

Original research article

Epidemiological study of oral lesions related to human papillomavirus (HPV)

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Abstract

Introduction and Objective: The aim of this study was to evaluate the epidemiological aspects of oral lesions related to human papillomavirus (HPV). **Material and methods:** The sample was composed of histopathological reports issued and archived by the Oral Pathology Department of the Public Laboratory of Mato Grosso, Brazil, between 2005 and 2013. The information's were collected from diagnosis requisition sheets and histopathological reports and were related to gender, age, histopathological diagnosis and anatomical localization. The statistical treatment analyzed data through frequency distribution. **Results:** Two hundred and thirty four reports (3.26%) presented a positive diagnosis for HPV. Among the positive lesions, squamous cell carcinoma was the most prevalent (n = 144, 61.53%) and the lesions occurred mainly between 51 and 60 years (n = 43; 29.86%). Verruga vulgaris were more prevalent in participants aged 41-50 years (n = 4; 23.52%) and the anatomical location in which it was most commonly found was lip (n = 6; 35.29%), while papilloma (n = 17; 23.87%) was more prevalent in participants between 41 and 50 years and in the oral mucosa. **Conclusion:** There was a high prevalence of oral HPV-related lesions in men and participants between 41 and 50 years. Squamous cell carcinoma was the most diagnosed lesion and the lip was the most affected anatomical region.

Introduction

Human papillomavirus (HPV) is a virus of the Papovaviridae family which has a non-enveloped icosahedral shape with 72 capsomers and a circular double-stranded DNA genome [37]. This virus does not multiply in cultures and is mostly epitheliotropic, that is, it infects the epithelium of the skin and mucous membranes and promotes its proliferation. HPV can lead to the development of several benign, premalignant and malignant lesions on mucosal and cutaneous surfaces [1, 24, 30]. The main route of transmission of the virus is sexual [1, 7, 31] and the highest incidence of HPV infection occurs between 20 and 40 years of age, which coincides with the peak of sexual activity [13].

Currently, more than 200 HPV types have been identified [2]. Considering the potential for malignancy of the virus, it can be classified as low (types 6, 11, 13, 32, 34, 40, 42, 44, 53, 54, 55 and 63) and high (types 16, 18, 31, 33 and 35) potential [12, 6]. Although the literature presents varied data regarding the frequency of HPV in oral lesions [10, 14], 24 viral types have already been found in lesions diagnosed in the oral cavity (types 1, 2, 3, 4, 6, 7, 10, 11, 13, 16, 18, 31, 32, 33, 35, 45, 52, 55, 57, 58, 59, 69, 72 and 73) [18, 32, 34, 36].

In the oral mucosa, HPV is the etiological agent of benign lesions such as papilloma, focal epithelial hyperplasia, verruga vulgaris and condyloma [4, 11, 15, 28, 29]. Papilloma is a lesion that affects the soft palate, tongue, lingual brake and lower lip and is usually single and small (<1 cm) [6]. It has exophytic growth and appears as a broad-based ovoid swelling or as a pedicled lesion. Its surface may have a rough warty outline or appear as small digitiform projections. Its color may vary from white to pink, depending on the degree of vascularization and keratinization [32]. Verruga vulgaris has often been localized to the lips, hard palate, gum and dorsal surface of the tongue [27]. This lesion presents clinical and histological features of a common skin wart [33].

The incidence of oral carcinoma has increased significantly over the past three decades, and HPV has been directly implicated as the cause [8]. Squamous cell carcinoma (SCC) represents 90% of all malignant tumors affecting the oral cavity [25]. Studies point HPV 16 as the most prevalent viral type in head and neck cancer lesions [16, 18, 30, 35]. Kreimer *et al.* [18] found a prevalence of HPV in SCC of 23.5%. Of this total, 16% were type 16. HPV 18 was the second most common oncogenic HPV type.

Mazon [25] evaluated the association between HPV presence and oral cancer using the immunohistochemistry technique. The author verified the presence of HPV in 38% of the lesions, with the presence of low potential HPV types (6 and 11) in benign lesions and high potential types (16 and 18) in malignant lesions. Tinoco *et al.* [35] studied the relationship between HPV infection and the development of malignant (SCC) and benign (papillomatous epithelial hyperplasia and papilloma) lesions in the oral cavity and oropharynx. The authors observed the presence of viral DNA in 16 (42.5%) of 38 cases of SCC, 19 (95%) of 20 cases of hyperplasia and in all eight cases (100%) of papilloma.

Considering the importance of epidemiological studies related to oral lesions associated to HPV, including oral cancer, and the lack of data pertinent to the state of Mato Grosso, the aim of the present study was to evaluate the prevalence of positive histopathological diagnoses for HPV virus in lesions in a subpopulation of Central Brazil.

Material and methods

This was a cross-sectional, descriptive and retrospective study performed by verifying histopathological reports of surgical specimens referred to the Mato Grosso State Government Oral Histopathology Laboratory (MT Laboratory, Cuiabá, Mato Grosso, Brazil), from 2005 to 2013. The search was developed from the exam requisition forms and their respective reports, all filed in the MT Laboratory Lesion Bank.

The inclusion criteria of this study were histopathological reports of oral lesions with positive diagnosis for HPV virus, duly filled. Records with unspecified data were excluded from the search. Data related to gender, age, histopathological diagnosis (verruca vulgaris, papilloma and squamous cell carcinoma) and anatomical location of the lesion (buccal floor, face, gum, lip, tongue, oral mucosa, oropharynx and palate) were collected and archived in digital spreadsheets. The variables were submitted to descriptive statistics. The study protocol was reviewed and approved by the Research Ethics Committee of the University of Cuiabá (UNIC) (CAAE 37414814.2.0000.5165).

Results and Discussion

In this study histopathological reports of surgical specimens sent to the MT Laboratory's

histopathological diagnosis service were analyzed, from 2005 to 2013. This period was selected because it corresponds to the beginning of the service's activities and its termination, since in 2014, the HPV vaccination campaign began in the state of Mato Grosso.

The Mato Grosso oral histopathology service was created through Ordinance 195 of the Mato Grosso State Health Department [23], which established the State Politics Care for Mouth and Face Diseases [22]. These actions were consolidated with the Law No. 8342, which determined that the basic health units of Mato Grosso should perform oral diagnostic tests (exfoliative cytology and biopsies) and established the MT Laboratory as the State Reference Center to perform the examinations [22, 23]. Thus, the MT Laboratory file concentrates the diagnoses of the mouth and face lesions of the entire state, as well as the demographic data (gender, age and origin) referring to these lesions. The concentration of the reports in one place facilitated the analysis developed in the present study.

Of the analyzed reports, 234 (3.26%) had a positive diagnosis for HPV-related lesions. Table I shows the distribution of HPV-associated lesion diagnoses according to the type of lesion and

year of diagnosis. Among HPV-positive lesions, squamous cell carcinoma was the most prevalent (n = 144; 61.53%) followed by papilloma with 73 records (31.19%) and verruga vulgaris with 17 records (7.26%). Similar result was found by Correa [9] who found that out of a total of 5081 evaluated lesions, 2.57% were HPV-associated lesions. Gillison *et al.* [16] found a prevalence of 6.9% in a population of 14-69 years in the USA. Considering the total number of records, it can be verified that the verruga vulgaris corresponded to 0.23%, the papilloma to 1.01% and the squamous cell carcinoma to 2.00% of the lesions. These results corroborate the findings of de Castro *et al.* [11]. However, Correa [9], when studying the prevalence of HPV-associated lesions, observed that papilloma was the most prevalent lesion, occurring in 60.30% of the sample. The prevalence of HPV in lesions located in the oral cavity and oropharynx region is not yet well understood [4, 26]. The variations found reflect differences in sample selection and size, in the technique of obtaining and treating surgical specimens and the different methodologies employed in collecting and analyzing data from each study [31].

Table I - Distribution of diagnoses of lesions associated with human papilloma virus (HPV) according to the type of lesion and year of diagnosis

Year of diagnosis	Type of lesion			Total lesions n (%)	Total n (%)
	Verruga vulgaris n (%)	Papilloma n (%)	Squamous cell carcinoma n (%)		
2005	1 (5.88)	6 (8.21)	8 (5.55)	15 (6.41)	294 (4.09)
2006	4 (23.52)	10 (13.69)	21 (14.58)	35 (14.95)	914 (12.73)
2007	2 (11.76)	14 (19.17)	30 (20.83)	46 (19.65)	1025 (14.28)
2008	2 (11.76)	11 (15.06)	20 (13.88)	33 (14.52)	928 (12.93)
2009	2 (11.76)	9 (12.32)	23 (15.97)	34 (14.52)	1061 (14.78)
2010	1 (5.88)	9 (12.32)	14 (9.72)	24 (10.25)	919 (12.80)
2011	2 (11.76)	5 (6.84)	11 (7.63)	18 (7.69)	688 (9.58)
2012	2 (11.76)	6 (8.21)	3 (2.08)	11 (4.70)	610 (8.50)
2013	1 (5.88)	3 (4.10)	14 (9.72)	18 (7.69)	737 (10.27)
Total	17 (0.23)	73 (1.01)	144 (2.00)	234 (3.26)	7176 (100)

The percentage was calculated for each type of injury, which demonstrates different distribution in the total number of cases

Verruga vulgaris and squamous cell carcinoma were most commonly found in the lip, 35.29% and 20.80%, respectively, while papilloma was more frequently observed in the oral mucosa (26.02%) (table II).

Tabela II - Distribution of oral lesions according to gender, age and anatomical location

Variable	Type of lesion			Total n (%)
	Verruga vulgaris n (%)	Papilloma n (%)	Squamous cell carcinoma n (%)	
Gender (n=234)				
Male	11 (64.70)	39 (53.42)	108 (75)	158 (67.52)
Female	6 (35.29)	34 (46.7)	36 (25)	76 (32.47)
Age (n=234)				
0 to 10 years	2 (11.76)	13 (17.80)	0 (0.00)	15 (6.41)
11 to 20 years	1 (5.88)	6 (8.21)	0 (0.00)	7 (2.99)
21 to 30 years	2 (11.76)	11 (15.08)	3 (2.08)	16 (6.83)
31 to 40 years	2 (11.76)	13 (17.80)	5 (3.47)	20 (8.54)
41 to 50 years	4 (23.52)	17 (23.87)	40 (27.97)	61 (26.06)
51 to 60 years	3 (17.64)	8 (10.95)	43 (29.86)	54 (23.07)
61 to 70 years	3 (17.64)	4 (5.47)	26 (18.05)	33 (14.70)
≥ 71 years	0 (0.00)	1 (1.36)	27 (18.75)	28 (11.96)
Anatomical location (n=239)				
Mouth floor	0 (0.00)	2 (2.73)	24 (16.10)	26 (10.87)
Face	2 (11.76)	0 (0.00)	6 (4.02)	8 (3.34)
Gum	0 (0.00)	3 (4.10)	14 (9.39)	17 (7.11)
Lip	6 (35.29)	17 (23.28)	31(20.80)	54 (22.59)
Tongue	4 (23.52)	15 (20.54)	26 (17.44)	45 (18.82)
Buccal mucosa	2 (11.76)	19 (26.02)	28 (18.79)	49 (20.50)
Oropharynx	0 (0.00)	0 (0.00)	2 (1.34)	2 (0.83)
Palate	3 (17.64)	17 (23.28)	18 (12.08)	38 (15.89)

The percentage was calculated for each type of injury, which demonstrates different distribution in the total number of cases

Regarding the anatomical location of the lesions, verruga vulgaris and squamous cell carcinoma were most commonly found in the lip, 35.29% and 20.80%, respectively, while papilloma was more frequently observed in the oral mucosa (26.02%). Data from this study are similar to the results obtained by previous studies [11, 27]. Miller & Johnstone [26] analyzed whether papilloma can be considered a risk factor for the development of squamous cell carcinoma. The authors found that HPV is more frequently detected in dysplastic and carcinomatous lesions and stated that the role of HPV in oral carcinogenesis appears to be lower compared to smoking and alcohol.

In the present study, most injuries were diagnosed in males (n = 158; 67.52%), with a male-female ratio of 2.07: 1 (table II). This result was

concordant to that observed in other studies [5, 11, 15, 21]. However, other studies indicate a reduction, or even an inversion in this gender disparity [3, 5, 17]. Gillison *et al.* [16] observed a prevalence of oral HPV three times higher in males and among them the prevalence of HPV 16 was five times higher, which could explain the higher incidence of malignant lesions in men, as found in this study. One possible explanation for the high prevalence among men could be the greater possibility of HPV transmission from females to males [20]. Hormonal differences between the sexes can affect the duration of the infection. Higher serum conversion rates among women in response to genital HPV infection could also, in theory, provide greater protection against subsequent oral infection [19, 20].

Analysis in relation to age showed that verruga vulgaris and papilloma occurred more frequently in individuals aged between 41-50 years, while squamous cell carcinoma was more frequent in the age group 51-60 years [31]. These data are in agreement with previous studies [15, 17]. Llewellyn *et al.* [19] observed that oral cancer occurs more often in individuals belonging to the fifth and sixth decades of life.

The lack of epidemiological data related to oral HPV-associated lesions in several geographic regions of Brazil motivated this study. The information gathered will certainly help in the development of prevention politics. Future prospective studies based on follow-up of these patients with a view to evaluate immunization protocols and their implications need to be developed.

Conclusion

The prevalence of HPV-associated oral lesions in the Mato Grosso Oral Histopathology Service is similar to that observed in studies conducted in other populations in which a high number of lesions are observed in males; the most affected age group is between 41-50 years old; the most commonly diagnosed lesion is squamous cell carcinoma; and the lip is the most affected anatomical region.

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