



## **Human Papilloma Virus and Oral Cancer: A Brief Review**

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**Abstract**

*Oral cancer poses a significant global health challenge, with approximately 300,000 new cases reported annually. Human papillomavirus (HPV) has emerged as a major risk factor for the development of oropharyngeal cancer, constituting around 60% of all oral cancer cases. This brief review will discuss the background of HPV, prevention of HPV and oral Cancer, methods for detection and management of the HPV associated oral cancer.*

**Key Words:** *Human papilloma virus, Oral cancer, Tumor cells.*

**Introduction**

In the development of various cancer types, infectious agents, especially viruses, play a substantial role. Approximately 20% of all cancers worldwide are believed to have an infectious origin, with viruses contributing to about 15% of the total cases [1,2]. Various viruses are associated with cancers that originate in specific anatomical regions, such as the liver, genital areas, and oral cavity [3-4]. Notably, a significant proportion of viral-induced cancers emerge in the oral cavity. These include head-and-neck squamous cell carcinoma linked to human papillomavirus (HPV), nasopharyngeal carcinoma associated with Epstein Barr virus (EBV), and oral Kaposi's sarcoma associated with Kaposi's sarcoma-associated herpesvirus (KSHV) [5]. Human papillomavirus (HPV) infection stands as a significant risk factor for a specific subset of head and neck squamous cell carcinomas, independent of conventional risk factors such as tobacco or alcohol use. Globally, approximately 38,000 cases of head and neck cancers are attributed to HPV, with 76% affecting the oropharynx, 12% the oral cavity, and 10% the larynx. It is well established that the HPV status influences the molecular profile and clinical behavior of these tumors, with HPV-positive patients generally exhibiting a more favorable prognosis and treatment response [6-10]. HPVs are small, non-enveloped, circular, double-stranded DNA viruses, approximately 8000 base pairs in length, with a specific tissue tropism that infects epithelial cells of the skin and mucous membranes in the anogenital and upper aerodigestive tracts [10]. Over 200 HPV types have been identified and categorized as low- or high-risk based on their cancer-causing potential. High-risk HPV (HR-HPV) can transform infected cells into cancer cells through the action of the E6 and E7 viral oncoproteins, which disable the TP53 and Rb tumor suppressor genes. A subset of 12 alpha HR-HPV types is classified as carcinogenic to humans by the International Agency for Research on Cancer

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[11-12]. HR-HPV, particularly genotypes 16 and 18, are considered the primary causative agents of cervical cancer, accounting for approximately 70% of cases. Moreover, research implicates HPV in other anogenital and head and neck cancers. While HPV16 has been extensively associated with oropharyngeal tumors, further investigation is needed to establish its relationship with different subtypes of head and neck squamous cell carcinoma [13]. According to Ault [14], approximately 6.2 million new cases of HPV infections occur annually in the United States, with over 20 million individuals estimated to be currently infected. HPV primarily spreads through skin-to-skin sexual contact and affects all sexually active populations. The Centers for Disease Control and Prevention (CDC) estimates that at least half of sexually active individuals will contract HPV at some point in their lifetime, while at least 80% of women in the US acquire HPV before turning 50. Additionally, statistics indicate that around 10% of the American population has an active HPV infection, 4% have cytological abnormalities resulting from HPV, and 1% have developed genital warts due to the virus. Young, sexually active females under the age of 25 are at the highest risk of contracting HPV infections.

### **Prevention of HPV and Oral Cancer**

Vaccines against human papillomavirus (HPV) prove effective in preventing infections caused by the most prevalent types. The vaccines are recommended for children aged 9-13 years, ideally before they become sexually active. This age range is important because the vaccine is most effective when administered before exposure to the virus. Additionally, cervical cancer screening, such as the Papanicolaou test or “pap smear,” can detect early signs of cancer and abnormal cells that may develop into cancer. Regular screening allows for early detection and treatment, leading to improved health outcomes. Indeed, consistent screening has demonstrated a reduction in both the occurrence and fatality rates of cervical cancer. Additionally, genital warts can be addressed through freezing methods. Overall, proactive measures to prevent and identify HPV infections can greatly enhance the likelihood of avoiding severe health complications [15]

### **Detection**

Presently, a range of molecular biological methods is accessible for the detection and genotyping of HPV at DNA, mRNA, and protein levels. These methods include polymerase chain reaction (PCR), real-time PCR, in situ hybridization, immunohistochemistry, and serum antibody assays. These advanced techniques have significantly improved our comprehension of HPV-related diseases. Moreover, next-generation sequencing approaches for HPV provide precise information on genotype composition and its potential impact on cellular

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processes. However, certain collection methods present challenges. Tumoral tissue biopsy, for example, is invasive and may not always be feasible, especially when dealing with inaccessible tumors. The collection of oral exfoliated cells using cotton swabs or cytobrush is limited to a specific area of the mouth, making it challenging to detect non-visible tumors or early molecular changes. To overcome these limitations, the analysis of HPV in oral exfoliated cells from saliva (with or without oral rinses) offers a convenient, non-invasive approach for screening high-risk populations for oral and oropharyngeal cancer. Despite numerous studies investigating the prevalence of salivary HPV DNA in patients with head and neck cancer, a comprehensive systematic review on this topic has been lacking until now. Our study aims to address this gap by providing a thorough overview of the existing literature on the subject.

## Treatment

If you are diagnosed with HPV-caused oral cancer, the choice of treatment depends on various factors, including the cancer's stage and location, your overall health, and personal preferences. Here are potential treatment options for oral cancer caused by HPV:

1. **Surgery:** Often the primary treatment for early-stage oral cancer, surgery involves removing the tumor and surrounding tissue. The objective is to eliminate all cancer cells while preserving as much normal tissue as possible.
2. **Radiation Therapy:** This treatment uses high-energy rays to destroy cancer cells. It can be employed alone or in combination with surgery. External beam radiation therapy directs radiation from outside the body to the affected area, while brachytherapy involves placing small radioactive rods or seeds directly into the tumor site.
3. **Chemotherapy:** Chemotherapy drugs target and destroy cancer cells throughout the body. This option may be used in conjunction with surgery or radiation therapy. Chemotherapy can be administered intravenously or taken orally in pill form.
4. **Targeted Therapy:** Targeted therapy medications specifically aim at cancer cells, minimizing damage to healthy cells. An example is cetuximab, a targeted drug approved for treating advanced oropharyngeal cancer, a type of oral cancer caused by HPV.
5. **Rehabilitation:** After treatment, rehabilitation may be necessary to regain normal function and appearance. Speech therapy, physical therapy, and occupational therapy can aid in restoring speaking, eating, and swallowing abilities.
6. **Cosmetic procedures** may address any changes in appearance. It's essential to remember that each

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person's situation is unique, and the most suitable treatment plan will depend on various individual factors. Consulting with a healthcare professional is vital to determine the best course of action [17].

In conclusion, the link between the oral human papillomavirus (HPV) family and oral cancer has become increasingly apparent. The growing body of evidence strongly suggests a causal connection between HPV and specific types of oral cancer, particularly those affecting the tongue and tonsils, prevalent among young individuals with no history of tobacco or alcohol use. This Review underscores the importance of raising awareness about HPV and its role in oral carcinoma as a critical prevention strategy. Future studies should continue to explore additional risk factors related to oral HPV and the involvement of other HPV types in oral cancer development. By enhancing our understanding of these connections, we can strive to improve early detection methods and effective treatments, ultimately lessening the burden of oral cancer.

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