

## Prevalence of oral papillomas in Brazilian children: a retrospective study of biopsied lesions

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**Abstract:** **Introduction:** Human papillomavirus (HPV) is an etiologic factor for several diseases of the oral mucosa and skin that can undergo a malignant process. Vaccination is the most important form of prevention, with girls being vaccinated between the ages of 9 and 13 and boys between the ages of 11 and 13. There is still no consensus on the prevalence of the HPV virus in children. **Aim:** To review the prevalence of HPV in children aged 1 to 13 years based on a database of reports of biopsied lesions diagnosed with papilloma analyzed in a national reference laboratory. **Material and methods:** Anatomic-pathologic reports of biopsies received at the Oral and Maxillofacial Pathology Laboratory of the Faculty of Dentistry of the College of São Paulo were analyzed over a 20-year period, between 2002 and 2022. Information on gender, lesion location and diagnostic hypotheses was also collected. **Results:** In a database of 93,950 reports, the age group analyzed accounted for 4,203 and 99 (2.3%) were diagnosed with papilloma. The proportion of male and female reports was similar at 50.5% and 49.5% respectively. The most common location of the lesion found was the lip region (48%). The most frequently cited diagnostic hypotheses were epulis and verruca vulgaris. **Conclusion:** The prevalence of papillomas in Brazilian children aged 1 to 13 years was 2.3%. Early diagnosis and advice on HPV vaccination can prevent and avoid exacerbation of the disease. Recognizing the clinical features of lesions is essential for correct diagnosis and early intervention and counseling.

**Key words:** Human Papillomavirus, Mouth, Children, Pediatric Dentistry, Prevalence.

## Prevalencia de papiloma oral en niños brasileños: un estudio retrospectivo de lesiones biopsiadas

**Resumen:** **Introducción:** El virus del papiloma humano (VPH) es un factor etiológico de diversas enfermedades de la mucosa oral y de la piel que pueden derivar en neoplasias malignas. La vacunación es la principal forma de prevención, inmunizando a las niñas de 9 a 13 años y a los niños de 11 a 13 años. Todavía no hay consenso sobre la prevalencia del virus VPH en niños. **Objetivo:** Verificar la prevalencia del VPH en niños de 1 a 13 años a partir de una base de datos de informes de biopsias de lesiones diagnosticadas de papiloma analizadas en un laboratorio nacional de referencia. **Material y métodos:** Se analizaron los informes anatomopatológicos de biopsias recibidas por el Laboratorio de Patología Oral y Maxilofacial de la Facultad de Odontología de la Universidad de São Paulo en un período de 20 años, de 2002 a 2022. También se recogieron informaciones sobre sexo, localización de la lesión e hipótesis diagnóstica. **Resultados:** En una base de datos de 93.950 informes, 4.203 comprendían el grupo de edad analizado y 99 (2,3%) tenían diagnóstico de papiloma. El porcentaje de varones y mujeres fue similar, 50,5% y 49,5% respectivamente. La localización más frecuente fueron los labios (48%). Las hipótesis diagnósticas más citadas fueron epúlides y verruga vulgar. **Conclusión:** La prevalencia del papiloma en niños brasileños de 1 a 13 años fue del 2,3%. El reconocimiento de las características clínicas de las lesiones es esencial para el diagnóstico correcto y la intervención precoz, así como la orientación.

**Palabras clave:** virus del papiloma humano, boca, niños, prevalencia.

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## Prevalência de papiloma oral em crianças brasileiras: um estudo retrospectivo de lesões biopsiadas

**Resumo: Introdução:** O papiloma vírus humano (HPV) é fator etiológico para diversas doenças na mucosa oral e na pele que podem sofrer processo de malignização. A vacinação é a principal forma de prevenção, imunizando meninas de 9 a 13 anos e meninos de 11 a 13 anos. Ainda não há um consenso sobre a prevalência do vírus HPV em crianças. **Objetivo:** Verificar a prevalência de HPV em crianças de 1 a 13 anos de idade com base em um banco de laudos de lesões biopsiadas com diagnóstico de papiloma analisadas em um laboratório de referência nacional. **Material e Métodos:** Foi feita a análise de laudos anatomopatológicos de biópsias recebidas pelo Laboratório de Patologia Bucal e Maxilofacial da Faculdade de Odontologia da Universidade de São Paulo em um período de 20 anos, compreendido entre ao anos 2002 a 2022. Informações de sexo, localização da lesão e hipóteses diagnósticas também foram coletadas. **Resultados:** Em um banco de 93.950 laudos, 4.203 compreendiam a faixa etária analisada e 99 (2,3%) tinham o diagnóstico de papiloma. A porcentagem de laudos do sexo masculino e feminino foi similar, sendo 50,5% e 49,5%, respectivamente. A localização da lesão mais frequente encontrada foi a região dos lábios (48%). Hipóteses diagnósticas mais citadas foram epúlide e verruga vulgar. **Conclusão:** A prevalência de papiloma em crianças brasileiras de 1 a 13 anos foi de 2,3%. Reconhecer características clínicas das lesões é essencial para um correto diagnóstico e intervenção precoce bem como para evitar o agravamento da doença.

**Palavras-chave:** Vírus do Papiloma Humano, Boca, Crianças, Odontopediatria, Prevalência.

### Introduction

HPV is the acronym for Human Papilloma Virus (HPV). They are viruses that can infect the skin, the anogenital area, the oral cavity and the mucous membranes<sup>1</sup>. In the oral mucosa, most lesions caused by HPV are benign. Pathological entities associated with HPV include verruca vulgaris, oral squamous epithelium, condyloma and focal epithelial hyperplasia (Heck's disease)<sup>2, 3</sup>.

In children, transmission can occur vertically, from mother to child at the time of birth, when the child is exposed to contaminated cells in the cervix and vaginal canal. The placenta and amniotic fluid are also considered routes of infection<sup>4</sup>. Horizontal transmission can also occur when an uninfected person has direct contact with the infected skin or mucous membrane of another person<sup>5</sup>.

Transmission through sexual contact during childhood and adolescence is part of possible sexual abuse situations, but in most cases it is not possible to determine the origin of the infection<sup>6</sup>.

Currently, more than 200 types of Human Papillomavirus (HPV) have been identified, classified according to their genetic similarity and the possibility of being involved in the development of different types of lesions, especially malignant ones. This DNA virus permanently infects cells in the deeper layers of the skin and mucosal epithelium after infection and can remain latent and subclinical or proliferative and cause lesions<sup>7</sup>.

As HPV screening in children is not routinely performed, data on HPV in childhood are insufficient for epidemiologic conclusions. The few studies that refer to the prevalence of

HPV in children show a wide range from 2 to 44% worldwide <sup>3, 8</sup>.

Vaccination is the most important method of preventing HPV infection in children and adolescents <sup>9</sup>. It was introduced in 2006 and there are currently at least two types of vaccines commercially available. The bivalent vaccine guarantees protection against virus types 16 and 18 and the tetravalent vaccine <sup>10, 11</sup> provides protection against HPV types 6, 11, 16 and 18. In 2014, the National Immunization Program of Brazil included tetravalent vaccination in the vaccination calendar of the Unified Health System (SUS), focusing on the immunization of girls aged 9 and 13 years and boys aged 11 to 13 years.

To our knowledge, there is no global estimate of HPV prevalence in children. However, recent reports indicate a relatively high prevalence of HPV in children and adolescents, which requires immediate preventive measures. A wide spectrum of definite and possible manifestations of HPV infection has been reported in early childhood <sup>4</sup>.

## Material and Methods

This project is part of a larger investigation entitled "Oral and maxillofacial diseases that have affected pediatric dentistry and pediatric dentistry patients in the last 20 years", approved by the Ethics Committee for Research of the Faculty of Dentistry of the College of São Paulo under the number CAAE: 67845217.6 .00000075.

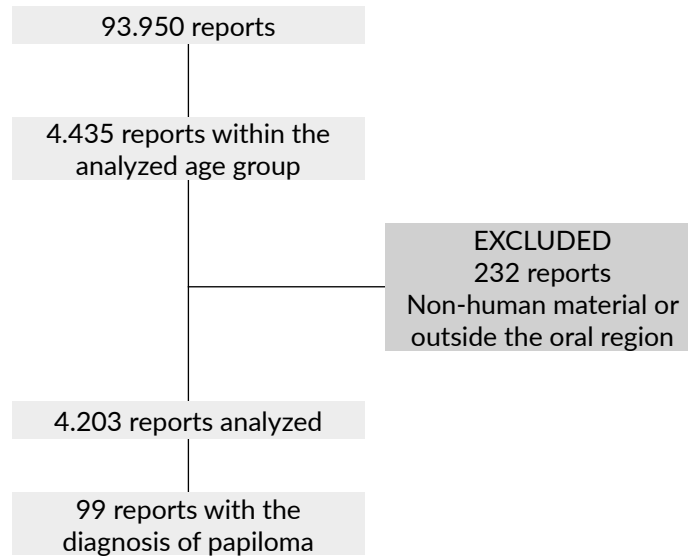
For this retrospective study, biopsy reports received between the years 2000 and 2020 in the laboratory of the Department of Oral Pathology of the Faculty of Dentistry of the College of São Paulo, which were anatomically diagnosed with papilloma, were collected. The age range of the patients analyzed ranged from 1 to 13 years. Detailed information such as gender, location of the lesion and diagnostic hypotheses were recorded using the Microsoft Excel program. For descriptive analysis of the results, the distribution of relative frequencies of HPV lesions in the recommended age range was performed. Reports of non-human material or localizations outside the oral region were excluded from the analyzes.

## Resultados

Following the exclusion and selection process (Figure 1), 99 reports with a diagnosis of papilloma were included in the descriptive analysis, representing 2.3% of the total reports.

Information on the sex and location of the lesion was collected and the results described (Table 1). The prevalence in women and men was similar, with a difference of 0.5%. The most common location of the lesions was the lip region.

Information on the diagnostic hypothesis was also collected and the results found were described (Table 2).



**Figure 1:** Flowchart of the report analysis.

**Table 1:** Demographic and clinical characteristics of the sample.

	N (%)
Gender	
Boys	50 (50.5%)
Girls	49 (49.5%)
Oral Lesion Location	
Lip	47 (48%)
Gingiva	11 (11%)
Palate	10 (10%)
Labial Comissure	8 (8%)
Tongue	7 (7%)
Buccal Mucosa	7 (7%)
Alveolar Ridge	5 (5%)
Other	4 (4%)

**Table 2:** Description of the diagnostic hypotheses found in the data analysis.

Diagnostic Hypotheses
Congenital epulis
Verruca vulgaris
Condyloma
Inflammatory fibrous hyperplasia
Fibroma
Peripheral giant cell lesion
Leukoplakia

## Discussion

This retrospective study describes the prevalence of reports of diagnosed papilloma in children aged 1 to 13 years sent to the FOU SP Oral and Maxillofacial Pathology Laboratory for analysis over a 20-year period.

The defined age range was from 1 to 13 years, an age that has been mandatory since 2014 for the quadrivalent vaccine for girls between 11 and 13 years and for boys between 11 and 13 years. Thus, the prevalence of papillomas was 2.3% out of a total of 4203 reports from patients recommended in the age range of this study.

This prevalence was similar to other retrospective studies looking at oral lesions in children. In Franklin *et al*, 2006<sup>12</sup>, the papilloma finding in the pediatric population was 2.13%. In Barbosa-do Vale, 2013<sup>13</sup>, the finding was 3.81% and in the data published by Cavalcante *et al*, 2016<sup>14</sup>, papilloma was found in 2% of the pediatric population.

One of the limitations in interpreting the results of the main advantage of the present study is that they were not specific for papillomas in all these studies, but rather a representation of the main pathologies observed in children and adolescents. Comparing the frequency in these samples with different methods and age groups of the population therefore makes it difficult to determine a true prevalence of this lesion in children up to 13 years of age. In terms of gender predilection, there was also agreement with the literature that there is no difference. In other words, it can occur in both boys and girls, and to a similar extent<sup>14-16</sup>.

HPV belongs to a group of circular DNA viruses that infect keratinocytes of the skin and mucous membranes of the human body. More than 200 different virus types belonging to the Papillomaviridae family have been described in the literature. The

most important lesions affecting the oral mucosa include oral squamous epithelium and condyloma acuminata, both of which are associated with HPV 6 and 11.

The verruca vulgaris is associated with types 2, 4 and 57. These types are among the 20 most frequently observed oral lesions in young children<sup>15,16</sup>. Therefore, it is plausible to observe the hypotheses of diagnoses of verruca vulgaris and condyloma in second and third place sent by dental surgeons. However, congenital epulis, inflammatory fibrous hyperplasia, fibroma, peripheral lesions of giant cells and leukoplakia are different pathologies in terms of clinical appearance, etiology and morphology<sup>13,17</sup>.

This makes us think about the importance of constant updating that pediatric dentists need to dedicate to semiology in children and adolescents. Even if the treatment is the same, that is, biopsy, diagnosis and, mainly, clinical and behavioral management in relation to care are important<sup>2, 5</sup>. The present research work aims precisely to draw attention to the importance of differential diagnosis between this group of injuries.

With several countries implementing HPV vaccination programs, data on adherence are beginning to emerge, but it is still far from being eradicated. Although the age range for comparison varies internationally, there is a large difference in HPV vaccine uptake between countries, from very high – 86.7% for 3 doses in teenage women of the target age in the UK to very low – 37% for 3 doses among the adolescent age group in the US.

The National HPV Vaccination Program in Australia began school delivery in April 2007 for girls and in February 2013 for boys, using the quadrivalent HPV vaccine [qHPV]. In Brazil, vaccination began in 2014 and, as in other countries, it is offered together with other vaccines in the national school vaccination program (for example, booster vaccines against diphtheria, tetanus and pertussis (DTaP) and against chickenpox)<sup>11, 18, 19</sup>.

Although HPV transmission is widely associated with sexual intercourse, the etiology of this lesion in children and adolescents and its impact on virus transmission still need to be elucidated (15). From the literature collected for this work, the authors argue that HPV transmission is easy due to its excellent survival on surfaces, increasing the incidence of papillomas in children. Knowledge of the etiology of the infection, behavioral analysis of the child and a careful anamnesis help explain its etiology and avoid cases of lawsuits related to false allegations of abuse. Therefore, it is important to keep in mind that when it comes to children, especially those under 3 years of age, with lesions possibly related to HPV, these are not necessarily consequences of sexual abuse<sup>3, 4, 7, 10, 11, 15, 19</sup>. Another limitation of the present study was the impossibility of relating the injuries to their origin of infection and route of contagion.

Finally, we highlight that epidemiological research on oral lesions in children and

in a given geographic region establishes the needs of this population, as well as providing professionals with updated knowledge of the lesions, making it easier to draw up treatment plans and preventive actions. Although the results presented here are compatible with most studies already carried out, there are few specific retrospective studies of HPV in children and adolescents, and this one has a longer period of observation, 20 years in a sample of 93,950 reports.

The pediatric dentist, who is frequently confronted with HPV-related lesions, must take a leading role in this scenario, both in the early diagnosis and treatment of HPV-related oral lesions and in raising awareness and the importance of HPV vaccination among patients, pediatricians and their parents and caregivers. Knowing these numbers makes us think about the importance of comprehensive health surveillance of children and adolescents, the importance of asking and checking with family and friends about vaccination, and the importance of giving people in your social network access to information about vaccination.

## Conclusion

The prevalence of papillomas observed in children aged 1 to 13 years was 2.3% in biopsy lesion reports over 20 years of analysis. There was no significant difference in prevalence compared to gender.

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Recibido: 06/11/2023

Aceptado: 03/02/2024

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