HUMAN PAPILLOMA VIRUS (HPV) INFECTIONS: A REVIEW

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ABSTRACT:

Worldwide, HPV infections are one of the most common sexually-transmitted infections (STI). It is of various types. Every category is associated with several conditions. It ranges from benign to severe. Benign are common warts and severe conditions are genital warts, vulvar intraepithelial neoplasia and invasive carcinoma of cervical epithelial cells. Worldwide, cervical cancer is one of the foremost causes of cancer deaths among women. The virus invades epithelial cells enabling its evasion of the host immune systems due to certain characteristics. HPV is spread by intimate contact with an infected partner. At present a vaccine is available as primary prevention against HPV infections. Effective and timely administration of this vaccine is crucial towards decreasing disease burden of HPV-induced genitourinary cancers. Unique approaches may need to be considered to increase uptake of the HPV vaccine. In India, awareness of this vaccination is not there and it is not in the national immunization schedule.

Keywords: Adolescent vaccine; Cervical Cancer; Human Papilloma Virus Infection; Warts

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INTRODUCTION

Worldwide, Human Papilloma Virus (HPV) infections are the most common sexually-transmitted infection (STI), have an effect on the reproductive tract especially oro-pharynx, and ano-genital region via skin-skin contact or exchange of bodily fluids. Genital warts and changes in epithelial cells that lead to genitourinary cancers in women are the common clinical manifestation, and are associated with oral cancers. These infections transmit through intimate contact and are highly prevalent worldwide. Owing to its duplication process, affected individuals may present years after original infection with HPV. Screening for this virus is challenging and not recommended. Vaccination offers primary prevention against HPV infection.

EPIDEMIOLOGY

HPV infections affect more in men and HPV-associated cancers are highest in non-industrialized countries. The prevalence of HPV among women with normal cytological findings is 11.7% worldwide and southeastern Asia has highest prevalence. The incidence of HPV infections is highest in women in the 3rd decade of life. If HPV infections are not detected in early stage then pre-cancerous type can lead to cancerous lesions as age increase, whereas in men such risks are not identified yet¹.

Human papilloma virus

Papillomaviridae is a non-enveloped, double-stranded DNA virus, that includes HPV, and is highly-tissue specific^{2,3} the spherical outer shell and DNA within the HPV⁴. Their genome consists of 8,000 base pairs that encode for proteins that promote cell growth⁵. HPV primarily affects epithelial cells by invading basal layers of skin. Early genes are expressed that stimulate the host cell DNA polymerase to replicate viral DNA during human cellular division^{6,7}. As the virus travels through the basal layers of the epidermis, it assembles its structural proteins^{7,8}. It grows very slowly and has low levels of gene expression. Fortunately, for immune competent individuals, the infection will clear spontaneously in 3–5 years⁸.

Risk factors

According to WHO (2017) HPV infection is classified as high or low-risk, based on their ability to predispose cancer in those infected. High-risk strains are responsible for 71% of cervical cancers globally. HPV-16 is associated with 60.6% of cervical cancers, while 10.2% results from HPV-18. Low risk strains are far less associated with cancers, but manifest as benign skin lesions, commonly seen as genital warts (Condyloma Acuminatum)

Clinical Manifestation

HPV infections includes common warts (Verruca Vulgaris) is common among 20% of school-aged children with prevalence declining with age (Kilkenny M, Merlin K, Young R, et al., 1998) Worldwide, genital lesions from HPV are acquired from sexual contact, making it the most common STI. Other clinical manifestations include genitourinary pre-cancerous lesions (such as low-grade squamous intraepithelial lesion and high-grade intraepithelial lesion) and cancers [such as vulvar intraepithelial neoplasia, vaginal intraepithelial neoplasia, and cervical intraepithelial neoplasia (CIN)]. The peak age for cervical cancer is from 35 to 44 years (WHO, 2019). Around 70–90% of HPV-related infections spontaneously resolve within 1–2 years in most healthy immune competent individuals (WHO, 2017).

Papanicolaou (Pap) smears are done in young adult women to detect early signs of cervical cancer. Persistent HPV lesions can progress towards various stages of precancerous lesions over subsequent months or years. Presence of infection or precancerous lesions should be noted at screening because these risk factors warrant follow-up to monitor for resolution. Lesions that persist require treatment to prevent disease progression to more advanced stages (WHO, 2017).

Diagnostic evaluation

Pap smear screening for cervical cancer is secondary prevention against cervical cancer (American cancer Society, 2017). Screening should begin at age 21, regardless of sexual activity, and repeated every 3 years. The recommendations regarding management of abnormal cervical cytology, high-risk HPV testing, or both, depend on age. Screening of immuno-competent girl of below 21 years and women of above 65 years of age have lower risk of cervical cancer, hence not recommended. HIV-positive women on immunosuppressant therapy require more frequent screening. Thus far, HPV immunization status does not change screening recommendations (Workowski KA, Bolan GA., 2015).

Medical Management

HPV infections resolve spontaneously for the individual with strong immunity. Individuals affected by non-cancerous HPV external ano-genital warts. The CDC treatment recommendations for these lesions are shown in Table 1 (CDC. 2015).

Table 1 CDC recommendations for treatment of external anogenital warts

Applied by patient	Administered by the provider
Imiquimod 3.75% or 5% cream	Cryotherapy with liquid nitrogen or cryoprobe
Podofilox 0.5% solution or gel	Surgical removal (tangential scissor excision, tangential shave excision, curettage, laser or electrosurgery)
Sinecatechins 15% ointment	Trichloroacetic acid or bichloroacetic acid 80–90% solution

CDC, Center for Disease Control and Prevention. Accessed 28 June 2019. Available online: <https://www.cdc.gov/std/tg2015/warts.htm>

In individuals affected by more than one high-risk type that leads to persistent infections resulting in life threatening conditions, treatment is dependent on the stage of disease.

HPV Vaccination

HPV vaccination is primary prevention against HPV infection and genitourinary cancers. Currently, Food and Drug Administration approved vaccine that protects against nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52 and 58. The 9-valent HPV vaccine is approved for use in males and females, and can be given as early as age 9 (especially for victims of sexual abuse). It is recommended for routine use in children between the ages of 11 and 12 with catch-up recommendations up to age 45 (**Meites E, Kempe A, Markowitz LE., 2016**).

Due to a better immune response, two doses are recommended when the vaccine series is initiated before age 15. After age 15, three doses are required to ensure protection against HPV. The vaccine is not recommended for pregnant adolescents and adults. It should not be given to anyone who is allergic to any components of the vaccine. Side effects of vaccine administration are generally well tolerated and include injection site reaction (pain, swelling and redness), syncope, lightheadedness, nausea, headache and mild fever (**Meites E, Kempe A, Markowitz LE., 2016**).

DISCUSSION

The role of the doctors and nurses is significant, when discussing HPV vaccination in the community as well as in hospital. One study found providers who make recommendations about the vaccine assuming parents' readiness to vaccinate had improved initiation of the vaccine among young adolescents (**Brewer NT, Hall ME, Malo TL, et al., 2017**). The highly effective HPV vaccine can be given as part of the other scheduled adolescent vaccines. In a systematic review of interventions done in unvaccinated college students found that increased uptake of the HPV vaccine correlated with encouragement from both peers and medical practitioners (**Barnard M, Cole AC, Ward L, et al., 2019**). Hence, finding creative ways to engage adolescents and families, and to show up myths about the infection and vaccine, is essential. The recommendations for the HPV vaccination are evolving. It is very important to highlight to families that getting immunized prior to exposure is the best way to prevent HPV associated infections.

CONCLUSION

The HPV is a highly infectious and widespread infection. Disease burden is high in otherwise healthy young women leading to significant consequences. Although the disease and economic burden of HPV infections is greater in women, men can also be affected by HPV. The available vaccine against HPV is a safe and effective means of primary prevention. Vaccine has been recently approved for use up to age 45 years. Challenges have occurred with administration of this vaccine however, leading to slower uptake when compared to other adolescent specific vaccines.

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