

Human Papillomavirus among Nigerian Women: An Overview

*Jabaka, R.D.¹, Kuta, F.A.², Adabara, N.U.³ and Shittu, K.O.⁴

¹Department of Microbiology, Faculty of Life Sciences, Kebbi State University of Science and Technology, Aliero, Kebbi State.

²Department of Microbiology, School of Life Science, Federal University of Technology Minna, Niger State.

³Department of Microbiology, School of Life Science, Federal University of Technology Minna, Niger State.

⁴Department of Biochemistry, School of Life Science, Federal University of Technology Minna, Niger State.

Corresponding Author: reginadoro1@gmail.com: 07036007818

Abstract: Human Papillomavirus (HPV), is a DNA virus from the family Papillomaviridae (De, Sanjosé *et al.*, 2018 and Virus Taxonomy, 2018). Capable of causing abnormal tissue growth, leading to warts and other changes to cells; thus, it is the major cause of cervical cancers globally. In Nigeria, the increase in the rate of cervical cancer infections and associated deaths is alarming. Thus, the present review was conducted to enrich the data bank of information on HPV in circulation amongst women, with particular focus on Nigeria. Adhering to the Cochrane Handbook for Systematic Reviews of Interventions/Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) instructions for documenting meta-analysis and systematic reviews, this study randomly sampled publications related to human papillomavirus in Nigeria from relevant databases, particularly published reviews and researches published on Google Scholar, PubMed, Web of Science and Scopus, with a cross-sectional approach. From a total of 220 identified studies, 18 pooled data studies were extracted using the developed systematic review protocol as a guide, which were subsequently used to analyze the extent of research on HPV performed in Nigeria with regards to the location. Findings by Manga *et al.*, (2015); Aondona *et al.*, (2021) uncovered that the common strains of HPV circulated within Nigeria are HPV 16, 18, 31, 33, 35 and 45. The study therefore recommended that research and sensitization programme on HPV be conducted in all the six (6) geopolitical zones of the country to create awareness and to suggest possible preventive measures that may mitigate the increasing rate of infection with cervical cancer within the country.

Keywords: Cervical cancer, HPV, virus, warts.

INTRODUCTION

Human Papilloma virus (HPV) is one of the most common sexually transmitted virus globally (Stanley, 2010; Jing *et al.*, 2018), commonly manifesting as *Condyloma acuminatum* a sexually transmitted disease characterized by a wart-like growth on the cervical or vulva mucosa in females, or on the glans or prepuce in males (McConnell, 2007; Faridi *et al.*, 2011; Jing *et al.*, 2018). These warts are generally caused by low-risk (LR) types of HPV, including 6, 11, 32, 40, 42, 44, 54, 55, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, 89, and 91 (Khan *et al.*, 2007), however, the High-risk (HR) types of HPV, including types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82 and 85 (Munoz *et al.*, 2003; Munoz *et al.*, 2006; De Villiers *et al.*, 2004; IARC *et al.*, 2007; Jing *et al.*, 2018), induce cervical dysplasia and can lead to the

development of several types of cancer including cervical, vulval, vaginal, anal, and penile cancers (Khan *et al.*, 2007; Jing *et al.*, 2018).

Cervical Cancer in particular is the second most common cancer affecting women worldwide, and is a major cause of morbidity and mortality (Sheng and Zhang, 2010; CDC, 2012). Persistent infection with HR-HPV is a necessary but not sufficient cause of this cancer, which develops over a long period of time through precursor lesions, which can be detected by cytological screening. The majority of these lesions regress spontaneously without treatment (Termini and Villa, 2008; Wentzensen and Klug, 2009).

Current estimates reveal that about 12,075 women are diagnosed with cervical cancer, with 7,968 deaths annually, out of the 56.2 million women in Nigeria (IARC, 2021).

Cervical cancer is the second most frequent cancer among women in Nigeria between the ages of 15 to 44 years (IARC, 2021). About 3.5% of women in the general population are infected with cervical HPV-16/18 at a given time, with 66.9% cases of invasive cervical cancers attributed to HPVs 16 or 18 (IARC, 2021). Nonetheless, Nigeria is yet to have optimum information on HPV, especially in the South-East and North-western geopolitical zones even though there has been cases of cervical cancer infection in circulation therein (Hassan and Awosan, 2018). The WHO is leading a global call for the elimination of cervical cancer by the year 2030 (Lawal *et al.*, 2021) and remains optimistic that cervical cancer will be eliminated as a disease of public health concern if 90% of girls receive the HPV vaccine by 15 years of age, 70% of women are screened by HPV testing at 35 and 45 years, and 90% of identified cases are treated. The success of this global call will significantly depend on the capacity to operationalize, finance, and implement the strategy in low and middle income countries (LMIC), where more than 80% of the disease burden resides.

Mode of Transmission

Human papilloma virus is transmitted through intimate skin to skin contact; via vaginal, anal or oral sex with an infected person. HPV warts can grow on lots of different body parts; almost anywhere on the skin, including the genitals, hands and feet; the throat, the airway, and lungs (Joanna *et al.*, 2019). For this reason, hand-genital transmission is common among young people who usually experience this type of sexual contact long before they have vaginal or anal intercourse. This is often a form of undesired sexual contact that may expose young children to risk for contacting HPV infection, and can involve transmission even with no manifestation of the symptoms of the disease in an infected person. The symptoms may develop months or even years after being infected (Sawaya and Miriam, 2015). The virus can be transmitted by sex partners who do not know they're infected. A pregnant mother who is infected with HPV can also transmit the virus to her infant during vaginal childbirth, which

may result in the baby having warts in the voice box or the throat (CDC, 2006; Kangmennaang *et al.*, 2018).

Pathogenesis

Upon infection, HPV viruses are carried on surfaces touched by someone who has warts, most especially inside shoes that have been worn by someone with plantar warts. Once a person has direct contact with an infected person or contaminated surface infected with HPV, the person becomes infected. Symptoms usually take 3-4 months to develop, however, in some cases, it may take up to 2-10 years (WHO, 2011; Montgomery *et al.*, 2015). Once infected, the virus will invade the skin, enter the cell and recombine its genetic material with the host cell DNA. Subsequently, it will cause the skin cells to multiply and form warts, from where the virus will be shed by passing unto others (HHP, 2019). Several researches (Richardson *et al.*, 2003; Chee *et al.*, 2019) stated that: common warts can be found on the hands of about one-fourth of people in the United States, especially children. For some unknown reason, plantar warts are said to be most common among teenagers and young adults. The infection with HR-HPV typically lasts from 12 -18 months and is eventually cleared by the immune system; (Richardson *et al.*, 2003). However, in some rare cases, approximately 10% of women fail to clear HPV infections, resulting in a persistent infection (Stanley, 2008; Chee *et al.*, 2019). The major effect of persistent infection with HR-HPV is the development of lesions that may progress to 'malignancy', and this contributes as a risk factor for the development of 'Cervical Cancer' (Stanley, 2008; Laiminsand and Moody, 2010; Bodily and Laimins, 2011).

Signs and Symptoms

Most people infected with genital HPV are asymptomatic and do not know that they are infected, however, others develop visible genital warts (Grabowski *et al.*, 2017). Some of the other symptoms that occur include: Vulvar warts; accompanied by pareunia, pruritus and burning discomfort; Penile warts; associated with occasional itching;

Urethral metal warts; causing hematuria or impairment of urinary stream; Vaginal warts; accompanied by discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy); and Perianal and intra-anal warts accompanied by pain, bleeding on defecation and itching (Grabowski *et al.*, 2017).

Prevention and Control of Human Papilloma Virus (HPV)

Amongst the most effective techniques for prevention of HPV is ensuring that sexual partners have been medically screened and declared free from HPV infection as well as other diseases. According to (Blomberger *et al.*, 2015; Igomu and Adebayo, 2020). Other preventive measures include:

- Unprotected sex should be avoided.
- Intimate skin to skin contact with an infected person should be avoided.
- Use of appropriate protection (condom) during sexual contact with partners that have not been medically screened should be adopted.

Vaccination

There are currently two (2) human papilloma virus vaccines in Nigeria and South Africa: the bivalent vaccines for type 16 and 18 and the quadrivalent vaccines for type 6, 11, 16 and 18, both of which are administered via injection (Igomu and Adebayo, 2020). Both have been found to be nearly 100% effective in preventing cervical intraepithelial neoplasia 2 (CIN2), CIN3, and condylomatous vulvar disease related to the HPV genotype covered by the vaccines (Blomberger, *et al.*, 2015; Tathiah *et al.*, 2015; Igomu and Adebayo, 2020). The vaccines are approved for administration to females aged 9-26 years. The vaccines were licensed and introduced in Nigeria in 2009, but they are being utilized only by a few amongst the privileged section of the populations (Tathiah *et al.*, 2015). Studies have shown that the knowledge of HPV infection and vaccine against the infection is quite low; and where available, the cost of the vaccine is beyond the reach of the average Nigerian (Laia and Xavier, 2009).

Treatment

Even though the reason for administering treatments to HPV patients is to control the disease, it is important to understand that the underlying HPV infection can't be cured (Tathiah *et al.*, 2015). Like any type of viral infection, HPV remains in the body and can cause warts to appear in the future, particularly when the immune system is suppressed. However; there are many ways to remove visible genital warts, depending on their size and location (Blomberg, *et al.*, 2015).

Smaller Warts can be removed by freezing them off through 'cryotherapy', burning them off with an acidic chemical, or removing them through laser surgery. All three procedures may require multiple follow-up visits or treatments (Laia and Xavier, 2009).

Some patients with HPV can also be treated with an antibiotic cream at home in less serious cell changes, however, if a woman has cervical dysplasia, the treatment depends on the severity of the diagnosis and the risk of sexual transmission (Blomberg *et al.*, 2015). Studies have shown that the knowledge of HPV infection and vaccine against the infection is quite low and if available, the cost is beyond the reach of the average Nigeria (Laia and Xavier, 2008).

Review Methodology

Based on the guidelines highlighted by Cochrane handbook for Systematic Reviews of Interventions (TCC, 2008) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) instructions for documenting meta-analyses and systematic reviews as described by (Liberati *et al.*, 2009; Moher *et al.*, 2009; Anthony *et al.*, 2021), this study developed, adopted and executed the systematic review protocol, using a cross sectional approach.

Search strategy

The search was focused on articles published using direct database search through Scopus, Web of Science, PubMed, Google Scholar and African Journal Online on Human Papilloma Virus.

The data sourced for by the authors included the author's first name, study design, publication date, research area, sampling method, criteria for inclusion of research study participants, laboratory protocol for the method of detection, geopolitical regions of the participants' enrolment, HPV genotypes, HPV severity and clinical manifestations of the study participants.

Research Impute and Distribution Pattern of HPV among Women in Some Part of Nigeria

This study revealed that the common strains of HPV in circulation in Nigeria are: HPV 16, 18, 31, 33, 35, and 45 (Okolo *et al.*, 2010; Dimie *et al.*, 2013; Manga *et al.*, 2015; Nyengidiki *et al.*, 2016; Aondona *et al.*, 2021). The high risk associated with the disease is due to the fact that humans are the host reservoir of the HPV infection (Zheng, *et al.*, 2022). Annually, there is a high incidence of about 12,075 women diagnosed with cervical cancer, with 7,968 deaths. Increase in the incidence of STDs, including HPV related cervical cancers, in Nigeria, is associated with high divorce rate especially in the North east, South-south and North-west (Ntoimo and Akokuwebe, 2022);

for instance, Kano state alone recorded over one million divorcees in the year 2019 (Ntoimo and Akokuwebe, 2022). Major risk factors accompanying HPV infection include: exchange of multiple sex partners and multiple marriages and separation. This hazard might have attributed to the wide spread of HPV infection among Nigerian women (Nejo *et al.*, 2018). Other hazardous factors might be found among researchers and health personnel's who are directly in contact with HPV infected patients, therefore, taking good protective and preventive measures will reduce the rate of nosocomial infections in the hospital. Some factors such as formal education, divorce, and unemployment has been significantly found to be associated with HPV infection (Manga *et al.*, (2015; Nejo *et al.*, 2018). These are some of the research gaps on HPV related cervical cancer highlighted by this study, and it recommends intense public awareness on cervical screening strategy for the prevention and control of cervical cancer (Nejo *et al.*, 2018). The key findings from the reviewed papers with regards to distribution of HPV amongst women in Nigeria are highlighted in the table below:

Table 1: Major findings from selected studies involving the risk factors and distribution of HPV amongst Nigerian women

S/No	Research Idea	Major findings	Reference
1	Investigation of the Human papilloma virus infection in women with and without cervical cancer in Ibadan, Nigeria	The research studied the HPV type prevalence among 932 women from the general population of Ibadan, Nigeria, from of 75 ICC cases using GP5+/6+ PCR based assay to detect 44 genital HPV types. The results showed that 245 (26.3%, 95% confidence interval (CI) 23.5% - 29.2%) women were HPV-positive in the general population, among whom the prevalence of HPV35 and HPV16 were equally frequent (12.2%, 95% CI 8.4% - 17.0%). In ICC, however, HPV16 predominated strongly (67.6% of 68 HPV-positive cases), with the next most common types being 18 (10.3%, 95% CI 4.2% - 20.1%), 35, 45 and 56 (each 5.9%, 95% CI 1.6% - 14.4%). Comparing among HPV-positive women only, HPV16 and 18 were over-represented in ICC versus the general population (prevalence ratios 5.52, 95% CI 3.7 - 8.3 and 1.4, 95% CI 0.6 - 3.3, respectively). Other high-risk HPV types, as well as low-risk and multiple HPV infections were less common in HPV-positive women with ICC than from the general population.	(Okolo <i>et al.</i> , 2010)
2	Age-specific prevalence of human papilloma virus and risk of cytologic abnormalities in rural Nigeria (south-west)	The population-based study in rural Nigeria on women aged 15+ using stratified random sampling revealed that out of two-thirds of the invited women who participated, 14.7% had detectable carcinogenic HPV, a proportion that did not decline with age (p-trend = 0.36) and showed slight peaks in the 15-29 and 60-69 age groups. Out of women aged 30-49 years, 12.8% were HPV positive, and the PPV for high-grade or worse cytology was 16.4%. Women aged < 30 were more likely to be HPV positive (18.9%, p = 0.03) with a lower PPV (4.2% p = 0.05). Among women at age 50 and above, HPV positivity was 14.2% with a PPV of 13.9%.	(Gage <i>et al.</i> , 2011)
3	Population-based cross-sectional study of age-specific risk factor for high risk human papilloma virus prevalence in Irun (a rural town in southwestern Nigeria)	In the study, 1,420 women were administered a clinic-based questionnaire on sexual and reproductive behavior, marital status (including co-wives), and malaria exposure, and the results showed that women with birth control use and age at first pregnancy were associated with HR-HPV (p-value = 0.03 and 0.05, respectively). Early age at sexual debut and multiple sex partners were risks factor for HR-HPV, but did not reach significance (p-value = 0.1 and 0.07, respectively). Neither self-reported malaria nor presence of co-wives in the household was associated with HR-HPV (p-value = 0.85 and 0.24, respectively) in this study. In age sub-categories, early age at sexual debut was a significant risk factor for HR-HPV among women at	(Clarke <i>et al.</i> , 2011)

- the age of 35-45 years (p-value = 0.02). Early age at first pregnancy remained a significant risk factor for women aged 56+ years (p-value = 0.04). Greater than 2 sex partners and use of birth control were associated (though not significantly) with HR-HPV in women aged 30-45 (p-value = 0.08, respectively).
- 4** Human papilloma virus (HPV) infection associated with HIV-1 infection and AIDS in HIV-infected adult patients from Zaria, Northern-western Nigeria. Based on assays of serum IgG antibodies to HPV by ELISA, the results showed that with regards to sero status, 1(3.8%) of the 26 HIV-negative participants and 26 (41.3%) of the 63 HIV-positive patients were HPV IgG sero positive. HIV-positive patients were 18 times more likely to be HPV sero positive than the HIV-negative adults (OR 17.6, 95% CI 2.2-138, p=0.0006). Univariate and multivariate (using logistic regression) analyses, revealed that CD4 cell count was the only independent variable associated with HPV sero positivity in HIV patients. Patients with CD4<200 cells/ μ l (indicative of AIDS) had 5 times more likelihood of been HPV IgG sero positive than those with CD4 cell count \geq 200cells/ μ l (OR 5.1, 95% CI 1.3-20.8, p=0.022). Only three 3(11.5%) of the 26 HPV sero-positive patients had clinical evidence of anogenital and facial warts. (Dimie *et al.*,2013)
- 5** Epidemiological patterns of cervical human papilloma virus infection among women presenting for cervical cancer screening in North-Eastern Nigeria. Among the 209 women who presented for cervical cancer screening at the Federal Teaching Hospital (FTH), Gombe state, the prevalence of cervical HPV infection among the participants with mean age of 39.6 ± 10.4 years was 48.1 %. The five most predominant genotypes were 18, 16, 33, 31 and 35, with prevalence of 44.7 %, 13.2 %, 7.9 %, 5.3 % and 5.3 % respectively. Other genotypes observed were 38, 45, 56, 58, 82 and KC5. Multiple HPV infections were detected among 7.9 % of participants. Risk factors such as level of education ($X^2 = 15.897$; p = 0.007), age at sexual debut ($X^2 = 6.916$; p = 0.009), parity ($X^2 = 23.767$; p = 0.000), number of life time sexual partners ($X^2 = 7.805$; p = 0.005), age at first pregnancy ($X^2 = 10.554$; p = 0.005) and history of other malignancies ($X^2 = 7.325$; p = 0.007) were found to have a statistically significant association with HPV infection. (Manga *et al.*, 2015)
- 6** Risk factors and distribution of oncogenic strains of human papilloma virus in women presenting for cervical cancer screening in Port Harcourt, Nigeria. The results revealed that the age range of patients between 19-62 years with prevalence of HR-HPV was 10%. The HR-HPV was found among patients with more than one life time sexual partner, the four HR-HPV genotypes identified were: 16, 18, 31 and 35. (Nyengidiki *et al.*, 2016)

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| 7 | Prevalence and risk factors for genital human papilloma virus infections among women in Southwest Nigeria | From 295 cervical swab specimens of women presenting for routine cervical cancer screening, STI clinic attendees and women who attended community based outreach programme, 55 samples were positive for HPV DNA (a prevalence of 18.6%). The key risk factors are: lack of formal education (P-value: 0.003), divorcee (P-value: 0.019), polygamy (P-value: 0.027), unemployment (P-value: 0.023), low income earnings (P-value: 0.018), younger age (< 18years) at sexual debut (P-value: 0.039) and passive smoking (P-value: 0.017). | (Nejo <i>et al.</i> , 2018) |
| 8 | Molecular characterization of genital human papilloma virus among women in South western, Nigeria | In the study, It was discovered that 51 (17.3%) individuals were positive for HPV DNA, with HPV-31 being the most predominant (32.8%), followed by HPV-35 (17.2%) and HPV-16 (15.5%) respectively. | (Yewande <i>et al.</i> , 2019) |
| 9 | Prevalence and incidence of genital warts and cervical Human Papilloma virus infections in Nigerian women | Out of 1020 women enrolled in a prospective cohort study, 56% (535/962) were HIV-negative and 44% (427/962) were HIV-positive; likewise, HIV was found to be associated with higher risk of prevalent genital warts (OR: 7.14, 95% CI: 2.41–28.7, $p < 0.001$) while higher number of sex partners in the past year was associated with increased risk of incident genital warts (OR: 2.86, 95% CI: 1.04–6.47. $p = 0.04$) and HPV11 was the only HPV associated with prevalent genital warts OR: 8.21, 95% CI: 2.47–27.3, $p = 0.001$). | (Dareng <i>et al.</i> , 2019) |
| 10 | National prevalence studies on Human Papilloma virus (HPV) genotypes in Nigerian women | The pooled prevalence and risk factors of genital HPV infection in Nigeria, as determined by a systemic review protocol revealed that the pooled prevalence of cervical HPV was 20.65% (95%CI: 19.7–21.7). Genotypes 31 (70.8%), 35 (69.9%) and 16 (52.9%) were the most predominant HPV in circulation. The study revealed that out of the six geopolitical zones in Nigeria, northeast had the highest pooled prevalence of HPV infection (48.1%), while the least was in the north-west (6.8%). | (Anthony <i>et al.</i> , 2021) |
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CONCLUSION AND RECOMMENDATIONS

This study had revealed that the majority of people in Nigeria are not aware of human papilloma viral infection and cervical cancer in Nigeria today, thus, there had not been full adherence to preventive measures in most localities, due to lack of proper awareness and sensitization. Furthermore, it was found that although various researches have been conducted in some parts of the country, particularly in some developed urban regional areas (South-south, South-west and North-central) of the country, however, there is no detailed information with regards to HPV in most of the states in the country, especially in the South-east and North-west regions.

Therefore, there is still the need for more information to enable generalizations about the existing strains in circulation within the country. The lack of awareness concerning the disease could be due to lack of finance and facilities to properly diagnose and investigate the etiologic agent, hence, there is need for government-backed interventions including efforts by international organization, such as WHO and CDC, spearheaded by researchers, to properly carry out a massive sensitization and investigate the distribution of HPV in each state so as to lay the background for mitigating the wide spread of cervical cancer across the country via vaccination. This major step may raise the hope of the control of cervical cancer in Nigeria, in the near future.

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