International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 11; November 2017; Page No. 7218-7222
DOI: http://dx.doi.org/10.24327/ijcar.2017.7222.1103

Research Article

A STUDY ON CLINICAL FORMS OF ORAL LEUKOPLAKIA WITH GRADES OF ORAL EPITHELIAL DYSPLASIA

Swati Dahiya and Kondajji Ramchandra Vijayalakshmi

Department of Oral Medicine & Radiology, Government Dental College & Research Institute, Bangalore

A R T I C L E I N F O

Article History:
Received 19th August, 2017
Received in revised form 9th September, 2017
Accepted 6th October, 2017
Published online 28th November, 2017

Key words:

Oral leukoplakia, Epithelial dysplasia, Tobacco

A B S T R A C T

Background & Objectives: Oral Leukoplakia (OL) has multifactorial etiology with tobacco being the major etiological factor. The management of the oral leukoplakia poses a challenge as it relies on its clinical presentation and histopathological grading. Hence, the study was aimed tostudy the clinical forms and histological grades of oral leukoplakia associated with habit of tobacco.
Methods: 60 cases of oral leukoplakia were selected according to selection criteria and were subjected to incisional biopsy, followed by histopathological grading. The obtained values of these parameters were tabulated, statistically analyzed and observations were drawn.
Results: Non-homogenous leukoplakia was significantly associated with moderate epithelial dysplasia and whereas homogenous form was significantly associated with mild dysplasia (p value <.05). Also, statistically significant association was noted between tobacco & alcohol with moderate grade of dysplasia (p value <.001)
Conclusions: This study suggests that severity of the clinical appearance of lesion is indicative of higher grade of epithelial dysplasia.

INTRODUCTION

Oral leukoplakia (OL) is defined as a white patch or plaque that cannot be characterized clinically or histopathologically as any other definable lesion. The prevalence of OL is about 2.6% globally whereas in India, it varies from 0.2% to 5.2% with malignant transformation ranging between 0.13% and 10%.[1,2]

Even though, etiology of OL is multifactorial, tobacco in different forms has been established as the main etiological factor as 80% of OL are present in tobacco users. Individuals smoking tobacco for more than 10 years has nearly 11 times greater risk of developing OL than non-smokers.[3] About 35-40 % of tobacco consumption in India is in the form of smokeless tobacco and it causes OL in 18-64 % of its users at the site where it is held.[4,5] The two main clinical forms of OL are the homogenous form, which includes flat, corrugated, wrinkled or pumice subtypes and the non-homogenous form with its subtypes namely verrucous, nodular, ulcerated and erythroleukoplakia.[6]

Currently, oral epithelial dysplasia is the most important prognostic indicator for determining the malignant transformation risk of OL.

Corresponding author:* **Swati Dahiya
Department of Oral Medicine & Radiology, Government Dental College & Research Institute, Bangalore

The presence of oral epithelial dysplasia often correlating with a clinical non-homogeneous, erythroleukoplakic subtype is generally regarded as the most important indicator of malignant potential. Hence this study was conducted with an objective to study various clinical forms of oral leukoplakia and related histological grades of epithelial dysplasia.

Aim

To study the clinical forms and histological grades of oral leukoplakia associated with habit of tobacco

MATERIAL AND METHOD

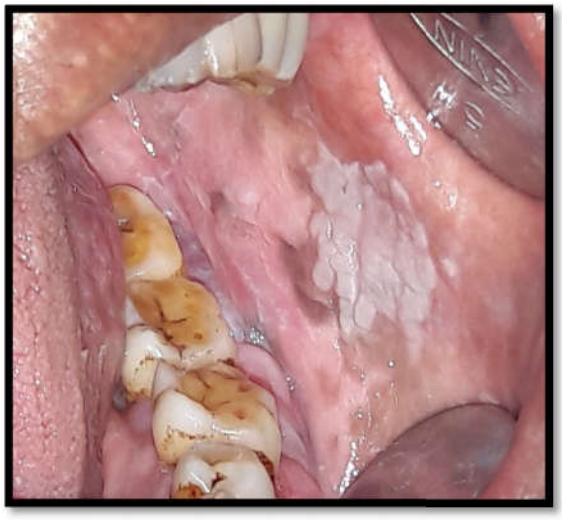
This study was conducted on 60 subjects of OL who were selected based on the selection criteria during the period of December 2014 to June 2016 visiting Department of Oral Medicine and Radiology, Government Dental College and Research Institute, Bangalore. The study was conducted in full accordance with ethical principles and was reviewed and approved by an ethical board of the institution.All the selected subjects were informed about the details of the study in their known local language and a written informed consent was obtained. A detailed case history, thorough clinical and oral examination was then carried out and documented on a specially designed case history proforma.

Inclusion Criteria

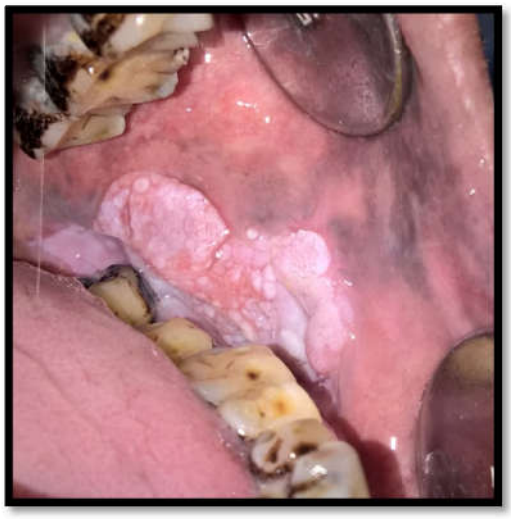
1. Patients with OL associated with smoke and smokeless tobacco habits in the age group of 18-60 years.
2. Patients with clinically diagnosed and histologically proven case of OL.
3. Patients not on any medication for OL for the past 2 weeks.

Clinical Categorization of Oral Leukoplakia

All the selected 60 cases were subjected to detailed examination of the lesion with emphasis on their number, size, site and texture. The oral leukoplakic lesions were grouped into two main types: Homogeneous and Non- homogeneous leukoplakia (figure 1) according to Pindborg *et al* 1997 (WHO International Histological Classification of Tumors) [6]



a



b

Figure 1 Showing homogenous leukoplakia (a) & non homogenous leukoplakia (b).

Measurement of Size of Oral Leukoplakia

Grid Preparation: A customized grid was prepared according to the size of clinical lesion by printing graph consisting of square boxes of 1x1 cm^2 on OHP sheet of thickness of 75 microns. Grid was then superimposed on the lesion and its outline was marked with a red color pen. The lesion was measured in both vertical and horizontal dimension and the dimension, which included maximum number of square boxes, was considered as the lesion size following this incisional biopsywas done from the most clinically representative area.[8]

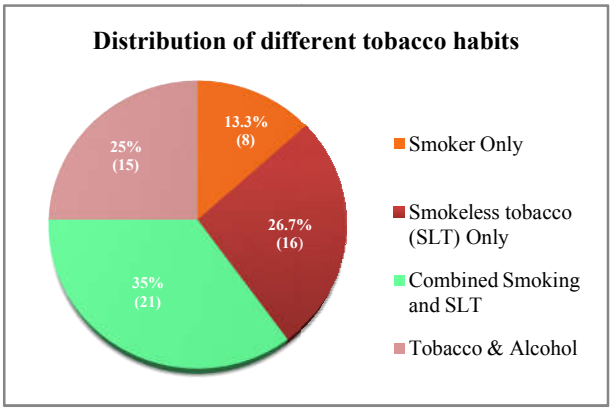
Histologic Grading& Staging of Oral Leukoplakia

A systematic histopathologic assessment and grading of the H & E stained sections was done by a oral pathologist into mild, moderate, severe dysplasia and carcinoma in situ based on architectural disturbances and cytologic atypia given by WHO classification of oral epithelial dysplasia (2005).[9] Following which staging was carried out based on Modified classification and staging system for oral leukoplakia (OLEP). [10]

RESULTS

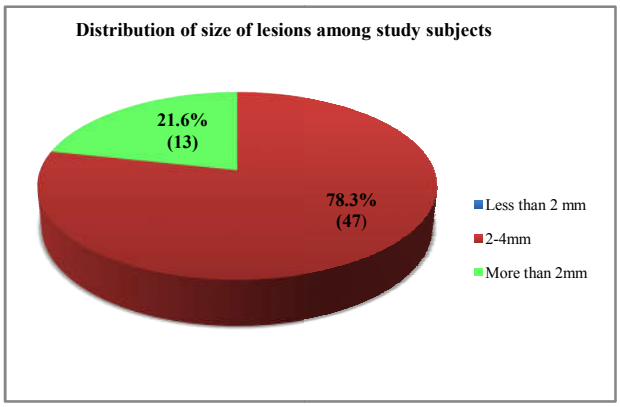
The study population comprised of 60 cases. All the 60 cases were in the age range of 26 to 60 years with mean age of 40 ± 9.24 years. Among 60 cases, 49(81.7%) were males and 11(18.3%) were females.

The tobacco habit varied among cases as shown in graph 1 with maximum number of individuals 21(35%) practiced combined smoking & smokeless tobacco habit.



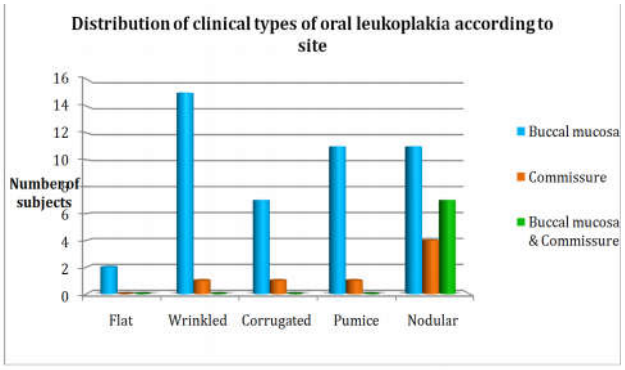
Graph 1 Pie chart showing distribution of different types of tobacco habits (cases)

The average frequency and duration of smoking habit was 8.4 ± 4.52 per day & 11.84 ± 7.28 years respectively whereas average frequency & duration of smokeless habit was 6.1 ± 2.93 per day and 10.62 ±6.11 years respectively. Among 60 cases, maximum number of subjects (68.3%) had single lesion. The lesion size for maximum number of individuals (68.3%) was in the range of 2-4 cm (Graph 2).



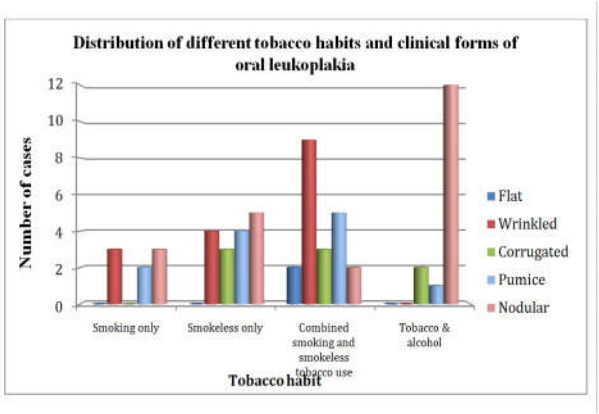
Graph 2 Pie chart showing distribution of size of lesions among cases

The predominant form noticed was homogenous 38 (63.3%) subjects, followed by non-homogenous form in 22(36.6%) subjects. The distribution of clinical typeof oral leukoplakia according to site is shown in graph 3.



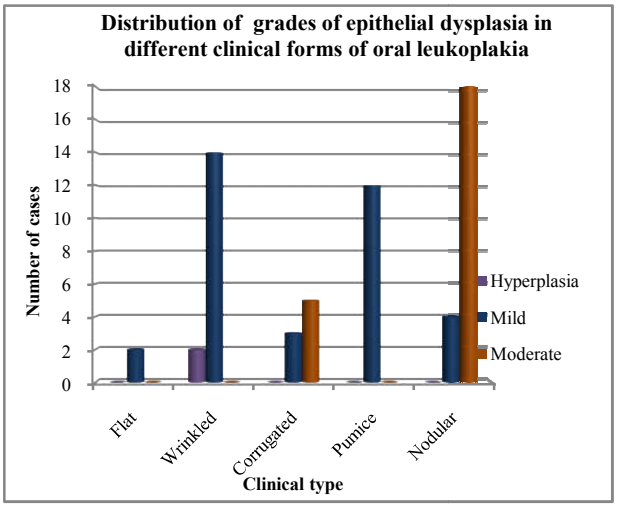
Graph 3 Showing distribution of clinical types of oral leukoplakia in different sites of oral cavity

Overall there was statistically significant association between site and clinical type of oral leukoplakia, with nodular form associated with both commissure and buccal mucosa and wrinkled form with buccal mucosa. Also, a statistically significant association was observed for combined tobacco and alcohol group with nodular non-homogenous leukoplakia with a p value of <.05 .(Graph 4).



Graph 4 Showing distribution of Clinical forms of oral leukoplakia according to tobacco habits

The Histological examination of the biopsy specimens revealed majority of the subjects with mild dysplasia(35) followed by moderate dysplasia (23) and hyperplasia(2).The distribution of grades of epithelial dysplasia in different clinical forms of oral leukoplakia is depicted in graph 5.



Graph 5 Showing distribution of grades of epithelial dysplasia in different clinical forms of oral leukoplakia

The association of grading of dysplasia with different tobacco habit is shown in table 1.Also, significant association was noted between tobacco & alcohol with grading of dysplasia (p value <.001) with moderate grade most commonly associated.

Table 1 Showing association between different types of tobacco habits and histologic grading of dysplasia in study group (cases)

Tobacco habits & Number	Grading of dysplasia			Total	χ^2 value	'p' value
	Hyperplasia	Mild dysplasia	Moderate dysplasia			
Smoking (8)	0 (0%)	7 (87.5%)	1 (12.50%)	8	3.26	.195
SLT Only (16)	1 (6.2%)	10 (62.5%)	5 (31.25%)	16	.91	.634
Combined smoking and smokeless (21)	1 (4.7%)	17 (80.9%)	3 (14.2%)	21	7.91	.019*
Alcohol and Tobacco (15)	0 (0%)	1 (6.7%)	14 (93.3%)	15	25.60	.000**
Total	2	35	23	60		

*denotes significant 'p' value
**denotes highly significant 'p' value

The distribution of cases according to OLEP staging showed maximum subjects in stage II (55%) followed by stage I (30%) and stage IV(15%).

DISCUSSION

Oral leukoplakia is potentially malignant disorder of the oral mucosa with tobacco established as its main etiological agent.[3] Several other factors including alcohol, areca nut alkaloids, dietary factors and viruses are also considered in its etiology.[11] Increased malignant potential of oral leukoplakia may be associated with certain clinical characteristics such as tobacco use, lesion type, size, site and dysplasia.[12] India is a region of relatively high prevalence of OSCC and leukoplakia. Homogenous leukoplakia is also said to have clinically significant malignant transformation, despite their supposed benign and low-risk nature.

The mean age of subjects with oral leukoplakia was 44.6± 7.3 years ranging from 26 to 60 years with male predominance in the ratio of 4:1. The reason for male predominance could be attributed to peer pressure, tension reduction/relaxation, addictive smoking and habit/automatism. The majority of subjects i.e. 21 (35%) were with the combined habit of smoke and smokeless tobacco and the mean age of subjects was 44.80±4.3yrs. These observations with habit, gender and age are in concurrence with the study conducted by Birur *et al* 2014,[7] Varshney *et al* 2015[13] and Bisht *et al* 2016.[14]

The mean duration of habit observed in subjects with only smoking was 11.8 ± 7.28 years whereas in smokeless tobacco group, the habit was practiced for 10.62 ±6.11 years. These observations were similar to that of study done by Bokor-Bratic M *et al*, 2002.[3] In the present study the mean frequency of smoking tobacco was higher (8.4 ± 4.52) than smokeless habit (6.1 ± 2.93 per day) which could be attributed to the fact that smokeless tobacco products release alkaloids, arecoline and other ingredients which are absorbed more in patients who keep it for longer duration and swallow it, hence producing a feeling of euphoria and well being in a user that ultimately decreases craving and accounts for its lesser frequency.[15]

Even though leukoplakia predominantly occurs in a single site however the presence of multiple lesions is not uncommon and can be attributed to the concept of field cancerization, which suggests origin of dysplastic cells in the adjacent epithelia of

oral leukoplakia thereby placing adjacent epithelium at a higher risk for malignant transformation.In this study, majority of subjects (68.3%) presented with single lesion, which was similar in observation to Ishii *et al*2003whereas similarity in size was observed in study byGurudath *et al* 2016who reported the size of leukoplakic lesions in the range of 1-4 cms.[16,17]

All the cases were categorized according to WHO clinical classification of oral leukoplakia in which the predominant form noticed was homogenous (63.3%) with buccal mucosa most common site for its occurrence (92.1%). These observations were in accordance with the studies done by Sharma *et al* 2011[18]; Ramesh *et al* 2013[19];Varshney *et al* 2015[13]; Birur *et al* 2014[7]and Bisht *et al*[14]. Also, we observed only nodular variant in all cases of non-homogenous leukoplakia (22,100%) with commissures being predominantly involved. This may be due to impact of tobacco smoke that carries large part of both burnt tobacco products and heat. The observation was in accordance with study conducted by Vazquer Alvarez *et al* 2010 who also reported commissure to be the common site for nodular leukoplakia.[12]

In the present study subjects with smokeless tobacco habit mostly presented with homogenous form (68.7%) of leukoplakia whereas those with only smoking commonly presented with nodular non-homogenous form (37.5%). Also, subjects in tobacco & alcohol group (80%) presented with non-homogenous leukoplakia, which can possibly be due to synergistic action of alcohol with tobacco as alcohol increases permeability of mucosal cells to tobacco carcinogens, which damages DNA via production of ROS thereby arresting the growth of fibroblasts irreversibly with features of cellular senescence.[20,21] Factors secreted by these senescent fibroblasts can then stimulate epithelial cell proliferation and disrupt epithelial differentiation.[21]

The most important and conclusive method of diagnosing oral leukoplakia is histopathologic examination of the biopsy specimen. The majority of the subjects in present study reported with mild epithelial dysplasia (58.3%), which was in concurrence with study conducted by Vazquez-Alvarez *et al* 2010[12]; Gopinath *et al* 2016[22]

The higher grades of dysplasia (93.3%) were found to be associated with habit of alcohol and tobacco. This is based on the assumption that ethanol produces reactive oxygen species which react with DNA, proteins and lipids in the mucosal cells, thus disrupting cellular structures and functions and causing oxidative damage which may contribute towards development of dysplasia.[20]

Further, taking into account size of leukoplakic lesion and presence or absence of epithelial dysplasia, a modified classification and staging system was used which facilitates uniform reporting of results of oral leukoplakia.[19] In the present study, out of 60 subjects, majority were categorized into Stage II (55%) followed by Stage III (30%). These results were in agreement with the study conducted by Shetty P *et al* 2016[23], however they were in conflict with study by Vazquez-Alvarez *et al* 2010who observed majority of subjects in Stage I & III.[12]

Bibliography

1. Mishra M, Mohanty M, Sengupta S, TripathiS. Epidemeological and Clinicopathological Study of Oral Leukoplakia. *Indian J Dermatol Venerol Leprol* 2005; 71:161-165.
2. Sridharan G. Epidemiology, control and prevention of tobacco induced oral mucosal lesions in India. *Indian J Cancer* 2014; 51:80-85.
3. Boker M, Vuckovic N. Cigarette Smoking As a Risk Factor With Oral leukoplakia. *Archive of Oncology* 2002; 10:67-70.
4. Gupta PC, Ray CS. Smokeless Tobacco And Health In India And South Asia. *Respirology* 2003; 8:419-431.
5. Connollyy GN, Winn DM, Hecht SS, Henningfield JE, Walker B, Hoffmann D. The Reemergence of Smokeless Tobacco. *N Engl J Med* 1986; 314:1020-1027.
6. Pindborg JJ. Precancerous Lesions. In: Pindborg JJ, Reichart PA, Smith CJ, Vander wall I, editors. Histological typing of oral cancer and precancer of oral mucosa. 2nd edition, Berlin Heidelberg New York, Springer 1997; p. 43-47
7. Birur P, Shubhasini AR, Bhanushree R, Mendonca P. Correlation of oral homogenous leukoplakia with grades of oral epithelial dysplasia. *IOSR J Dent Med Sci.*2014; 13:98-103.
8. Ramdas K. Oral Precancerous. In: E Lucas (ed), A manual for early diagnosis of oral neoplasia. France, International Agency For Research on Cancer, 2013; p 17-35
9. Branes L, Eveson JW, Reichart P, World DS. Tumours of the oral cavity and oropharynx. *Pathol Genet* 2005; 67:177-179.
10. Van der Waal L, Schepman KP, Van der Meij EH *et al*. A modified classification and staging system for oral leukoplakia. *Oral Oncol* 2000; 36:264-266.
11. D'Costa J, Saranath D, Sanghvi V, Mehta AR: Epstein-Barr virus in tobacco- induced oral cancers and oral lesions in patients from India. *J Oral Pathol Med* 1998; 27:78-82.
12. Vázquez-Álvarez R, Fernández-González F, Gándara-Vila P, Reboiras- López D, García-García A, Gándara-Rey JM. Correlation between clinical and pathologic diagnosis in oral leukoplakia in 54 patients. *Med Oral Patol Oral Cir Bucal.* 2010; 15:832-838.
13. Varshney S, Sandhir S, Mishra S. A study of oral pre-malignant lesions and related risk factors. *Indian J Comm Health*. 2015; 27:130-134.
14. Bisht RS, Singh AK, Sikarwar V, Darbari A. Study over the clinical picture and histopathology of leukoplakia and to establish the correlation between causative factors in the patients of Garhwal hill region. *Natl J Maxillofac Surg* 2013; 4:177-180.
15. Singh S, Gaikwad P, Sapra G, Chauhan R. Clinico-Pathological Evaluation and Correlation of Stages of Oral Submucous Fibrosis with Different Habits.*J Interdiscipl Med Dent Sci* 2015;3:1-6
16. Ishii J, Fujita K, Komori T. Laser surgery as a treatment for oral leukoplakia. *Oral Oncol* 2003;39:759-769
17. Gurudath S, Naik RM, Ganapathy KS, Guruprasad Y, Sujatha D, Pai A. Superoxide dismutase and glutathione peroxidase in oral submucous fibrosis, oral leukoplakia, and oral cancer: A comparative study. *J Orofac Sci* 2012; 4:114-119.
18. Sharma N, Mubeen K. Non -invasive diagnostic tools in early detection of oral epithelial dysplasia. *J Clin Exp*

Dent. 2011; 3:184-188.
19. Ramesh S, Jhincy T, Rani PM, Daniel VA, Sunila T, Vivek V. Frequency of leukoplakia in patients visiting a dental college located in a rural area of south kerala:A Pilot Study. *J Indian Aca Oral Med Radio* 2013;25:109-111
20. Petti S, Scully C. Association between different alcoholic beverages and leukoplakia among non- to moderate-drinking adults: A matched case–control study. *European J Cancer*2006; 42:521-527.
21. Coppe JP, Boysen M, Sun CH. A Role for Fibroblasts in Mediating the Effects of Tobacco-Induced Epithelial Cell Growth and Invasion. *Mol Cancer Res*. 2008;6: 1085–1098.
22. Gopinath D, Thannikunnath BV, Neermun SF. Prevalence of Carcinomatous Foci in Oral Leukoplakia: A Clinicopathologic Study of 546 Indian Samples. *J Clinical Diagnostic Res*. 2016;10:78-83
23. Shetty P, Hegde S, Vinod KS, Kalra S, Goyal P, Patel M. Oral leukoplakia: Clinicopathologic correlation and its relevance to regional tobacco related habits index. *J Contemp Dent Pract* 2016; 17:601-608.

How to cite this article:

Swati Dahiya and Kondajji Ramchandra Vijayalakshmi (2017) 'A Study on Clinical Forms of Oral Leukoplakia With Grades of Oral Epithelial Dysplasia', *International Journal of Current Advanced Research,* 06(11), pp. 7218-7222.
DOI: http://dx.doi.org/10.24327/ijcar.2017.7222.1103

****