

# HUMAN PAPILLOMAVIRUS IN HEAD AND NECK CARCINOMAS: PREVALENCE AND CLINICOPATHOLOGICAL RELATIONSHIP

*PAPILOMAVÍRUS HUMANO EM CARCINOMAS DE CABEÇA E PESCOÇO: PREVALÊNCIA E RELAÇÃO CLINICOPATOLÓGICA*

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## ABSTRACT

**Introduction:** The human papillomavirus (HPV), associated with other factors such as smoking and drinking, increases the risk of head and neck carcinomas. The presence of the HPV-16 genome, considered as highly carcinogenic, increases the risk by 50%. **Objectives:** To assess the prevalence and clinicopathological relationship of HPV associated with the head and neck carcinomas. **Methods:** This is a systematic literature review, from a bibliographical search on LILACS and MEDLINE databases. **Results:** Thirteen studies were reviewed, which altogether evaluated 1,216 cases of head and neck carcinomas, where HPV was detected, on average, in 36.45% of the cases. HPV-16 was the most prevalent genotype, present in 22 to 100% of positive cases for HPV. A higher prevalence of male subjects was observed in cases where the HPV genome was detected. A lower average age in HPV-positive cases was described in all the studies. An inverse association between the presence of HPV and habits such as smoking and alcohol consumption has been reported, with HPV seeming to be more prevalent in tumors presented by nonsmokers and nondrinkers. **Conclusion:** Despite being associated with smoking and alcohol consumption in some studies, improved prognosis and lower recurrence were reported in head and neck carcinomas with the presence of the HPV genome and a higher prevalence and growing incidence of these tumors in younger individuals.

**Keywords:** Papillomaviridae; head and neck neoplasm; epidemiology.

## RESUMO

**Introdução:** O papilomavírus humano (HPV) associado a outros fatores, como tabagismo e etilismo, aumenta os riscos de surgimento de carcinomas de cabeça e pescoço, sendo que a presença do genoma do HPV 16, considerado de alto poder cancerígeno, aumenta esse risco em até 50%. **Objetivos:** Avaliar a prevalência e relação clinicopatológica do HPV associado aos carcinomas de cabeça e pescoço. **Método:** Revisão sistemática da literatura, a partir de um levantamento bibliográfico nos bancos de dados LILACS e MEDLINE. **Resultados:** Foram revisados 13 estudos que, em conjunto, avaliaram 1.216 casos de carcinoma de cabeça e pescoço onde o HPV foi detectado, em média, em 36,45% dos casos. Nos 13 estudos, o HPV 16 foi o genótipo mais prevalente, presente em 22 a 100% dos casos positivos para o HPV. Maior prevalência de indivíduos do sexo masculino nos casos em que o genoma do HPV foi detectado. Foi descrito, em todos os estudos, uma menor média de idade nos casos HPV positivo. Associação inversa entre a presença do HPV e hábitos como tabagismo e etilismo tem sido relatada, sendo que o HPV parece ser mais prevalente nos tumores de pacientes não fumantes e não etilistas. **Conclusão:** Apesar de ter sido associado ao tabagismo e etilismo em alguns estudos, foi relatado melhor prognóstico e menor recorrência em carcinomas de cabeça e pescoço que apresentam o genoma do HPV, assim como maior prevalência e uma crescente incidência desses tumores em indivíduos mais jovens. **Palavras-chave:** Papillomaviridae; neoplasias de cabeça e pescoço; epidemiologia.

## INTRODUCTION

Human papillomavirus (HPV) shows a high prevalence in cervical carcinomas and other genital areas. However, its prevalence and etiological relationship in head and neck carcinomas are still being investigated, and several studies have been carried out in recent years that support this idea<sup>(1-3)</sup>.

Head and neck carcinomas originate from the aggression caused by chemical, physical, or biological agents that lead to the formation

of differentiated cells that can develop into a tumor<sup>(4)</sup>. Changes in cell genetics lead to the formation of an abnormal process that culminates in cell proliferation, which, if not diagnosed and treated in time, cause the formation of a tumor process with unfavorable prognosis for the patient<sup>(5)</sup>.

Its evolution depends on causal factors beyond the affected site. Separately, factors such as tobacco and alcohol consumption and the presence of high-risk HPV can trigger the carcinogenesis but with a lower speed and aggressiveness than when these factors are associated<sup>(6)</sup>.

The prognosis of these tumors is still grim, despite the developments in diagnostic techniques and treatment, because they have low survival rates at 5 years, around 58.3% for oral cavity carcinomas and 52.7% for oropharyngeal carcinomas<sup>(7,8)</sup>. HPV vaccination campaigns are measures that can influence the natural history of cancers associated with the virus<sup>(9)</sup>.

From a systematic review of literature, this study aims to present articles that investigated the prevalence of samples of HPV in head and neck carcinomas and covering the important aspects about the clinical implications of this relationship.

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## METHOD

This is a systematic review of the literature, from a bibliographical search in the LILACS and MEDLINE databases. The following keywords were used: human papillomavirus; head and neck carcinoma; and prevalence. For the construction of the prevalence table, complete studies were included, which used the polymerase chain reaction (PCR) as the HPV detection method and associated findings to the clinicopathological factors of carcinomas.

## RESULTS AND DISCUSSION

Studies carried out in different geographical regions have investigated the presence of HPV-DNA in head and neck carcinomas (**Table 1**). The identification of the main HPV genotypes present in these tumors was also performed in order to predict the effects of potential HPV vaccines in head and neck carcinomas.

As described in **Table 1**, the presence of HPV-DNA in the reviewed studies ranges from 5% in a study conducted in the United States that evaluated 29 tumors<sup>(13)</sup>, to 100% in a study that analyzed 20 tumors in Malaysia<sup>(11)</sup>. A study in Brazil showed the presence of HPV in 19.5% of the cases evaluated<sup>(14)</sup>. In total, the 13 studies described in **Table 1** evaluated 1,216 cases of head and neck carcinomas, and HPV was detected, on average, in 36.45% of cases. In the 13 studies shown in **Table 1**, HPV-16 was the most prevalent genotype present in 22 to 100% of cases positive for HPV detection.

All the studies shown in **Table 1** used the PCR to detect the HPV genome in the carcinomas evaluated. The PCR method has a high sensitivity for the detection of viral genome, but different results can be obtained as a result of the different sets of primers used in the reaction<sup>(19)</sup>.

Head and neck carcinomas have always revealed smoking and alcohol consumption as the main risk factors. From the studies conducted in the 1980s, HPV has become associated as a risk agent for these carcinomas. However, in the past 15 years, from the numerous antismoking and antialcohol campaigns around the world, many with positive results, the percentage of head and neck carcinomas associated with the virus has increased<sup>(20)</sup>. In the studies presented

in **Table 1**, this relationship is clear, especially, by the presence of HPV-16, considered as of high risk, with high carcinogenic power.

The detection method of the virus genome in the samples is of fundamental importance for the survey of more accurate and reliable results. The PCR is considered a method of high sensitivity and more reliability for this type of study<sup>(21,22)</sup>. All the studies listed in **Table 1** used the PCR as the HPV detection method.

We can observe a high difference in the values presented in different studies, ranging from 5 to 100%. Behavioral and social factors influence the prevalence of the virus in carcinomas of one group studied. In regions where smoking and drinking rates are high, as in some European countries or in some regions within a country, this can influence a lower prevalence of HPV. However, the association between HPV and behavioral factors linked to sexual activity, particularly, oral sex, shows a considerable importance in the prevalence of the virus in these carcinomas<sup>(19)</sup>.

Given the high consumption of alcohol and tobacco by young people and a greater tendency to promiscuity and a greater number of partners, the incidence of these tumors in young people is increasing, as reported in the studies on head and neck carcinomas related to HPV<sup>(23)</sup>.

Studies have shown a better prognosis with greater survival rates among HPV-positive patients when compared with HPV-negative patients. Lower tendency to metastasis and fewer deaths were more common in HPV-positive groups<sup>(10)</sup>. In all the studies described in **Table 1**, there was a higher prevalence of male subjects.

The association of HPV in head and neck carcinomas reveal an important influence on the profile and clinicopathological characteristics of patients<sup>(14)</sup>. HPV-positive groups tend to present a lower average age, lower tendency to metastasize, and fewer deaths when compared with HPV-negative groups<sup>(7,10)</sup>. All the studies surveyed reported a lower average age in HPV-positive groups. HPV was associated with smoking habits in several studies<sup>(8,14,16)</sup>, with no significant values that counteract a higher prevalence of HPV in groups with smoking habits.

## CONCLUSION

In the 13 studies analyzed, HPV was detected, on average, in 36.45% of cases, and HPV-16 was the most prevalent genotype, present in 22 to 100% of HPV-positive cases. The highest prevalence of cases was in male subjects, and the same occurred only in cases in whom the HPV genome was detected. Lower average age, in HPV-positive cases, has been reported in all studies. An inverse association between the presence of HPV and habits such as smoking and drinking has been reported (i.e., HPV seems to be more prevalent in tumors in nonsmoking and nondrinking patients). However, HPV was associated with smoking and alcohol consumption in some studies. The best prognosis and lower recurrence are reported for the head and neck carcinomas that reveal the HPV genome and a higher prevalence of tumors in younger individuals.

## Conflict of interests

The authors report no conflict of interests.

**Table 1** – Detection of HPV-DNA and genotyping of HPV-16 in patients, with head and neck squamous cell carcinomas in different countries, from 2000 to 2013.

Year	Authors	Country/region	n	HPV (%)	HPV-16 (%)
2000	Gillison <i>et al.</i> <sup>(10)</sup>	USA/Baltimore	253	25.0	90.0
2002	Ringström <i>et al.</i> <sup>(1)</sup>	USA	89	20.0	100.0
2007	Lim <i>et al.</i> <sup>(11)</sup>	Malaysia	20	100.0	30.0
2007	Gonzales <i>et al.</i> <sup>(12)</sup>	Argentina	16	43.7	28.6
2008	Simonato <i>et al.</i> <sup>(13)</sup>	USA	29	5.0	17.2
2008	Oliveira <i>et al.</i> <sup>(14)</sup>	Brazil	87	19.5	22.0
2009	Zhao <i>et al.</i> <sup>(15)</sup>	China	52	40.4	63.5
2010	Montaldo <i>et al.</i> <sup>(16)</sup>	Italy	68	60.3	51.0
2010	Hong <i>et al.</i> <sup>(6)</sup>	Australia	198	42.0	87.0
2011	Snietura <i>et al.</i> <sup>(17)</sup>	Poland	66	14.0	100.0
2011	Elango <i>et al.</i> <sup>(2)</sup>	Asia	60	50.0	96.0
2012	Huang <i>et al.</i> <sup>(18)</sup>	Taiwan	103	30.1	51.6
2013	Quintero <i>et al.</i> <sup>(8)</sup>	Colombia	175	23.9	82.0

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