

Research Article

Prevalence of Cervical Human Papillomavirus (HPV) Infection Among Women in Some Areas of North-central Nigeria

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ABSTRACT

The prevalence of cervical human papilloma virus (HPV) infection varies worldwide with Sub-Saharan Africa having the highest prevalence (12.0%) with Nigeria having the highest prevalence in Sub-Saharan Africa. Some risk factors associated with HPV infection are multiparity, smoking habits, use of contraceptives and early age sexual debut. A large number of HPV-associated risk factors and poor diagnosis in Nigeria have led to inadequate records of the prevalence and distribution of HPV genotypes. Hence, this study is aimed at determining the prevalence of cervical HPV infections and its associated risk factors among women in some parts of North-central Nigeria. Cervical swab samples were collected from 250 women who consented and attended cervical cancer screening units of three tertiary health institutions in Plateau and Nasarawa States and Abuja, Nigeria. Socio-demographic and risk factor information was obtained through structured questionnaires while HPV DNA was detected using Nested PCR. Results revealed an HPV prevalence of 30.9% in Plateau State, 82.6% in Nasarawa State and 30.3% in Abuja. Demographic/ risk factors such as age (p=0.02; r=0.37), marital status (p=0.01; r= 0.45), age at first pregnancy (p= 0.04; r= 0.27), educational status (p=0.04; r=0.56), employment status (p=0.02; r=0.37), use of contraceptives (p=0.02; r=0.43) and history of STI (p=0.01; r= 0.35) were significantly associated with HPV infection. This study observed a high prevalence of HPV infection and its associated risk factors in all three study locations. Therefore, public health education and campaigns about associated risk factors and cervical cancer screening are essential for the prevention and control of Human papilloma virus (HPV).

Keywords: Cervical Human papilloma virus (HPV), prevalence, risk factors, Nested PCR, North-central Nigeria.

Introduction

One of the viruses contributing to the statistics of cancerous diseases is the human Papillomavirus (HPV). HPVs are a group of small circular, unenveloped, double-stranded DNA viruses belonging to the family of *Papillomaviridae* that infect the cutaneous and mucosal epithelium. More than 100 genotypes of HPV have been identified out of which a measure infects the genital tract and are shown to be connected with benign and malignant epithelial lacerations in humans (Manga, 2015). Infection of HPVs leads to the development of cervical cancer, particularly the high-risk types. The

virus can be spread sexually (the most common sexually transmitted virus) and high-risk HPV DNA is found to be present in 99.7% of cervical cancer samples (Okunade, 2020). Cervical cancer is the seventh most common cancer worldwide and the fourth most common type of cancer among the female population with an incidence of 527,624 in the year 2012 alone and approximately 84.3% of these occur in developing countries (Ferlay *et al.*, 2019). It is the second most common cancer next to breast cancer in Nigeria (Nejo *et al.*, 2018) and an important cause of cancer death in Nigerian women with over 9000 deaths recorded annually (Toye *et al.*, 2017).

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A joint analysis and survey of HPV prevalence carried out by the International Agency for Research on Cancer (IARC) stated that Nigeria has the highest HPV prevalence in Sub-Saharan Africa (Adegbesan-Omilabu et al., 2014). According to universal data on HPV infection, the main occurrence originates in Africa (22.1%) (de Sanjose et al., 2007). Uganda has a reported prevalence of 16.3%, South Africa 20.4%, Guinea 50.8%, Sudan 2.2%, the Benin Republic 33.2%, the Republic of Congo 23.5%, Morocco 76%, Burkina Faso 25.4% and Rwanda 34% (Serwadda et al., 1999; Allan et al., 2008; Keita et al., 2009; Salih et al., 2010; Piras et al., 2011; Boumba et al., 2014; Birrou et al., 2015; Traore et al., 2016 and Ngabo et al., 2016) respectively. Diverse HPV prevalence has been reported in Nigeria that ranged from 26.3% in Ibadan, 37% in Abuja to 10% in Port Harcourt (Thomas et al., 2004; Akarolo-Anthony et al., 2014 and Kennedy et al., 2016) respectively.

The prevalence of HPV infection upsurges soon after the beginning of sexual activity with the peak value in the teenage years and middle age after which, it drops between ages 20 and 39 years (Castellsague et al., 2009). A distinct peak in HPV prevalence seems to occur in younger women in Asia, Europe and Northern America while figures from Central and South America seem to have a descending drift as age increases (Smith et al., 2008). There is variance in the age-specific prevalence of HPV across countries in Africa. The prevalence peaked in younger women and slowly declines with age in Kenya, Uganda and Zimbabwe, but usually touched a peak around 40 years of age in Nigeria and Mozambique (Castellsague et al., 2001; Thomas et al., 2004). Peak prevalence in young women was displayed by further studies from rural Nigeria, Senegal, and South Africa and they go together with a second but minor increase in prevalence among older women (Clarke et al., 2011; Gage et al., 2012). However, in Gambia, women from 15- to 54-year-olds have a moderately constant prevalence (Wall et al., 2005). The reason Africa has a discrepancy in HPV prevalence patterns remains uncertain but can probably be connected to disparities in sexual behavioural practices, sexual hygiene, co-morbidities, polygamy, male sexual partner behaviour and male circumcision (Veldhuijze et al., 2011). Some of the risk factors associated with HPV infection are level of education, age at sexual debut, parity, number of lifetime sexual partners, age at first pregnancy, and history of other malignancies (Manga *et al.*, 2015).

The large number of HPV-associated risk factors and poor diagnosis in Nigeria has led to inadequate records of the prevalence and distribution of HPV genotypes. Hence, this study is aimed at determining the prevalence of cervical HPV infections and its associated risk factors among women in some parts of North-central Nigeria. Socio-demographic and risk factor information was obtained through structured questionnaires while HPV DNA was detected using Nested PCR which is a more reliable technique.

Materials and Methods

Sample location

The study obtained ethical approval from the Medical Research and Ethics Committees of Jos University Teaching Hospital (JUTH/DCS/ADM/127/XXVIII/ 1343), Federal Medical Centre Keffi (FMC/KF/HREC/ 244/18) and National Hospital Abuja (NHA/ADMIN/ 236/V.VII) before the commencement of the study. These health institutions are located in Plateau State, Nasarawa State, and Abuja, Nigeria's Federal Capital. JUTH is located between latitude 9.90657° N and longitude 8.9547° E of the equator, FMC Keffi is located between latitude 8.84652° N and longitude 7.88489° E of the equator while NHA Abuja is located between latitude 9.0406° N and longitude 7.46174° E of the equator. Figure 1 shows the geographical locations of the study sites.

Sample size calculation

The sample size for this study was determined by using a statistical formula (Charan and Biswas, 2013) at a 95% confidence level and a reported 18.6% prevalence of human papillomavirus infection among women in the Southwestern part of Nigeria (Nejo *et al.*, 2018). A total of 250 women from age 15 to 70 years were enrolled between December 2020 and November 2021.

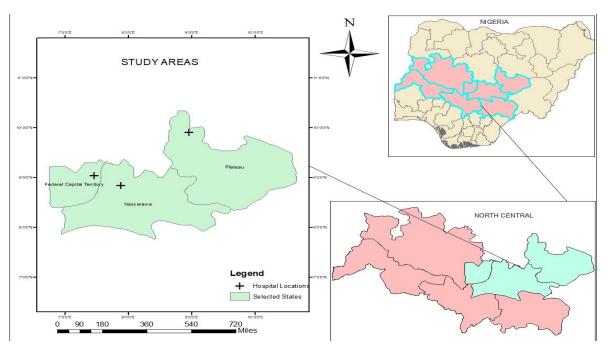


Figure 1: Geographical locations of the study sites

Sample/Data collection and analysis

Cervical swab samples were collected from women who presented for cervical cancer screening (Pap smear) in any of the three tertiary institutions (located in Plateau State, Nasarawa State, and Abuja, Nigeria) either being referred by Doctors or healthcare workers following complaints of symptoms suggestive of either genital tract infection or cervical cancer or based on their personal decision. Informed consent was obtained from all subjects before their study enrollment. Prospective participants were briefed about the purpose of the study and asked questions regarding the inclusion and exclusion criteria of the study. All women who have not undergone a hysterectomy, not menstruating, or were not pregnant at the time of sample collection and have consented to participate were recruited in the study.

The Socio-demographic and risk factor characteristics of each participant were obtained through the use of a structured questionnaire. A cytobrush was used to collect cervical swab samples from the ectocervix of each participant. The cytobrush, containing the cervical cells was placed into a labelled screw-capped vial containing 10ml liquid-based cytological processing/ preservative reagent and was transported to the laboratory on ice packs. It was vortexed for 60 sec after which the cervical cell suspension was transferred into cryovials and stored at -80°C until analyzed.

Viral DNA extraction and polymerase chain reaction (PCR)

Viral genomic DNA extraction from the cervical swab samples was carried out using a column-based commercially available viral RNA+DNA extraction kit (JENA Bioscience, Jena, Germany) following the manufacturer's instructions. The consensus region of the HPV DNA was amplified by polymerase chain reaction (PCR) using primers that target the E6/E7 gene region [one forward primer (GP-E6-3F) and two back primers (GP-E7-5B and GP-E7-6B)] as described by Sotlar *et al.* (2004). Detection of the amplified DNA was done using 2% gel electrophoresis.

Statistical analysis

IBM SPSS statistics version 21 software was used to analyze the data collected alongside chi-square statistics test and binomial logistic regression to test for significant differences in the relationship between HPV infection and associated risk factors (with p values of <0.05 considered as statistically significant) and to estimate the degree of correlation between the variables respectively.

96

Results

Data obtained showed that the age range of the participants was between 20 and 70 years with a mean age range of 44.5 ± 11.9 years. Most of the participants, 80 (32.0%) were within the age group 40-49 years while the least were within the age group of \geq 70 years 2 (0.8%). Out of the 194 swab samples analysed from Plateau State, 60 were positive giving a prevalence of 30.9%, of

the 23 swab samples analysed from Nasarawa State, 19 were positive giving a prevalence of 82.6% while of the 33 swab samples analysed from Abuja, 10 were positive giving a prevalence of 30.3%. The result of the prevalence of HPV in each location is as shown in Figure 2 below.

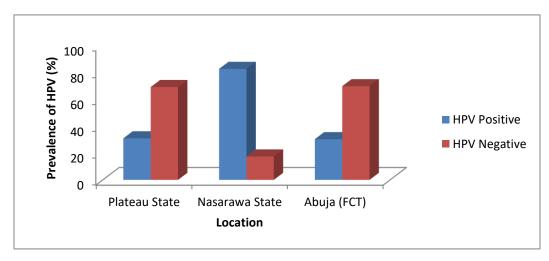


Figure 2: Percentage Distribution of the Participants within the Study Locations.

The prevalence of HPV infection in relation to sociodemographic/ risk factors by location of sample collection of the participants is shown in Figures 3 to 9. The result of the prevalence of HPV infection in relation to age group is as shown in Figure 3. Result showed that Plateau State had the highest HPV prevalence among the age group 30 - 39 years (18.56%), Nasarawa State had the highest prevalence among the age group 40 - 49 years (26.09%) while Abuja had the highest prevalence among the age group 20 - 29 years (12.12%) (p=0.02; r=0.37).

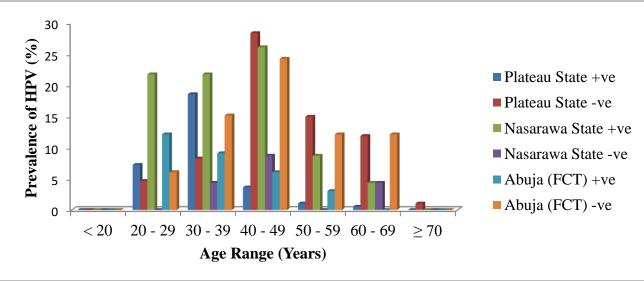


Figure 3: Prevalence of HPV infection in relation to age

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The result of the prevalence of HPV infection in relation to marital status of the participants is as shown in Figure 4. Results showed that the highest prevalence of HPV infection was recording in married women in all locations of Plateau State, Nasarawa States as well as Abuja with a prevalence rate of 17.5%, 52.17% and 12.12% respectively (p=0.01; r=0.45).

The result of the prevalence of HPV infection in relation to age range at first pregnancy of the participants is as shown in Figure 5. The result showed that the age range of 20 - 24 years recorded the highest infection rate in Plateau State and Abuja (FCT) which had 20.62% and 15.15% respectively. While the age range ≥ 25 years had the highest infection rate of 39.13% in Nasarawa State (p=0.04; r=0.27).

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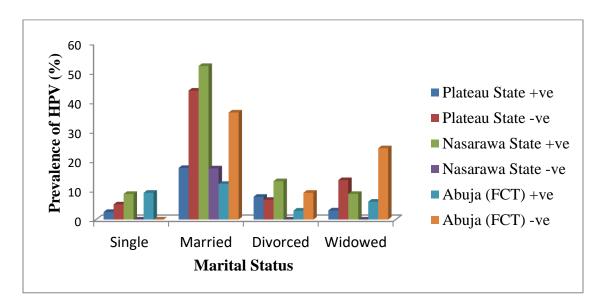


Figure 4: Prevalence of HPV infection in relation to marital status

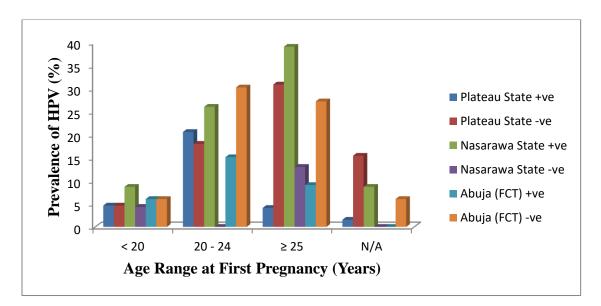


Figure 5: Prevalence of HPV infection in relation to age range at first pregnancy Legend: NA= Not applicable

The result of the prevalence of HPV infection in relation to educational status of the participants is as shown in Figure 6. The result showed that the participants with tertiary level of education in Plateau, Nasarawa and Abuja had the highest HPV prevalence of 12.89%, 34.78% and 24.24% respectively (p=0.04; r=0.56).

The prevalence of HPV infection in relation to employment status of the participants is as shown in Figure 7. The result showed that the participants who are housewives in Plateau and Nasarawa States had the highest HPV infection rate of 16.49% and 43.45% respectively. While women who are skilled/professionals had the highest infection rate of 15.15% in Abuja (FCT) (p=0.02; r=0.37).

99

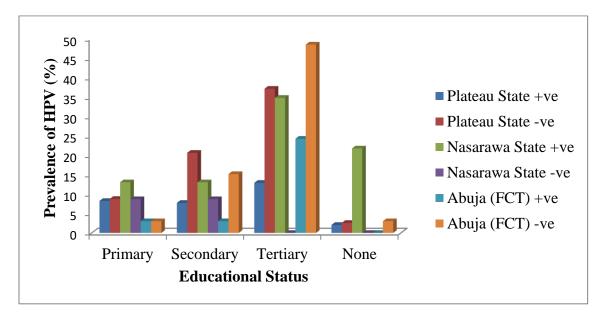


Figure 6: Prevalence of HPV infection in relation to educational status

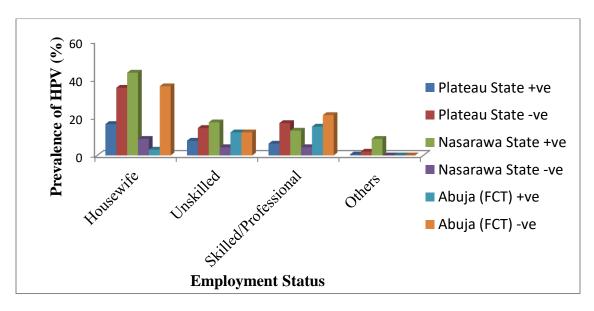


Figure 7: Prevalence of HPV infection in relation to employment status

The prevalence of HPV infection in relation to the use of contraceptives by the participants is as shown in Figure 8. The result showed that the women who use IUCD in Plateau and Nasarawa States had the highest infection rate of 11.34% and 30.43% respectively. While participants associated with use of condoms in Abuja had the highest infection rate of 12.12% (p=0.02; r=0.43).

The prevalence of HPV infection in relation to the history of sexually transmitted infections by the participants is as shown in Figure 9. The result showed that the women with HIV infection in Plateau State had the highest HPV prevalence of 14.72% while women without any history of STI in Nasarawa State and Abuja (FCT) had the highest prevalence of 43.49% and 30.3% respectively (p=0.01; r=0.35).

100

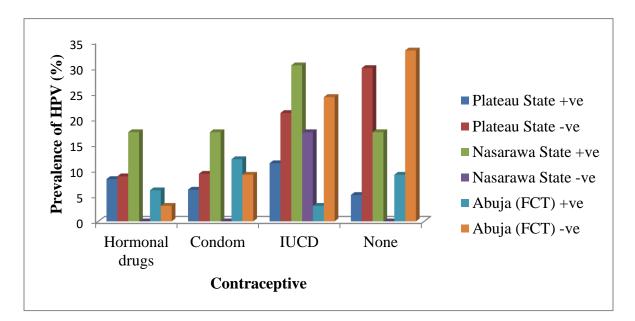


Figure 8: Prevalence of HPV infection in relation to use of contraceptives

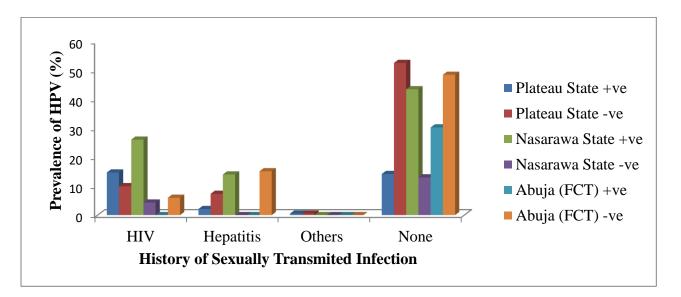


Figure 9: Prevalence of HPV infection in relation to history of sexually transmitted infections

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Discussion

The high infection rate recorded in Nasarawa State (82.6%) could be linked to the participants being referred by a physician as a result of signs/symptoms presented by the participant. The signs/symptoms which are already present led to a high number of HPV-positive results in the State. The prevalence reported in this study is higher than the previously reported seroprevalence of HPV-16 (32.0%) in the state by Adoga *et al.* (2021) and another reported prevalence of 54.1% by Yakub *et al.* (2019).

The 30.9% prevalence reported in Plateau State is moderately high. Lower prevalence and incidence rates have been reported by some studies conducted in Jos Plateau state. These studies reported a prevalence of 13.2% among adolescent girls and an incidence of 31.1% (Cosmas *et al.*, 2022; Zakari *et al.*, 2016) respectively.

In Abuja, a moderately high HPV prevalence of 30.3% was also reported. Previous studies in Abuja reported a higher prevalence of 37% and a lower prevalence of 21.3% (Akarolo-Anthony *et al.*, 2014; Adebamowo *et al.*, 2017) respectively. Studies in other parts of Nigeria reported a lower HPV prevalence of 21.6% and 19.6% both in South West Nigeria (Fadahunsi *et al.*, 2013; Ezechi *et al.*, 2014) respectively while Auwal *et al.* (2013) reported a higher prevalence of 76.0% in a study carried out in Kano state, Northwest Nigeria.

The high prevalence of HPV infection in this continent (especially in Nigeria) might be connected to the insufficient knowledge and awareness of the virus in Africa alongside the prevalence of most positive risk factors for HPV (Vinodhini *et al.*, 2012) in addition to some hypothesis which has projected that the origin of the development of some if not all HPV types might be drawn to Africa. The inconsistency in HPV prevalence patterns in the three study locations is not yet certain but could also be linked to discrepancies in sexual behavioural practices, sexual hygiene, co-morbidities, polygamy, male sexual partner behaviour and male circumcision (Veldhuijze *et al.*, 2011).

In this study, women within the childbearing age (20 - 29, 30 - 39 and 40 - 49 years) had the highest prevalence of HPV infection in Abuja, Plateau and Nasarawa States respectively. The high prevalence noticed within this age range which is a childbearing age could be due to the fact that this research is

hospital-based, thus it involved more women of childbearing age that tend to go to the hospital more often. Another reason for the high prevalence could also be projected that the high prevalence of HPV in middle and older aged women, precisely, in the Ghanaian and Nigerian societies where polygamy is commonly recognized, a percentage of the spouses or partners of these women may remain to have numerous sexual contacts/partners throughout their life and therefore re-infecting themselves and these women in the course. The high prevalence within the age range of 30 - 39 and 40 - 49 years recorded in Plateau and Nasarawa States corroborates similar findings in Lagos (Adegbesan-Omilabu et al., 2014) and in Ibadan (Thomas et al., 2004) where older females were found more likely to be infected with high-risk HPV. The high prevalence detected within the age range of 20 - 29years in Abuja is a sign that HPV infection also has a high prevalence in younger women as observed by dos Santos et al. (2022). This might be a result of sexual transmission since it overlaps with the start of sexual activity. The age pattern of the prevalence of HPV infection differs from one country to another, nonetheless, the main reported pattern displayed an early peak in the young age groups, following the start of sexual intercourse (de Sanjose et al., 2003), followed by a stable decline in middle age, after clearance of a large percentage of acquired infections, and a stable state in the age group 40 and above (Ng'andwe et al., 2007).

With respect to marital status, the highest prevalence of HPV infection in Plateau, Nasarawa and Abuja was among married women (17.5%, 52.17% and 12.12%) respectively. This substantiates the findings of Akarolo-Anthony et al. (2014) who reported a higher prevalence of HPV among the married (61.0%) over the unmarried (39.0%). The high prevalence among married women may perhaps be linked with their spouses having multiple sexual partners and the practice of polygamous marriage which is a common practice in Northern Nigeria. On the other hand, a higher positivity among singles than married was reported by Thomas et al. (2004) and Zakari et al. (2016) but the associations in the former were not significant. Nejo et al. (2018) also reported a higher infection rate among the divorced than the married. Prevalence of HPV infection predominates among participants whose first pregnancy was between ages 20 and 24 years in Plateau and Abuja (20.62% and 15.15%) respectively.

The reports of Opoku et al. (2021) from a study carried out in eight developing countries recognized that both age at first coitarche and age at first pregnancy are risk factors for cervical cancer which are triggered by insistent HPV infection irrespective of other known risk factors for cervical cancer. There is a possible added increase in risk when the early event of first sexual intercourse is shortly followed by pregnancy. Pandey et al. (2019) reported that young women between 20 and 30 years are at extreme risk of HPV infection though they are mostly symptomless and get cleared naturally due to a strong immune system. Women are more sexually active at this age. This age range forms a key unit among pregnant women in developing nations. Hormonal changes and immune response might favour the occurrence or persistence of HPV infection (Pandey et al., 2019).

Women with a tertiary level of education had the highest infection in Plateau, Nasarawa and Abuja (12.89%, 34.78% and 24.24%) respectively. This supported the findings of Nweke et al. (2013) who conducted research in Lagos, Nigeria. This high rate of infection among educated women (tertiary level) can be credited to the fact that more than half of the participants in each of the study locations were educated up to the tertiary level. It can be recommended that the attainment of HPV infection which is frequently thought to be related to sexual lifestyle may not certainly be influenced by education as a propensity to involve in unprotected sexual activities cut across all groups of respondents regardless of educational status (Okunade et al., 2017). On the other hand, studies carried out in Western Nigeria by Nejo et al. (2018), Thomas et al. (2004) and Kennedy et al. (2016) discovered that persons with no formal education (illiterates) are at higher risk of attaining HPV infection with a significant association between HPV infection and education in the last two studies. Other studies conducted on Colombian women also showed that absence of education has a significant relationship with HPV infection as it had been linked with high-risk sexual practices and a poor healthseeking attitude which accumulates to the increased presence of sexually contagious infections like HPV (Molano et al., 2002). The apparent significance of tertiary education as a risk factor against HPV infection may not be unrelated to the tilted spreading of the respondents in terms of educational qualification. These findings further confirm the need for a bigger and community-based study to avert the uneven spreading of the participants as most of them are educated and screening is mostly based on referral by healthcare workers.

Participants that are housewives (unemployed) had the highest rate of infection (16.49% and 43.48%) in Plateau and Nasarawa states respectively. This supports the findings of Baloch et al. (2016) and Traore et al. (2016) who did not find any association between employment status and HPV infection. Another previous study revealed that the rate of HPV infection was higher among the unemployed and an association was found between HPV infection and low-income earners (Nejo et al., 2018). It is possible that most of these unemployed are low-income earners and this might intensify their level of poverty as well as highrisk sexual practices consequential in gaining sexually transmitted infections like HPV. The infection rate predominates in the skilled /professionals in Abuja (15.15%). This could be attributed to the high number of women examined in that group.

It has been established in our study that the use of contraceptives was a significant risk factor for HPV infection with a moderately strong correlation as HPV prevalence was higher in subjects who use contraceptives than those who did not use any contraceptive. Plateau and Nasarawa States had the highest prevalence in women who used IUCD (11.34% and 30.43%) respectively. This result is comparable to the findings of Roura *et al.* (2016) who also recorded a significant association between HPV infection and the use of birth control. The use of condoms having the highest infection rate in Abuja (12.12%) corroborates the reports of Nejo *et al.* (2018) that the use of condoms is a significant risk factor for HPV infection.

Among the participants in our study, a significant association between HPV infection and history of STI was shown. Although more than half of the participants in the three study locations were without STI, the rate of HPV infection was highest in Plateau State among those with HIV (14.72%) while in Nasarawa and Abuja, those without any history of STI had the highest prevalence (43.49% and 30.3%) respectively. The result in Nasarawa and Abuja is in contrast to other reported studies such as that of Alotaibi *et al.* (2020) who reported that sexually transmitted Infections (STIs) may play a crucial role in HPV persistence, leading to serious complications, including cervical cancer. Paba *et al.* (2008) also reported that an STI may facilitate the

entry of multiple HR-HPVs as well as decrease the host's ability to resolve the HPV infection. This high prevalence of HPV infection in women with no history of STI may be a result of the high number of women without a history of STI that were examined. This study observed a high prevalence of HPV infection and its associated risk factors in all three study locations. Therefore, public health education and campaigns about associated risk factors and cervical cancer screening are essential for the prevention and control of human papillomavirus.

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