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**Review article**

# DIFFERENT FACES OF HUMAN PAPILLOMA VIRAL INFECTIONS IN A TROPICAL RURAL PRACTICE IN NIGERIA

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## ABSTRACT

**Introduction:** The human papilloma virus (HPV) is a ubiquitous virus that manifest in different parts of the body in various ways. It particularly has a unique ability to affect the skin and mucous membranes. It can present benignly or in an aggressive malignant manner depending on the part of the body involved. **Methods:** This review describes several different ways in which it presents in our tropical rural practice in Nigeria. This ranges from sexually transmitted infections of the skin and mucous membranes of the genitalia to non-sexual transmissions of the skin and mucous membrane of other parts of the body apart from the genitalia. It also describes the benign and the malignant manifestations of this infection. The peculiarities of the various types are discussed. **Conclusion:** The human papilloma virus has evolved a unique ability to attack various parts of the human body where keratinocytes are present ranging from benign lesions to malignant ones. The infections are becoming commoner with various conditions that compromise the body`s cell mediated immunity particularly infections like HIV. The recognition of these lesions may aid in the prompt commencement of the appropriate therapy for this group of patients and may help to reduce morbidity and sometimes mortality of malignant ones.

**Keywords:** Human papilloma virus, Tropical, Rural practice

## INTRODUCTION

The human papilloma virus (HPV) is a ubiquitous DNA virus that is capable of infecting the human keratinocytes on the skin and mucous membranes. The papilloma virus genus is a member of the Papovaviridae family. They are small, non-enveloped viruses measuring about 55 nm in diameter[1]. It establishes productive infections only in the keratinocytes of the skin or mucous membranes.

It is transmitted in various ways, such as sexually (genital, anal and oral) and it is the most frequent sexually transmitted infection in the world[2, 3]. It is also transmitted perinatally from mother to child[4] and non -sexually by contact of infected hands to another part of the body[5] as well as via sharing of contaminated objects. It has also been postulated that it can be transmitted via blood transfusion[6]. HPV is restricted to the basal layer of the stratified epithelium where they replicate via proliferation of infected basal keratinocytes[7]. Infection occurs via traumas and mild bruises that expose segments of the basement membrane. The infectious process takes 12–24 hours for initiation of replication. Once an HPV virion invades a cell, an active infection occurs, and the virus can be transmitted. The lesion that such an infection causes depends on the part of the affected and this review describes 5 different ways it presents in our tropical rural practice in Nigeria.

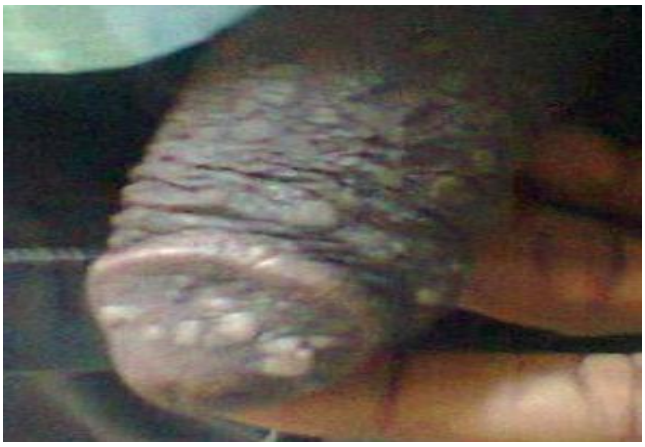

**Fig 1: Genital warts**.

Condyloma acuminatum or genital warts are benign growths occurring in the skin and mucous membranes of the genital areas and anus due to infection with the human papillomavirus. This is the commonest way for it to manifest (as seen in figure 1 above). Genitals (condylomata acuminata or venereal warts) are the most easily recognized.

Typical lesions are found on the penile shaft of males as raised circular plaque like lesions clustered in groups. They are usually painless and it is only the appearance and gritty feeling by the patients that makes them seek attention. Ninety percent of cases occurring around the genitalia are caused by types 6 and 11 and are acquired through micro lacerations of the skin[8]. Auto inoculation of virus onto nearby adjacent skin is common. This type of infection usually spreads through the skin and not through the blood. Cell mediated immunity (CMI) appears to play a significant role in its regression making patients with CMI deficiency such as those with HIV infection to be particularly susceptible to the infection and notoriously difficult to treat[9]. The highest incidence of genital warts is found in young adults aged years with a female-to-male ratio reported to be 1.4:1 in some series[10].

Warts on other parts of the body, such as on the hands and inner thighs are caused by other types of HPV different from that infects the genitalia. Barrier protection with condoms (particularly in males) does not completely protect from the infection since they do not cover exposed areas such as the inner thighs that may still be smeared with infected secretions[11].Most infections are however mild and can resolve on its own without any treatment.

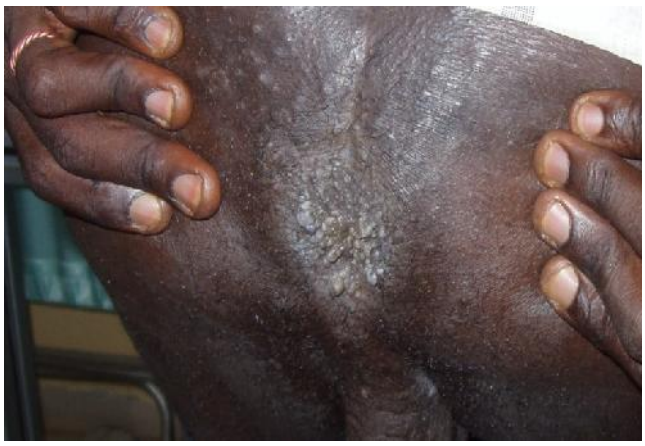

**Fig 2: Anal warts.**

These are similar to the above in appearance, but are located around the anal orifice as seen in figure 2 above. Anal sex is the usual predisposition. Infections in this area are transmitted primarily via sexual activity[11].The importance of this relatively benign infection is that it is associated with an increased risk of secondary malignancy. This is particularly common with types 16,18,31,33 and 45. It occurs in up to 75% of sexual contacts[12].

**Fig 3: Verrucous carcinoma of genitalia (giant Condyloma of Buschke-Löwenstein)**

This is a low-grade, locally invasive, squamous cell carcinoma that is associated with HPV types 6 and 11. This giant genital mass (figure 3 above) was seen in an HIV positive woman.

Patients with genital warts have an increased risk of anogenital malignancy[13]. Of the 120 known human papillomavirus, 51 species and three subtypes infect the genital mucosa. Of these, 31 are considered to present a low risk of carcinogenesis; 17 are considered to be high risk and 6 are of intermediate risk. Infection with HPV is the primary cause of cervical malignancy, although most patients with HPV-infected cervices have a benign outcome. Up to

90% of cervical cancers are caused by HPV infection of the cervix. Strong epidemiologic evidence suggests that 10% of patients who had a high-grade squamous intraepithelial lesion (HGSIL, which includes so-called moderate-to-severe dysplasia, carcinoma in situ, and cervical intraepithelial neoplasia II and III) would have persisted of lesions that eventually would progress to invasive cancer without treatment. Patients with perianal warts, patients who are HIV positive, and those with a history of receptive anal intercourse are at increased risk for anal HGSIL. No direct evidence suggests that this would progress to invasive anal cancer, as lesions of the cervix are capable of doing. Nonetheless, penile, vulvar, vaginal, ovarian, and anal carcinomas have been linked to HPV infection. Female patients with genital warts should therefore be advised to have an annual screening examination and Papanicolaou test even after receiving a preventive vaccination. Cervical cancer screening recommendations have not changed for females who receive HPV vaccine[14].Without continued screening; the number of cervical cancers preventable by vaccination alone is less than the number of cervical cancers prevented by regular screening alone[15].

**Fig 4: Focal epithelial hyperplasia**

Focal epithelial hyperplasia or Heck's disease is a rare viral infection of the oral mucosa caused by human papillomavirus. It was first described in Native Americans in 1965 by Archard et al[16]but since then several cases have been reported from other parts of the world including Nigeria[17, 18]. It is a rare benign lesion of the oral mucosa produced by the subtypes 13 or 32 of human papillomavirus (HPV) [19]. It primarily occurs in children (as seen in figure 4 above in this 7 years old girl) with no gender predilection. The subtype 32 of HPV tends to cause the disease in the older age groups while the subtype 13 of HPV seems to be equally involved in the development of the disease in both young and old patients. This condition is characterized by the occurrence of multiple or unique whitish or normal in color small papules or nodules in oral cavity, especially on labial and buccal mucosa, lower lip and tongue, and less often on the upper lip, gingiva and palate[20].The frequency of this disease varies widely from one geographic region to another[21]. A site-specific predilection for keratinized and non-keratinized surfaces has been observed in these HPV infections[22].

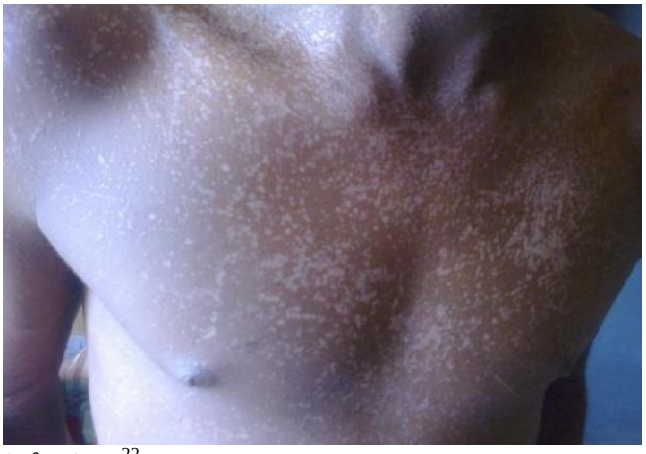

**Fig 5: Epidermodysplasia verruciformis**.

Epidermodysplasiaverruciformis (EV) is a rare cutaneous disorder characterized by persistent widespread, generalized human papillomavirus (HPV) infection[23]. HPV causes epidermo dysplasia verruciformis in immuno compromised individuals as demonstrated by some of the patients seen in figures 5 above. This viral infection manifests by excessive keratin production as a result of inefficient immune containment or regulation leading to typical lesions of plain warts[24].Epidermodysplasia verruciformis (EV) in the classical form without HIV infection results from a genetically determined defect in cutaneous immunity that leaves afflicted individuals susceptible to persistent HPV infection and later development of squamous cell carcinoma of the skin. Many of the HPV types found in EV lesions are non-pathogenic to the general population[25]. Its occurrence in patients with HIV infection has been reported severally in the Nigerian literature due to the high prevalence of HIV infection[26-28]. EV is a rare disorder of cutaneous immunity characterized by an inherited susceptibility to infection with specific HPV. It was first described by Lewandowsky andLutz[29] in 1922. There does not appear to be any racial or geographic predilection, although there have been few reports of EV in

individuals of African descent[30]. The initial cutaneous changes seen with EV often occur at a young age[31] EV typically presents with two main types of cutaneous lesions. Flat wart like lesions that present as scaly hyper- or hypopigmented confluent patches and linear streaks are widely distributed on the hands, arms, and face such those seen in the patients in figure 5 above (there are prominent Koebnerization visible in all the patients due to the following lines of scratching. HIV infection is the common denominator in all the patients). In addition, verrucous or seborrheic keratosis-like lesions are commonly seen. Skin cancers commonly occur in these patients, especially in sun-exposed areas[32]There is increasing evidence that the major predisposing factor to the development of EV is a dysfunction in cell-mediated immunity; however, the specific immune defect has not been fully elucidated[33].The underlying abnormality involves the inability to recognize EV-associated HPVs, which is marked by the inhibition of natural killer cells and cytotoxic lymphocytes[34].Its association with HIV infection has been reported by several authors[35-37]. HIV infection as a potent suppressor of all forms of immunity predisposes patients to all forms of infection including viral infections with HPV. These will develop as the immune status of the patient continues to decline. Other opportunistic infections may occur before or after the development of EV. Steger et al[38] suggested that up to 20% of the population may sub clinically harbour certain EV-associated HPVs. Progression of HIV infection may therefore convert this subclinical infection to a full blown disease. The disease manifests as a congenital form in infancy (about 7.5%). During childhood (61.5%: in years), or at puberty (22.5%). Epidermo dysplasiaverruciformis in association with HIV infection may be a pointer to underlying HIV infection and early commencement of antiretroviral therapy in such patients might sometimes lead to the resolution of the disease. The above presentations are a few ways in which different strains of human papilloma virus present clinically to our tropical rural dermatology practice. The occurrence of HIV infection increases the frequency of occurrence of some while in others, it occurs rarely with few reported associations with or without HIV infection. Recognizing these different types helps the managing clinician to approach its care in a logical scientific manner as demonstrated by several studies where human papilloma virus and HIV infection co-exists and may even lead to reversal of clinical features in some cases[39].

## CONCLUSION

In conclusion, though human papilloma viral infection is restricted to the keratinocytes in the skin and mucous membranes, it can still be a significant cause of morbidity and mortality particularly in tropical Africa.

**Conflict of Interest:** Nil

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