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

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ABSTRACT

Background: The prevalence of cervical human papillomavirus (HPV) infection varies worldwide with Sub-Saharan Africa having the highest prevalence (12.0%) and Nigeria having the highest prevalence in Sub-Saharan Africa. The polymerase chain reaction (PCR) is the conventional assay for HPV detection using type-specific primers that allow the accurate typing of HPV infections. The poor diagnosis of HPV infection and its associated risk factors in Nigeria have led to inadequate records and the distribution of HPV genotypes hence, the spread of the infection/cervical cancer. There is a need to fight cervical cancer through HPV testing using methods that allow particular typing of the HPV infections and are sensitive to detecting high-risk HPV genotypes as an alternative to cytology. **Objectives:** Consequent to this, the 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. Method: 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. Result: An HPV prevalence of 82.6% was revealed in Nasarawa State, 30.9% in Plateau State and 30.3% in Abuja. The HPV prevalence observed shows increased virus transmission in Northcentral Nigeria. 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. Conclusion: 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 preventing and controlling the Human papillomavirus (HPV).

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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 cervical 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).

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 a variance in the age-specific prevalence of HPV across countries in Africa. The prevalence peaked in younger women and slowly declined 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 disparities sexual connected to in behavioural practices, sexual hygiene, comorbidities, polygamy, male sexual partner behaviour, male circumcision and the methods used in testing HPV (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).

PCR is broadly used in several epidemiological studies for HPV typing due to its high sensitivity for detecting HPV DNA. This method of HPV detection is deficient in this part of the world, therefore, contributing to the unknown circulation of some high-risk HPV types and hence the incongruity in the HPV prevalence in Nigeria.

The moderately high prevalence of cervical cancer in Nigeria can be prevented through screening with new methods such as the use of type-specific primers. 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 is aimed at determining prevalence of cervical HPV infections and its associated risk factors among women in some parts of North-central Nigeria. Sociodemographic 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 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 9.906570 N and longitude 8.95470 E of the equator, FMC Keffi is located between latitude 8.846520 N and longitude 7.884890 E of the equator while NHA Abuja is located between latitude 9.04060 N and longitude 7.461740 E of the equator. Figure 1 shows the geographical locations of the study sites.

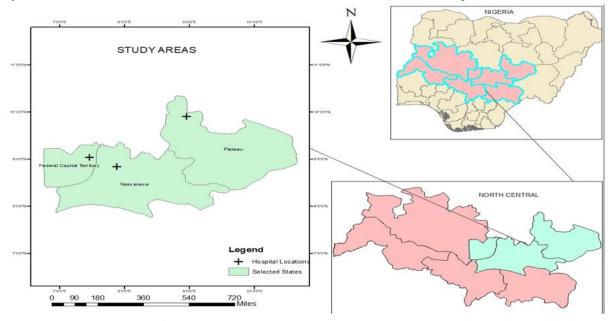


Fig. 1: Geographical locations of the study sites.

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 the age of 20 - 70 years were enrolled between December 2020 and November 2021.

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 enrolment. 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 had not undergone a hysterectomy, not menstruating, or were not pregnant at the time of sample collection and had 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 reverse primers (GP-E7-5B and GP-E7-6B)] as described by Sotlar *et al.* (2004). Detection of the amplified DNA was done using 2% agar rose gel electrophoresis.

Statistical Analysis:

IBM SPSS statistics version 21 software was used to analyze the data collected alongside a 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.

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±11.9years. Most of the participants, 80 (32.0%) were within the age group 40 - 49 years while the least were within the age group of ≥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% (Table 1).

Table 1: Prevalence of HPV infection in	each of the study locations.
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Location	No. Examined	No. positive	Prevalence (%)
Plateau State	194	60	30.9
Nasarawa State	23	19	82.6
Abuja (FCT)	33	10	30.3
Total	250	89	

The prevalence of HPV infection in relation to socio-demographic/ risk factors by location of sample collection of the participants is shown in Figures 2 to 8. Results 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). The result of the prevalence of HPV infection in relation to the age group is shown in Figure 2.

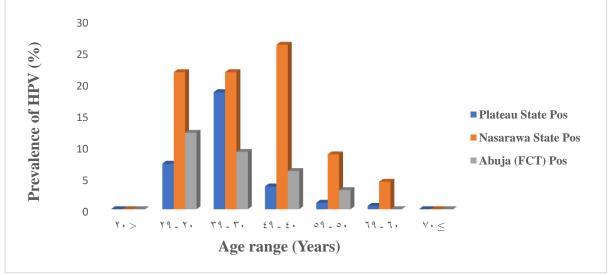


Fig. 2: Prevalence of HPV infection in relation to age.

Results showed that the highest prevalence of HPV infection was recorded 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 the marital status of the participants is shown in Figure 3.

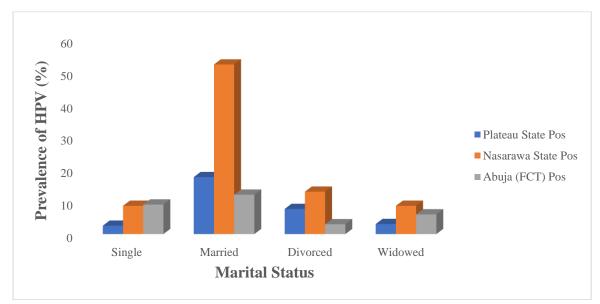


Fig. 3: Prevalence of HPV infection in relation to marital status.

The result of the prevalence of HPV infection in relation to the age range at first pregnancy of the participants is shown in Figure 4. 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).

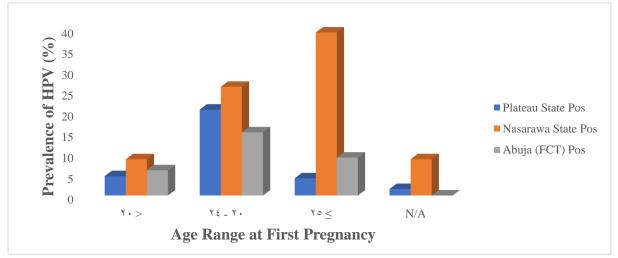


Fig. 4: Prevalence of HPV infection in relation to age range at first pregnancy. Key: NA= Not applicable.

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) (Fig. 5).

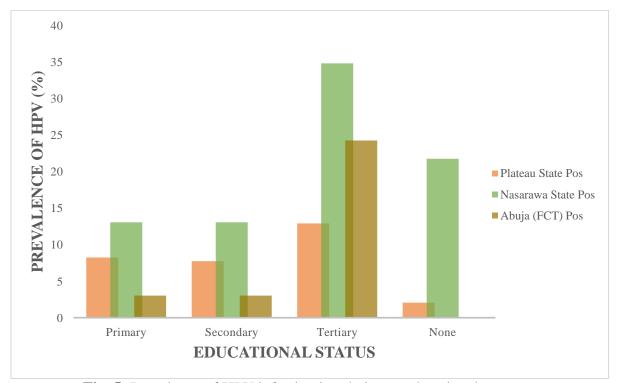


Fig. 5: Prevalence of HPV infection in relation to educational status.

The prevalence of HPV infection in relation to the employment status of the participants is shown in Figure 6. The result showed that the participants who are housewives in Plateau and Nasarawa States had the highest HPV infection rates of 16.49% and 43.45% respectively. While the women who are skilled/professionals had the highest infection rate of 15.15% in Abuja (FCT) (p=0.02; r=0.37).

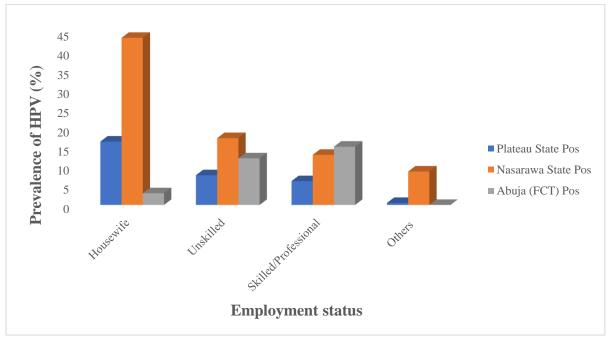


Fig. 6: Prevalence of HPV infection in relation to employment status.

The prevalence of HPV infection in relation to the use of contraceptives by the participants is shown in Figure 7. The result showed that the women who use IUCD in Plateau and Nasarawa States had the highest infection rates of 11.34% and 30.43% respectively. While participants associated with the use of condoms in Abuja had the highest infection rate of 12.12% (p=0.02; r=0.43).

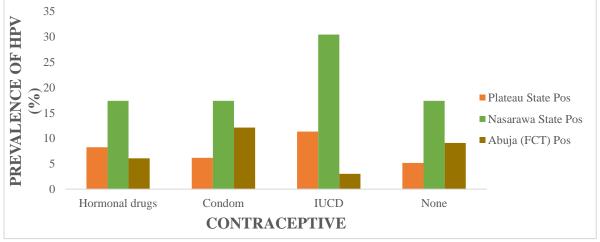


Fig. 7: Prevalence of HPV infection in relation to use of contraceptives.

The prevalence of HPV infection in relation to the history of sexually transmitted infections by the participants is shown in Figure 8. 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).

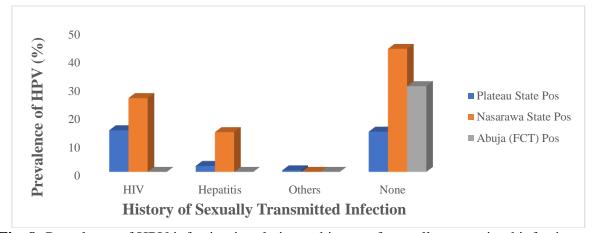


Fig. 8: Prevalence of HPV infection in relation to history of sexually transmitted infections.

DISCUSSION

Nasarawa state had a very high infection rate (82.6%) which could be linked to most of the participants being referred by a physician as a result of signs/symptoms presented. 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. Although most of the participants from Plateau State and Abuja visited the clinics for cervical cancer screening based on self-decision, the locations still recorded a moderately high prevalence of HPV infection which is an indication of high HPV prevalence in 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, hygiene, co-morbidities, polygamy, male sexual partner behaviour and 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, involved more women it 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 women, precisely, in the Ghanaian and Nigerian societies where polygamy is commonly recognized, a percentage of the spouses or partners of these women may to have numerous remain 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 - 49years 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 - 29 years 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 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 be involved 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 health-seeking 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 who 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 high-risk 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 contraceptive. Plateau 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 a 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, which indicates an increased transmission of HPV infection amongst sexually active women in Northcentral Nigeria. 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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