Epidemiology and correlation of the clinicopathological features in oral epithelial dysplasia: analysis of 173 cases

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Abstract

Oral epithelial dysplasias (OEDs) are potentially malignant disorders characterized by diverse degrees of cellular atypia. The early and careful diagnosis has extreme importance, allowing prevention of the progression to the oral squamous cell carcinoma. This study aimed to determine the epidemiology and then correlate it with the clinicopathological features of OED. One hundred seventy-three cases of oral lesions retrieved from the files of a Service of Pathological Anatomy, covering a 38-year period, were submitted to descriptive statistical analysis through the Pearson χ^2 test. The majority of cases were from affected females (57.9%), with a peak of occurrence in the age group of 41 and 55 years (37.3%), white patients (64.8%), and those with lesions located on the gingiva/alveolar ridge (25.1%). The lesions predominantly presented with white color (56.8%) and were described as nodules (27.4%), with a rough surface (76.7%), an exophytic growth (79.1%), and a sessile base (95.6%). The majority of the lesions with degree of mild (34.6%) and moderate (34.9%) OED had clinical diagnosis of leukoplakia, whereas 33.3% of the lesions with degree of severe had clinical diagnosis of squamous cell carcinoma ($P < .05$). Tobacco use was the risk habit more related with OED (42.6%) ($P > .05$). The knowledge of OED epidemiology and clinical features provide a better understanding of the factors that possibly are associated with the malignant transformation of OED. Furthermore, these results contribute to supporting a prompt and accurate recognition of these lesions in clinical practice.

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1. Introduction

The term *potentially malignant disorders* (PMD) has been used to describe clinical presentations that may have a potential to become cancer [1-4]. These lesions show variable clinical presentation such as leukoplakia, erythroplakia, submucous fibrosis, actinic keratosis, palatal lesions in reverse smokers, lichen planus, discoid lupus erythematosus, and hereditary disorders such as dyskeratosis congenita and epidermolysis bullosa [1,5-7]. The presence of epithelial dysplasia is generally accepted as one of the most important predictors of malignant development in lesions [1]. Nevertheless, it is recognized that, occasionally, nondysplastic lesions may turn into cancer, whereas not all dysplastic lesions become malignant neoplasms [2-4].

The histopathological feature of oral epithelial dysplasia (OED) is characterized when architectural disturbance is accompanied by cytological atypia with loss of normal maturation and stratification of keratinocytes [8,9]. Conventionally, dysplasia is divided into grades: mild, moderate, and severe [2]. The presence of moderate or severe dysplasia

has been accepted to have the greatest likelihood for malignant transformation [5].

Oral erythroplakia shows the highest malignant transformation rates among all potentially malignant disorders of the oral mucosa. More than 90% of the cases already exhibit dysplasia, carcinoma in situ, or invasive carcinoma [10].

Estimates of the so-called malignant transformation rates of PMD in the literature vary enormously, from site to site within the mouth, from population to population, and from study to study. Schepman et al [11] and Silverman et al [12] reported a range from 1.4% to 7%. In 1995, Lumerman et al [13] reported that 6.6% to 36% of epithelial dysplasias may transform to oral squamous cell carcinoma. In a recent study [5], the malignant transformation rate of PMD was estimated to be from 1.9% to 5.4%. In accordance with cited studies, Ho et al [8] reported that the risk of transformation of OED to cancer has a range from 1.4% to 7.62% per year. The variation in rates from study to study is attributed to differences in follow-up times, study group selection, and tobacco habits [7].

Oral epithelial dysplasia, not associated with any specific clinical appearance, is a term assigned to the histopathological changes associated with increased risk of malignant transformation [5]. Oral epithelial dysplasia typically presents itself as a predominantly white, red, or mixed white and red mucosal lesion [14]. The accurate clinical diagnosis of these pathologies and also the epidemiological data knowledge have a huge value in giving directions to the microscopic study of cytological and architectural alterations. Thus, a precise histopathological diagnostic must be done, further making possible a better understanding of clinical factors that are commonly associated with potentially malignant disorders. The early diagnosis of these pathologies may prevent their transformation in squamous cells carcinoma, consequently implying a better prognosis.

There are little available data in the literature about the clinical features of OED. Thus, the aims of this study were to determine the epidemiology and the clinical pattern of OEDs and then correlate the clinicopathological features in the different grades of these lesions.

2. Materials and methods

A retrospective study of 173 cases of OED in which biopsy was performed that were obtained over a period of 38 years, from 1970 to 2008, was designed.

The histopathological features were classified into mild, moderate, and severe OED. All lesions were diagnosed by specialist oral pathologists and defined according to the criteria of classification of the World Health Organization [2].

Our sample was composed of all specimens histopathologically diagnosed as various degrees of OED, except those that showed intense inflammatory infiltrate.

The records of these cases were reviewed and analyzed. Information regarding the frequency, sex, age, race, biopsy type, and clinical features were collected. In addition, site, color of the lesion, clinical diagnosis and presence of risk habits (tobacco and alcohol use) were correlated with the degree of OED.

The data were tabulated and analyzed statistically using the Statistical Package for the Social Sciences software version 17.0 (SPSS, Chicago, IL). The Pearson χ^2 test was used to compare differences between groups, which were regarded as significant when the *P* value was less than .05.

The study was approved by the Research Ethics Committee.

3. Results

One hundred seventy-three of 9621 oral soft and hard tissue lesions from the histopathology records of our service were confirmed histologically to be OED, giving an incidence rate of 1.79%. One hundred eight (62.4%) of the patients had lesions with histopathological features of mild OED, 50 (28.9%) were moderate, and 15 (8.7%) were severe.

Among the 173 cases of OED biopsies, there were 99 females (57.9%), 72 males (42.1%), and 2 unknown cases, with a female to male ratio of 1.37:1, with age ranging from 15 to 90 years old and peak of occurrence in the fifth and sixth decades of life. White patients were the most common (n = 94; 64.8%), and black patients (n = 33; 22.8%) were the second most frequent. This information was not available in 28 records.

Most of the lesions were described as nodules (27.4%), with a rough surface (76.7%), an exophytic growth (79.1%), and sessile base (95.6%) (Table 1).

The majority (n = 90; 59.2%) of cases were surgically excised, 62 (40.8%) were incisional biopsies, and 21 were unknown cases.

The alveolar ridge/gingiva (24.4%) and lower lip (23.8%) were the most commonly affected oral sites, followed by the palate (19.1%) and buccal mucosa (14.3%). Severe OED was more likely in lesions of the tongue (26.7%) or floor of the mouth (20%), whereas mild OED was more likely in lesions of the lower lip. There were no statistically significant associations between the site of lesion and degree of OED (*P* > .05) (Table 2).

Eighty-nine (56.8%) lesions presented with white color, whereas 27 (17%) were red and 20 (12.6%) presented with white and red. The white color was related with all degrees of OED, and the mixed white and red lesions were more related with severe OED (30.8%) (Table 3). There was no statistical significance (*P* > .05).

The majority of the lesions with degree of mild (34.6%) and moderate (34.9%) OED had clinical diagnosis of leukoplakia, whereas 33.3% of the lesions with degree of severe had clinical diagnosis of squamous cell carcinoma (Table 4). There were statistically significant associations between degrees of OED and the clinical diagnosis of lesions (*P* < .05).

Table 1
Clinical features of OED in Brazilians

Aspect	n (%)	Surface	n (%)	Growth	n (%)	Implantation	n (%)
Nodular	32 (27.4)	Rough	23 (76.7)	Exophytic	68 (79.1)	Sessile	109 (95.6)
Ulcerated	23 (19.7)			Endophytic	17 (19.8)		
Patches	7 (6.0)	Flat	7 (25.3)	Exophytic/endophytic	1 (1.2)	Pedunculated	5 (4.4)
Others	55 (47.0)						
Total	117 (100)*	Total	30 (100)*	Total	86 (100)*	Total	114 (100)*
Missing*:	56 cases	Missing*:	143 cases	Missing*:	87 cases	Missing*:	59 cases

Natal/RN–2010.
  * For each Total number there is an amount of cases not evaluated due to lack of data.

Almost half of the patients were only smokers (54.1%), and the use of the tobacco was the habit more related with all degrees of OED (Table 5). There was statistical significance ($P < .05$).

4. Discussion

The clinical and histopathological diagnosis of potentially malignant disorders can be difficult, and it is important that clinicians are able to recognize those mucosal lesions that can be OED [15]. The present work was done with data from lesions histopathologically diagnosed as OEDs, providing the epidemiology and clinicopathological correlation of these pathologies.

One hundred seventy-three of 9621 oral soft and hard tissue lesions from the histopathology records of our service were confirmed histologically as OED, giving an incidence rate of 1.79%, in agreement with other studies [13].

The female to male ratio in this study was 1.37:1, unlike the other studies [5,10,15,16]. This can be due to the increase of the number of exposed women to the factors of risks currently, such as the tobacco use and the consumption of alcohol.

The age at presentation is an important clinical parameter when the differential diagnosis of a lesion is being formulated. In our study, the age range was 15 to 90 years with a mean of almost 54 years and with a peak in the sixth decade. The age at presentation of our patient population was consistent with previous reports [4,5,13,15,17,18]. The development of these lesions in the cited age group coincided with one previous to decade affected by the oral cancer. This fact reinforces the theory that some OEDs can originate malignant lesions.

The predominance of white patients was observed. This is in accordance with previous studies [15,17]. Almost 24% of OEDs were in inferior lip, which suggests that the solar radiation was the main cause of a reasonable amount of those lesions. This can explain a larger number of white patients with OED because they are more susceptible to this etiological factor. These data also can be related to the fact that white patients, because of their socioeconomic features, have more opportunities to access oral health services in Brazil.

Clinical characteristics can help in the diagnostic evaluation of the lesions that are suspected of being epithelial dysplasia [19]. In these series, the most common clinical feature of OED was the presence of white sessile nodule with rough surface. The clinical features of OED are compatible with lesions like leukoplakia, erythroplakia, or erythroleukoplakia [15,20].

Cowan et al [18] showed increased numbers of biopsies from 1985 onward, suggesting a change at clinical practice in terms of using biopsy as an investigation tool. Although surgery is the first choice in the management of oral leukoplakia by most relevant specialists [21], the hypothesis that the removal of potentially malignant oral lesions could prevent the onset of oral cancer remains unproved. However, Lodi and Porter [22] suggested that even if excisional biopsy of leukoplakia is not effective as an intervention of primary prevention (ie, to prevent malignant transformation), it may have a role as intervention of secondary prevention (ie, to detect very early cancer undetected by an incisional biopsy).

Table 2
Correlation among the degree of OED and site of the lesions (n = 168)*

Degree of OED				Site of the lesions				
	Alveolar ridge/gingiva n (%)	Lower lip n (%)	Palate n (%)	Buccal mucosa n (%)	Tongue n (%)	Floor of the mouth n (%)	Upper lip n (%)	Total n (%)
Mild	29 (27.9)	26 (25)	18 (17.3)	16 (15.4)	11 (10.6)	2 (1.9)	2 (1.9)	104 (100)
Moderate	10 (20.8)	11 (22.9)	12 (25)	7 (14.6)	4 (8.3)	3 (6.3)	1 (2.1)	48 (100)
Severe	1 (6.7)	3 (20)	2 (13.3)	2 (13.3)	4 (26.7)	3 (20)	0 (0)	15 (100)
Total n (%)	41 (24.4)	40 (23.8)	32 (19)	25 (14.9)	19 (11.3)	8 (4.8)	3 (1.8)	168 (100)

Natal/RN-2010. Pearson χ^2 ($P > .05$).
  * Missing: 5 cases.

Table 3
Correlation among degree of OED and color of the lesions (n = 159)*

Degree of OED			Color of the lesions		
	White n (%)	Red n (%)	White/red n (%)	Others n (%)	Total n (%)
Mild	56 (56)	19 (19)	9 (9)	16 (16)	100 (100)
Moderate	26 (56.5)	15 (7)	7 (15.2)	6 (13)	46 (100)
Severe	7 (53.8)	1 (7.7)	4 (30.8)	1 (7.7)	13 (100)
Total n (%)	89 (56)	27 (17)	20 (12.6)	23 (14.5)	159 (100)

Natal/RN–2010. Pearson χ^2 ($P > .05$).
   * Missing: 14 cases.

Table 5
Correlation among the degree of OED and risk habits from patients (n = 61)*

Degree of OED			Risk habits		
	Tobacco n (%)	Alcohol n (%)	Tobacco + alcohol n (%)	No habits n (%)	Total n (%)
Mild	19 (51.4)	1 (2.7)	2 (5.4)	15 (40.5)	37 (100)
Moderate	12 (63.2)	0 (0)	0 (0)	7 (36.8)	19 (100)
Severe	2 (50.0)	0 (0)	0 (0)	2 (50)	4 (100)
Total n (%)	33 (54.1)	1 (1.6)	2 (3.3)	25 (41.0)	61 (100)

Natal/RN–2010. Pearson χ^2 ($P < .05$).
   * Missing: 112 cases.

In our cases, the majority of cases were surgically excised; and this can be justified by the lesions' size, which varied from 0.1 to 2.0 cm. Examination of the sequentially excised specimens showed that there was a range of grades of dysplasia in different portions of the specimen [13,18]. This suggests that incisional biopsy samples cannot be representative of the true nature of the lesion and that histologic examination of the entire clinical lesion is necessary for an accurate grading of dysplastic lesions.

In the present study, the alveolar ridge/gingiva (25.1%) and lower lip (23.8%) were the most frequent sites of OED. Some studies have reported that the tongue, floor of the mouth, and the lower lip were the most common sites for OED [13,16,23]. The supposed areas of greatest risk for malignant changes when exposed to carcinogenic factors— the floor of mouth and tongue [24]— accounted for only 11.3% and 4.8%, respectively, of OED lesions in the present study. Nevertheless, there was a higher frequency of severe OED in these locations compared with the other sites, in agreement with the previous studies [15].

The white lesions were more related with all the degrees of the OED. However, the colors white and red (speckled leukoplakias) were more related with severe OED, similar to the other studies [4,25]. In the present study, the clinical presentation of lesions was not a significant predictor of degree of OED; but with increased degrees of OED, we found more speckled lesions.

Leukoplakia was the more frequent clinical diagnosis, being the lesion classically associated with dysplastic changes, mainly mild and moderate OED, in agreement

with other studies [1,4,5]. Our study has shown a suitable agreement between the clinical and histopathological diagnostic.

Risk factors associated with oral carcinoma development, such as alcohol or tobacco use, weak diet in antioxidants like C and E vitamins and carotenes, occupational exposure to carcinogens, viral infections, and also genetical and hereditary factors, can influence the establishment and behavior of potentially malignant disorders [26]. In this study, however, it was not possible to analyze if others risk factors in addition to tobacco and alcohol use were associated with the OED development because the investigation was retrospective and made with medical registers, many of them lacking these informations. Among the analyzed factors, the tobacco use was the most prevalent.

Almost half of the patients had risk habits associated with OED, and most of them were related to the habit of smoking. In the present study and in agreement with previous reports [17], no degree of OED was particularly influenced by social habits related to tobacco use, implying that this risk factor is associated with all OED degrees.

It is concluded that lesions with OED manifest clinically mainly as leukoplakias with mild dysplasia and occur mainly on the alveolar ridge/gingiva and lower lip. Conventional clinical and histopathological (degree of the OED) characteristics are still the most important parameters for the prediction of malignant transformation in oral potentially malignant disorders in routine diagnostic oral pathology. These findings analyzed together contribute to supporting a prompt and accurate recognition of these lesions in clinical practice.

Table 4
Correlation among the degree of OED and clinical diagnosis of the lesions (n = 165)*

Degree of OED											
	LK n (%)	SCC n (%)	ET n (%)	ELK n (%)	AC n (%)	LP n (%)	NS n (%)	FK n (%)	FH n (%)	SP n (%)	Others n (%)	Total n (%)
Mild	37 (34.6)	5 (4.7)	4 (3.7)	2 (1.9)	7 (6.5)	5 (4.7)	4 (3.7)	1 (0.9)	16 (15.0)	3 (2.8)	23 (21.5)	107 (100)
Moderate	15 (34.9)	8 (18.6)	0 (0)	0 (0)	9 (20.9)	0 (0)	1 (2.3)	0 (0)	4 (9.3)	1 (2.3)	5 (11.6)	43 (100)
Severe	2 (13.3)	5 (33.3)	0 (0)	0 (0)	2 (13.3)	1 (6.7)	0 (0)	0 (0)	2 (13.3)	3 (20.0)	0 (0)	15 (100)
Total n (%)	54 (32.7)	18 (10.9)	4 (2.4)	2 (1.2)	18 (10.9)	6 (3.6)	5 (3.0)	1 (0.6)	22 (13.3)	7 (4.2)	28 (17.0)	165(100)

Natal/RN-2010. Pearson χ^2 ($P < .05$). LK indicates leukoplakia; SCC, squamous cell carcinoma; ET, erythroplakia; ELK, erythroleukoplakia; AC, actinic cheilitis; LP, lichen planus; NS, nicotinic stomatitis; FK, frictional keratosis; FH, fibrous hyperplasia; SP, squamous papilloma.
   * Missing: 8 cases.

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