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Correlation of oral homogenous leukoplakia with grades of oral epithelial dysplasia

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Abstract : Background and objectives*: Management of the oral leukoplakia poses a challenge in the general dental set up. It relies heavily on clinical presentation and grading of the histopathological diagnosis.Hence this study was done to correlate oral homogenous leukoplakia with the histopathological grades.*

Materials and methods*:Study was conducted in 126 patients with the clinical diagnosis of oral homogenous leukoplakia and histopathological diagnosis. Data on age, gender, history of habits, lesion site at the initial diagnosis were correlated with the various grades of the oral epithelial dysplasia.*

Results: *The results revealed mean age of 42.12 years, with wide range. 66.6% of the patient population were in younger age group. The site of occurrence were multiple with the buccal mucosa being frequently involved site in 71.6%. Predominantly 65.1% of the patients had the habit of chewing tobacco. 46% of the patients with homogenous leukoplakia had mild dysplasia, 26.2% moderate dysplasia, 13.5% of the severe dysplasia and 3.2% of the microinvasive squamous cell carcinoma. According to the binary system of grading dysplasia 42.9% patients had high risk grade.*

Conclusion*: This study suggests that, severity does not depend on the clinical appearance alone, oral homogenous leukoplakia should be considered along with varying clinical factors.*

Keywords: *Oral potentially malignant disorders, Oral homogenous leukoplakia, Microinvasive Squamous cell carcinoma, Epethelial dysplasia, Binary system*

I. INTRODUCTION

Oral and pharyngeal cancer, grouped together, as the sixth most common cancer in the world. The annual estimated incidence is around 275,000 for oral and 130,300 for pharyngeal cancers [1]. Two thirds of Oral squamous cell carcinoma (OSCC) occurs in developing countries. An age-adjusted rate of oral cancer in India is high that is, 20 per 100,000 population and accounts for over 30% of all cancers in the country [2]. OSCC could be preceded by clinically evident oral potentially malignant disorders (OPMDs) [3, 4]. Oral leukoplakia(OL) is the most common OPMDs of the oral cavity clinically [5]. OL were subdivided into a homogeneous type and a non-homogeneous type (erythroleukoplakia and Verrucous leukoplakia)[6]. Malignant transformation is diverse ranging from 0.13 to 17.5% of lesions [7].

Currently, oral epithelial dysplasia is the most important prognostic indicator for determining the malignant transformation risk of OL [7, 8]. 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 [9]. Oral epithelial dysplasia and the risk of malignant transformation is said to be considerably less in the oral homogenous leukoplakia [10]. Eventhough they are of low risk, oral homogenous leukoplakia are considered the most common OPMDs, suggesting a clinically significant rate of malignant transformation [9]. Hence there is need to understand the behavior of these lesions especially the presence of dysplastic changes and their severity. It will provide us guiding path and help in early detection of OSCC.

This study was conducted with an objective to correlate the oral homogenous leukoplakia and related factors with various histological grades of oral epithelial dysplasia.

II. MATERIALS AND METHODS

This retrospective study was conducted at KLE society's institute of dental sciences, Bangalore. Ethical clearance was obtained. The study included cases between June 2011 to 2013 and consisted of 126 patients with the clinical diagnosis of oral homogenous leukoplakia along with the histopathological diagnosis. Informed consent was obtained from the individual patients. Data on age, gender, history of habits and lesion site at the initial diagnosis of oral homogenous leukoplakia were recorded.

Homogeneous leukoplakia, predominantly white lesion of uniform flat, thin appearance that may exhibit shallow cracks and that has a smooth, wrinkled or corrugated surface with a consistent texture throughout was included in the study [11]. The exclusion criteria of the study was, any patient with the diagnosis of oral leukoplakia and concomitant oral cancer at the initial visit, patient with the nonhomogenous leukoplakia, any patient with the white lesions of the normal variations of oral cavity such as linea alba,

leukoedema and other potentially malignant disorders such as lichen planus, oral submucous fibrosis, discoid lupus erythematosis.

Histopathological diagnosis of all the cases was analysed. The procedure for all the cases involved biopsy to obtain tissue, following which the tissue was fixed in the 10% formalin, embedded in the paraffin and processed for routine histologic examination. The histopathologic evaluation was done by an oral pathologist. The histopathological diagnosis of the lesions were classified according the WHO 2005 classification as squamous hyperplasia, mild dysplasia, moderate dysplasia, severe dysplasia and carcinoma in situ [12]. Histopathologic diagnosis were also classified according to the binary system of grading dysplasia by Kujan et al (2006) as, ''low-risk"(No⁄Questionable⁄ Mild) and ''high-risk" lesion((Moderate/ Severe/Carcinoma insitu) [13,14].The grades of the oral epithelial dysplasia were correlated with the varying clinical factors related to the oral homogenous leukoplakia.

2.1 Statistical analysis:

All statistical analysis was carried out using Statistical Package for Social Science (SPSS, V 10.5). The correlation between the clinical variables and the binary system was done using the chi-square test. The level of statistical significance was set as $p<0.05$.

III. RESULTS

The study consisted of 126 patients diagnosed clinically with oral homogenous leukoplakia. Patients were in the age group of 17 to 73 years, with the mean age of 42.12years (Standard deviation 13.54). Among 126 patients, 23 were female and 103 were male patients. All patients gave tobacco habit history and it varied from chewing tobacco, smoking, both variants and some patients had the habit of alcohol consumption along with the tobacco consumption (Table 1).

Majority of the patients had the habit of chewing tobacco in 65.1% (n =82). The types of the chewable tobacco varied from the traditional betel quid consisting of the leaf of the betel vine wrapped around areca or betel nut (nut of Areca catechu L), slaked lime, catechu (extract of Acacia) and tobacco. Other variants were Gutka, Hans, Pan Parag and other commercially available tobacco products. 24.6 % (n=31) had smoking habit either beedi or cigarette smoking. The site of occurrence of the oral homogenous leukoplakia varied (Table 1). The buccal mucosa was the most common site involved, 71.6% patients with the lesions located in the buccal mucosa (n=91).

Histological examination, of the biopsy specimens revealed 46% (n=58) patients having mild epithelial dysplasia, this being the most common pathology diagnosis among the study group. Moderate dysplasia was the second most common in 26.2% (n=33) patients. Severe epithelial dysplasia were noted in the 13.5 % (n=17) patients. Squamous hyperplasia without dysplasia was noted in the 11.1% (n=14) patients. Interestingly we found 3.2% (n=4) patients with the microinvasive squamous cell carcinoma (Fig.1). The clinical factors age, gender, habit history and the site of oral homogenous leukoplakia were correlated with the WHO grades of the oral epithelial dysplasia (Table 2).

According to the binary system of grading dysplasia, high risk lesions were noted in the 42.9% (n=54) patients and low risk lesions were noted in the (57.2%)(n= 72) patients. The clinical factors of oral homogenous leukoplakia were also correlated with the binary grades of the oral epithelial dysplasia (Table 3).

On correlation there was a statistical significance between the age and the grades (p=0.008). However with the correlation of the gender and habits with the grades there was nonsignificant association (p=0.594, p=0.143).

Table No.1 Clinical data of 126 oral homogenous leukoplakia

Clinical features	**Frequency**	**Percentage (%)**
Gender:		
Male	103	81.7
Female	23	18.3
Habits:		
Smokeless(Chewing tobacco)	82	65.1
Smoking	31	24.6
Both	6	4.8
Alchohol with smoking and smokeless	7	5.6

Site:		
Buccal mucosa	91	71.6
Retrocomissures	12	9.5
Labial mucosa	12	9.5
Buccal mucosa and the retrocommisures	2	1.6
Buccal vestibule	2	1.6
Lateral border of the tongue	2	1.6
Multiple sites of the oral mucosa	2	1.6
Buccal mucosa and vestibule	1	0.8
Gingiva	1	0.8
Dorsum of the tongue	1	0.8

Table 2. Correlation of clinical factors with the grades of oral epithelial dysplasia

Clinical factors		**Histopathological grades**					
		Squamous Hyperplasia	**Mild Dysplasia**	**Moderate Dysplasia**	**Severe Dysplasia**	**Microinvasive Squamous cell carcinoma**	**Total**
Age	**<45year**	11(13.1%)	44(52.4%)	18(21.4%)	8(9.5%)	3(3.6%)	84(100%)
	>45 years	3(7.1%)	14(33.3%)	15(35.7%)	9(21.4%)	1(2.4%)	42(100%)
Gender	**Female**	2(8.7%)	10(43.5%)	6(26.1%)	3(13%)	2(8.7%)	23(100%)
	Male	12(11.7%)	48(46.6%)	27(26.2%)	14(13.6%)	2(1.9%)	103(100%)
Habits	**Chewable tobacco**	9(11.1%)	43(52.4%	20(24.4%)	8(9.8%)	2(2.4%)	82(100%)
	Smoking	3(9.7%)	13(41.9%)	10(32.3%)	4(12.9%)	1(3.2%)	31(100%)
	Both	1(16.7%)	1(16.7%)	3(50%)	-	1(16.7%)	6(100%)
	Alcohol with tobacco habit	1(14.3%)	1(14.3%)	-	-	5(71.4%)	7(100%)
Site	**Buccal mucosa**	12 (13.2%)	42(46.2%)	23(25.3%)	11(12.1%)	3(3.3%)	91(100%)
	Retrocommisures	1 (8.3%)	4 (33.3%)	5(41.7%)	1(8.3%)	1(8.3%)	12(100%)
	Labial mucosa	-	7(58.3%)	2(16.7%)	3(25%)	-	12(100%)
	Buccal mucosa &retrocommisures	-	-	2(100%)	-	-	2(100%)
	Buccal mucosa &Vestibule	-	1(100%)	-	-	-	1(100%)
	Buccal vestibule	1(50%)	1(50%)	-	-	-	2(100%)
	Dorsum of the tongue	-	1(100%)	-	-	-	1(100%)
	Lateral border of the tongue	-	-	1(50%)	1(50%)	-	2(100%)
	Gingiva	-	1(100%)	-	-	-	1(100%)
	Multiple site	-	1(50%)	-	1(50%)	-	2(100%)
	Total	14(11.1%)	58(46%)	33(26.1%)	17(13.4%)	4(3.2%)	126(100%)

Table 3. Cross tabulation of the clinical factors with the High risk and the Low risk grades of binary grading of the oral epithelial dysplasia

		Binary system grades			
Clinical factors		**Low Risk**	**High risk**	**Total**	**P value**
Age	**<45 years**	55(65.5%)	29(34.5%)	84(100%)	0.008*
	>45 years	17(40.5%)	25(59.5%)	42(100%)	
Sex	**Female**	12(52.2%)	11(47.8%)	23(100%)	
	Male	60(58.3%)	43(41.7%)	103(100%)	0.594
Habits	**Smokeless**	52(63.4%)	30(36.6%)	82(100%)	
	Smoking	16(51.6%	15(48.4%)	31(100%)	0.143
	Both	4(66.7%)	2(33.3%)	6(100%)	
	Alchohol with tobacco	2(28.6%)	5(71.4%)	7(100%)	
Site	**Buccal mucosa**	54(59.4%)	37(40.7%)	91(100%)	-
	Retrocommisures	5(41.6%)	7(58.3%)	12(100%)	
	Labial mucosa	7(58.3%)	5(41.7%)	12(100%)	
	Buccal mucosa & Retrocommisures	-	2(100%)	2(100%)	
	Buccal mucosa &Vestibule	1(100%)	-	1(100%)	
	Buccal Vestibule	1(100%)	-	2(100%)	
	Dorsum of the tongue	1(100%)	-	1(100%)	
	Lateral border of the tongue	-	2(100%)	2(100%)	
	Gingiva	1(100%)	-	1(100%)	
	Multiple Site	1(50%)	1(50%)	2(100%)	

*Significant

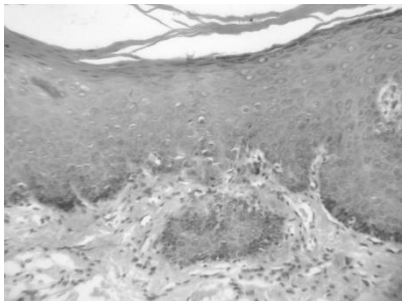

Fig..1- Photomicrograph of microinvasive squamous cell carcinoma

IV. DISCUSSION

Oral leukoplakia (OL) is the most common potentially malignant disorder of the oral mucosa [15].The risk of malignant transformation of the OL is difficult to assess, the clinical risk factors for the OL transformation vary among different study populations [16]. The presence of epithelial dysplasia is a marker of the malignant potential of oral leukoplakia, and the risk of an individual leukoplakic lesion to progress to carcinoma increases with the increase of the grade of the epithelial dysplasia [17-20].

Nonhomogenous type of oral leukoplakia is often associated with epithelial dysplasia and carcinoma[21]. Increased degree of malignant transformation is found in nonhomgenous leukoplakia than the homogenous leukoplakia [22, 23]. India is a region of relatively high prevalence of OSCC and leukoplakia[16].Here presence of homogenous leukoplakia which is the most common oral potential malignant disorder cannot be neglected [9]. Homogenous leukoplakia is also said to have clinically significant malignant transformation, despite their supposed benign and low-risk nature [9]. Hence this study was undertaken to compare the clinical features with the oral epithelial dysplasia.

In the developed nations, oral leukoplakias are usually found between the 4^{th} and 7^{th} decades, while in the developing world they may occur 5–10 years earlier [16]. In our study the mean age of occurrence was 42.12 years, with a wide variation in the age group between the 17 to 73 years. The earlier age of occurrence is related to the tobacco chewing habit prevalent in India. The male-to-female ratio was noted to vary enormously from district to district in India [23, 24]. In agreement in our study males were predominantly affected with a large

proportion (81.7%) compared to the females (18.3%). The 10-year leukoplakia review in India claimed that if there were no tobacco habit, there would be no leukoplakia [23]. Similarly all the patients in our study had the history of habits and the majority of the patients had tobacco chewing habit in 65.1%, which included traditional as well as commercially available products.

In most studies from western countries, the predominant OPMDs sites are the tongue and floor of the[25, 26]. But studies from India, Taiwan and other Southeast Asian countries, indicated that the buccal mucosa is the most common site of premalignancy [27, 28]. In our study the site of occurrence varied with the involvement of the multiple site, but the most common site of occurrence was, buccal mucosa in 71.6% which was followed by the retrocommisures as well as the labial mucosa in 9.5%, only 2.4% of the cases with the tongue involvement. This is due to the pattern of tobacco usage especially with the practice of chewing tobacco and placement of quid in the relative sites.

In our study, histopathological analysis provided a valuable data. The grades of oral epithelial dysplasia as well as binary system of grading dysplasia were considered. In the study 46% of the patients had mild epithelial dysplasia, however the presence of 26.2% moderate dysplasia, 13.5% of the severe dysplasia and 3.2% of the microinvasive Squamous cell carcinoma in clinically benign appearing oral homogenous leukoplakia were the matter of concern.

According to the binary system of grading oral dysplasia, 80% of high risk lesions progressed to malignancy, compared to only 15% of low risk lesions [13]. It has been shown to have merit in that better agreement was reached between those experienced in examining oral biopsies [13, 14]. Hence we considered this system in our study to correlate with the clinical factors of oral homogenous leukoplakia. When we considered the patients, above and the below 45 years of age group and correlated with the grades of risk, there was a statistical significant difference (p=0.008) and 66.6% of the patient population were in younger age group. Among 4 cases of microinvasive squamous cell carcinoma, 3 cases were found in this age group and also 34.5% of the patients in this group had high risk grade. There was no statistical significant difference between the males and females when related to binary system of grades of dysplasia (p=0.594).There was also no significant difference between the habits and grades of risk. It is related to the wide variations in the habits. However, tobacco habit prevailed specially in chewable form and 36.6% of the patients were in the high risk grade.

V. CONCLUSION

This study was undertaken, to provide an indicator for the clinical diagnosis at patients initial presentation and to carry out immediate intervention without further delay. Severity does not depend on the clinical appearance alone. Oral homogenous leukoplakia poses challenging situation and as presented in the data, there might be dysplastic features with significant risks. It is the conglomerate of the varying factor namely age, sex, especially habit. Hence oral homogenous leukoplakia should be considered along with other clinical factors, especially habit history should lead to suspicion. Biopsy should be undertaken at initial visit and the management should be done accordingly.

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