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CASE SERIES

HUMAN PAPILLOMAVIRUS –RELATED ORAL LESIONS IN KUWAIT – CLINICAL CASE SERIES

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Abstract

Human papillomaviruses (HPV) are known to be a causative agent for a number of papillary lesions. The variants HPV-16 and HPV-18 have been linked with cervical, oropharyngeal, and lung cancers. HPV is also responsible for HPV-related oral lesions (HPVOL), which can clinically manifest as squamous papilloma, verruca vulgaris, condyloma acuminatum, and multifocal epithelial hyperplasia.

This review paper presents cases of benign oral manifestations of HPV infections in patients attending oral medicine clinics in Kuwait. We present a case series of human papillomavirus-related oral lesions (HPVOL) presented to our oral medicine clinics, with emphasis on the possible risk factors for its increased incidence.

Known risk factors for the development of an HPV infection have been highlighted with emphasis on changing sexual practices, smoking, alcohol consumption, and poor oral hygiene in the EMENA region. While the prevalence of oral HPV in men and women aged between 14 and 69 years is around 7%, unsafe sex practice was scored the lowest in Kuwait. Further, there tends to be a higher prevalence of HPV oral infection with smoking and alcohol intake, and both can act synergistically in the presence of an oral HPV infection, further increasing the oncogenic potential of HPVOL. Poor oral hygiene is also a known factor in HPVOL.

The role of dental practitioners is to raise awareness of the risk of developing HPV and the preventive measures to reduce that risk. These include engaging in safe sexual practices, smoking cessation, and improving oral hygiene. Incorporating the HPV vaccine into the national immunization scheme could contribute to increase in vaccine uptake and hence better population immunity. The recognition of the clinical presentations of HPVOL as presented herein, facilitates dentists' diagnostic skills and aids in making appropriate referrals.

Keywords: Human papillomavirus (HPV), HPV-related oral lesions (HPVOL), HPV vaccine

INTRODUCTION

Human papillomaviruses (HPV) are recognized as causative agents for a group of clinically presenting papillary lesions. Specifically, high-risk HPV types such as HPV-16 and HPV-18 have been linked with cervical, oropharyngeal, and lung cancers.[1] HPV is also responsible for HPV-related oral lesions (HPVOL), such as squamous papilloma (α group) and verruca vulgaris (β group), as it targets the squamous epithelium of mucous membranes.[2] The molecular basis of HPV carcinogenesis involves the integration of viral DNA into the host genome, which leads to genomic instability and ultimately progression to malignancy.[3-5]

The most common route of infection is sexual transmission, including oral sex, or through saliva via mouth-to-mouth contact. Oral sex is one of the major risk factors for HPV infection.

Alternative routes of transmission, including non-sexual ones, have also been reported. However, a main issue with HPV infection is the high percentage of asymptomatic cases, allowing unintentional transmission.[6] HPVOL can manifest in various clinical forms, such as squamous papilloma, verruca vulgaris, condyloma acuminatum, and multifocal epithelial hyperplasia. Although the clinical features of these entities vary, common features include the

presence of newly noticed mucosal abnormality, a burning sensation in the mouth, and the presence of verrucous or papillary lesions around the lips, tongue, and inner sides of the cheeks and lips.[7] Additionally, HPV presence has also been depicted across a spectrum from benign lesions to potentially malignant lesions, being more prevalent among more advanced cases.[8,9] This suggests that dentists play a critical role in the early detection and monitoring of HPVOL through thorough history taking and clinical examination at routine visits.

Although HPV is a known causative agent of oral lesions globally, evidence investigating HPVOL in Kuwait is severely lacking.

Herein, we present a case series of HPVOL attending the Oral Medicine Clinic, with emphasis on the possible risk factors for its increased incidence within the Kuwaiti population.

Case Series

The most common entity of all HPVOL is squamous papilloma (SP). This entity usually manifests as a small cauliflower-like lesion with a white granular or papillomatous surface (Figure 1).

Figure 1. Cauliflower-like lesion with a white granular or papillomatous surface at the junction of hard and soft palate.

Some lesions, however, may appear larger (Figure 2 and 3). They are usually solitary but multiple lesions may occur in the same patient.

Figure 2. Large squamous papilloma involving the hard palate.

Figure 3. Large squamous papilloma involving the hard palate.

SP commonly involves the soft and hard palate, but other sites may be affected such as the tongue (Figure 4), and labial or lip mucosa (Figure 5).

Figure 4. Squamous papilloma involving the dorsum surface of the tongue in a female.

Figure 5: Cauliflower-like lesion involving the upper labial/lip mucosa consistent with squamous papilloma.

Verruca vulgaris (VV) is another entity induced by HPV. They clinically present as asymptomatic, small exophytic growths with finger-like projections, often clinically indistinguishable from SP (Figure 6). The The soft palate and tongue are common sites of involvement (Figures 6 and 7). It is increasingly being detected in females (Figures 8 and 9).

Figure 6. Verruca vulgaris involving the right lateral tongue.

Figure 7. Verruca vulgaris involving the junction of hard and soft palate.

Figure 8. Verruca vulgaris involving the tongue in a young female.

Figure 9. Verruca vulgaris involving the tongue in a young female.

Condyloma acuminatum is rare in the oral cavity, however common in the anogenital region. Oral condyloma is therefore likely in patients whose sexual partners are affected with genital condyloma. In the oral cavity, lesions clinically appear as soft, pink nodules that coalesce into cauliflower-like growths (Figure 10). They tend to be larger in size compared to other HPVOL.

Figure 10. Oral condyloma appearing clinically as soft, pink nodules that coalesce into cauliflower-like growths.

Multifocal epithelial hyperplasia is another uncommon entity of HPVOL. They are clinically characterized by multiple asymptomatic papulonodular lesions. The clinical presentation usually reveals multiple well-demarcated papules with papillomatous surfaces (Figure 11). The gingiva is a common site of involvement (Figure 11).

Figure 11. Multiple papulonodular involving the gingiva consistent with multifocal epithelial hyperplasia.

Risk factors

Several risk factors have been linked to an increased incidence of HPVOL. This considerable increase is explained by changes in sex behavior and the increased practice of oral sex. HPVOL was observed more frequently among male gender than their female counterparts. A recent meta-analysis found that all types of oral HPV are higher in cases where

men have sex with men than with females (12.2% versus 2.9%).[10] Although unsafe sex is recognized as a risk factor for HPVOL, Kuwait has recorded one of the lowest global age-standardized mortality rates (ASMR) and age-standardized DAILY rates (ASDR) attributable to unsafe sex practices.[11] Moreover, HPVOL has been reported to be more prevalent among current smokers and alcohol drinkers.[12] Prior evidence conducted a study investigating prevalence of smoking in the region, it was found that around 34.4% of participants were current smokers, and smoking was most prevalent among young age groups (≤ 20 years).[13] This highlight smoking as a major risk factor for HPVOL in the Kuwaiti population, suggesting that dentists can significantly contribute to mitigating HPVOL incidence through smoking cessation and reducing alcohol consumption.

Poor oral hygiene can increase the susceptibility to HPV infection. Gingivitis and periodontitis have been identified as potential routes for HPV infection.[14] Furthermore, a higher infection rate was observed among denture users, indicating that injuries to oral mucosa, resulting from mechanical stimulation of dentures coupled with poor denture hygiene may contribute to HPV infection.[10,14] Other risk factors such as oral and facial piercings, have been implicated in infectious diseases such as hepatitis B, and hepatitis C and human immunodeficiency virus (HIV), yet their role in HPVOL remains an area of ongoing investigation.[15]

The HPV vaccine is a well-established method to mitigate the risk of HPV and HPVOL. A recent report has reported higher willingness to accept vaccine in the region if vaccine was offered free-of charge versus when payment is required (69.8% versus 23.1%).[6] However, hesitancy towards the HPV vaccine included factors such as a lack of confidence in the vaccine, and complacency regarding the risks of HPV disease. Nevertheless, the findings of this study cannot be generalized as it only included university students and excluded male participants from the study.[6]

Discussion

This case series illustrated cases of benign oral manifestations of HPV infections in patients attending an oral medicine and pathology clinics in Kuwait. These include squamous papilloma, verruca vulgaris, condyloma acuminatum and multifocal epithelial hyperplasia, which are most commonly caused by low-risk HPV subtypes 6,11,2 and 4.[16]

A review of the literature reported 481 cases of squamous papilloma of which 50% were HPV positive, and 284 cases of oral condylomas of which 75% were HPV positive.[17]

Prevalence

Little to no data regarding the prevalence of HPVOL in the Kuwaiti population is present in the literature. With regards to genital HPV infections, a single study was found which investigated the prevalence of HPV infections in 3011 women with normal cervical cytology attending a gynecology clinic in Kuwait.[18] Of all women, 2.4% tested positive for the presence of HPV DNA, of which 71.8% were infected with low-risk HPV subtypes and 32.3% were infected with high-risk HPV subtypes.[18] No oral examination was undertaken to look for concomitant oral HPV infection in the Kuwaiti women. A US-based study identified the prevalence of oral HPV in men and women between ages of 14 and 69 at 7.3%, and at 1.1% for HPV 16, with higher rates in men than women.[19] Evidence regarding the concordance of genital and oral HPV is conflicted in the literature. A study found that the risk of subclinical oral HPV is higher in both women with cervical HPV as well as their male partners.[20] Men with a genital HPV infection were found to be four times more likely to present with an oral HPV infection.[21] However, another study found no higher risk of oral HPV in female participants with cervical HPV.[22] Studies investigating the prevalence of HPV in the Extended Middle East and North Africa (EMENA) region have focused mainly on cervical HPV rather than oral HPV. Review of the literature concluded that the overall prevalence of HPV infections in the region is lower than those estimated from western countries.[23] It has been hypothesized that the comparatively lower prevalence could be due to the fact that socially accepted sexual behaviors in the region are more conservative.[24]

Modes of HPV transmission

To predict the trends of HPV prevalence in any given population, the risks of transmission need to be examined. The mode of transmission of HPV can be horizontal; through sexual intercourse, including oral sex, or through saliva via mouth-to-mouth contact.[16] HPV may also be transmitted vertically from an infected mother to her offspring at birth.[17] As with other sexually transmitted diseases, engaging in sexual intercourse earlier in life and with a higher number of sexual partners increases the risk of transmission.[19] Some studies have attributed an increase in risk of oral HPV infection to an increase in the frequency of oral sex.[16] Other studies have contested this claim, stating that it is mouth-to-mouth transmission via saliva, rather than oral sex, that poses a significant risk of infection between partners.[17] A study that followed up Finnish couples over a seven-year period found that a change in marital status and frequency of sexual intercourse

had an impact on the incidence of genital HPV in men, while the number of sexual partners had an impact on the incidence of oral HPV infections.[24] This supports the claim that having a stable monogamous relationship can reduce the risk of both oral and genital HPV infections.[24] The data on the average number of sexual partners and average age of initiation of sexual activity in the Kuwaiti population is not currently available. Although low, the rising trend in sexually transmitted diseases (STDs), including HPV, in the EMENA region has been attributed to changes in sexual behavior of young people.[9] These include engaging in premarital sex, oral and anal sex, and unprotected sex.[25] In areas where the practice of temporary marriage is socially legitimatized, the probability of having multiple partners is higher.[25] Further contributing to this trend is a lack of sexual and reproductive health services in the region, as well as the social stigma associated with STDs acting as a barrier to treatment seeking behavior and disease notification.[25]

A group of patients whose diagnosis maybe be missed and hence may contribute to an increased risk of transmission in the population, are those who have not yet had sexual intercourse. Although rare, the risk of an HPV infection in a child with an HPV positive mother is higher when compared to children with an HPV negative mother.[17]

A population group in which the prevalence of HPV is found to be higher than the general population are those who are current users or have a history of injectable drug use.[26] Among this group, those who were HIV positive and had a lower CD4 count were reported to be at an increased risk of oral HPV infection, compared to HIV positive patients with a higher CD4 count, indicating that HIV induced immunosuppression may increase patients ' vulnerability to oral HPV.[26]

HPV Vaccination

With the introduction of HPV vaccines, HPV infections have become largely preventable. Evidence showing an increase in HPV antibodies in saliva following HPV vaccination, may indicate the role of the vaccine in protecting against oral HPV infections.[17] The effectiveness of the vaccine in reducing the risk of transmission on a population level relies on the reach of the program and the resultant herd immunity.[17] Global coverage of eligible females is reported at 17%.[27] Although the vaccine is available in Kuwait, it has not yet been incorporated into the national immunization scheme. A study which interviewed female schoolteachers in Kuwait found that 88% were unaware of the availability of an HPV vaccine, and of those that were aware, 83% were unvaccinated.[28] Beyond the lack of a nationwide government endorsed vaccination scheme, the barriers to uptake of HPV vaccination in Kuwait seem to include lack of public awareness of the impact of the disease and the effectiveness of the vaccine as a protective measure.[28,29] This highlights the importance of social awareness campaigns to promote the uptake of the vaccine. Additionally, disseminating information regarding the risks of transmission, including those associated with sexual behavior, can help encourage protective sexual practices. It is important for those at risk of infection to be aware of the need for regular review at a dental clinic as oral HPV infections can be subclinical.[16] This could potentially help increase early detection, thus limiting the spread of infection. Dental professionals have a role in educating their patients on how to reduce their risk of oral HPV infections and how to protect others from infection.

High-risk HPV types

It is important to note that high risk HPV subtypes 16 and 18 can result in oral lesions with potential for malignant change.[16] In a systemic review conducted by Kreimer et al, 23.5% out of 2,642 oral squamous carcinoma cases and 35.6% of 969 oropharyngeal carcinoma tested positive for HPV.[29] Smokers tend to have a higher incidence of oral HPV infection with an increased risk of persistence.[17,19] Furthermore, tobacco use and alcohol intake are both risk factors for the development of oral cancers and may act synergistically in the presence of an oral HPV infection, further increasing the oncogenic potential of the HPVOL.[30]

Conclusion

This review paper presented cases of benign oral manifestations of HPV infections in patients attending oral medicine clinics in Kuwait. Further data is required to develop a better understanding of the prevalence and impact of HPVOL as well as the trends of transmission within the Kuwaiti population. Known risk factors for the development of an HPV infection have been highlighted with emphasis on changing sexual practices, smoking, alcohol consumption, and poor oral hygiene in the EMENA region. The role of dental practitioners is to raise awareness of the risk of developing HPV and the preventive measures to reduce that risk. These include engaging in safe sexual practices, smoking cessation, and improving oral hygiene. Incorporating the HPV vaccine into the national immunization scheme could contribute to increase in vaccine uptake and hence better population immunity. The recognition of the clinical presentations of HPVOL as presented herein, facilitates dentists 'diagnostic skills and aids in making appropriate referrals.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The authors declare to have conducted their research in accordance with the World Medical Association Declaration of Helsinki.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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REFERENCES

1. Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A. and Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021; 71(3): 209–249.https://doi.org/10.3322/caac.21660
2. Gheit, T., Muwonge, R., Lucas, E., Galati, L.et al. Impact of HPV vaccination on HPV-related oral infections. Oral Oncol. 2023; 136:106244:https://doi.org/10.1016/j.oraloncology.2022.106244
3. Christensen, N.D. HPV disease transmission protection and control. Microb Cell 2016; 3(9):475–489: https://doi.org/10.15698/mic2016.09.530
4. Gravitt, P. and Winer, R. Natural History of HPV Infection across the Lifespan: Role of Viral Latency. Viruses. 2017 9(10): 267: https://doi.org/10.3390/v9100267
5. Santacroce, L., Di Cosola, M., Bottalico, L., Topi, S., Charitos, I.A., Ballini, A., Inchingolo, F., Cazzolla, A.P. and Dipalma, G. Focus on HPV Infection and the Molecular Mechanisms of Oral Carcinogenesis. Viruses.2021;13(4): 559: https://doi.org/10.3390/v13040559
6. Alsanafi, M., Salim, N.A. and Sallam, M. Willingness to get HPV vaccination among female university students in Kuwait and its relation to vaccine conspiracy beliefs. Hum Vaccin&Immunother.2023;19(1).: https://doi.org/10.1080/21645515.2023.2194772
7. Hendawi, N., Niklander, S., Allsobrook, O., Khurram, S.A., Bolt, R., Doorbar, J., Speight, P.M. and Hunter, K.D. Human papillomavirus (HPV) can establish productive infection in dysplastic oral mucosa, but HPV status is poorly predicted by histological features and p16 expression. Histopathology.2019;76(4):592–602: https://doi.org/10.1111/his.14019
8. Azevedo, P.L., de Abreu, P.M., Gregório Có, A.C., de Podestá, J.R.V., Freitas Cordeiro-Silva, M. de, Gouvea, S.A., do Valle, I.B. and von Zeidler, S.L.V. Clinical features of oral and oropharyngeal squamous cell carcinoma HPV related. BMC Proc. 2014;8(4):49: https://doi.org/10.1186/1753-6561-8-S4-P49
9. Mravak-Stipetić, M., Sabol, I., Kranjčić, J., Knežević, M. and Grce, M.Human Papillomavirus in the Lesions of the Oral Mucosa According to Topography. PLoS ONE,2013;8(7):69736: https://doi.org/10.1371/journal.pone.0069736
10. Shigeishi. H and Sugiyama, M. Risk Factors for Oral Human Papillomavirus Infection in Healthy Individuals: A Systematic Review and Meta-Analysis. J Clin Med Res.2016; 8(10):721-729:https://doi.org/10.14740/jocmr2545w
11. Qiu, P., He, H., Zhao, Y. et al.Global disease burden attributed to unsafe sex in 204 countries and territories from 1990 to 2019: results from the Global Burden of Disease Study 2019. Sci Rep. 2023;13(1): 12900: https://doi.org/10.1038/s41598-023-40001-2
12. Yu, S., Zhu, Y., He, H., Hu, Y., Zhu, X., Diao, W., Li, S., Shan, G. and Chen, X. Prevalence and risk factors of oral human papillomavirus infection among 4212 healthy adults in Hebei, China. BMC Infec Dis. 2023;23(1): https://doi.org/10.1186/s12879-023-08759-y

13. Memon, A., Moody, P.M., Sugathan, T.N., el-Gerges, N., al-Bustan, M., al-Shatti, A. and al-Jazzaf, H. Epidemiology of smoking among Kuwaiti adults: prevalence, characteristics, and attitudes. Bull World Health Organ. 2000; 78(11): 1306–15:
14. Nishimura Y, Maeda H, Hattori M, Azumaya F, Muramatsu I, Kameyama Y, Tanaka Y. et al. Human papillomavirus infection in the oral cavity of denture wearers. Nihon Hotetsu Shika Gakkai Zasshi. 2004; 48(5): 713-722: doi: 10.2186/jjps.48.713
15. Plastargias I, Sakellari D. 2014. The consequences of tongue piercing on oral and periodontal tissues. ISRN Dent.2014; 2014:876510: doi:10.1155/2014/876510
16. Fiorillo, L., Cervino, G., Surace, G., De Stefano, R., Laino, L., D'Amico, C., Fiorillo, M.T., Meto, A., Herford, A.S., Arzukanyan, A.V., Spagnuolo, G. and Cicciù, M. Human Papilloma Virus: Current Knowledge and Focus on Oral Health. BioMed Res Int. 2021; 2021(1): 6631757–10:
17. Syrjanen, S. Oral manifestations of human papillomavirus infections. Eur J of Oral Sci .2018; 126(1): 49–66
18. Al-Awadhi, R., Chehadeh, W. and Kapila, K. Prevalence of human papillomavirus among women with normal cervical cytology in Kuwait. J Med Virol.2011;83(3):453–460.
19. Sanders, A., Slade, G. and Patton, L. National prevalence of oral HPV infection and related risk factors in the U.S. adult population. Oral Dis. 2011; 18(5): 430–441.
20. Cossellu, G., Fedele, L., Badaoui, B., Angiero, F., Farronato, G., Monti, E., Liverani, C.A., Gorni, C. and Botti, S. Prevalence and concordance of oral and genital HPV in women positive for cervical HPV infection and in their sexual stable partners: An Italian screening study. PloS one. 2018; 13(10): doi: 0205574–0205574.
21. Sonawane, K., Suk, R., Chiao, E.Y., Chhatwal, J., Qiu, P., Wilkin, T., Nyitray, A.G., Sikora, A.G. and Deshmukh, A.A. Oral Human Papillomavirus Infection: Differences in Prevalence Between Sexes and Concordance With Genital Human Papillomavirus Infection NHANES 2011 to 2014. Ann Intern Med . 2017; 167(10): 714–724.
22. Meyer, M.F., Huebbers, C.U., Siefer, O.G., Vent, J., Engbert, I., Eslick, G.D., Valter, M., Klussmann, J.P. and Preuss, S.F. Prevalence and risk factors for oral human papillomavirus infection in 129 women screened for cervical HPV infection. Oral Oncol. 2014; 50(1): 27–31.
23. Vaccarella, S., Bruni, L. and Seoud, M. Burden of Human Papillomavirus Infections and Related Diseases in the Extended Middle East and North Africa Region. Vaccine . 2013;31(S6):32–44.
24. Kero, K.M., Rautava, J., Syrjänen, K., Kortekangas-Savolainen, O., Grenman, S. and Syrjänen, S. Stable marital relationship protects men from oral and genital HPV infections. Eur J Clin Microbiol Infect Dis. 2014; 33(7): 1211–1221.
25. El-Kak, F. Sexuality and Sexual Health: Constructs and Expressions in the Extended Middle East and North Africa. Vaccine. 2013; 31(6):45–50.
26. Robbins, H.A., Fennell, C.E., Gillison, M., Xiao, W., Guo, Y., Wentz, A., Kirk, G.D., Mehta, S.H. and D'Souza, G. Prevalence of and Risk Factors for Oral Human Papillomavirus Infection among HIV-Positive and HIV-Negative People Who Inject Drugs. PloS one.2015; 10(11):0143698–0143698.
27. WHO. Human Papillomavirus (HPV) vaccination coverage. World Health Organization. https://immunizationdata.who.int/pages/coverage/hpv.html?CODE=Global&ANTIGEN=15HPVC_F&YEAR=
28. Rezqalla, J., Alshatti, M., Ibraheem, A., Omar, D., Houda, A.-F., AlHaqqan, S., AlGhurair, S. and Akhtar, S. Human Papillomavirus (HPV): unawareness of the causal role of HPV infection in cervical cancer, HPV vaccine availability, and HPV vaccine uptake among female schoolteachers in a Middle Eastern country. J Infect Public health [Internet]. 2021; 14(5): 661–667.
29. Kreimer, A.R., Clifford, G.M., Boyle, P. and Franceschi, S. Human Papillomavirus Types in Head and Neck Squamous Cell Carcinomas Worldwide: A Systematic Review. Cancer Epidemiol Biomarkers Prev. 2005; 14(2): 467–475.
30. Reis, H.L., Rabelo, P., de Santana, M.R., Ferreira, D. and Filho, A. Oral squamous papilloma and condyloma acuminatum as manifestations of buccal-genital infection by human papillomavirus. Indian J Sex Transim Dis AIDS. 2009; 30(1): 40-42.