

# Human Papilloma Virus-Induced Cervical Cancer in Nigeria: Epidemiology, challenges, prevention and future perspective

Jephthah Yacham Bagayang, Kimbi Enoch Danbaki\* and Ojule Inumanye

Department of Preventive and Social Medicine, Faculty of Clinical Sciences, University of Port Harcourt, Nigeria.

\*Corresponding author. Email: [enochkimbi@gmail.com](mailto:enochkimbi@gmail.com). Co-author: [jbagayang@gmail.com](mailto:jbagayang@gmail.com), [Inumanye.ojule@uniport.edu.ng](mailto:Inumanye.ojule@uniport.edu.ng)

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**ABSTRACT:** Cervical cancer is the fourth prevalent cancer among women worldwide, and Human Papillomavirus (HPV) infection is recognised as a major risk factor for its development. Sub-Saharan Africa records the highest rates of cervical cancer globally, emerging as the predominant cause of mortality among women in 21 out of the 48 countries within the region. In Nigeria, the prevalence of HPV-induced cervical cancer is a major public health concern. The review aimed at examining the burden of HPV-induced cervical cancer and exploring potential solutions. An English-language literature search was conducted on PubMed, Scopus, and Embase, as well as existing systematic reviews, speciality journals, and several websites, including Google. Medical Subject Headings (MeSH) terms were used to search for relevant articles before March 2, 2024. Lack of awareness and education about HPV and cervical cancer, limited access to HPV vaccination and screening programs, stigma and sociocultural barriers in seeking early diagnosis and treatment for cervical cancer were identified as challenges in tackling HPV-induced cervical cancer in Nigeria. The major noted key strategies for the prevention and control of HPV induced cervical cancer in Nigeria were: Promoting HPV vaccination programs and awareness campaigns, strengthening screening and early detection initiatives, improving access to quality treatment and care services and enhancing healthcare infrastructure and workforce capacity were considered as the strategies for prevention and control of HPV-induced cervical cancer in Nigeria. Moving forward, collaborative efforts are crucial, necessitating encouraging multi-sectoral collaboration and partnerships, advocating for policy changes and implementation, integrating cervical cancer programs into primary healthcare and monitoring and evaluation of HPV-induced cervical cancer programs.

**Keywords:** Cervical cancer, epidemiology of HPV, HPV vaccination, Human Papilloma Virus, HPV challenges in Nigeria, HPV preventive measures.

## INTRODUCTION

Cervical cancer is the fourth prevalent cancer among women worldwide, and Human Papillomavirus (HPV) infection is recognised as a major risk factor for its development (WHO, 2022). In 2022, there were 660,000 new cases of cervical cancer worldwide (WHO, 2024a). The disease claimed 350,000 lives, with approximately 94% of these deaths occurring in low- and middle-income countries (WHO, 2024a). Cervical cancer accounted for 6.9% of all newly diagnosed cancer cases in 2020, making it the eighth most prevalent cancer among both men and women (Gupta *et al.*, 2022; Ozaydin-Yavuz *et al.*, 2021).

In developing nations, cervical cancer stands as the primary cause of cancer-related fatalities among women (Dzinamarira *et al.*, 2022). The incidence of new cases is reported at 34.8 per 100,000 women, with 22.5 deaths per 100,000 women attributed to cervical cancer (Arbyn *et al.*, 2008). Sub-Saharan Africa records the highest rates of cervical cancer globally, emerging as the predominant cause of mortality among women in 21 out of the 48 countries within the region (Dzinamarira *et al.*, 2022). Currently, there is no effective antiviral chemotherapeutic agent against HPV (WHO, 2021).

Adolescent girls (10-19 years) constitute a significant population most at risk, with those under 25 showing the highest rates of HPV infection (Schiffman and Wentzensen, 2013; Krüger Kjaer *et al.*, 2001).

In Nigeria, the prevalence of HPV-induced cervical cancer is a major public health concern. Data reveal that the country grappled with one of the highest rates of cervical cancer in 2020, with 12,075 new cases diagnosed and 7,968 fatalities yearly in Sub-Saharan Africa (SSA) (HPV Centre, 2023). Data from the Nigerian states with HPV Centres revealed that over 8,000 women in Nigeria lose their lives to cervical cancer, out of approximately 12,000 new cases identified annually (Akor, 2023). In Nigeria, cervical cancer ranks as the second most prevalent malignancy among women between the ages of 15 and 44 (Akor, 2023). The review aimed at examining the burden of HPV-induced cervical cancer and exploring potential solutions.

### Types of cervical cancer-inducing HPV

HPV infection is the most common sexually transmitted infection (STI) observed and affects sites like the lower genital tract, head & neck, and oesophagus (Wallin *et al.*, 2000). According to the International Agency for Research on Cancer (IARC) 2007 report, low-risk HPV types (2, 3, 6, 7, 10, 11, 13, 27, 28, 29, 32, 40, 42, 43, 44, 54, 57, 61, 62, 71, 72, 74, 78, 81, 83, 84, 86, 87, 89, 90, 91, and 94) are linked to anogenital warts and benign epithelial lesions, while high-risk HPV types (16, 18, 26, 30, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, and 85) are linked to cancer (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2007). In addition, HPV 77, 97, 102, 106, 114, 117, 125, 160, and 117 have been classified as HPV of undetermined risk (Ur) because of limited research confirming the carcinogenicity of these HPV types (Meiring *et al.*, 2012). Furthermore, 3.5% of women harbour HPV types 16 and 18 in their cervix (ICO/IARC Information Centre on HPV and Cancer, 2021).

### Risk factors of HPV-induced cervical cancer

Risk factors for HPV infection encompass young age, early menarche, various forms of sexual activity (vaginal, anal, or oral), sexual debut at or before 15 years of age, multiple sexual partners, unprotected intercourse, multiparity, immunosuppression, family history, smoking, and other sexually transmitted diseases. Sexual intercourse stands out as a major transmission risk for HPV, often acquired within months of the first sexual encounter (CDC, 2013; Vinodhini *et al.*, 2012; Cervantes and Doan, 2018). Nearly 30% of young women tested positive for HPV within a year of their sexual debut in one study (Doufekas *et al.*, 2019).

### Burden of HPV in Nigeria

Cervical cancer poses a significant health risk for Nigerian women, particularly in the absence of effective prevention and early detection strategies. An estimated 60.9 million Nigerian women aged 15 years and older are at heightened risk of developing cervical cancer without the implementation of cost-effective interventions (HPV Centre, 2023).

Ajegbo and Uchenna (2022) conducted a hospital-based study, screening 27,333 patients using Pap smears across five centres in Enugu State, which revealed that 13% (3,528) showed positive signs for cervical cancer. The mean age of positive cases was 38.82 years, with the highest incidence (62%) in the 30-39 age group. A t-test analysis revealed a significant increase in the testing rate compared to a previous attempt ( $t = 5.7$ ,  $p = .002$ ) (Ajegbo *et al.*, 2022).

In 2023, Dom-Chima *et al.* conducted a study using next-generation sequencing (NGS) to analyse 90 samples from a Nigerian cohort, identifying 44 different HPV types. Type-specific polymerase chain reaction (PCR) confirmed the presence of 25 out of these 44 HPV types within Nigeria, with ten types being the most prevalent. The top five prevalent HPV types were HPV71 (17%), HPV82 (15%), HPV16 (16%), HPV6 (10%), and HPV20 (7%). Among the PCR-confirmed HPV types, 40.98% were categorised as high-risk, 27.22% as low-risk, and 31.15% as undetermined risk types. Notably, only six of the 25 HPV types Dom-Chima's survey found in Nigeria are covered by the current nine-valent HPV vaccine. Additionally, there was a high prevalence of multiple HPV infections within one individual, with some samples containing up to nine different HPV types (Dom-Chima *et al.*, 2023).

Another study included 83,593 women from three Nigerian states (Kaduna, Lagos, and Rivers), of which 6,043 (7%) were women living with HIV (WLHIV). They screened 67,371 (81%) women using Visual Inspection with Acetic acid (VIA) and 16,173 women (19%) using HPV DNA testing, with a very small number receiving both tests simultaneously. VIA positivity was 7% among WLHIV and 3% in the general study population, while HPV prevalence was 16% among WLHIV and 8% in the general population. Following a positive HPV test result, 21% of women referred for further examination completed the triage. Impressively, 96% of women diagnosed with precancerous lesions received treatment, and 44% of women with suspected cancer were successfully referred to oncology centres for advanced treatment (Lawson *et al.*, 2023).

### Roll out of HPV vaccines in Nigeria

On October 24, 2023, the federal government, through the Federal Ministry of Health, rolled out HPV vaccination into its routine immunisation system, aiming to reach 7.7

million girls under 14 years. A single dose of Gardasil-4 protects against four HPV types that are known to cause up to 70% of cervical cancer. This exercise is aimed at achieving herd immunity, thereby reducing the incidence of cervical cancer in decades to come. The vaccine is provided free in partnership with GAVI, the Vaccine Alliance, UNICEF, the WHO and other partners. Over 16million Girls under 14 years are expected to be vaccinated in Nigeria by the year 2025 (Akor, 2023; Gavi, 2023; UNICEF, 2023)

### Some research into HPV vaccines

A first-in-human Phase I clinical trial of Vvax001, an alphavirus-based therapeutic cancer vaccine targeting HPV-induced cancers, for immunological activity, safety, and tolerability. Vvax001 uses Semliki Forest virus replicon particles encoding HPV16 antigens E6 and E7. Twelve participants with a history of cervical intraepithelial neoplasia received escalating doses ( $5 \times 10^5$  to  $2.5 \times 10^8$  particles) in three immunisations at 3-week intervals. Blood samples were taken before and after immunisations for monitoring. The vaccine was safe and well-tolerated, causing only mild injection site reactions, and elicited CD4+ and CD8+ T cell responses against E6 and E7. The lowest dose effectively induced E6/E7-specific IFN- $\gamma$  responses in all participants (Komdeur *et al.*, 2021)

A study in China involved 99 patients in Group A and 91 in Group B, with comparable baseline characteristics. At six months, Groups A1 and B1 showed significantly higher high-risk HPV (hrHPV) clearance rates than their control groups (A1/A2: 80.0% vs. 20.4%; B1/B2: 64.4% vs. 15.2%,  $p < 0.001$ ). The effective rates were 84% for Group A1 and 68.9% for Group B1, with side effect incidences of 11.5% and 11.1%, respectively, mainly involving local discomfort. The intervention had an odds ratio (OR) of 12 (95% CI 4.431-32.50,  $p < 0.001$ ) for clearing persistent HPV infection and an OR of 10.1 (95% CI 3.68-27.7,  $p < 0.001$ ) for cervical low-grade squamous intraepithelial lesion (LSIL), indicating its significant efficacy (Chen *et al.*, 2023).

### Vaccines in current use

HPV Vaccination is most effective when given to boys and girls before they become sexually active and exposed to the virus. Age 9-14 years is most recommended. Widespread vaccination can translate to herd immunity, protecting unvaccinated individuals by reducing the incidence of the disease (CDC, 2023). Three vaccines are in current use worldwide:

1. Cervarix - protects against high-risk HPV strains, which are 16,18, usually implicated in cervical cancer
2. Gardasil-4. Provides protection against four strains of HPV, which usually cause cervical cancer, anal

cancer, throat cancer, and genital cancer, including genital warts.

3. Gardasil-9. Protects against nine strains of HPV, including the seven most common strains that cause 80% of cervical cancer.

### SEARCH STRATEGY

An English-language literature search was conducted on PubMed, Scopus, and Embase, existing systematic reviews, speciality journals, several websites and other search engines such as Google. Medical Subject Headings (MeSH) terms were used to search for relevant articles before March 2, 2024, using a combination of the following keywords: Cervical cancer (with or without HPV) or cervical cancer in Nigeria or HPV prevalence or HPV challenges in Nigeria or HPV preventive measures or HPV epidemiology, and HPV North Central Nigeria or HPV North East Nigeria or HPV North West Nigeria or HPV South East Nigeria or HPV South South Nigeria or HPV South West Nigeria. Titles and/or abstracts of the search results were screened to determine the relevance of the studies. Full-texts of selected studies were also reviewed. (Search date 02/ 4/2024-02/8/2024). When required, we contacted the authors and also manually searched the reference lists of all identified publications and recent systematic reviews.

### CHALLENGES IN ADDRESSING HPV-INDUCED CERVICAL CANCER IN NIGERIA

Challenges in addressing HPV-induced cervical cancer in Nigeria include limited access to HPV vaccination, inadequate screening programs, poor healthcare infrastructure, cultural stigmas, and lack of awareness. Additionally, financial constraints and insufficiently trained healthcare personnel hinder effective prevention, early detection, and treatment efforts, thereby exacerbating the disease burden. The challenges are discussed briefly below.

#### Lack of awareness and education about HPV and cervical cancer

The lack of awareness and education about HPV and cervical cancer poses a significant challenge in addressing the impact of HPV-induced cervical cancer in Nigeria. Insufficient knowledge among the population regarding the link between HPV and cervical cancer contributes to delayed diagnosis and limited preventive measures. According to Oboro *et al.* (2023) study, only 20.2% of participants were aware of the causal association between HPV infection and cervical cancer. Some (3.1%) practised unprotected sexual intercourse. The absence of awareness also contributes to the persistence of socio-

cultural barriers, including stigma and fear surrounding gynaecological examinations, hindering women from seeking timely and essential preventive care.

### **Limited access to HPV vaccination and screening programs**

Limited access to HPV vaccination and screening programs poses a significant challenge in addressing HPV-induced cervical cancer in Nigeria. Accessibility issues, including inadequate healthcare infrastructure, geographical constraints, and economic disparities, hinder the implementation of widespread vaccination initiatives and cervical cancer screening services. Ohareri *et al.* (2020) found that a lack of awareness about the HPV vaccine and low educational levels were major obstacles to vaccination among adults in Oyo State. Specifically, 89% of their participants lacked sufficient knowledge about the vaccine, and 81% had limited educational backgrounds. Ojule and Anika's study among In-school girls in Port Harcourt, Nigeria, noted that fear of creating an impression of being sexually active was a major hindrance even when the vaccine was provided free (Ojule and Anika, 2020). This limitation is particularly pronounced in rural and underserved areas, where health knowledge is low and healthcare facilities are scarce. Additionally, the cost of HPV vaccines and screening tests may be prohibitive for many women, further exacerbating the disparities in access. Without comprehensive vaccination coverage and effective screening programs, early detection and prevention of HPV infections and related cervical cancers are compromised, contributing to higher incidence rates (WHO, 2024a) and delayed interventions.

### **Stigma and sociocultural barriers in seeking diagnosis and treatment**

Stigma and sociocultural barriers present formidable challenges in addressing HPV-induced cervical cancer in Nigeria. Deep-rooted cultural beliefs and societal taboos surrounding reproductive health topics contribute to the stigmatisation of individuals seeking diagnosis and treatment for cervical cancer. Ohareri *et al.* (2020) found that sociocultural barriers to HPV vaccination among adults in Oyo State were of an average age of 30.2 years, including fears of promoting promiscuity (82%) and concerns about potential adverse effects (80%). These apprehensions significantly hinder vaccine uptake in the population. This stigma is particularly pronounced in the context of gynaecological examinations, with many women facing reluctance or inhibitions due to societal norms and misconceptions. The resulting delay in seeking medical care can lead to the progression of HPV-related infections to advanced stages (2), impacting early treatment and overall prognosis.

### **Insufficient healthcare infrastructure and resources**

Insufficient healthcare infrastructure and resources pose a formidable challenge in addressing HPV-induced cervical cancer in Nigeria. Nigeria's health sector suffers from a lack of government commitment as the annual budget falls far short of the agreed 15% outlined in the Abuja Declaration of 2001. In 2022, only 4.2% of the budget was allocated to health, out of which 72% was spent on salaries and office maintenance in the past 11 years (Oboro *et al.*, 2023). The inadequacy of medical facilities, diagnostic equipment, and trained healthcare personnel hampers the timely detection, diagnosis, and treatment of HPV infections and cervical cancer. More so, the massive emigration of Nigerian health professionals sees a significant shortage in the country. The Nigerian Association of Resident Doctors (NARD) in 2022 reported that only 10,000 doctors remained, with 35,000 doctors leaving for preferred destinations like the UK, Canada and the USA. Factors contributing to the push include inadequate working environments and poor welfare packages (Oboro *et al.*, 2023). In many regions, particularly rural areas, the scarcity of well-equipped health facilities exacerbates disparities in access to preventive services such as HPV vaccination and quality healthcare services. Limited availability of screening programs and vaccination clinics further impedes efforts to curb the prevalence of HPV. The lack of a robust healthcare infrastructure undermines the implementation of comprehensive prevention and treatment strategies, hindering the ability to reach a significant portion of the population.

## **STRATEGIES FOR PREVENTION AND CONTROL OF HPV-INDUCED CERVICAL CANCER IN NIGERIA**

### **Promoting HPV vaccination programs and awareness campaigns**

To prevent and control HPV-induced cervical cancer in Nigeria, crucial strategies include promoting widespread HPV vaccination programs and conducting comprehensive awareness campaigns. These initiatives aim to increase vaccine coverage, educate the public about HPV transmission and cervical cancer risks, and foster a proactive approach towards preventive healthcare measures among Nigerian women (UNICEF, 2023; UNICEF, 2024).

### **Strengthening screening and early detection initiatives**

Critical strategies for preventing and controlling HPV-induced cervical cancer in Nigeria involve enhancing screening and early detection initiatives. Strengthening existing healthcare infrastructure, particularly in under-

served regions, is essential for improving access to regular cervical cancer screenings. Additionally, implementing education programs to raise awareness about the importance of early detection can empower women to seek timely medical attention. By integrating effective screening measures into routine healthcare practices, Nigeria can significantly reduce the impact of HPV-induced cervical cancer on its population (UNICEF, 2023; UNICEF, 2024).

### **Improving access to quality treatment and care services**

Key strategies for preventing and controlling HPV-induced cervical cancer in Nigeria include improving access to quality treatment and care services. This entails enhancing healthcare infrastructure, training medical personnel, and establishing specialised facilities for cervical cancer management. Ensuring affordability and accessibility to cutting-edge treatments is vital to mitigate the impact of the disease, providing comprehensive care and support for affected individuals across diverse socio-economic backgrounds (UNICEF, 2023; UNICEF, 2024).

### **Enhancing healthcare infrastructure and workforce capacity**

Crucial strategies for preventing and controlling HPV-induced cervical cancer in Nigeria involve enhancing healthcare infrastructure and workforce capacity. This includes substantial investments in medical facilities, diagnostic equipment, and training programs for healthcare professionals. Strengthening the healthcare system will ensure effective implementation of prevention and treatment measures that address the growing burden of cervical cancer in the country (UNICEF, 2023; UNICEF, 2024).

## **FUTURE PERSPECTIVE FOR HPV-INDUCED CERVICAL CANCER IN NIGERIA**

### **Encouraging multi-sectoral collaboration and partnerships**

Encouraging multi-sectoral collaboration and partnerships is essential for addressing HPV-induced cervical cancer in Nigeria. By bringing together stakeholders from various sectors, including government, healthcare providers, NGOs, and community leaders, a comprehensive and coordinated approach can be developed. This all-inclusive collaboration can help in raising awareness about HPV and cervical cancer, improving access to vaccination and screening programs, reducing stigma, sociocultural barriers and strengthening healthcare infrastructure and resources. Additionally, partnerships can facilitate the

integration of cervical cancer programs into primary healthcare and advocating for policy changes and implementation. Partnerships are crucial in monitoring and evaluating the effectiveness of the various programs to ensure their success in preventing and controlling HPV-induced cervical cancer in Nigeria (WEF, 2022; WHO, 2024b).

### **Advocating for policy changes and implementation**

Advocating for policy changes and implementation is crucial for addressing the challenges of HPV-induced cervical cancer in Nigeria. Policy changes are needed to prioritise and allocate resources for education and awareness campaigns about HPV and cervical cancer, as well as for establishing decentralised vaccination and screening programs. Implementation of these policies is essential to ensure that all Nigerian women have access to HPV vaccination and screening, regardless of their socio-cultural backgrounds or geographic locations. Additionally, policy changes should address the stigma and sociocultural barriers that prevent women from seeking diagnosis and treatment, while also enhancing the healthcare infrastructure and resources available for cervical cancer prevention and control. Through effective policy advocacy and implementation, Nigeria can make significant progress in reducing the burden of HPV-induced cervical cancer and improving the overall health outcomes for Nigerian women (Ohareri *et al.*, 2020; WHO, 2024b).

### **Integrating cervical cancer programs into primary healthcare**

Integrating cervical cancer programs into primary healthcare is a crucial step in addressing HPV-induced cervical cancer in Nigeria. By incorporating these programs into existing primary healthcare systems, more women will have access to prevention, screening, and treatment services. This integration will require comprehensive training for healthcare workers on cervical cancer prevention and management. Additionally, it is important to ensure the availability of necessary equipment and supplies for screening and treatment. Through this integration, cervical cancer services can be made more accessible and affordable, ultimately leading to earlier detection and improved outcomes for Nigerian women (WHO, 2024b).

### **Monitoring and evaluation of HPV-induced cervical cancer programs**

In fostering collaboration and policy recommendations for HPV-induced cervical cancer in Nigeria, a paramount aspect involves establishing robust monitoring and evaluation

mechanisms for cervical cancer programs. Regular assessment of program effectiveness, vaccination coverage, and screening outcomes is imperative for informed decision-making. Collaboration between governmental bodies, non-profit organisations, and international partners is crucial for resource optimisation. Policymakers should emphasise data-driven strategies, ensuring the continual refinement of initiatives to address the evolving landscape of HPV-induced cervical cancer in the Niger (Lawson *et al.*, 2023).

## CONCLUSION

The high prevalence rates of high-risk HPV types in Nigeria present a serious public health concern about the consequences, such as HPV-induced cervical cancer. The problem is made worse by the lack of understanding, cultural hurdles, and lack of equity in access to healthcare. Promising approaches to prevention and control include continuous political commitment, public awareness efforts, routine cervical screening programs, and mass HPV vaccine initiatives. It is imperative to make efforts to fortify the healthcare system and incorporate cervical cancer prevention into primary health care. Future prospects for HPV-related cervical cancer in Nigeria depend on continued support from the national government, medical professionals, and foreign allies. Nigeria can significantly lower the incidence of HPV-induced cervical cancer through more surveillance, better healthcare delivery and community participation.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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