Al-Salam Journal for Medical Science
Journal Homepage: http://journal.alsalam.edu.iq/index.php/ajbms
E-ISSN: 2959-5398, P-ISSN: 2958-0870

Insights into the relevance of viral infections to the onset of oral malignancies, review study

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DOI: https://doi.org/10.55145/ajbms.2025.4.1.010
Received July 2024; Accepted September 2024; Available online September 2024

ABSTRACT: The purpose of this article is to summarize what is now known about the link between oral cancer, viral infections, and influencing variables by reviewing the scholarly literature on the subject. Inflammatory reactions can be triggered by a variety of hereditary and environmental variables that impact the mouth cavity and its multitude of bacteria. Important functions of this reaction include determining a patient's viral illness susceptibility, promoting chronic inflammation that may lead to oral carcinogenesis, and regulating the human immune system. Researchers have looked at the correlation between viral manifestation and the likelihood of cancer by studying how inflammation of the afflicted epithelium increases the risk. A large body of research indicates that viral infections increase the likelihood of developing various malignancies due to their systemic effects. Alcohol use, smoking, and poor dietary habits are among the many confounding variables linked to oral cancer. The following search engines were utilized: MEDLINE, PubMed, Google Scholar, and ScienceDirect. The keywords that were entered were: head and neck cancer (HNC), oral squamous cell carcinoma (OSCC), and other oral malignancies, viral infections (HSV, CMV, HIV, EBV, HPV), and so on. This review set out to search the relevant literature for a better understanding of the connection between viral infections and oral cancer.

Keyword: oral cancer, viral infections, chronic inflammation

1. INTRODUCTION

Oral cancer rates differ substantially across countries, regions, age groups, racial and ethnic groups, socioeconomic position, and other variables. It is the sixteenth most common cancer and the fifteenth most dangerous disease in the world [1]. Healthcare record quality, preventive education, life expectancies, and population habits differ significantly between developed and developing nations. This disparity is most likely caused by distinct national circumstances, such as low income, low literacy, severe disease stage, limited healthcare access, and insufficient treatment facilities. Several different medical conditions, environmental factors, and genetic variables increase the likelihood of developing cancer of the oral cavity [2]. Oral cancer risk factors include a number of lifestyle choices and behaviors, such as smoking, heavy alcohol consumption, unhealthy diet, radiation exposure, racial/ethnic background, immunosuppression, use of mouthwash, syphilis, dental problems, occupational hazards, and a partner [3]. The hypothesis that some viral infections increase the risk of mouth cancer is still up for discussion. A number of studies have shown, however, that certain Candida species are capable of producing endogenous nitrosamines from nitrites found in saliva and other oral components [4]. Cancer of the head and neck ranks sixth among malignant tumors, making it one of the most urgent public health concerns worldwide [5]. Oral cancer encompasses a wide variety of cancers that can develop anywhere in the mouth or throat, including the lips [6]. There are various types of oral cavity cancers, but the most common is squamous cell carcinoma, which accounts for around 90% of cases [7]. Similar to other types of cancer, OSCC symptoms might vary in form, size, invasion level, and when the disease was detected [8]. Until symptoms appear, many patients with oral cancer are unaware they have the disease, which can mean it has progressed significantly. Early squamous cell carcinomas might manifest as lesions with a combination of red and white patches (erythroplakia) or white plaques (leukoplakia), or even both. Endophytic lesions are characterized by a depressed ulcerated surface and a raised, rolling border, while other lesions progress into exophytic masses with fungating, papillary, or ulcerated

surfaces [9]. The fact that oral cancer is often detected at a very late stage, contributing to the high mortality rate, is largely to blame. The dearth of studies and publications on this cancer type means that the key role of the etiology, which is still not fully understood and is still controversial, goes unexplored. Gaining a better grasp of the links between the topic and specific viral infections should lead to a better approach to treating this illness and provide the framework for upcoming studies.

2. Search Strategy and Selection Criteria

All of the references used in this review are from publications published between 2018 and 2020 that were indexed in databases such as Google Scholar, MEDLINE, Scopus, and the Web of Science. We also searched the reference lists of the publications that were considered for inclusion in the review as well as databases of abstracts pertaining to cancer. There were also proceedings volumes for the "an international conference on "Oral Medicine and Medically Complex Patients for General Dental Practice" and "120 Years of Organized Dental Medicine in the Republic of Croatia" " symposium including. Articles that could only be found in English or a translated version of them were searched for using the following terms: "A review of oral squamous cell carcinomas (OSCCs), "OSCCs: current research and future directions," and "Prevalence of Herpes Simplex Virus (HSV) and Cytomegalovirus (CMV) in oral squamous cell carcinoma patients with a history of alcohol and nicotine abuse."," "Investigation of somatic genetic aberrations and the tumor microenvironment in juvenile B-cell non-Hodgkin lymphoma," "Cytoly," and "Excess cancers among HIV-infected individuals in the United States." Each source's contribution to the Review's overarching subject and aims was one of the deciding factors in its inclusion in the final reference list. Search engines like Citations found in databases such as PubMed, Google Scholar, Web of Science, Medline, and EMBASE.com (owned by Elsevier) were used to scour historical publications and reviews for this review, using a variety of keywords such as oral cancer, viral-related oral cancer, and oral malignancies. Research on viral infections and associated malignancies was also culled from internet archives, with additional input from risk variables published on the World Health Organization's (WHO) website. Since the accuracy of diagnoses for head and neck cancer and related terms is debatable, we opted to do a free-style search rather than use MeSH (Medical Subject Headings). Reviews that provided medical definitions of mouth cancer in English were reviewed. Articles addressing the incidence, diagnosis, and treatment of oral cancer throughout various time periods were considered for inclusion. These publications were included because of their medical and historical importance; they dealt with viral infections, mouth cancer that developed from these infections, and clinical features of this disease. In particular, we sought out primary publications that focused on oral cancer risk factors and viral interactions and steered clear of secondary sources that offered detailed explanations of oncology. We were able to reach conclusions that were in line with the most recent research in the field once we incorporated the data.

3. Oral cancer risk factors

Many factors that lead o oral cancer developing involve both hereditary and environmental variables which are considered s risk factors [10].

Table 1. - An overview of the known and suspected causes of oral cancer risks

Precursor Conditions	Environmental variables	hereditary variables
Chronic candidiasis can be caused by infections such HRV, Treponema pallidum, HIV, Epstein-Barr virus, and others.	Lifestyle choices (including excessive alcohol use, cider brewing, tobacco use Using marijuana, not taking care of one's teeth, chewing betel quid or guṭkha, and smoking or chewing tobacco	Fanconi's anemia
Problems with the mouth that don't go away (such as very harsh mouthwashes, faulty dental implants, gum disease , Gastroesophageal reflux disease GERD)	Low socio-economic status (lack of availability of dental hospitals and clinics)	Xeroderma pigmentosum, scleroderma, and congenital dyskeratosis are hereditary genodermatoses.
Immune suppression and immune disorders (i.e., graft-versus-host	Asbestos, formaldehyde, sulfuric acid, pyrene, methyl pyrene, and workers in the	Syndrome of Plummer-Vinson, also known as

Precursor Conditions	Environmental variables	hereditary variables
disease is a chronic inflammatory syndrome that affects people who have undergone a transplant. (GVHD)	leather and textile professions are all examples of industrial pollutants or occupational exposures.	Patterson-Brown-Kelly
	Inadequate intake of fresh produce, especially carrots, tomatoes, and peppers; genetically engineered meals, such as fried foods; deficiencies in zinc, vitamin A, and vitamin E	Variations in enzyme-encoding genes (such as P450 and XMEs)
	Exposure to radiation (ultraviolet rays, ionizing radiation, radiation treatment)	Diabetes

4. Viral infections related to oral cancer

Some studies have shown that some viruses can raise the risk of mouth cancer [11]. Herpesviruses and human papillomaviruses account for the vast majority of viral infections in the mouth that lead to oral illnesses and cancers. according to Andrei et al. (2022) [12]. If an infection evolves from being asymptomatic to generating symptoms over time, or if an existing problem gets worse over time, like HPV-associated dysplasia turning into invasive malignancy, then changes in oral health can manifest [13]. The diseases that are mentioned cover a wide range of conditions, including HSV-1 and 2, herpes zoster or shingles, oral ulcers and retinitis/uveítis, oral hairy leukoplakia, oral cancers caused by oncoviruses like Epstein-Barr virus, Kaposi's sarcoma-associated herpesvirus, and 'high-risk' HPVs, including HHV-5, HHV-8, and HPV-16, 18, 31, and 33 [14]. Many different kinds of oral cancers exist, including a subgroup of them that impact the upper aerodigestive tract, Kaposi's sarcoma, and Burkitt's lymphoma (BL) [15]. Cancer can be directly caused by oncoviruses like hepatitis C and B viruses (HBV) by a variety of mechanisms, including but not limited to: cell division, genetic instability, migration of cells, and suppression of cell death [16, 17]. These viruses can cause cancer indirectly by causing chronic inflammation.

4.1 Human Papilloma Virus

Human papillomavirus (HPV) infection is a major factor in some types of ontologies involving the head and neck, alongside more traditional risk factors such as smoking and alcohol consumption [18]. Approximately 38,000 cases of ontologies involving the head and neck, are linked with HPV infection worldwide. The oropharynx is affected by around 76% of these malignancies, the oral cavity by about 12%, and the larynx by around 10% [19]. Human papillomavirus (HPV) researchers have found over 200 distinct strains, each with its own level of cancer-causing potential. [20]. Worldwide, the prevalence of oropharyngeal cancers in young individuals is increasing as a result of human papillomavirus (HPV) infections, mirroring trends observed in North America and Europe [21]. There is overwhelming evidence linking HPV to oropharyngeal SCC on a global scale. The following are some of the studies that have been linked to HPV squamous cell carcinoma (HPV-16 + 98% associated with HPV-18), acuminate condylomata and leukoplakia (HPV-6), cutaneous warts in individuals with HIV infection (HPV-7), and several other types of cancer. [22-25].

4.2 Epstein Barr Virus

Infecting about 95% of the world population, it is one of the most prevalent and often encountered human viruses. Following acute infection, whether or not symptoms are present, latent EBV infection persists for life [26]. Thus, EBV can initiate a latent infection, a type of quiet viral infection in which the virus's genes aren't activated, leading to a lack of cytotoxic effects and infectious virus production. Higdon et al. (2023) states that Infectious mononucleosis is caused by the Epstein-Barr virus. [27]. According to Novalic (2020), EBV infects two types of oral target cells: B-lymphocytes and the oro/nasopharynx and/or salivary gland epithelial cells. Thus, EBV is thought to have a role in OSCC and premalignant lesions [28]. The lymphocyte-rich region behind the nose is the site of development for nasopharyngeal carcinoma (NPC), a tumor type of epithelial cells. Only native North Americans, Tunisians, and East Africans, as well as those from Southern China, are endemic to the disease. In contrast to the 1% average in Western nations, 20% of tumors among native North Americans and Cantonese Chinese are non-small cell lung cancers (NPCs)

[29]. While BL cells do not carry EBV, all anaplastic NPC cells do. Genetic susceptibility, environmental factors, and dietary considerations are thought to have a role in the etiology of NPC, according to Wu et al. (2024) [30]. The virus is mainly stored in B lymphocytes, and infected individuals usually have EBV found in lymphoid tissues of the throat and mouth [31]. As expected, Staniewicz and Karpiński (2022) established a correlation between Epstein-Barr virus (EBV) and malignancies such as oral Burkitt's lymphoma, oral squamous cell carcinoma (OSCC), salivary gland epithelioma, and oral diffuse large B-cell non-Hodgkin's lymphoma. [32]. Although EBV may not play a direct role in cancer development, it is frequently linked with immunodeficiency [33]. In persons with compromised immune systems, "oral hairy leukoplakia" is a non-malignant white lesion that forms on the lateral aspect of the tongue and is linked to Epstein-Barr virus (EBV). [34]. The non-Hodgkin, low-differentiation-grade monoclonal B-lymphocyte cancer known as Burkitt's lymphoma (BL) is most commonly found in the jaw and is native to Papua New Guinea and equatorial Africa. Children make up over half of the patients [35]. There are more than 90% of BL that have EBV genomes in these areas. Outside of these regions, sporadic occurrences are the sole ones observed. According to Gong (2024), EBV is identified in only 10% to 20% of tumors in patients of sporadic Bell's lymphoma. Although the association between EBV and cancer has long been known, the precise function of EBV in carcinogenesis remains a mystery [36].

4.3 Human Cytomegalovirus

The opportunistic nature of HCMV infection can cause serious disease or mortality in vulnerable groups, including those undergoing organ transplantation, living with HIV/AIDS, or battling cancer [37]. Griffiths and Reeves (2022) report that the global prevalence of HCMV infection ranges from 70% to 90% of the earth's population. Upon infection of a host, the virus enters a latent state that it sustains for the duration of the host's life. [38]. Nevertheless, it has the potential to reactivate and cause severe sickness in those with compromised immune systems. Infection with HCMV speeds up the progression of some human malignancies, such as breast cancer [40] and brain cancer [39]. A potential involvement of CMV in the pathogenesis of oral squamous cell carcinoma (OSCC) lesions is reported in this study.Multiple international investigations have demonstrated a CMV prevalence in these people ranging from 0% to 90% [41]. Zheng and Savitz (2022) state that herpesviruses, including CMV, have been associated with specific types of human carcinomas. But there is still a risk of oral cancer from CMV [42].

4.4 Herpes Simplex Virus HSV

Infection with the herpes simplex virus (HSV) is highly prevalent worldwide. Although vaginal lesions have been identified as HSV-1 and oral lesions as HSV-2, it is the oro-pharyngeal region that experiences the highest incidence of HSV-1 infections, while the genital region is the primary site of HSV-2 infections. [43]. In genital herpes, the sacral ganglion is involved, while in facial herpes, it may be the trigeminal ganglion. A primary infection and subsequent recurrence of the same site are the most common manifestations of herpes simplex infection [44]. Infections of the eyes, vaginal skin or mucous membranes, congenital skin lesions, infections of the mouth or perioral areas, and severe systemic illnesses like encephalitis and newborn sickness are among the indications and symptoms that can accompany an HSV-1 infection, although many people with the virus show no symptoms at all [45]. Regarding the connection between oral squamous cell carcinoma (OSCC) and cancer, researchers have discovered contradictory information concerning the type 1of herpes simplex virus for many years. As cancer advances, anti-HSV-1 titers tend to rise, according to some research [46]. Research has demonstrated that antibodies against HSV-1 are more prevalent in patients with OSCC lesions or precancerous lesions compared to healthy individuals [47]. While Dayyani et al. (2021) discovered a link between OSCC and HSV-1, they did not find a similar association with HSV-2 [48]. Detectable levels of HSV DNA in the brush samples of 29% of toombak users, according to another study, imply a relationship between HSV and oral cancer [49]. Unlike studies involving other microorganisms, However, researchers studying the relationship between herpes simplex virus (HSV) and oral squamous cell cancer (OSCC) have unfortunately received insufficient money and attention. Only when herpes simplex virus (HSV) is bound to TAR (tobacco-associated residues) can it induce oral cancer. The inhibition of thymidine kinase and DNA polymerase synthesis by TAR molecules was discovered in studies by Inchingolo et al. (2020) and Ahsan et al. (2023). Consequently, this causes an upsurge in infected cell α-proteins (ICP4 and ICP27) and impedes virus shedding [1] [50]. The oral cavity is a prime location for oral Kaposi sarcoma (KS), and HHV-8, also known as Kaposi's sarcoma-related herpesvirus, has been tied to the development of oral cancers in people with HIV [51]. It was found that many KS lesions in AIDS patients contained HHV-8 DNA [32]. According to Moro et al. (2023), the oral microbiota and HIV/HHV-8 co-infection can interact to affect the development and progression of KS [52]. Despite HHV-8's close association with HIV, the virus has only been associated with one case of KS [53]. Despite ongoing investigations, the herpes virus remains unproven as a direct carcinogen in oral squamous cell carcinoma (OSCC).

4.5 Human Immunodeficiency Virus HIV

The human, professional, and monetary spheres are all profoundly affected by the spread of HIV/AIDS, Among the most severe illnesses globally [54]. As immunosuppression develops, the asymptomatic phase of an HIV infection gives way to the symptomatic phase; the infection persists over time. However, AIDS always ends up being the result

[55]. When viruses attack T-helper cells, it drastically lowers a person's immunity [56]. An imbalance in the microbiota of the mouth, brought on by a number of opportunistic infections, can lead to systemic lesions [57]. Some people think of HIV as a "oncovirus," although in reality, it mostly affects people indirectly by making them more immunosuppressed [58]. Activation of the immune system is associated with HIV, which can lead to chronic inflammation and cancer, as stated by Cribbs et al. (2020) [59]. Alterations to the oral microbiome, a decrease in local immune surveillance, and the onset of chronic inflammation are all possible outcomes. It is possible that HIV directly activates B cells by raising levels of activation-induced cytidine deaminase (AID) [60]. Apart from HIV, Speicher et al. (2016) identified numerous other risk factors for head and neck cancers (HNC), including cigarette or smokeless tobacco smoking, betel quid chewing, alcohol or drug usage, and several viral infections. [61]. The International Agency for Research on Cancer concluded in 2009 that HIV, due to its enhanced immunosuppressive effects, raises the likelihood of developing KS, non-Hodgkin's lymphomas, Hodgkin's lymphoma, anal and cervical cancer, oral cavity/pharyngeal cancer, and liver cancer. By 2015, Robbins and colleagues. Necrotizing ulcerative gingivitis, oral candidiasis, oral hairy leukoplakia, Kaposi's sarcoma, linear gingival erythema, nonspecific lymphoma, and necrotizing ulcerative periodontitis are often observed oral lesions in individuals with HIV. [62]. The inflammation of the gums and the progressive loss of attachment are hallmarks of HIV-associated periodontitis, in contrast to conventional periodontitis [63]. Inflammation of the periodontium and immunosuppression are strongly correlated, increasing the risk of LGE, NUG, and NUP [64]. Under conditions of immunological weakness, such as a decrease in the quantity of CD4 T cells in the bloodstream, oral lesions might develop. [65]. The Centers for Disease Control and Prevention (CDC) states that a CD4 count below 200 (<15%) is the clinical definition of AIDS, because HIV mainly impacts CD4 cells [66]. Both an increased risk of infection and the reactivation of latent infections can cause oral diseases in HIV-positive patients [67].

5. Conclusion

Squamous cell carcinomas account for almost 90% of oral cancer cases. These cancers can metastasize to any region of the mouth or neck, including the lips. Many environmental and genetic factors contribute to the start of oral cancer, including the herpes simplex virus (HSV), TAR molecules that restrict viral shedding, alcohol consumption in HIV-related hepatocellular carcinoma (HNC), and oral squamous cell carcinoma (OSCC). The development of oral cancer can be attributed to infections caused by human herpes viruses, including HPV, EBV, CMV, and HSV. Viral infections such as EBV, CMV, and HSV might indirectly contribute to oral carcinogenesis by inducing immunosuppression and chronic inflammation. These viruses, along with HPV-18 and HBV-16, are strongly linked to squamous cell carcinoma (98%) in humans. Salivary gland tumors, oral Burkitt's lymphomas, ovarian squamous cell carcinoma, and non-small cell lung cancer are identified as some of the most common malignancies associated with EBV. The progression of oral cancer is expedited by HIV, which induces immunosuppression and, more precisely, stimulates B-lymphocytes. Cancer risk may increase when two or more viruses interact, as is shown by the fact that HIV and HHV interact to influence the development and progression of KS. There is still a lack of knowledge on the oral biota, the natural history of these viral infections, and their interactions with one another, making it difficult to grasp how they differ. We need new biomarkers and detection methods that are more specific to viruses if we want to investigate the link between the two.

Funding

None

ACKNOWLEDGEMENT

The research team extends its sincere thanks to the Iraqi Center for Cancer and Medical Genetics Research-Mustansiriyah University for provide support and facilities.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

REFERENCES

[1] F. Inchingolo et al., “Oral cancer: A historical review,” Int. J. Environ. Res. Public Health, vol. 17, no. 9, p. 3168, 2020.

[2] N. Goyal et al., “Risk factors for head and neck cancer in more and less developed countries: Analysis from the INHANCE consortium,” Oral Dis., vol. 29, no. 4, pp. 1565–1578, 2023.

[3] J.-H. Seo, Y.-D. Kim, C.-S. Park, K. Han, and Y.-H. Joo, “Hypertension is associated with oral, laryngeal, and esophageal cancer: a nationwide population-based study,” Sci. Rep., vol. 10, no. 1, p. 10291, 2020.

[4] X. Wang, W. Zhang, W. Wu, S. Wu, A. Young, and Z. Yan, "Is Candida albicans a contributor to cancer? A critical review based on the current evidence," Microbiol. Res., vol. 272, p. 127370, 2023.

[5] J. Bouaoud et al., "Unmet needs and perspectives in oral cancer prevention," Cancers (Basel), vol. 14, no. 7, p. 1815, 2022.

[6] N. Lazim and Z. I. M. Mat, "Head and Neck Malignancy: Highlights of Clinical Presentation," Assessment and Treatment, 2023.

[7] S. Givony, "Oral squamous cell carcinoma (OSCC) an overview," J. Med. Sci, vol. 8, pp. 67–74, 2020.

[8] Y. Tan et al., "Oral squamous cell carcinomas: state of the field and emerging directions," Int. J. Oral Sci., vol. 15, no. 1, p. 44, 2023.

[9] B. Sivapathasundharam, "Epithelial neoplasms of the oral cavity," Shafer's Textbook of Oral Pathology E-book, vol. 146, 2020.

[10] M. F. Khan, R. P. Hayhoe, and R. Kabir, "Exploring the risk factors for oral cancer in Pakistan: A systematic literature review," Dent. J., vol. 12, no. 2, 2024.

[11] S. Irani, "New insights into oral cancer-risk factors and prevention: A review of literature," Int. J. Prev. Med., vol. 11, no. 1, p. 202, 2020.

[12] E. C. Andrei et al., "Oral papillomatosis: Its relation with human papilloma virus infection and local immunity-an update," Medicina (Kaunas), vol. 58, no. 8, p. 1103, 2022.

[13] E. Mcilvanna, C. Mccarthy, and K. Gurzawska-Comis, "The Impact of the COVID-19 Pandemic on Oral and Oropharyngeal Cancer," Current Oral Health Reports, pp. 1–9, 2023.

[14] M. Puig, M. Weiss, R. Salinas, D. A. Johnson, and A. Kheirkhah, "Etiology and risk factors for infectious keratitis in South Texas," J. Ophthalmic Vis. Res., vol. 15, no. 2, pp. 128–137, 2020.

[15] P. E. Zeinaty, C. Lebbé, and J. Delyon, "Endemic Kaposi's sarcoma," Cancers (Basel), vol. 15, no. 3, p. 872, 2023.

[16] E. J. Saheb and L. F. Ali, "Interleukin-32 (IL-32) gene expression in Iraqi chronic hepatitis B virus patients," Biochemical & Cellular Archives, vol. 23, no. 2, 2023.

[17] I. B. Kalarani, K. Thasneem, and R. Veerabathiran, "Oncoviruses: future prospects of molecular mechanisms and therapeutic strategies," in Oncogenic viruses, Academic Press, 2023, pp. 81–107.

[18] A. Barsouk, J. S. Aluru, P. Rawla, K. Saginala, and A. Barsouk, "Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma," Med. Sci. (Basel), vol. 11, no. 2, 2023.

[19] M. Pinkiewicz, K. Dorobisz, and T. Zatoński, "Human Papillomavirus-associated head and neck cancers. Where are we now? A systematic review," Cancer Manag. Res., vol. 14, pp. 3313–3324, 2022.

[20] K. A. Tadlaoui, N. Hassou, B. Bennani, and M. M. Ennaji, "Emergence of oncogenic high-risk human papillomavirus types and cervical cancer," in Emerging and Reemerging Viral Pathogens, Academic Press, 2020, pp. 539–570.

[21] S. Ndon, A. Singh, P. K. Ha, J. Aswani, J. Y.-K. Chan, and M. J. Xu, "Human Papillomavirus-associated oropharyngeal cancer: Global epidemiology and public policy implications," Cancers (Basel), vol. 15, no. 16, 2023.

[22] D. M. G. A. Gálvez, "Treatment of Erythroplasia and Cervical HPV in a Young Patient with a Coriolus versicolor Vaginal Gel," BY HUMAN PAPILLOMA VIRUS, vol. 30, 2023.

[23] D. Spirito, F. Pantaleo, G. Di Palo, M. P. Amato, A. Raimondo, and A. Amato, "Oral Human Papillomavirus Benign Lesions and HPV-Related Cancer in Healthy Children: A Systematic Review," Cancers, vol. 15, no. 4, 2023.

[24] S. Singh, S. Ahmad, A. N. Srivastava, and J. S. Misra, "A review on role of human papilloma virus (HPV) in health-related diseases," Advances in Medical, Dental and Health Sciences, vol. 3, no. 3, pp. 34–40, 2020.

[25] N. K. Ghoshal and S. Singh, "Non-Smoker's Cancer-Human Papilloma Virus (HPV) Induced Head & Neck Squamous Cell Carcinoma (HNSCC)," Medical Science Journal for Advance Research, vol. 4, no. 4, pp. 248–258, 2024.

[26] H. Yu and E. S. Robertson, "Epstein-Barr virus history and pathogenesis," Viruses, vol. 15, no. 3, 2023.

[27] L. E. Higdon, J. C. Tan, and J. S. Maltzman, "Infection, rejection, and the connection," Transplantation, vol. 107, no. 3, pp. 584–595, 2023.

[28] Z. Novalic, Cytolytic Virus Activation Therapy for Epstein-Barr virus associated nasopharyngeal and gastric carcinoma, 2020.

[29] T. Huang, "Dietary Habits, Commensal Microbiome, and Nasopharyngeal Carcinoma (Doctoral dissertation)," Karolinska Institutet, 2020.

[30] C.-C. Wu, M.-S. Chen, and J.-Y. Chen, "The application of emodin treatment on nasopharyngeal carcinoma therapy," Biomedicines, vol. 12, no. 3, p. 486, 2024.

[31] G. Houen and N. H. Trier, "Epstein-Barr Virus and systemic autoimmune diseases," Front. Immunol., vol. 11,

p. 587380, 2020.

[32] M. Stasiewicz and T. M. Karpiński, "The oral microbiota and its role in carcinogenesis," Semin. Cancer Biol., vol. 86, no. Pt 3, pp. 633–642, 2022.

[33] B. Fournier and S. Latour, "Immunity to EBV as revealed by immunedeficiencies," Curr. Opin. Immunol., vol. 72, pp. 107–115, 2021.

[34] K. F. Macsween, T. Haque, and I. Johannessen, "Human herpesviruses: Infectious mononucleosis and other non-malignant diseases," in Viral Infections of Humans, New York, NY: Springer US, 2022, pp. 1–64.

[35] A. Blain, Investigation of somatic genomic abnormalities and the tumor microenvironment in pediatric B-cell non-Hodgkin lymphoma (Doctoral dissertation), 2023.

[36] S. Gong, "Precision medicine in burkitt and burkitt-like lymphomas," in Molecular Pathology Library, Cham: Springer International Publishing, 2023, pp. 159–178.

[37] C. Yu, S. He, W. Zhu, P. Ru, X. Ge, and K. Govindasamy, "Human cytomegalovirus in cancer: the mechanism of HCMV-induced carcinogenesis and its therapeutic potential," Front. Cell. Infect. Microbiol., vol. 13, p. 1202138, 2023.

[38] P. Griffiths and M. Reeves, "Pathogenesis of human cytomegalovirus in the immunocompromised host," Nat. Rev. Microbiol., vol. 19, no. 12, pp. 759–773, 2021.

[39] H. L. Fulkerson, M. T. Nogalski, D. Collins-McMillen, and A. D. Yurochko, "Overview of human Cytomegalovirus pathogenesis," Methods Mol. Biol., vol. 2244, pp. 1–18, 2021.

[40] A. K. Richardson et al., "Breast cancer and cytomegalovirus," Clin. Transl. Oncol., vol. 22, no. 4, pp. 585–602, 2020.

[41] S. Gadde and S. Poda, "Prevalence of Herpes Simplex Virus (HSV) and Cytomegalovirus (CMV) in Oral Squamous Cell Carcinoma patients with a history of Nicotine and Alcohol abuse," Current Trends in Biotechnology and Pharmacy, vol. 17, no. 2, pp. 873–884, 2023.

[42] H. Zheng and J. Savitz, "Effect of Cytomegalovirus infection on the central nervous system: Implications for psychiatric disorders," Curr. Top. Behav. Neurosci., vol. 61, pp. 215–241, 2023.

[43] Z. Tarle *et al.*, "Book of abstracts of the congress '120 Years of Organized Dental Medicine in the Republic of Croatia' and symposium 'Oral Medicine and Medically Complex Patients for General Dental Practice', with international participation," *Acta Stomatol. Croat.*, vol. 57, no. 4, pp. 406–411, 2023.

[44] A. S. Maris, L. Tao, and J. E. Schmitz, "Herpes simplex viruses," in Molecular Medical Microbiology, Elsevier, 2024, pp. 2559–2575.

[45] J. Lau and R. Balasubramaniam, "Oral Herpes Simplex Virus Infections. Sexually Transmissible Oral Diseases," pp. 159–167, 2023.

[46] X. Gong, H. Chi, Z. Xia, G. Yang, and G. Tian, "Advances in HPV-associated tumor management: Therapeutic strategies and emerging insights," J. Med. Virol., vol. 95, no. 7, p. e28950, 2023.

[47] J. K. Strzelczyk et al., "Low prevalence of HSV-1 and Helicobacter pylori in HNSCC and chronic tonsillitis patients compared to healthy individuals," Diagnostics (Basel), vol. 13, no. 10, 2023.

[48] F. Dayyani, S. Tavakolian, H. Goudarzi, F. Y. Biucki, and E. Faghihloo, "Prevalence of HSV, varicella-zoster, CMV, ebv and hpv in the oral cavity and the larynx carcinoma in Iran," Future Virol., vol. 16, no. 2, pp. 141–151, 2021.

[49] G. Yang et al., "A systematic review of oral biopsies, sample types, and detection techniques applied in relation to oral cancer detection," BioTech (Basel), vol. 11, no. 1, p. 5, 2022.

[50] M. S. Ahsan Emon, R. Islam, M. S. Reja, and M. M. Islam, "Unraveling the Social Consequences of Tobacco Products on Health and Environment: A Case Study in Gopalganj District," J Clin Rev Case Rep, vol. 8, no. 9, pp. 230–238, 2023.

[51] R. N. Demba, Molecular Epidemiology and Characterization of K1, K15p and Orf75 Genes of Hhv-8 Associated With Hiv/aids Kaposi's Sarcoma in Patients at Kenyatta National Hospital (Doctoral dissertation), 2020.

[52] F. Moro et al., "Pemphigus: trigger and predisposing factors," Front. Med. (Lausanne), vol. 10, p. 1326359, 2023.

[53] G. U. van Zyl, "New technological developments in identification and monitoring of new and emerging infections," in Encyclopedia of Infection and Immunity, Elsevier, 2022, pp. 463–479.

[54] D. Kohnert, *On the socio-economic impact of pandemics in Africa-Lessons learned from COVID-19, Trypanosomiasis, HIV, Yellow Fever and Cholera*, 2021.

[55] S. R. Prabhu and N. Van Wagoner, "Human Immunodeficiency Virus Infection and Acquired Immunodeficiency Syndrome (HIV/AIDS): An Overview," Sexually Transmissible Oral Diseases, pp. 51–71, 2023.

[56] S. Maloth, T. R. Shrinivas, B. Krishna Pramod, and P. J. Nagarathna, "Prevalence of oromucosal lesions in

HIV positive patients receiving haart-A prospective clinical study," J. Family Med. Prim. Care, vol. 9, no. 9, pp. 4821–4825, 2020.

[57] M. Ptasiewicz et al., "Armed to the teeth-the oral mucosa immunity system and Microbiota," Int. J. Mol. Sci., vol. 23, no. 2, p. 882, 2022.

[58] J. Proulx, M. Ghaly, I.-W. Park, and K. Borgmann, "HIV-1-mediated acceleration of oncovirus-related non-AIDS-defining cancers," Biomedicines, vol. 10, no. 4, p. 768, 2022.

[59] S. K. Cribbs, K. Crothers, and A. Morris, "Pathogenesis of HIV-related lung disease: Immunity, infection, and inflammation," Physiol. Rev., vol. 100, no. 2, pp. 603–632, 2020.

[60] S. Chakravorty, B. Afzali, and M. Kazemian, "EBV-associated diseases: Current therapeutics and emerging technologies," Front. Immunol., vol. 13, p. 1059133, 2022.

[61] D. J. Speicher, V. Ramirez-Amador, D. P. Dittmer, J. Webster-Cyriaque, M. T. Goodman, and A.-B. Moscicki, "Viral infections associated with oral cancers and diseases in the context of HIV: a workshop report," Oral Dis., vol. 22, Suppl 1, pp. 181–192, 2016.

[62] H. A. Robbins, R. M. Pfeiffer, M. S. Shiels, J. Li, H. I. Hall, and E. A. Engels, "Excess cancers among HIV-infected people in the United States," J. Natl. Cancer Inst., vol. 107, no. 4, 2015.

[63] S. M. Peters, Viral and Fungal Infections. In Dental Science for the Medical Professional: An Evidence-Based Approach, Cham: Springer International Publishing, 2023.

[64] M. Aparna, Periodontal Status and Oral Mucosal Lesions Among Human Immunodeficiency Virus Seropositives with and Without Antiretroviral Therapy Reporting at District Hospital, Mangalore: A Cross Sectional Study (Doctoral dissertation), 2019.

[65] W. Shu, F. Du, J. S. Bai, L. Y. Yin, K. W. Duan, and C. W. Li, "A real-world evidence-based management of HIV by differential duration HAART treatment and its association with incidence of oral lesions," Current HIV Research, vol. 20, no. 1, pp. 91, 2022.

[66] P. L. Esser et al., "Torque Teno Virus load is associated with CDC stage and CD4+ cell count in people living with HIV but unrelated to AIDS-defining events and Human Pegivirus load," J. Infect. Dis., 2024.

[67] P. Thakkar, J. M. Banks, R. Rahat, D. A. Brandini, and A. R. Naqvi, "Viruses of the oral cavity: Prevalence, pathobiology and association with oral diseases," Rev. Med. Virol., vol. 32, no. 4, p. e2311, 2022.