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Prevalence and Risk Factors of High-Risk HPV E6 /E7 Oncoproteins Among Women in Benin-City, Nigeria: Implications for Cervical Cancer Prevention

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Abstract

Cervical cancer remains a major public health issue in Nigeria, primarily driven by persistent infection with high-risk Human Papilloma Virus (HPV) types 16 and 18, particularly through the expression of viral oncoproteins E6 and E7. These oncoproteins are known to disrupt tumor suppressor pathways, contributing to the development of pre-cervical and invasive cervical cancer. This study aimed to assess the prevalence of HPV E6 and E7 oncoproteins and associated risk factors in parts of Benin-City, Edo State. A cross-sectional study design was employed, and 120 cervical samples were collected from consenting participants who met the inclusion criteria. The study population had a mean age of 26.4 years (SD = 2.11), with the majority aged between 18–27 years (51.7%). Most participants were single (65.8%), Christian (76.7%), and students (45.0%), with the highest level of education being secondary (57.5%) and tertiary (26.7%). The overall prevalence of E6/E7 oncoproteins was 4.2%, with the highest positivity observed among participants with early sexual activity ($p = 0.001$). Multiple sexual partners, abnormal vaginal bleeding, and lack of HPV vaccination were found to have significant association with HPV infectivity among the study participants ($p = 0.006$, $p = 0.022$, $p = 0.046$ respectively). Notably, 80% of E6/E7-positive cases were associated with HPV type 16, and 20% with type 18. The findings underscore the importance of E6/E7 oncoprotein screening in identifying women at higher risk of cervical neoplasia and reinforce the importance of integrating molecular-based HPV testing into routine cervical cancer prevention programs. Public health strategies that promote early HPV vaccination and accessible molecular diagnostics are essential to mitigate the burden of cervical cancer in Edo State and similar settings.

Introduction

Cervical cancer remains a major public health concern and ranks as one of the leading causes of cancer-related deaths among women worldwide (Bray *et al.*, 2024). Sub-Saharan Africa, including Nigeria, bears a disproportionate burden of the disease due to limited access to preventive measures such as HPV vaccination and regular cervical screening programs (Jemal *et al.*, 2011). The primary etiological agent of cervical cancer

is Human Papilloma Virus (HPV), a double-stranded Deoxyribonucleic acid (dsDNA) virus from the family *Papillomaviridae* (Ramberg, 2022). Among the over 200 identified HPV types, high-risk strains such as HPV-16 and HPV-18 are responsible for approximately 70% of cervical cancer cases globally (Ferlay *et al*., 2021).

A critical step in HPV-driven carcinogenesis is the persistent expression of two viral oncoproteins, E6 and E7, which play a central role in disrupting cellular tumor suppressor pathways. The E6 protein facilitates the degradation of p53, impairing DNA repair and apoptosis, while E7 inactivates the retinoblastoma protein (pRb), promoting uncontrolled cellular proliferation (Fernandes & De Medeiros Fernandes, 2012). These oncoproteins serve as molecular markers of high-risk HPV infections, making them valuable for early detection and targeted therapeutic strategies.

While high-income countries have made substantial progress in reducing cervical cancer incidence through vaccination and advanced screening techniques, many low- and middle-income countries, including Nigeria, struggle with high disease prevalence (Ferlay *et al*., 2014). In Edo State, factors such as inadequate healthcare infrastructure, cultural misconceptions, poor awareness of HPV, and the lack of access to molecular-based diagnostic tools exacerbate the challenges of early detection and prevention

However, existing screening programs in the region focus primarily on cytological methods, such as Papanicolaou test (Pap smears), which are less effective in identifying high-risk HPV strains and their oncogenic activity (World Health Organization (WHO), 2022). This is because Pap smears detect cellular abnormalities that may result from HPV infection but do not directly identify the virus or determine its specific strain. As a result, they may miss early HPV infections or fail to distinguish between low-risk and high-risk types, limiting their effectiveness in assessing cervical cancer risk (Radosevich, 2012).

Screening for E6 and E7 oncoproteins offers a more sensitive and specific approach to identifying women at risk of developing pre-cervical cancer and cervical cancer. This method not only aids early detection but also provides a critical opportunity to target high-risk populations for timely (WHO, 2006). By evaluating the effectiveness of E6 and E7 oncoprotein screening for pre-cervical cancer in parts of Benin City, Edo State, this study aimed to demonstrate their potential as a diagnostic tool for early detection of pre-cervical cancer and cervical lesions, allowing for timely clinical interventions. This could support the integration of molecular screening into existing cervical cancer prevention programs, improving early intervention strategies and improved patient outcomes (WHO, 2023).

Methodology

A total of 120 cervical samples were collected aseptically using sterile cervical swabs, from women at Faith Mediplex Hospital from August 2024 to October 2024. Sample collection was carried out using sterile cervical swabs and in accordance with recommended clinical standards to ensure patient safety and specimen integrity.

Each participant was positioned in the lithotomy posture, and a sterile speculum was gently inserted to visualize the cervix. Using the Delphi vaginal self-sampler, the sample was collected by inserting the sampler into the vagina and pressing the activation button to absorb the cervical secretions. The sample, which often appeared cloudy and could contain mucus (a normal finding), was then released into a labeled, dry transport tube by depressing the button on the sampler while the sampler was held upright within the tube. Samples were immediately labeled with the participant's identification

code and date of collection to maintain traceability and prevent cross-contamination.

Results

This study included 120 participants, with a mean age of 26.4 years (SD = 2.11). The age distribution showed that the majority of respondents were between 18-27 years (51.7%), followed by 28-37 years (33.3%), 38-47 years (10.0%), and those older than 47 years (5.0%). In terms of marital status, most participants were single (65.8%), while others were married (27.5%), widowed (5.0%), and divorced (1.7%). Religious affiliation was predominantly Christian (76.7%), with smaller proportions identifying as Muslim (20.0%), Traditionalist (0.8%), and other religions (2.5%). Regarding education, 3.3% of participants had no formal education, 12.5% had primary education, 57.5% had secondary education, and 26.7% had tertiary education. Occupational status varied, with 12.5% employed, 32.5% self-employed, 5.8% unemployed, 45.0% students, and 4.2% falling into other occupational categories (Table 1). The prevalence of E6/E7 Oncoproteins of Human Papilloma Virus among participants was found to be 4.2% (5/120) as shown in figure 1.

Table 1. Sociodemographic Characteristics of Participants

Variable	Number (n=120)	Percentage (%)
Age		
18-27 year	62	51.7
28-37 years	40	33.3
38-47 years	12	10.0
>47 years	6	5.0
Marital Status		
Single	79	65.8
Married	33	27.5
Divorced	2	1.7
Widowed	6	5.0
Religion		
Christian	92	76.7
Islam	24	20.0
Traditional	1	0.8
Others	3	2.5
Education		
None	4	3.3
Primary	15	12.5
Secondary	69	57.5
Tertiary	32	26.7
Occupation		
Employed	15	12.5
Self employed	39	32.5
Unemployed	7	5.8
Student	54	45.0
Others	5	4.2

Mean age=26.4±2.11 years.

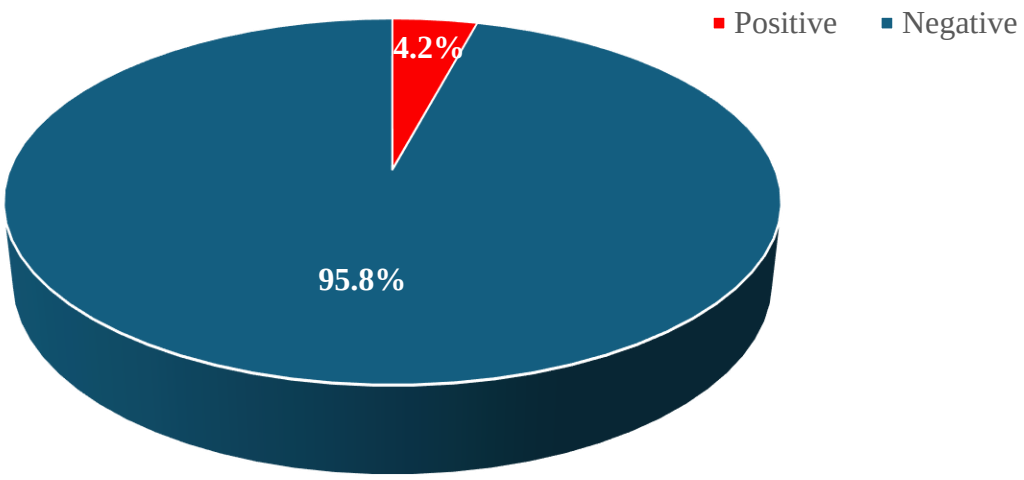

Figure 1. Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus among participants.

Relationship Between Sociodemographic Parameters and Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus

Table 2 shows the relationship between sociodemographic parameters and the prevalence of E6/E7 oncoproteins of Human Papilloma Virus (HPV). The results showed no statistically significant associations between any of the sociodemographic variables and HPV oncoprotein prevalence. Among participants aged 18-27 years, 3.2% were infected, while 5.0% of those aged 28-37 years were infected. No infections were found in participants aged 38-47 years, and 16.7% of those over 47 years were infected. However, the differences were not statistically significant ($\chi^2 = 3.077$, $p = 0.380$). The infection rate was 5.1% among single participants, 3.0% among married participants, and 0% among divorced and widowed participants. This variation was not statistically significant ($\chi^2 = 0.614$, $p = 0.893$). Among Christians, 4.3% were infected, while 4.2% of Muslims were infected. No infections were observed among participants practicing traditional religions or other religions. These differences were not statistically significant ($\chi^2 = 0.181$, $p = 0.981$). The prevalence of infection was 0% among participants with no formal education, 6.7% among those with primary education, 4.3% among those with secondary education, and 3.1% among those with tertiary education. This was not statistically significant ($\chi^2 = 0.501$, $p = 0.919$). The prevalence of infection was 6.7% among employed participants, 0% among self-employed participants, 14.3% among unemployed participants, 5.6% among students, and 0% among those in other occupations. These differences were not statistically significant ($\chi^2 = 4.204$, $p = 0.379$).

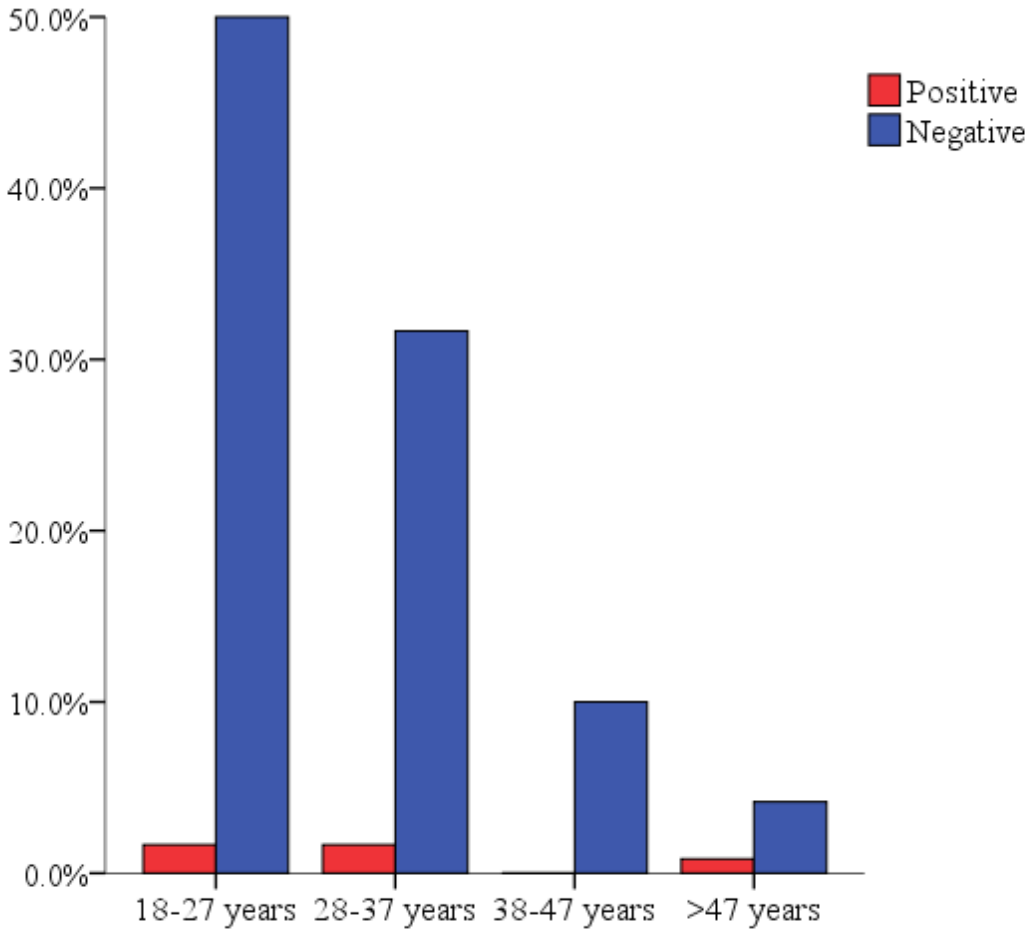

Figure 2. Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus infection among different age groups of participants

Table 2: Relationship Between Sociodemographic Parameters and Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus

Variable	No. Examined (%)	No. Infected (%)	Test Statistics	p value
Age				
18-27 year	62 (51.7)	2 (3.2)	3.077	0.380
28-37 years	40 (33.3)	2 (5.0)		
38-47 years	12 (10.0)	0 (0)		
>47 years	6 (5.0)	1 (16.7)		
Marital Status				
Single	79 (65.8)	4 (5.1)	0.614	0.893
Married	33 (27.5)	1 (3.0)		
Divorced	2 (1.7)	0 (0)		
Widowed	6 (5.0)	0 (0)		
Religion				
Christian	92 (76.7)	4 (4.3)	0.181	0.981
Islam	24 (20.0)	1 (4.2)		
Traditional	1 (0.8)	0 (0)		
Others	3 (2.5)	0 (0)		
Education				
None	4 (3.3)	0 (0)	0.501	0.919
Primary	15 (12.5)	1 (6.7)		
Secondary	69 (57.5)	3 (4.3)		
Tertiary	32 (26.7)	1 (3.1)		
Occupation				
Employed	15 (12.5)	1 (6.7)	4.204	0.379
Self employed	39 (32.5)	0 (0)		
Unemployed	7 (5.8)	1 (14.3)		
Student	54 (45.0)	3 (5.6)		
Others	5 (4.2)	0 (0)		

P<0.05 indicates significance

Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus in association with Cervical Cancer

Table 3 shows the association between the prevalence of E6/E7 oncoproteins of Human Papilloma Virus (HPV) and various risk factors for cervical cancer. Among sexually active participants, 4.4% were infected with HPV oncoproteins compared to 3.4% of those who were not sexually active. However, this difference was not statistically significant (OR = 1.287, 95% CI: 0.138-12.000, p = 0.824). The prevalence of HPV oncoproteins was significantly higher among participants who had their first sexual experience before the age of 18 (25.0%) compared to those aged 18-24 years (2.2%) and those who were over 24 years (0%). This difference was statistically significant (p = 0.001). Participants with more than three sexual partners in the past year had a significantly higher prevalence of HPV oncoproteins (14.8%) compared to those with one partner (0%) or 2-3 partners (2.0%). This difference was statistically significant (p = 0.006). Participants who reported having unprotected sex had a higher prevalence of HPV oncoproteins (9.4%) compared to those who consistently used protection (2.3%). However, this difference was not statistically significant (OR = 4.448, 95% CI: 0.708-27.954, p = 0.085). The prevalence of HPV oncoproteins was 4.7% among those who consistently used protective barriers during sex, compared to 2.9% among those who did not. This difference was not statistically significant (OR = 1.679, 95% CI: 0.181-15.577, p = 0.645). Participants with a history of sexually transmitted infections (STI) had a higher prevalence of HPV oncoproteins (12.5%) compared to those without a history of STIs (3.6%). This difference was not statistically significant (OR = 3.857, 95% CI: 0.379-39.281, p = 0.222).

Table 3: Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus in association with Cervical Cancer

Variable	No. Examined (%)	No. Infected (%)	OR	95%CI	p value
Sexually Active					
Yes	91 (75.8)	4 (4.4)	1.287	0.138-12.000	0.824
No	29 (24.2)	1 (3.4)			
Age of First Sexual Experience					
<18 years	12 (10.0)	3 (25.0)			0.001
18-24 years	89 (74.2)	2 (2.2)			
>24 years	19 (15.8)	0 (0)			
Number of Partners in Past Year					
1	42 (35.0)	0 (0)			0.006
2-3	51 (42.5)	1 (2.0)			
>3	27 (22.5)	4 (14.8)			
Unprotected Sex					
Yes	32 (26.7)	3 (9.4)	4.448	0.708-27.954	0.085
No	88 (73.3)	2 (2.3)			
Consistent Protection Usage					
Yes	85 (70.8)	4 (4.7)	1.679	0.181-15.577	0.645
No	35 (29.2)	1 (2.9)			
History of STI					
Yes	8 (6.7)	1 (12.5)	3.857	0.379-39.281	0.222
No	112 (93.3)	4 (3.6)			

P<0.05 indicates significance

Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus in association with HPV-related Medical History of Participants

Table 4 shows the relationship between the prevalence of E6/E7 oncoproteins of Human Papilloma Virus (HPV) and HPV-related medical history of participants. Participants who reported abnormal vaginal bleeding had a significantly higher prevalence of HPV oncoproteins (16.7%) compared to those without this symptom (2.8%) (OR=7.000, 95% CI: 1.044-46.949, p = 0.022). Participants with persistent pelvic pain had a higher prevalence of HPV oncoproteins (11.1%) compared to those without this symptom (3.6%), the association was not statistically significant (OR = 3.344, 95% CI: 0.333-33.554, p = 0.278). The prevalence of HPV oncoproteins was higher among participants with unusual vaginal discharge (6.9%) compared to those without (3.3%), but this difference was not statistically significant (OR = 2.173, 95% CI: 0.345-13.687, p = 0.398).

Participants who reported painful intercourse had a higher prevalence of HPV oncoproteins (7.9%) compared to those without this symptom (2.4%). However, this association was not statistically significant (OR = 3.429, 95% CI: 0.548-21.432, p = 0.164). None of the participants who had been vaccinated were infected with HPV oncoproteins, compared to 7.4% of those who were not vaccinated. This difference was statistically significant (OR = 1.079, 95% CI: 1.009-1.154, p = 0.046).

Table 4: Prevalence of E6/E7 Oncoproteins of Human Papilloma Virus in association with HPV-related Medical History of Participants

Variable	No. Examined (%)	No. Infected (%)	OR	95%CI	p value
Abnormal vaginal bleeding					
Yes	12 (10.0)	2 (16.7)	7.000	1.044-46.949	0.022
No	108 (90.0)	3 (2.8)			
Persistent pelvic pain					
Yes	9 (7.5)	1 (11.1)	3.344	0.333-33.554	0.278
No	111 (92.5)	4 (3.6)			
Unusual vaginal discharge					
Yes	29 (24.2)	2 (6.9)	2.173	0.345-13.687	0.398
No	91 (75.8)	3 (3.3)			
Painful intercourse					
Yes	38 (31.7)	3 (7.9)	3.429	0.548-21.432	0.164
No	82 (68.3)	2 (2.4)			
Vaccination					
Yes	52 (43.3)	0 (0)	1.079	1.009-1.154	0.046
No	68 (56.7)	5 (7.4)			

P<0.05 indicates significance

Discussion

Human Papillomavirus (HPV), particularly its high-risk strains expressing E6 and E7 oncoproteins, is widely recognized as a significant etiological agent in the development of cervical cancer globally (de Martel *et al.*, 2020). In Nigeria, cervical cancer remains one of the leading causes of cancer related mortality among women, largely attributed to limited HPV vaccination coverage and insufficient public awareness regarding cervical cancer screening practices (Sung *et al.*, 2021; WHO, 2022).

In this research, 120 participants were screened for E6 and E7 oncoproteins of HPV, and the overall prevalence was 4.2%. This prevalence indicates the presence of oncogenic HPV strains in the community and underscores the need for active surveillance and preventive strategies. This also suggests that high-risk HPV strains continue to represent a latent threat, even in regions with low incidence rates. Comparable studies have reported varying prevalence rates across Nigeria. For instance, in a study of 405 women in Awka, Southeastern Nigeria, the prevalence was 19.5%, while estimates ranged from 14.7% in Irun to 21.6% in Okene, 26.3% in Ibadan, and 37.0% in Abuja (Ezechi et al., 2023). A systematic review and meta-analysis of 18 studies likewise estimated a pooled high-risk HPV prevalence of 25% among Nigerian women, with HPV-16 and -18 at 9% and 10%, respectively (Ezechi et al., 2023). Such heterogeneity likely reflects differences in demographic profiles, sexual behavior, laboratory methods, and access to screening and vaccination programmes.

With respect to sociodemographic characteristics of the participants in this study, variables such as age, marital status, religion, education, and occupation did not show any statistical association with the prevalence of E6 and E7 oncoproteins, with p values, 0.380, 0.893, 0.981, 0.919, and 0.379 respectively. This finding is consistent with earlier research, such as that by Akarolo-Anthony *et al*., (2014), which also observed no significant associations between sociodemographic characteristics and HPV infection prevalence. In their study, the lack of correlation was ascribed to the widespread distribution of HPV infection across different demographic groups, suggesting that factors such as age, marital status, and education level may not be the primary determinants of infection risk. The highest infection rate (16.7%) occurred in women above 47 years of age, followed by those in the 28–37 age range (5.0%). This is supported by Piras *et al*. (2011), whose European study showed that persistent HPV infection in older women is likely due to cumulative sexual exposure over time, particularly in populations with delayed access to screening. However, these differences were not statistically significant ($\chi^2 = 3.077$, $p = 0.380$). Single women had a slightly higher prevalence (5.1%) than married women (3.0%), diverging from research associating marriage with prolonged HPV exposure. This may be linked to factors such as lack of parental supervision, peer pressure, economic vulnerability, and limited access to sexual health education and services among single women, which could increase the likelihood of early sexual initiation and multiple sexual partnerships. These conditions have been observed in various settings and may contribute to increased HPV exposure (Narasimhan *et al*., 2015). The high rate of infection among unemployed individuals observed in this study (14.3%) could be attributed to the multiple burdens participants in this category face such as poverty, social isolation, and a lack of consistent healthcare access. Without a source of income or structured routine, unemployed individuals may be more vulnerable to engaging in risky sexual behaviors, including transactional sex, as a means of survival. Additionally, many unemployed individuals may lack the education or awareness necessary to understand the importance of regular HPV screening, vaccination, and safe sex practices, further increasing their susceptibility to infection. These findings correspond with research by Okolo *et al*. (2016), who stated that unemployed women had significantly higher HPV prevalence due to economic instability, reduced healthcare access, and a tendency to engage in survival-driven sexual behaviors.

While these sociodemographic variations may suggest underlying behavioral or access related factors, statistical analysis did not confirm them as significant contributors for HPV infectivity. However, some studies contrast with these observations. For example, Ezechi *et al*. (2017), in a study conducted in Ibadan, South-Western Nigeria, reported a high prevalence (20.3%) for high-risk HPV strains and found a strong correlation with low socioeconomic status alongside contributing factors such as poor personal hygiene, early initiation of sexual activity, multiple sexual partners, and severely limited access to cervical screening programs. The disparity in findings is likely due to the rural setting marked by persistent poverty, overcrowding, and a poorly resourced healthcare system, which may have amplified these risk factors and revealed associations that were inevident in this study. Early sexual activity has been widely recognized as a key risk factor for HPV acquisition and subsequent cervical neoplasia (WHO, 2022). Participants with first sexual activity before 18 years of age had a 25.0% infection rate, which is substantially higher than the 2.2% rate among those aged 18–24, showing statistical significance ($p = 0.001$). These findings correlate with global data linking early sexual activity to increased HPV susceptibility due to cervical immaturity (Gichangi *et al*., 2018). Conforming with findings of Moscicki *et al*. (2020), who studied over 300 adolescent girls in California and concluded that early sexual initiation was associated with higher HPV incidence, emphasizing the importance of delaying sexual interaction through community sensitization, formal sex education in schools, and engagement of parents in adolescent reproductive health awareness. Also, participants with more than three sexual partners in the past year had a higher prevalence (14.8%), compared to those with one partner (0.0%) and those with 2–3 partners (2.0%) ($p = 0.006$). This is in line with research findings of Bruni *et al*. (2022), who conducted a global meta-analysis of over 1 million women across 70 countries in 5 continents and found a strong positive correlation between multiple sexual partners and persistent

HPV infection. This trend was also seen in Nigerian studies such as Chukwuma *et al*. (2018) in Port Harcourt and Efanga *et al*. (2020) in Calabar, who reported higher HPV prevalence among women with multiple partners in cohorts of 200 to 300 participants. Behavioral changes and communication strategies that promote monogamy or fewer sexual partners might be a valuable approach to HPV prevention, as multiple sexual partners increase the likelihood of exposure to different HPV strains and reduce the effectiveness of natural immune responses (Burd, 2021).

Participants who engaged in unprotected sexual intercourse also demonstrated a higher prevalence (9.4%) compared to those who used protective barriers (2.3%), though this was not statistically significant ($p = 0.085$). According to previous research, regular condom use may reduce but not eliminate the risk of HPV transmission (CDC, 2023). Gravitt *et al*. (2017) noted that condoms can effectively reduce viral load and the likelihood of co-infections with other sexually transmitted pathogens, reinforcing their role as an important component in prevention efforts. Likewise, participants with a history of sexually transmitted infections (STIs) had a higher HPV prevalence (12.5%) than those without (3.6%), again corresponding with previous studies suggesting that STIs can compromise mucosal integrity and facilitate HPV infection (LazcanoPonce *et al*., 2021). This finding supports the work of Clifford *et al*. (2013), who conducted a comprehensive meta-analysis examining the co-

infection of HPV with other STIs, particularly *Chlamydia trachomatis* and *Herpes Simplex Virus type 2 (HSV-2)*. Their study proposed that prior or concurrent infections may induce chronic mucosal inflammation, epithelial disruption, and immune modulation, promoting the entry and persistence of HPV.

HPV E6/E7 oncoprotein expression was notably linked to abnormal vaginal bleeding ($p = 0.022$), suggesting this symptom may serve as an early clinical manifestation of cervical epithelial changes. A prevalence of 16.7% was recorded among women who presented with abnormal vaginal bleeding, compared to 2.8% in those without it. This supports the findings of Arbyn *et al.* (2021), who in a European pooled analysis of 15,000 patients identified abnormal bleeding as a significant symptom of early cervical lesions. Although other symptoms such as persistent pelvic pain, unusual vaginal discharge, and painful intercourse were more common among infected individuals, they were not statistically significant ($p = 0.278$), ($p = 0.398$), ($p = 0.164$) respectively. Nevertheless, these findings highlighted the importance of clinical surveillance, particularly in regions with limited access to screening infrastructure. Namujju *et al.* (2021) also established abnormal vaginal bleeding as a frequent warning sign of advanced cervical pathology and should trigger prompt clinical evaluation, including HPV testing and colposcopy. Early detection and timely intervention are essential in halting the progression from HPV infection to cervical intraepithelial neoplasia and, eventually, invasive cervical cancer. The protective benefit of HPV vaccination was clearly demonstrated in this study as none of the vaccinated participants tested positive for E6 or E7 oncoproteins, in contrast to a 7.4% infection rate among unvaccinated individuals. This clear difference reinforces the effectiveness of HPV vaccines, particularly those targeting high risk strains like HPV-16 and HPV-18, in preventing oncogenic infections and their associated lesions. Similar trends have been observed globally, with widespread vaccination contributing to substantial declines in HPV prevalence and related diseases (Drolet *et al.*, 2019; Bruni *et al.*, 2021). However, HPV vaccination coverage in Nigeria remains limited due to barriers such as cost, accessibility, and lack of awareness (Gatumo *et al.*, 2018). These findings highlight the urgent need to strengthen and expand vaccination efforts, particularly among pre-adolescent girls before their sexual debut, to curb the burden of HPV-related conditions.

Conclusion

This study provides important insights into the prevalence and associated risk factors of E6 and E7 oncoproteins of Human Papillomavirus in Benin City, Edo State. The 4.2% prevalence indicates ongoing HPV transmission and the potential for progression to cervical cancer in affected individuals. Significant associations with early sexual activity, multiple sexual partners, abnormal vaginal bleeding, and lack of vaccination emphasize the need for targeted public health interventions. These findings support the efficiency of HPV vaccination, highlight the importance of screening programs and sexual health education in reducing the burden of HPV related diseases and progression to cervical cancer in Nigeria.

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