopathological findings. The calculated value of Chi-square was 13.988, which was found significant as p value is 0.000 at 1 degree of freedom and of 95% confidence level.

In the present study, we found some degree of correlation between the clinical types and histopathological features of leukoplakia, erythroplakia, tobacco pouch keratosis, smokers' melanosis, smokers' palate, and OSMF while there was no definite correlation between the clinical staging and histopathological grading of OSCC.

Discussion

Oral lesions are linked to the use of tobacco with or without betel quid and cigarette smoking. Chewing tobacco with betel quid increases the exposure to carcinogenic tobacco-specific nitrosamines and nitrosamines derived from areca nut alkaloids. Reactive nitrogen species, which originate in cigarette smoke, are implicated in multistage carcinogenesis and are considered to trigger the process leading to malignant transformation.[12]

Leukoplakia, erythroplakia, and OSMF are well-defined precancerous states, while there are some lesions, like tobacco pouch keratosis, smoker's melanosis, and smoker's palate, which are associated with tobacco consumption but are not considered as precancerous states. The biological behavior of these precancerous states is rather unpredictable, as some precancers may regress, whereas about one-third may progress to invasive malignancy.[12]

In spite of the accessibility of the oral cavity to direct examination, these lesions are often not detected until the late stages. Early detection followed by appropriate treatment can increase cure rates to 80 or 90% and can greatly improve the quality of life by minimizing extensive, debilitating treatments.[13]

Of the 270 patients with tobacco-related lesions, 237 were males and 33 were females, making the male:female ratio of 7.1:1. The findings were in agreement with Bouquot and Gorlin[14] who also reported a male predominance.

In the present study, among the 270 tobacco-related lesions, the prevalence of leukoplakia, OSCC, OSMF, tobacco pouch keratosis, smoker's melanosis, smoker's palate, and erythroplakia was similar to the findings of Saraswathi et al.,[15] Mehta et al.,[4] Pindborg et al.,[3] Gupta, and Ray.[1] These studies have shown that the most prevalent tobacco-related lesions were leukoplakia and OSCC while the prevalence of other lesions varied according to the use of specific tobacco products.

In the present study, the duration of tobacco consumption was <20 years in the maximum number of both homogeneous i.e. 76 patients and nonhomogeneous leukoplakia i.e. 12 patients. The frequency of tobacco consumption was 11–20 times/day in the maximum number of both homogeneous i.e. 95 patients and nonhomogeneous leukoplakia i.e. 19 patients. These findings were in agreement with the results of Macigo et al.[16] according to whom,

Table 4: Distribution of 46 cases of OSCC based on clinical (TNM) staging and histopathological (Bryne's) grading

		Histopathological grade		
Clinical (TNM) stages	*No. of Pts.*	*I*	*II*	*III*
I	10	8	2	0
II	5	2	3	0
III	24	13	10	1
IV	7	2	3	2

Table 3: Distribution of 71 cases of leukoplakia and 4 cases of erythroplakia based on histopathological grading of epithelial dysplasia according to the WHO 2005 classification scheme

		Histopathological grade				
Clinical type	*No. of Pts.*	*No dysplasia*	*Mild*	*Moderate*	*Severe*	*CA in situ*
Homogeneous						
Thin	16	13	3	0	0	0
Thick	38	19	16	3	0	0
Nonhomogeneous						
Granular	6	2	1	3	0	0
Verrucous	5	2	2	1	0	0
Speckled	6	1	1	4	0	0
Erythroplakia	4	0	0	2	1	1

the prevalence of leukoplakia tends to increase with the frequency of consumption of tobacco rather than the duration of tobacco.

All the clinical types of leukoplakias were commonly seen on the buccal mucosa irrespective of the type of tobacco consumption, similar to the findings of Tomar et al.[17] and Freitas et al.[18] When we correlated all the leukoplakia lesions (irrespective of type) with the degree of dysplasia, it was found that they were significantly more in the low-risk category. These findings were in accordance with the studies of Vander Wall et al.[6] which showed that as the clinical nature of leukoplakia changes from homogeneous to nonhomogeneous, the grade of epithelial dysplasia increases.

Our observations regarding erythroplakia were that this lesion was more common in males in the young (<30 years) to middle age-group (30–60 years) with the habit of smokeless tobacco. The buccal mucosa was the only site involved in all the six cases. These findings were similar to the findings of Shafer and Waldron[19] and Reichart and Philipsen[20] High-risk lesion like erythroplakia showed severe degree of histopathological changes suggestive of a correlation between the clinical and histologic pictures in erythroplakia, similar to the findings of Shafer and Waldron.[19]

In the present study, we studied malignancy OSCC, along with premalignancy and OSCC was detected in 54 cases. The common site was buccal mucosa. These findings are similar to the observations in studies of Ariyawardana et al.[21] and Muwonge et al.[22] Histopathological analysis of 46 patients with OSCC according to the Bryne's grading system showed that 25 cases of OSCC were categorized as grade I (well differentiated) whereas 18 cases fell under the category of grade II (moderately differentiated) and only three cases were categorized as grade III (poorly differentiated). It suggests that as the clinical stages increased, no significant increase in histopathological grades was seen. So, there was no significant correlation between the clinical and histologic features in OSCC (Table 4).

Our findings suggest that tobacco pouch keratosis was common in males in the middle age-group population. The most prevalent site was lower labial mucosa and vestibule, similar to the findings of Speight et al.[23]

The findings of our study suggest that smoker's melanosis was common in males, in the younger aged population. The most prevalent site was the involvement of bilateral buccal mucosa similar to the findings of Yousuf et al.[24]

In the present study, smoker's palate was common in middle-aged males, associated with smoked tobacco consumption similar to the findings of Mirbod and Ahing.[25] According to their studies, smoker's palate was seen in middle to older age-group associated with tobacco smoking habit and commonly affected the hard palate.

While carrying out the present study, we found 40 cases of OSMF. These patients gave a history of gutkha chewing (form of smokeless tobacco) in our findings. These findings were similar to the findings of Pandya et al.[26] Based on the histopathological features, the maximum number of patients (which was 52.94%) was seen in the moderately advanced cases which were followed by early cases in 47.06% of patients (Table 5). The above-mentioned findings were suggestive that, in the maximum patients with OSMF, the clinical diagnosis coincided with the histopathological diagnosis, similar to the observation of Pandya et al.[26]

Table 5: Distribution of 35 cases of OSMF based on Lai (1995) clinical classification system and histopathological staging according to Pindborg (1966) classification system

		Histopathological stages			
Clinical groups	*No. of Pts.*	*Very early*	*Early*	*Moderately advanced*	*Advanced*
Group A (IIO >35 mm)	4	0	4	0	0
Group B (IIO = 30–35 mm)	14	2	5	5	2
Group C (IIO = 20–30 mm)	17	0	8	9	0
Group D (IIO <20 mm)	0	0	0	0	0

Limitations of the Study

Data analysis was based on the responses given by the respondents. Because the information regarding the habits was gathered through the questionnaire method, there could be an information bias. Since, the clinical appearance and punch biopsy of the lesion have their own limitations in predicting the potential seriousness of oral mucosal lesions, excisional biopsy or adequate incisional biopsy is indicated.

Conclusion

From the above-mentioned results, the present study concluded that tobacco use among people is existing and increasing at a higher pace. Interestingly, this study also served as a mirror for those patients who were unaware of the lesions they were giving abode to in their oral cavities. The appropriate clinical assessment and categorization of all these lesions aided us in motivating patients to undergo necessary treatments and also to discontinue their habits in order to prevent deterioration of their conditions.

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