Original Study

PREVALENCE OF EPITHELIAL DYSPLASIA IN ORAL LEUKOPLAKIA AND ITS CLINICAL CORRELATION; A RETROSPECTIVE STUDY

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ABSTRACT

Aim: The aim of this study is to evaluate the prevalence rate of epithelial dysplasia (ED) among leukoplakia and its clinical characteristics among south Indian population.

Materials and Methods: This cross sectional retrospective observational study was conducted in two centers including a private dental hospital and a private dental college, India. Twenty nine patients' details were included, the clinical findings such as age, gender, clinical appearance, site of involvement, associated tobacco habits and the histotopathological findings were retrieved from the medical records of OL patients reported between 2015-16.

Statistical analysis: The data were statistically analyzed with chi-square test for comparing the tobacco habit, site of occurrence of clinical type of OL and presence of ED using SPSS version 21 [IBM, Armonk, NY, USA].

Results: Among the twenty nine cases, 26 (89.65%) OL cases were males and 3 (10.35%) were females and the ratio was 1:0.11. The predominant clinical type observed was homogenous (19; 65.50%) followed by 10 non-homogenous (34.50%). Histopathological examination revealed epithelial dysplasia (ED) in 16 (55.17%) cases, out of which 4 (25%) were mild, 7 (43.75%) were moderate and 5 (31.25%) showed severe dysplastic changes with statistical significant difference among homogenous and non-homogenous types with chi-square value of 18.092a and p value of 0.00.

Conclusion: This study showed a high prevalence of dysplasia in both homogenous and non-homogenous OL and emphasizes that the decision for microscopic analysis and early intervention should be independent of the clinical type of OL.

Key words: Oral leukoplakia, Precancerous conditions, Carcinoma in situ, Squamous cell carcinoma.

Introduction

Head and neck Squamous cell carcinomas are amongst the most aggressive tumors, with oral Squamous cell carcinoma (OSCC) representing the clear majority.[1] The tendency for local and regional metastases because of the proximity and uninhibited infiltration of local lymph nodes is supposed to be the greatest contributor to the morbidity and mortality associated with OSCC. [2] Although OSCC do not have linear development, there is general agreement that it begins as a simple epithelial hyperplasia and progresses through oral epithelial dysplasia (OED), with more severe dysplastic changes signifying more extensive genetic aberrations. WHO Collaborating Centre for Oral Cancer and Precancer suggested the criteria and classification of oral epithelial dysplasia for uniformity among pathologist in grading and malignant potential prediction. [3] However, the duration for this process is not known, but is thought to be a relatively slow process, with malignant transformation occurring within 10 years. [4] Early detections at the "precancerous" stage would improve the morbidity and the survival rates in these individuals. OSCC could be preceded by clinically evident oral potentially malignant disorders (OPMDs). [5] Based on the size, clinical type and dysplastic pathological changes (LCP) grading was proposed to clinically stage leukoplakia for better treatment planning. [6]

Oral leukoplakia (OL) is the most common OPMDs of the oral cavity. The risk factors for OL include all forms of tobacco including smoking cigarette, cigar, beedi, pipe, cheroot, snuff powder and tobacco in chewable form in betel quid chewing. Other contributing factors which act synergistically are alcohol, chronic irritation, candidal infection, galvanic current from dissimilar metal restorations, syphilis, micronutrient deficiencies like B complex vitamins, iron and ultraviolet rays. OL are clinically classified as homogeneous and non-homogeneous types. Clinically, non-homogeneous leukoplakia is considered to carry a considerably higher risk for malignant change than homogeneous ones. Its existence is often regarded as the most important indicator of epithelial dysplasia. [6] Hence non-homogeneous OL are readily biopsied and treated immediately. Of concern are homogeneous types of OL. Their benign nature has resulted

in a general, perhaps inaccurate consensus that homogeneous OL have low rates of OED and malignant transformation rate, thereby considering surveillance as the first-line management option which further enhances the risk of OSCC development. [7]

Currently, OED is the most important prognostic indicator for determining the malignant transformation risk of OL. The Increased prevalence rate of OED reported among homogeneous type of OL warrants a need to understand the biologic behavior of these lesions, thereby providing the clinician a guiding path in its early detection at first presentation and to undertake more definitive treatment for this OPMD irrespective of its clinical type. [8] Hence this study was conducted with an aim to analyze the prevalence rate of OED among oral leukoplakia and its correlation with its clinical types and characteristics.

Materials & Methods:

A retrospective descriptive study for OL cases was carried out among patients reported to two centers including a private Sanker Ganesh Dental Hospital and the Department of Oral Medicine, in Sree Mookambika Dental College, India between 2015 and 2016. Patients who were diagnosed clinically as OL case and underwent biopsy for histopathological evaluation were included in this study. Patients diagnosed clinically as OL cases and histopathologically proved as other mucosal lesions were excluded. Out of thirty nine reported cases of OL, ten cases were excluded because of incomplete details/lack of histopathology report. Twenty nine cases of OL, which were clinically diagnosed and histotopathologically confirmed were included in this study. The study was approved by institutional review board (Lr.No 21/2016). The clinical data such as age, gender, clinical type of the lesion (homogenous or non-homogenous), anatomical sites and histopathologic evidence for the presence or absence of epithelial dysplasia and the grades of dysplasia were retrieved from the medical records and tabulated. Chi-square test was done for comparing the tobacco habit, site of occurrence, clinical types of OL and the presence of ED. The data were statistically analyzed using SPSS version 21 [IBM, Armonk, NY, USA].

Results:

Among 29 patients of oral leukoplakia 26 (89.65 %) were males and 3 (10.34%) were females. The male to female ratio was 1:0. Patients were in the age range of 21 to 75 years with a mean of 52. Clinically, the lesions were categorized as homogenous in 19 (65.50%) cases (Figure 1, 2) and non-homogenous in 10 (34.50%) cases. Among the non-homogenous types 7 (70%) were speckled (figure 3), 1 (10%) was granular, 1 (10%) was nodular, and 1 (10%) was ulcerative (Table 1).

Pan chewing was found to be the commonest associated habit seen in 11 (37.93%) patients, Betel quid chewing combined with smoking was seen in 10 (34.48%) patients, and smoking alone was seen in 7 (24.13%) patients. In the present study buccal mucosa was the most frequently involved site and seen in 25 (86.2%) cases, followed by ventral surface of the tongue in 2 (6.9%) and lesion involving multiple sites in 2 (6.9%) cases. There was statistically significant correlation between the oral habits and site of occurrence of OL lesions with Chi-square value of 21.392 and p value of 0.002 (Table 2).

Histopathologic examination of 29 OL revealed oral epithelial dysplasia in 16 (55.17%) cases and no dysplasia in 13 (44.82%) cases. Among 16 dysplastic lesions, 4 (25%) were reported to be mild epithelial dysplasia (figure 4), 7(43.75%) being moderate dysplasia (figure 5) and 5(31.25%) were severe dysplasia (figure 6). Among the 16 OL with OED cases 6 cases (31.57%) were homogenous type and 10 (68.42%) were non homogenous type. Among the cases with mild dysplasia 3 (75%) were homogenous and 1 (25%) was non homogenous. Among cases with moderate dysplasia 3 (42.90%) were homogenous and 4 (57.10%) were non homogenous. All the cases with severe dysplasia 5 (100%) were non homogenous. All the study variables between homogenous and non-homogenous clinical types showed statistical significance chi-square value of 18.092a and p value of 0.00 (Table 3).

Discussion:

Oral leukoplakia is the most common precancerous lesion of the oral mucosa. Epidemiological data on the prevalence of OL have shown ranges from 0.7 to 24.8%. Marked differences are found between the prevalence rates in various countries, in different parts of one country and in the same population. Reasons for the variation in prevalence rates could relate to methodology, the diagnostic criteria and the study population selection. [9]

In developed nations OL are usually found between the 4th and 7th decades, while in the developing nations they may occur 5–10 years earlier. The present study showed that OL occurred more frequently in men of 50 years' age which supports the previous findings. [10] This could be due to the widely prevalent usage of the implicating factors such as chewing and smoking of tobacco among the adult population.

The etiology of OL is considered multifactorial. Number of concomitant factors such as tobacco, alcohol, oral sepsis, chronic friction, syphilis, galvanism and ultraviolet radiation has been discussed to explain the etiology of OL. Earlier descriptive studies especially those performed in India and Denmark have shown that the frequency of OL among smokers is so high that, in the absence of controls, the habit could be considered as causative. [11] However, in contrary to this, we observed tobacco chewing in the form of pan quid to be the most important implicating factor in 37.93% of the patients. Smoking as a single factor was found to be the causative factor only in 24.13% of the patients.

The distribution of OL within the oral cavity differs in different parts of the world. The intraoral locations varied depending upon the chewing and smoking habits involved. The common site of occurrence of OL is buccal mucosa, tongue, and gingiva. In buccal mucosa OL in smokers occurs anteriorly towards commissure, whereas in tobacco chewers it occurs posteriorly involving buccal sulcus also. [12] However, our observations coincide with most of the Asian studies as the buccal mucosa was the most frequently involved site in our study. This can be attributed to the pattern of tobacco usage especially with the prevalent practice of chewing tobacco and placement of quid in the relative sites. There was statistically significant correlation between the oral habits and site of occurrence of OL lesions with Chi-square value of 21.392 and p value 0.002.

The results of this study showed that 19 (65.5%) cases were non-homogenous type; this is in accordance with previous studies that showed homogeneous OL were much more prevalent than non-homogeneous. [11] The present study also showed that 10 (68.42%) cases of the OL with OED were clinically non-homogenous type. Non-homogeneous leukoplakia is considered to carry a considerably higher risk for malignant change than homogeneous ones. Proliferative verrucous leukoplakia (PVL) is considered as a distinct variant, which is common in females and involve multiple intra-oral sites. It has a high rate of malignant transformation.[13] In a retrospective study conducted by Wang, T.Y. et al. (2018) from Taiwan showed malignant transformation rate of 26.40 fold in OL cohort. [14] Neville BW (2002) reported that epithelial dysplasia in OL lesions ranges from 15.6% to 39.2%.[15] However, the present study observed OED in 16 (55.17%) of the patients and no sign of dysplasia in 13 (44.82%) cases. Various immunohistochemical bio markers like podoplanin, P53 and Ki67 can predict epithelial dysplasia and thereby the malignant potential of OL. [16] Liu. Y. et al. (2017) in a study discussed an exfoliative cytology method developed to quantitatively assess the oral cancer risk using DNA index value in patients with OL. [17]

In this study we observed that among the 19 homogenous type of OL, 6 cases (31.57%) had OED and among this, 3 (50%) showed mild dysplasia and another 3 (50%) showed moderate dysplasia. A similar study conducted by Praveen, B., et al (2014) exclusively on 126 homogenous leukoplakia reports higher prevalence rate of 46% mild dysplasia, 26.2% moderate dysplasia, 13.5% severe dysplasia and even micro invasive Squamous cell carcinoma in 3.2% of patients. [18] The result of the present study suggests that OED is highly prevalent among OL lesions of both homogenous and non-homogenous types. Hence homogenous OL also should be looked with suspicion and given a consideration of investigation and a more definite treatment at the earliest time by abandoning the routine wait and watch management strategy. However, there were some limitations which were observed while conducting the research. The present study results cannot be generalized, as the sample size was small. Advanced mmunohistochemical techniques were not used for the expression of podoplanin, p53 and Ki67 for predicting epithelial dysplasias.

Conclusion:

This study observed a higher prevalence of OL in men in the fifth decade. Buccal mucosa was the predominant site involved. Homogenous type was found to be more prevalent (19; 65.5%). OED was seen in 16 (55.17%) of OL cases. This study results emphasize the high prevalence rate of dysplasia among non-homogenous OL (68.42%) and homogenous OL (31.57 %) and emphasize the unpredictable biologic behavior of homogenous OL. Hence all OL lesions should be considered as potentially malignant lesions and requires serious consideration in carrying out immediate investigation and intervention without any delay.

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Clinical features			Frequency	Percentage
Age	21-30		1	3.44%
	31-40		3	10.34%
	41-50		8	27.58 %
	51-60		10	55.47%
	61-70		4	13.79%
	>70		3	10.34%
Gender	Male		26	89.65 %
	Female		3	10.34%
Habits	Tobacco chewing		11	37.93%
	Tobacco chewing and smoking		10	34.48%
	Smoking		7	24.13%
Site	Buccal mucosa		25	86.2%
	Ventral tongue		2	6.9%
	Multiple sites		2	6.9%.
Clinical type	Homogenous		19	65.50%
	Non homogenous		10	34.50%
		Speckled	7	70%
		Nodular	1	10%
		Granular	1	10%
		Ulcerative	1	10%

Table 1: Clinical characteristics of Oral Leukoplakia

		Current pattern of Risk usage				Total	Chi-square	P Value
		Non user	Pan Chewing Only	Smoking Only	Pan Chewing and smoking			
Specific Site of Lesion	Buccal Mucosa	0	10	5	10	25	21.392	0.002
		0.0 %	90.9 %	71.4 %	100.0 %	86.2 %		
	Ventral Surface of the tongue	1	1	0	0	2		
		100.0 %	9.1 %	0.0 %	0.0 %	6.9 %		
	Multiple Sites	0	0	2	0	2		
		0.0 %	0.0 %	28.6 %	0.0 %	6.9 %		
	Total	1	11	7	10	29		
		100.0 %	100.0 %	100.0 %	100.0 %	100.0 %		

*Table 2: Specific Site of Lesion * Current pattern of Risk usage Cross tabulation*

	Mild Dysplastic Changes	Moderate Dysplastic Changes	Severe Dysplastic Changes	Total Dysplastic changes	No Dysplastic Changes	Total	Pearson Chi-Square Value	df	Asymp. Sig. (2-sided)
Homogenous OL exhibited OED	3	3	0	6	13	19	18.092a	3	0.00
	75.00 %	42.90 %	0.00 %	31.57 %	100.00 %	65.50 %			
Non Homogenous OL exhibited OED	1	4	5	10	0	10			
	25.00 %	57.10 %	100.00 %	68.42 %	0.00 %	34.50 %			
	4	7	5	16	13	29			
	25.00 %	43.75 %	31.25 %	55.17 %	44.82 %	100.00 %			

Table 3: Prevalence of Oral Epithelial Dysplasia Among 29 leukoplakia

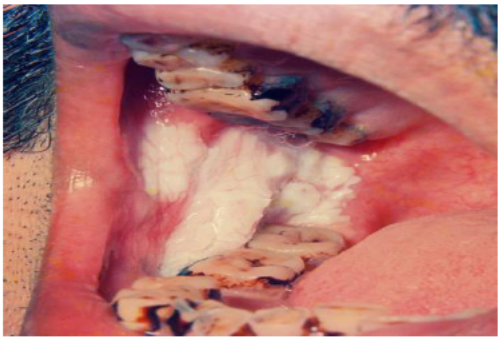

Figure 1: Homogenous oral leukoplakia in the buccal mucosa

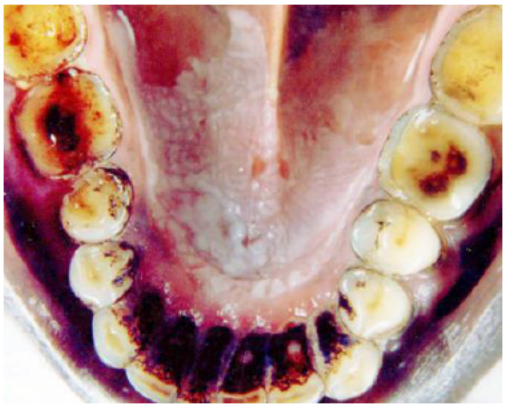

Figure 2: Homogenous oral leukoplakia in the floor of the mouth.

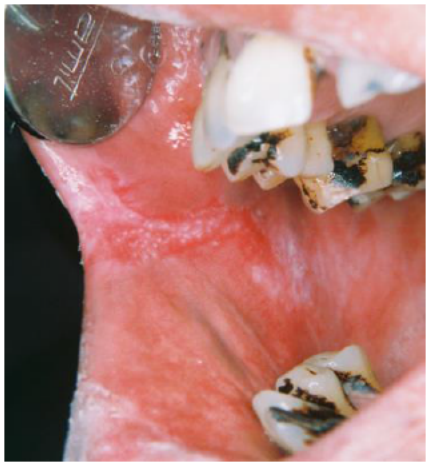

Figure 3: Speckled leukoplakia in the buccal mucosa

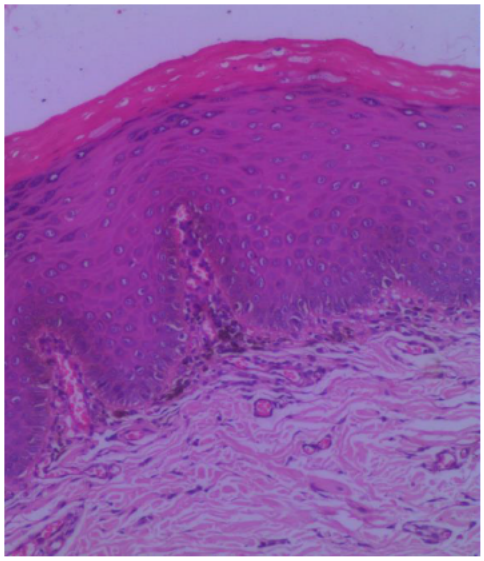

Figure 4: Photomicrograph of 10X magnification showing mild dysplasia

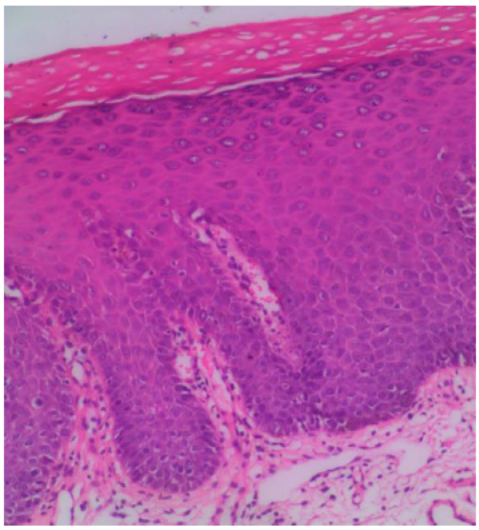

Figure 5: Photomicrograph of 10X magnification showing moderate dysplasia with bulbous rete pegs.

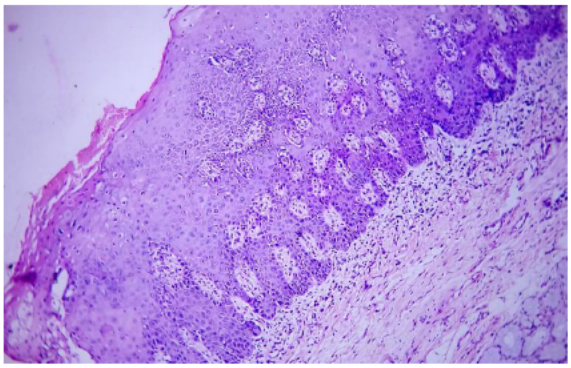

Figure 6: Photomicrograph of 10X magnification showing severe dysplasia from top to bottom of epithelium.