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## Human papilloma virus infection and risks of developing cervical cancer: A review in the context of Nigerian situation

**Babatunde Ajayi Olofinbiyi, Michael Olumide Gbala, Tolulope Samuel Fawole, Dominic Oluwale Olaogun, Babatunde Olaniyi Rosiji, Olawale Ayobami Abayomi, Awolowo Anthony Thomas, Gbenga Damilola Akinlua, Benedict Tolulope Adeyanju and John Ayodeji Owoyemi**

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### Abstract

Human Papillomavirus (HPV) infection poses a significant risk factor for the development of cervical cancer, particularly in regions with limited access to preventive measures. This study conducts a comprehensive assessment of the dose-response relationship between HPV infection and the subsequent risk of cervical cancer development in Nigeria.

Exposure evaluation was conducted through an extensive review of epidemiological data, including HPV prevalence rates and cervical cancer incidence rates across various regions in Nigeria. The evaluation highlighted a notable correlation between the prevalence of HPV infection and the incidence of cervical cancer, suggesting a dose-response relationship. Risk characterization revealed that Nigerian women, particularly those in underserved communities, face a heightened risk of developing cervical cancer due to persistent HPV infection. Factors such as lack of awareness, limited access to screening programs and socioeconomic disparities further exacerbate this risk.

Based on the findings, recommendations for mitigating the risk of cervical cancer in Nigeria include implementing widespread HPV vaccination programs targeting adolescent girls, enhancing access to cervical cancer screening and early detection services, and promoting public awareness campaigns on HPV infection and its link to cervical cancer. Additionally, efforts to improve healthcare infrastructure and address socioeconomic barriers are crucial for effectively reducing the burden of cervical cancer in Nigeria.

This study underscores the urgent need for comprehensive strategies aimed at preventing HPV infection and reducing the incidence of cervical cancer in Nigeria, ultimately improving women's health outcomes nationwide.

**Keywords:** Human papilloma virus infection, risks of cervical cancer, HPV vaccine, Nigeria

### Introduction

Cervical cancer, the fourth most common malignancy in women and the commonest gynaecological cancer globally, is a major contemporary issue in the reproductive health issues spectrum; its management and prevention is of great reproductive health importance <sup>[1, 2]</sup>. Given the high morbidity and mortality rates associated with malignancies, cervical cancer is of particular importance. Around 604,000 new cases were diagnosed worldwide in 2020, and 342,000 people died as a result <sup>[3]</sup>. About 80% of cervical cancer cases occur in developing nations, and given the cervical cancer mortality trend in these nations, a 25% increase in mortality may be seen over the course of the next 10 years <sup>[4]</sup>. According to Sowemimo, Ojo, and Fasubaa (2017), the average incidence of cervical cancer in sub-Saharan Africa is 19.1/100,000; with average worldwide incidence being 15.2 <sup>[5]</sup>. The most prevalent gynecological malignancy in Nigeria and sub-Saharan Africa is cervical cancer, with 14,089 new cases annually documented in Nigeria (Sitas *et al.*, 2008; Bisi-Onyemaechi, Chikani, and Nduagubam, 2018) <sup>[6, 7]</sup>. In Nigeria, 36.6 million women over the age of 15 were at risk of contracting the illness in 2007 <sup>[8]</sup>; according to Pisani *et al.*, the incidence was 250/100, 00 women <sup>[9]</sup>. However, anecdotal evidence suggests that in some rural sections of the nation, the prevalence is substantially higher.

Due to inadequate screening facilities, cervical cancer incidence is particularly high in

**Corresponding Author:**  
**Babatunde Ajayi Olofinbiyi**  
<sup>1</sup>Department of Obstetrics and Gynaecology, College of Medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria  
<sup>2</sup>School of Public Health, University of South Wales, United Kingdom

underdeveloped nations like Nigeria [5]. Therefore, the majority of patients in developing countries arrive late, which has a high morbidity and mortality rate. Recurrent bleeding, post-coital bleeding, anaemia, pelvic infections, uraemia, renal failure, job loss, marital conflict, divorce and a wide range of psychiatric illnesses, including suicide, are among the burdens placed on the individual. Family, the economy of the country and the resources of health facilities are all severely pressured; the nation also experiences a detrimental impact on its Gross Domestic Products [9].

A sexually transmitted double stranded (M) DNA virus known as the human papilloma virus (HPV) has been identified as the primary aetiological factor in the emergence of cervical cancer [10]. About 99.7% of cervical cancer cases have the virus present, according to studies [11]. A study from Northern Nigeria found the virus in 66.6% of cervical cancer specimens [12]. According to Okunade, the most frequent cancer in women connected with HPV is cervical cancer [13]. Early exposure to sexual activity, having several sexual partners and immunosuppression all contribute to the development and progression of cervical cancer [14]. Thus, HPV vaccination is a key component of global strategies to eradicate cervical cancer [15].

According to studies, HPV is the most prevalent sexually transmitted virus, infecting roughly 75% of sexually active individuals at some point in their life [16]. Due to its link to the emergence of cancer, particularly cervical cancer, HPV is extremely important in public health. HPV and cervical cancer are strongly associated, according to substantial clinical, molecular, and epidemiological data [11]. Cervical cancer has been linked to at least 13 different HPV genotypes, with high-risk genotypes 16 and 18 being particularly prominent [17]. Therefore, the main objective of vaccination strategies against the infection is persistent high risk HPV infection [17]. Prepubescent, pubescent and young individuals (9-26 years old) should all receive a cervical cancer vaccine as a main preventive intervention on a worldwide scale. As there is evidence that more adolescents are being exposed to sexual activity, vaccination of this young population is not only a Hobson's choice in the Nigerian context but also highly desirable [18].

However, it is intriguing to learn that vaccine uptake in Nigeria is still less than 50%, and in many Nigerian communities, it is even zero [17]. The low vaccination uptake is thus a significant problem; this is not unrelated to low vaccine awareness, parental dread of the unknown, vaccine cost, accessibility to vaccine, and vaccine availability [19].

Therefore, it has become essential to continually review HPV infection and cervix cancer in order to have more knowledge and insight about the relationship between the two; this will have a significant impact on the formulation, implementation and execution of policy in the prevention of cervix cancer. The Nigerian government has taken a proactive approach to the battle against cancer, including cervical cancer. The National Cancer Control Plan (NCCP) was established to provide high-quality care to cancer patients as well as to deploy effective primary prevention initiatives to safeguard the unaffected population [20, 21]. The Federal Ministry of Health in Nigeria launched the National Cancer Control Plan, co-opting the state ministries of health and the basic, secondary and tertiary healthcare institutions under each of them (Romero *et al.*, 2018) [20]. Other stakeholders include the American Cancer Society, the Clinton Health Access program, the Nigeria Cancer Society, the National Cancer Institute and the Society for Family

Health, to name a few. The program is fully functioning and has their backing.

### **Risk assessment**

**Method:** In Ekiti State, Nigeria, the prevalence of cervical cancer associated with HPV infection was examined. Anecdotal accounts from communities, medical facilities and the Reproductive Health and Cancer Unit of the Ekiti State Ministry of Health and Human Resources were used to compile the data. There was also a review of the literature on HPV infection and cervical cancer.

### **Identification of the Risk**

The human papillomavirus infection is a sexually transmitted disease that is spread by microtrauma experienced during routine sexual contact. There is evidence that even one coital encounter can cause infection [22]. According to Deschuyteneer *et al.*, the organism is a double stranded DNA virus with roughly 8000 base pairs [23]. The native tumour suppressor gene products P53 and pRB are altered by the viral genome upon entrance, most likely by endocytosis, to cause aberrant cell proliferation and immortalization (Balasubramaniam *et al.*, 2019) [14]. The virus enters a brief period of inactivity before integrating into the host DNA. This results in the production of viral proteins and numerous accompanying nuclear enlargements, dyskeratosis, koilocytosis (i.e. features of Cervical Intraepithelial Lesion-CIN) and other histological signs of HPV infection at the cellular level. CIN is a kind of early histopathological transition in which cells with varied degrees of dysplasia replace all or a portion of the cervical epithelium. If dysplasia is not promptly identified and treated, it can lead to cervical epithelial invasion, which eventually develops into cervical cancer. The immune system of the host typically clears the majority of the infectious process in 12 to 24 months. The chromosomal makeup of the lesion, the oncogenic potential of the infecting virus (Subtypes), immunosuppression, smoking and patient age all have a role in the persistence of infection and development to frank cervical. Other benign diseases, such as vulva warts, Vulva Intraepithelial Neoplasia (VIN), laryngeal papillomatosis from vertical transmission to the unborn child, etc., can occur alongside HPV infection. The quality of life may be negatively impacted by intense vulval itching caused by vulva warts. Treatment options for vulva warts can make the morbidity worse. Additionally, because of the risk of vertical transmission, florid vulval warts may be an indication for an elective Caesarean section. Invasion and early infection are typically asymptomatic. Postcoital bleeding, frank bleeding, anemia, infection with foul-smelling vaginal discharge, uraemia and renal failure, fistulae, electrolyte imbalance, and death are signs of cervical cancer development.

### **Dose response evaluation**

Data on dose-response evaluation of HPV & CA in Nigeria are generally scarce. The most prevalent sexually transmitted illness in the world is the human papilloma virus, and by the age of 50, 80% of people have already been exposed. Women who are sexually active, smokers on oral contraceptives or who have impaired immune systems are particularly vulnerable. Less exposure occurs in women using barrier methods of contraception, primarily condoms. According to a population-based study, smoking is associated with a higher risk of developing cervical cancer

(RR for CA of 2.7; 95% CI=1.1-6.7), which is also higher among women who have tested positive for HPV and as there are more live births (P<sub>trend</sub>=0.004) [24]. The study also found that using barrier contraceptives decreased the probability of getting CA (RR=0.39; 95% CI=0.16-0.96) [24]. HPV infection rates are highest among adolescents and young adults in Nigeria, where they are startlingly high during the beginning of puberty and in new partnerships [25]. A descriptive cohort study from central Nigeria found that adolescent urban females had a high incidence of HPV (13.2%) [26]. In a thorough study and meta-analysis, HPV positive people had a greater incidence of cervical cancer development than HPV negative people (OR 1.37; 95% CI, 1.15-1.62; P 0.001) [27]. According to Fan *et al.*, women who tested positive for HPV were more likely to develop cervical cancer (57% tested positive, 95% CI=43.7%-70.4%; 48.5% tested positive for HPV 16; 12.5% tested positive for HPV 18; 95% CI=8.8%-16.2%) [28]. Smoking tobacco, whether it be active or passive, has been linked to an increased risk of HPV infection, according to research by Kum-Nji *et al.* (OR=4.16; 95% CI=1.36-12.67) [29].

### Exposure evaluation

Age at first sexual encounter, number of partners, type of sex, type of contraceptive used, level of immunity, genotype of virus exposed, location, occupation, socioeconomic class and level of education all play a role in the development of cervix cancer and the risk of HPV infection. Cross-sectional research by Otohe *et al.* revealed that 61.3% of Nigerian secondary school girls had experienced their first sexual encounter, with the majority having done so between the ages of 16 and 20 [30]. This finding indicates a significant risk of HPV exposure in this age group.

Studies have also revealed an increased risk of HPV infection in commercial sex workers, who may also be at an increased risk for cervical abnormalities that develop into cervical cancer [31-33]. This is not unrelated to their high-risk sexual behaviours, such as abusing substances during sex, not using barrier contraception and frequently engaging in extravaginal sex. Multicentre institution-based research conducted in Nigeria found a substantial correlation between HPV infection and formal education deficiency, divorce, polygamy, unemployment, and younger age at first sexual experience, as well as poor income earning and smoking [24, 34, 35].

### Characterization of risk

According to the HPV subtypes and genome, the harmful effects of HPV infection range from benign symptoms to malignant characteristics, with cervical cancer serving as their focal point [36, 37]. Vulva condyloma, a frequently occurring benign HPV lesion that manifests as discomfort and pruritus of varied intensities, is both physically and psychologically upsetting [38]. Another frequent appearance is a premalignant lesion of the cervix (CIN). Even though the condition is curable and treatable, morbidities from the various treatment modalities may have a negative impact on quality of life [39, 40]. Cervical cancer, which is one of the most prevalent causes of cancer morbidity and mortality among Nigerian women, is the most common disease caused by HPV infection and its peak presentation [34]. The quality of life of victims of cervix cancer is severely impacted by the disease's local and systemic manifestations, complications from treatments (surgery, chemo, and radiotherapy), and their families, communities, and

healthcare facilities as a whole [41, 42].

### Management of risk

Understanding the natural history of HPV, contributing factors to disease development, additional risk factors for transmission, early identification of early illness and management of consequences are necessary for risk management in HPV infection and cervical cancer [43, 44]. This will necessitate both immediate and long-term disease prevention initiatives that are mounted at the primary, secondary, and tertiary levels. This will need to be implemented using both a top-down and bottom-up strategy. Due to the high prevalence of HPV and cervical cancer growth in Africa, several nations on the continent have developed their own strategic strategies to combat the disease. Each nation's ministry of health has a crucial role to play in this risk management. Survivorship, early HPV detection and HPV prevention are at the core of all these strategies.

Nigeria joined the African cancer control program because of the unacceptable out-of-pocket health costs that make it impossible for the underprivileged masses to handle HPV/cervical cancer prevention and management [45]. As a result, the Nigerian government is currently striving to implement the National Health Scheme's promise of universal health care. In order to lower the expense of treating cervical cancer, the Nigerian government is also encouraging the idea of public-private partnerships. According to the Nigeria National Cancer Control Plan (2018-2022), cervical screening programs including HPV testing, visual inspection with acetic acid (VIA), and care of premalignant cervix lesions should be completed by at least 50% of women in the reproductive age group [20]. Additionally, the WHO, financing international organizations, and non-governmental organizations are involved in the National Cancer Control Plan and Implementation [20]. The legislation supporting girls' education and empowerment, which has a beneficial influence on their sex preferences and lifestyle changes, is part of the government action plan. Additionally, there are numerous national policies that encourage the use of barrier methods of contraception, most notably condoms, which have been proven to significantly reduce the spread of HPV. The formation of cancer centers, their facility-level equipment, and the development of handling skills for instances of cervical cancer are all encouraged by national policies in Nigeria. The management and coordination of screening techniques as well as various kinds of therapy for premalignant forms of cervical cancer will be taught to nurses and other allied professions. Central and local tumor management boards are also created by various healthcare organizations at various levels, with guidelines for their operation. Prepubescent, pubescent, and young women are required to receive immunization against HPV virus exposure since it has been shown to be an effective main preventative measure. Although the HPV vaccine is becoming more widely known, few communities have embraced it. The HPV vaccination is often advised for individuals between the ages of 9 and 24.

Nigeria is putting up measures to boost advocacy for excellent sexual and reproductive health, particularly among adolescents and young adults, using a bottom-up approach. The management and prevention of sexually transmitted diseases, particularly those caused by the human immunodeficiency virus (HIV) and HPV, are crucial in this

domain. There have been a number of help-link projects to raise awareness of these STIs; these use media handles, visiting schools, churches, and radio and television programs. Additionally, there is an upsurge in advocacy for barrier methods of contraception, particularly condom use for HPV protection. There are jingles here and there that urge people not to smoke because it is still a significant contributor to HPV transmission. The promotion of sexual and reproductive health education in the country, both at home and in schools, aids adolescents and young adults in making educated decisions regarding their reproductive health concerns.

Controlling HPV infection and its effects is still a challenge in Nigeria. According to their sociocultural perspective, sexual and reproductive health in Nigerian communities continues to be a sacred and intensely private subject! As a result, gaining universal support for sexual and reproductive health education is difficult; some teachers in schools actively oppose the concept of teaching this material.

### Recommendation and Conclusion

Cervical cancer and HPV infection management and presentation are still very difficult in Nigeria. In the areas of advocacy, screening and treatment and immunization against HPV infection, there are several administrative and socioeconomic gaps that need to be closed. Government should demonstrate the necessary political will to support different STI/cervical cancer reduction measures. Funding should be made accessible for information sharing and education at all levels, and those who are being organized for advocacy should be offered incentives with security. The promotion of reproductive health education through radio, television, and other media outlets has to be stepped up.

With the mobilization and involvement of local leaders, more community seminars and programs on HPV infection/cervical cancer awareness should be organized. The de-mystification of HPV vaccine, cervical cancer and other topics relating to reproductive health should be a priority. The nation has to be more aggressive in boosting its coverage because the HPV vaccination is typically not well-taken up by the young demographic for whom it is advised. In addition to being desired, reducing the price of the vaccination is a possibility that should be investigated. Many parents who want to give their daughters the immunization but lack the money sometimes cannot. The risks of early marriage, early sexual exposure, having numerous partners, smoking, and advancements in barrier contraception should also be emphasized.

Education about sexual and reproductive health should be taught in schools at various levels and made mandatory. To increase screening and treatment coverage for HPV infection/cervical cancer, more healthcare professionals should be mobilized and attracted. Along with this, the necessary tools and materials for various screening techniques and treatment modalities should be made available, and funding should be made available for the development of these sectors' capacity. There is a critical need to develop well-equipped, adolescent-friendly reproductive health facilities across the nation where their needs may be met at a reasonable cost without stigma and compulsion.

The success of policies relating to sexually transmitted infections and national cancer control should always be reviewed. Reports on all HPV infection/cervical cancer prevention efforts from all levels of healthcare are required.

It is important to encourage and fully finance research into issues connected to HPV infection and cervical cancer, including the necessity to re-examine immunization of male children.

### Conflict of Interest

Not available.

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#### Author's details

##### Babatunde Ajayi Olofinbiyi

<sup>1</sup> Department of Obstetrics and Gynaecology, College of Medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria

<sup>2</sup> School of Public Health, University of South Wales, United Kingdom

##### Michael Olumide Gbala

Department of Obstetrics and Gynaecology, University of Medical Sciences Teaching Hospital Ondo, Ondo State, Nigeria

##### Tolulope Samuel Fawole

Department of Obstetrics and Gynaecology, Ysbyty Gwynedd, Betsi Cadwaladr University Health Board, Wales, United Kingdom

**Dominic Oluwole Olaogun**

Department of Obstetrics and Gynaecology, College of Medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria

**Babatunde Olaniyi Rosiji**

Department of Obstetrics and Gynaecology, State Specialist Hospital, Ikole-Ekiti, Ekiti State, Nigeria

**Olawale Ayobami Abayomi**

Department of Radiology, College of Medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria

**Awolowo Anthony Thomas**

Department of Radiology, College of Medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria

**Gbenga Damilola Akinlua**

Department of Obstetrics and Gynaecology, Afe Babalola University Multisystem Hospital, Ado Ekiti, Ekiti State, Nigeria

**Benedict Tolulope Adeyanju**

Department of Obstetrics and Gynaecology, Afe Babalola University Multisystem Hospital, Ado Ekiti, Ekiti State, Nigeria

**John Ayodeji Owoyemi**

Department of Family Medicine, College of medicine, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria

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