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Prevalence and Predictors of High-Risk HPV in Nigeria

Aigbe Gregory Ohihoin[1*], Patrick Azuka Okwuraiwe[1], Adesola Zaidat Musa[1], Gbenga Olorunfemi[2], Chika Kingsley Onwuamah[1], Fehintola Ige[1], Olufemi Samuel Amoo[1], Rosemary Audu[1], Felix Okogbo[3], Babafemi Daniyan[4], Terrumun Swende[5], Geoffrey Chukwubuike Onyemelukwe[6], Haruna Daru[7], Hadiza Usman[8], Oladapo Shittu[6], Jonah Musa[7], Oliver Chukwujekwu Ezechi[1], Innocent Achanya Ujah[7]

[1]Nigerian Institute of Medical Research (NIMR), Lagos, Nigeria
[2]School of Public Health, University of Witwatersrand, Johannesburg, South Africa
[3]College of Medicine Ambrose Alli University, Edo State, Nigeria
[4]National Obstetric Fistula Center Abakaliki, Ebonyi State, Nigeria
[5]Benue State University, Benue State, Nigeria
[6]Ahmadu Bello University Zaria, Kaduna State, Nigeria
[7]University of Jos, Jos, Nigeria
[8]University of Maiduguri, Borno State, Nigeria
Email: *aigbe.ohihoin@yahoo.com, *aigbe.ohihoin@nimr.gov.ng

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Abstract

Introduction: Cervical cancer remains a major cause of morbidity and mortality among the female population in sub-Saharan Africa. Vaccination against human papillomavirus (HPV), the main causative agent, has the potential to eradicate cervical cancer. In-country evidence of sub-types of HPV associated with cervical cancer is scanty, thus necessitating this study. **Methods:** A cross-sectional study was performed using a multistage sampling technique. A molecular technique using the Cobas 4800 machine was used for genotyping. **Results:** 570 participants were recruited for the study. The mean age of the participants was 32.4 ± 5.2 years. The age of sexual debut ranged from 15 - 24 years with a median of 19 years. 194 participants were positive for high-risk HPV giving a prevalence of 34%. 3% (n = 17) were positive for HPV, 16. 4% (23) had a positive result for HPV, 18. 27% (n = 154) had a positive result for other high-risk groups (OHR) other than HPV 16 or 18. Positive status for high-risk HPV is associated with the presence of genital warts (OR = 7.5), a Positive HIV status (OR = 3.48), abnormal vaginal discharge (OR = 2.20), multiple sexual partners (OR = 2.30), and obesity (OR = 2.70). The prevalence of HIV in the study population was 6.84% (n = 39). **Conclusion:** Another High-risk HPV other than 16 and 18 appears to be the predominant form of HPV infection in Nigerian women. The risk of being positive

for high-risk HPV is associated with the presence of genital warts, abnormal vaginal discharge, a positive HIV status, multiple sexual partners and Obesity. It is therefore necessary to disaggregate and study these high-risk sub-types.

Keywords

HPV, Cervical Cancer, Prevalence, Predictors, Nigeria

1. Introduction

Human Papilloma Virus (HPV) has been recognized as the main aetiological basis for the development of cervical cancer, the second commonest cancer of women in Nigeria [1].

Human Papilloma Virus (HPV) is from the family Papovaviridae. It is regarded as one of the most common causes of sexually transmitted diseases in both men and women worldwide [2]. HPV continues to be an important topic, as rates of infection appear to continue to be rapidly increasing. The virus has been known to invade human epithelial cells, including the anal and genital areas. The time between exposure to the virus and having symptoms can be 3 to 4 months, yet the virus can be transmitted to someone else during this time [3]. Although HPV is considered a sexually transmitted infection (STI), it can also be transmitted by skin-to-skin contact; therefore traditional methods of protecting against STI, such as condoms can reduce, but not eliminate the risk of HPV infection [3].

Individuals who pose a higher risk for HPV infection include those with numerous lifetime sexual partners, early age of first intercourse, history of other STIs, alcohol and drug use related to sexual behaviours, and partner's number of sexual partners [4].

The infection is most prevalent in women in the 20-24-year-old age group, with 15 -19 year olds being the second largest group [5]. Prevalence decreases with age, dropping significantly after age 30 as it is thought that the younger, developing cervix is more likely to be infected, but these infections tend to be short-lived and are usually cleared by the immune system [5] [6].

About 100 different strains of HPV have been identified. In terms of HPV's association with cervical cancer and precursor lesions, HPVs can be grouped into high-risk and low-risk HPV types. Low-risk HPV types include types 6, 11, 42, 43, and 44. High-risk HPV types include types 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and 70.

Epidemiologic studies indicate that the risk of contracting genital HPV infection and cervical cancer is influenced by sexual activity [7] [8]. An individual is at greater risk of becoming infected with HPV if he or she has had multiple sexual partners at any time or is the partner of someone who has had multiple sexual partners [9] [10]. Sexual activity at an early age also places an individual at

increased risk, as does a history of other sexually transmitted diseases, genital warts, abnormal Pap smears, or cervical or penile cancer in an individual or sexual partner [11] [12].

In addition to sexual activity, age is an important determinant of the risk of HPV infection. Most cervical cancers arise at the squamocolumnar junction between the columnar epithelium of the endocervix and the squamous epithelium of the ectocervix. At this site, there are continuous metaplastic changes. The greatest risk of HPV infection coincides with the greatest metaplastic activity. The greatest metaplastic activity occurs at puberty and first pregnancy and declines after menopause. HPV infection is most common in sexually active young women, 18 to 30 years of age [6]. There is a sharp decrease in prevalence after 30 years of age. However, cervical cancer is more common in women older than 35 years, suggesting infection at a younger age and slow progression to cancer [6] [13] [14]. Persistence of infection is more common with the high-risk oncogenic HPV types and is an important determinant in the development of cervical cancer [14].

Detection of high-risk HPV is necessary but may not be sufficient for the development of cervical cancer. Studies suggest that whether a woman will develop cervical cancer depends on a variety of additional factors that act in concert with cancer-associated HPV types in the process that leads to cervical cancer [11] [13] [14].

It appears that smoking is the most important risk factor independent of HPV infection for higher grades of cervical disease [15] [16]. In women with mild cervical disease, only the presence of high-risk HPV infection was a significant risk factor. Other factors such as alcohol consumption and diet have not been well established [17] [18]. There has been some suggestion that sexually transmitted viruses may serve as cofactors in the development of cervical cancer. It has been postulated that coinfection with herpes simplex virus type 2 may play a role in the initiation of cervical cancer. Cytomegalovirus (CMV), human herpesvirus 6 (HHV-6), and HHV-7 have also been detected in the cervix. Coinfection offers the opportunity for these viruses to interact with HPV [11] [19] [20].

Considering the pivotal role that HPV in association with other variables plays in the development of cervical cancer, it is, therefore, pertinent to determine the prevalence and predictors of high-risk HPV in Nigeria.

2. Methods

A cross-sectional study that assembled responses to a structured questionnaire captured clinical evaluation findings on the subjects and documented findings on the laboratory tests performed on specimens collected from the participants. The study was conducted between the period January 2015 to December 2019 across selected centres within the six geo-political zones of Nigeria. The six zones are the SS (South-South), SW (South-West), SE, (South-East), NC (North-Central), NW (North-West), and NE (North-East).

2.1. Procedure

Participants were counselled to complete an informed consent form. The assessment of participants took place in healthcare facilities close to the residence of the participants. The Women were recruited from randomly selected outpatient clinics, family planning clinics and gynaecology oncology clinics across the six geo-political regions of the country using a multistage sampling technique. The geo-political zones were based on the established by the National Population Commision [21]. Those who signed informed consent were enrolled on the study. Study-specific numbers linked to participants' hospital files were given to each participant.

After signing the informed consent form, participants were interviewed by research assistants and the information required in the study was collected by CRF. Thereafter the participants had a pelvic examination. They were placed in a modified lithotomy position, and the cervix was exposed with the help of a disposable Cusco bivalve speculum and examined. Cervical cell scrapings were collected by a cytobrush. The tip of the cytobrush was placed into a transport medium and sent to the laboratory for storage at 2˚C to 8˚C. The stored sample along with the CRF was batched and transported to the Human virology laboratory at NIMR for analysis.

2.2. HIV Test

HIV testing was conducted according to Nigerian national HIV counselling and testing guidelines in participants who agreed to be tested. Diagnosis of HIV was based on positive test results using a double enzyme-linked immunosorbent assay algorithm.

2.3. Human Papilloma Virus Detection and Genotyping

The HPV genotype tests were conducted using the automated *COBAS*® 4800 system (*Roche*, Germany). The *COBAS*® 4800 system is made up of the *COBAS*® X480 (extraction) and the *COBAS*® Z480 (analyser) instruments. The *COBAS*® 4800 HPV test is based on two major processes: 1) automated specimen preparation to simultaneously extract HPV and cellular DNA; 2) PCR amplification of target DNA sequences using both HPV and β-globin (acting as internal control) specific complementary primer pairs and real-time detection of cleaved fluorescent-labelled HPV and β-globin specific oligonucleotide detection probes. The system software version 1.0 links the operation of the *COBAS*® X480 and Z480. One millilitre of the sample was transferred into pre-labelled 10ml plain tubes placed on the sample rack. Sample codes were entered on the Work Order. Lastly, uncapped samples and reagents were loaded onto the X480, and the assay commenced. After the successful completion of sample preparation, a plate carrier containing processed samples was unloaded and put manually into the Z480 for amplification and detection. The assay takes about 3 hours and 30 minutes in total. The test identifies HPV16, HPV18 and other high-risk (OHR) genotypes at

clinically relevant infection levels.

2.4. Statistical Analysis

After the retrieval of the data, data entry clerks doubly entered the data on the NIMR REDCap platform and exported to SPSS for statistical analysis and descriptive statistics used to summarize the data. Inferential statistics was done to determine the predictors of HPV positivity by use of odd ratios and corresponding 95% Confidence Interval and calculated using unconditional multiple logistic regression adjusted for cofounders.

Variables that demonstrated statistically significant associations with a positive HPV status were incorporated in the same model and evaluated overall to determine independent predictors of a positive status for HPV.

3. Results

A total of 570 samples were obtained from randomly selected clinics from the six geo-political zones of the country. The mean age of the participants was 32.4 ± 5.2 years. The majority of the patients were married (63.1%), and had at least a secondary school education (72.0%) as shown in Table 1. The age of sexual debut ranged from 15 - 24 years with a median age of 19years. A total of 194 participants were positive for high-risk HPV giving a prevalence rate of 34%. 3% (n = 17) were positive for HPV 16. 4% (23) had a positive result for HPV 18. 27% (n = 154) had a positive result for other high-risk groups (OHR) other than HPV 16 or 18. A total of 376 participants (66%) had a negative result for HPV as shown in Table 2. Positive status for high-risk HPV is associated with the presence of genital warts (OR = 7.5), a Positive HIV status (OR = 3.48), abnormal vaginal discharge (OR = 2.20), multiple sexual partners (OR = 2.30), and obesity (OR = 2.70) as shown in Table 3. The prevalence of HIV in the study population was 6.84% (n = 39). The use of oral contraceptive pills did not show a significant association with the development of high-risk HPV (p = 0.572). Condom use did not also influence the risk of developing high-risk HPV (p = 0.323). Other factors that did not significantly influence the development of high-risk HPV include the age of coitarche, previous termination of pregnancy and age of marriage (p = 0.787, p = 0.347, p = 0.870 respectively).

4. Discussion

A total of 570 participants participated in the study and 194 participants were positive for high-risk HPV, giving a prevalence of 34%. The prevalence of HPV 16 was 3% (n = 17), while the prevalence of HPV 18 was 4% (n = 23). 376 participants (66%) had a negative result for HPV. The mean age of the participants was 32.4 ± 5.2 years. The majority of the patients were married (63.1%) and had at least a secondary school education (72.0%). The age of sexual debut ranged from 15 - 24 years. Positive status for high-risk HPV is associated with the presence of genital warts (OR = 7.50), a Positive HIV status (OR = 3.48), abnormal

Table 1. Socio-demographic and sexual history of the study population.

Variable	Frequency (%)
Age (years)	
<25	91 (16.0)
25 - 34	216 (38.0)
35 - 44	143 (25..0)
45 - 54	70 (12.2)
>55	50.0 (8.8)
Marital Status	
Single	133 (23.3)
Married	360 (63.1)
Divorced	11 (2.0)
Widowed	34 (6.0)
Separated	32 (5.6)
Highest Education Attained	
Primary	69 (12.0)
Secondary	410 (72.0)
Tertiary	91 (16.00)
Age at sexual debut (years)	
Range: 15 - 24	
<15	74 (13.0)
15 - 24	365 (64.0)
25 and above	131 (23.0)
Mean (±SD)	20.4 (±3.9)
Total lifetime sexual partners	
Range: 2 - 10	
1	182 (32.0)
2 - 4	380 (66.6)
>5	8.0 (1.4)
Mean (±SD)	2.9 (±2.5)

Table 2. Prevalence of HPV subtypes.

HPV TYPE	NUMBER	PREVALENCE (%)
16	17	3
18	23	4
OHR (OTHER HIGH RISK)	154	27
NEGATIVE FOR HPV	376	66
TOTAL	570	100

Table 3. Variables showing significant association with high-risk HPV after multiple logistic regression.

VARIABLE	OR	P-value	CI
GENITAL WARTS	7.5	0.0082	15.90 - 32.64

Continued

POSITIVE HIV STATUS	3.48	0.010	1.92 - 3.72
ABNORMAL VAGINAL DISCHARGE	2.20	0.021	1.5 - 3.3
MULTIPLE SEXUAL PARTNERS	2.30	0.009	2.1 - 8.0
OBESITY	2.70	0.0138	1.74 - 3.3

vaginal discharge (OR = 2.20), multiple sexual partners (OR = 2.30), and obesity (OR = 2.70). The prevalence of HIV in this cohort was 6.84% (n = 39)

The prevalence of high-risk HPV in this study was 34%. This is higher than earlier reports in Ibadan [22] but almost similar to that reported in Lagos [23] [24]. The study from Ibadan gave a prevalence of 18.6% while in Lagos the prevalence was 36.5%.

In this study, samples from participants were drawn from different geo-political zones in the country while in the Ibadan study, samples were taken from participants who reside within Ibadan and environs. It is not surprising that the prevalence rate from the Lagos study is close to our Nationwide study as Lagos being a highly cosmopolitan and heterogeneous city has representatives from all of the various parts of the country, thus findings from Lagos state is usually reflective of findings from a sum aggregate of the nation. Moreover, Lagos state constitutes an average of 10% of the population of the country [21].

The prevalence of HPV 16 and 18 in this study was 3% and 4% respectively. HPV 16 and 18 have been documented as the specific aetiological basis for cervical cancer [9]. Earlier Vaccines that were designed targeted these sub-types of HPV. These vaccines are gradually being replaced by vaccines with a wider spread [5]. The prevalence of HPV 16 and 18 in this study is less than other high-risk HPV. This finding justifies the need for the use of a vaccine with broader coverage instead of the bivalent and quadrivalent options. These vaccines can cover only for two and four subtypes of HPV respectively.

Another possible explanation for variation in prevalence of HPV across different studies may be related to the diverse methods used for HPV detection across the various studies. In our study, the molecular method used for the detection of HPV involved the use of the COBAS 480 system for nucleic material extraction and Polymerase Chain Reaction. This method of HPV detection is known to have a high validity [19].

The prevalence of high-risk HPV from this study is higher than the reported worldwide prevalence of 10.4% [25]. Studies on HPV prevalence tend to show higher prevalence in sub-Saharan Africa than in most other parts of the world. This spread also reflects the high distribution of cases of cervical cancer in sub-Saharan Africa than in the western part of the world. Most developed parts of the world have embraced vaccination against HPV and they have incorporated HPV vaccination into their National Immunization programmes. This strategy has led to a decrease in the incidence of HPV and cervical cancer in most developed western nations of the world. Vaccine deployment for the pre-

vention of HPV is yet to be incorporated into the National immunization programmes of many countries in sub-Saharan Africa, hence the prevalence of HPV is still high in most of these countries and cervical cancer still ranks high in incidence and in cancer mortality.

Other local studies in Nigeria and some regional studies within the west—African sub-regions have also revealed HPV prevalence with a wide range of 14.7% - 44.9%. This is captured by our prevalence rate but higher than the global prevalence rate [12] [23] [26].

In this study, the majority of participants were married and had at least a secondary school education. The type of marriage did not influence the risk of being positive for HPV ($p = 0.134$). The age of marriage did not also influence the chance of being positive for HPV ($P = 0.870$).

Early age of sexual intercourse is associated with a positive status for high-risk HPV [27]. It is thought that early age of marriage and invariably early coitarche should be associated with a positive status for high-risk HPV. This is however not the case in this study. The impact of HPV on the immature cervix of young women and teenage women is more aggressive than on the mature cervix, hence there is genuine concern about the age of coitarche, risk of HPV transmission and development of cervical cancer [27].

The presence of genital warts is associated with a positive status for HPV. Genital warts are caused by certain strains of HPV. Hence it did not come as a surprise that patients with genital warts had a more than seven-fold increase in being positive for high-risk HPV (OR: = 7.5).

The prevalence of HIV in this study was 6.8%. This value is higher than the national average of 2.1%. The higher prevalence of HIV in this cohort of individuals tends to mirror the relatively high prevalence of HPV. Both HIV and HPV are sexually transmissible infections. HPV is regarded as the commonest sexually transmissible infection [4]. The similarity in the mode of transmission of both HPV and HIV likely explains the high prevalence of HIV in this cohort of participants when compared to the National average. Furthermore, the study revealed that being positive for HIV had a more than three-fold increase in being positive for high-risk HPV. HIV patients are known to have an extra risk for developing cervical cancer at an earlier age when compared to their HIV-negative counterparts [4]. The relationship between HIV infection and HPV has been well documented as the risk of becoming positive for HIV is twice higher for patients who are positive for HPV [4]. This relationship appears to be synergistic as either infection tends to have a high prevalence in settings when the other has a high prevalence [4]. This finding is possibly explained by the fact that both HPV and HIV are both transmitted sexually hence this synergistic behaviour between HIV and HPV.

The study showed that participants with abnormal vaginal discharge had a two-and-a-half-fold risk of being positive for high-risk HPV. The abnormal vaginal discharge could be a surrogate for background sexually transmissible infection and this can account for the increased risk of a positive status for HPV in

this category of patients. It is important to also note that HPV is a sexually transmissible infection hence the same risk factor that predisposes the affected participants to increased risk of HPV will also increase their risk for other sexually transmissible infections. Furthermore, the presence of abnormal vaginal discharge could also be indicative of Bacteria Vaginosis. There is some evidence to suggest that Bacteria Vaginosis could be associated with a greater risk of being positive for high-risk HPV [7].

In this study, it was revealed that participants who had multiple sexual partners had a higher chance of being positive for high-risk HPV (OR-2.20). This also did not come as a surprise as HPV is mainly a sexually transmissible infection thus sexual habits and promiscuity, as depicted by the number of sexual partners predict the risk of becoming positive for high-risk HPV [15]. This study also showed that being obese was associated with a more than two-fold increase in the risk of being positive for HPV (OR = 2.70). This finding is at variance with the report from Liu *et al.*, (2013) who demonstrated that there was no difference in HPV prevalence between obese and non-obese women [18]. Another study, however, reported a lower prevalence of high-risk HPV infection in obese individuals when compared to non-obese individuals [16]. The reasons for this difference are not quite clear and will require further studies. The limitation of this study is the inability of the authors to disaggregate the classification OHR (Other high risk) HPV variants as this will enable specific identification of other variants of HPV.

In conclusion, the study has shown that high-risk HPV other than HPV 16 and 18 appears to be the predominant form of HPV affecting Nigerian women. The risk of being positive for high-risk HPV is associated with the presence of genital warts, abnormal vaginal discharge, a positive HIV status, multiple sexual partners and Obesity. There is, therefore, an urgent need to disaggregate these other high-risk types different from HPV 16 and 18 to ascertain their role in cervical cancer and other HPV-related malignancies. Public health measures to address the factors identified to be predictors of high-risk HPV should be instituted to mitigate the impact of these risk factors in the development of high-risk HPV.

5. What Is Already Known on This Topic

Human Papilloma Virus (HPV) has been recognized as the main aetiological basis for the development of cervical cancer, the second commonest cancer of women in Nigeria [1]. It is regarded as one of the most common causes of sexually transmitted diseases in both men and women worldwide. Epidemiologic studies indicate that the risk of contracting genital HPV infection and cervical cancer is influenced by sexual activity [20] [28] [29]. An individual is at greater risk of becoming infected with HPV if he or she has had multiple sexual partners at any time or is the partner of someone who has had multiple sexual partners. In addition to sexual activity, age is an important determinant of the risk of HPV

infection. It appears that smoking is the most important risk factor independent of HPV infection for higher grades of cervical disease [30] [31] [32].

6. What This Study Adds

1) The study shows that other than HPV 16 and 18, other variants of high-risk HPV appear to be the predominant form of HPV affecting Nigerian women.

2) It also shows that the risk of being positive for high-risk HPV among Nigerian women is associated with the presence of genital warts, abnormal vaginal discharge, a positive HIV status, multiple sexual partners and Obesity.

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Ethical Approval and Consent to Participate

Ethical approval was obtained for the conduct of this study from the Institutional Review Board (IRB) of the Nigerian Institute of Medical Research (NIMR). A written informed consent was obtained from the participants.

Consent for Publishing

All authors gave their consent for publishing.

Availability of Supporting Data

Supporting data are available on request.

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Conflicts of Interest

The authors report no competing (commercial/academic) interests.

References

[1] Agaba, P.A., Thacher, T.D., Ekwempu, C.C. and Idoko, J.A. (2009) Cervical Dysplasia in Nigerian Women Infected with HIV. *International Journal of Gynecology & Obstetrics*, **107**, 99-102. https://doi.org/10.1016/j.ijgo.2009.06.006

[2] Akarolo-Anthony, S.N., Famooto, A.O., Dareng, E.O., Olaniyan, O.B., Offiong, R., Wheeler, C.M. and Adebamowo, C.A. (2014) Age-Specific Prevalence of Human Papilloma Virus Infection among Nigerian Women. *BMC Public Health*, **14**, Article No. 656. https://doi.org/10.1186/1471-2458-14-656

[3] Ault, K.A. (2006) Epidemiology and Natural History of Human Papillomavirus Infections in the Female Genital Tract. *Infectious Diseases in Obstetrics and Gynecology*, **2006**, Article No. 40470. https://doi.org/10.1155/IDOG/2006/40470

[4] Averbach, H.S., Gravitt, P.E., Nowak, G.R., Celentano, D.D., Dunbar, S.M., Morri-

son, S.C., Grimes, B. and Padian, N.S. (2010) The Association between Cervical HPV Infection and HIV Acquisition among Women in Zimbabwe. *AIDS*, **24**, 1035-1042. https://doi.org/10.1097/QAD.0b013e3283377973

[5] Brotherton, J.M.I. (2018) Human Papillomavirus Vaccination Update: Nonavalent Vaccine and the Two-Dose Schedule. *Australian Journal of General Practice*, **47**, 417-421. https://doi.org/10.31128/AJGP-01-18-4462

[6] Cage, C.J., Ajenifuja, O.K., Wentzensen, A.N., *et al.* (2011) The Age-Specific Prevalence of Human Papilloma Virus and Risk of Cytologic Abnormalities in Rural Nigeria: Implications for Screen and Treat Strategies. *International Journal of Cancer*, **10**, 1002-26211.

[7] Cerdeira, R.C., Sanchez-Blanco, E. and Alba, A. (2012) Evaluation of Association between Vaginal Infections and High-Risk Human Papillomavirus Types in Female Sex Workers in Spain. *ISRN Obstetrics and Gynecology*, **2012**, Article ID: 240190. https://doi.org/10.5402/2012/240190

[8] Clifford, G.M., Smith, J.S., Plummer, M., Muñoz, N. and Franceschi, S. (2003) Human Papillomavirus Types in Invasive Cervical Cancer Worldwide: A Meta-Analysis. *British Journal of Cancer*, **88**, 63-73. https://doi.org/10.1038/sj.bjc.6600688

[9] Clifford, G.M., Gallus, S., Herrero, R., Munoz, N., Snijders, P.J., Vaccarella, S., *et al.* (2005) Worldwide Distribution of Human Papillomavirus Types in Cytologically Normal Women in the International Agency for Research on Cancer HPV Prevalence Surveys: A Pooled Analysis. *The Lancet*, **366**, 991-998. https://doi.org/10.1016/S0140-6736(05)67069-9

[10] De Sanjosé, S., Almirall, R., Lloveras, B., *et al.* (2003) Cervical Human Papillomavirus Infection in the Female Population in Barcelona, Spain. *Sexually Transmitted Diseases*, **30**, 788-793. https://doi.org/10.1097/01.OLQ.0000080177.82204.E0

[11] Ezechi, O.C. (2014) The Battleground of Two Infections and Cancer: Human Papilloma Virus, Premalignant Lesions of the Cervix and Their Interaction with Human Immunodeficiency Virus in Southwestern Nigeria. Dissertation, Lund University, Lund.

[12] Gage, J.C., Ajenifuja, K.O., Wentzensen, N., *et al.* (2013) Effectiveness of a Simple Rapid Human Papillomavirus DNA Test in Rural Nigeria. *International Journal of Cancer*, **131**, 2903-2909.

[13] Herrero, R., Castle, P.E., Schiffman, M., *et al.* (2005) Epidemiologic Profile of Type-Specific Human Papillomavirus Infection and Cervical Neoplasia in Guanacaste, Costa Rica. *The Journal of Infectious Diseases*, **191**, 1796-1807. https://doi.org/10.1086/428850

[14] Idelot-Rousseau, M.N., Nagot, N., Costes-martineau, V., *et al.* (2006) Human Papilloma Virus Genotype Distribution and Cervical Squamous Intraepithelial Lesions among High-Risk Women with and without HIV-1 Infection in Burkina Faso. *British Journal of Cancer*, **95**, 355-362. https://doi.org/10.1038/sj.bjc.6603252

[15] Idso, C. (2009) Sexually Transmitted Infection Prevention in Newly Single Older Women: A Forgotten Health Promotion Need. *Journal for Nurse Practitioners*, **5**, 440-446. https://doi.org/10.1016/j.nurpra.2009.02.015

[16] Jung, U.S., Choi, J.S., Ko, J.H., *et al.* (2013) Decreased Prevalence of High-Risk Human Papillomavirus Infection Is Associated with Obesity. *European Journal of Gynaecological Oncology*, **34**, 70-74.

[17] Kahn, J.A., Rosenthal, S.L., Succop, P.A., Ho, G.Y. and Burk, R.D. (2002) Mediators of the Association between Age of First Sexual Intercourse and Subsequent Human Papillomavirus Infection. *Paediatrics*, **109**, E5. https://doi.org/10.1542/peds.109.1.e5

[18] Liu, S., Rostich, F.A., Viscidi, P.R., Michelle, I.S., Burke, A.E. and Gravitt, E.P. (2013) Obesity and Human Papillomavirus Infection in Perimenopausal Women. *The Journal of Infectious Diseases*, **208**, 1071-1080. https://doi.org/10.1093/infdis/jit297

[19] Mette, T., Jensen, S.J., Bech, H.B., Blaaker, J., Svanholm, H. and Andersen, B. (2018) Good Concordance of HPV Detection between Cevico-Vaginal Self Samples and General Practitioner-Collected Samples Using the Cobas 4800 HPV DNA Test. *BMC Infectious*, **18**, Article No. 348.

[20] Muñoz, N., Bosch, F.X., de Sanjose, S., *et al.* (2003) Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer. *The New England Journal of Medicine*, **348**, 518-527. https://doi.org/10.1056/NEJMoa021641

[21] National Population Commission (2020) Nigeria Population and Housing Census. http://ghdx.healthdata.org/organizations/national-population-commission-nigeria

[22] Nejo, Y.T., Olaleye, D.O. and Odaibo, G.N. (2018) Prevalence and Risk Factors for Genital Human Papillomavirus Infections among Women in Southwest Nigeria. *Archives of Basic and Applied Medicine*, **6**, 105-112.

[23] Nweke, I.G., Banjo, A.A.F., Abdulkareem, F.B. and Nwadike, V.U. (2013) Prevalence of Human Papillomavirus DNA in HIV Positive Women in Lagos University Teaching Hospital (LUTH) Lagos, Nigeria. *Microbiology Research Journal International*, **3**, 400-413. https://doi.org/10.9734/BMRJ/2013/4151

[24] Okunade, K.S., Nwogu, C.M., Oluwole, A.A. and Anorlu, R.I. (2017) Prevalence and Risk Factors for Genital High-Risk Human Papillomavirus Infection among Women Attending the Out-Patient Clinics of a university Teaching Hospital in Lagos, Nigeria. *The Pan African Medical Journal*, **28**, Article No. 227. https://doi.org/10.11604/pamj.2017.28.227.13979

[25] Salazar, E.L., Mercadom, E. and Calzada, L. (2005) Human Papillomavirus HPV-16 DNA as an Epitheliotropic Virus That Induces Hyperproliferation in Squamous Penile Tissue. *Archives of Andrology*, **51**, 327-334. https://doi.org/10.1080/014850190923396

[26] Schnatz, P.F., Markelova, N.V., Holmes, D., Mandavilli, S.R. and O'Sullivan, D.M. (2008) The Prevalence of Cervical HPV and Cytological Abnormalities in Association with Reproductive Factors of Rural Nigerian Women. *Journal of Women's Health* (*Larchmt*), **17**, 279-285. https://doi.org/10.1089/jwh.2006.0295

[27] Ter Meulen, J., Eberhardt, H.C., Luande, J., *et al.* (1992) Human Papillomavirus (HPV) Infection, HIV Infection and Cervical Cancer in Tanzania, East Africa. *International Journal of Cancer*, **51**, 515-521. https://doi.org/10.1002/ijc.2910510403

[28] Thomas, J.O., Herrero, R., Omigbodun, A.A., *et al.* (2004) Prevalence of Papilloma Virus Infection in Women in Ibadan, Nigeria: A Population-Based Study. *British Journal of Cancer*, **90**, 638-645. https://doi.org/10.1038/sj.bjc.6601515

[29] Trottier, H. and Franco, E.L. (2006) The Epidemiology of Genital Human Papillomavirus Infection. *Vaccine*, **24**, S1-S15. https://doi.org/10.1016/j.vaccine.2005.09.054

[30] Wall, S.R., Scherf, C.F., Morison, L., *et al.* (2005) Cervical Human Papillomavirus Infection and Squamous Intraepithelial Lesions in Rural Gambia, West Africa: Viral Sequence Analysis and Epidemiology. *British Journal of Cancer*, **93**, 1068-1076. https://doi.org/10.1038/sj.bjc.6602736

[31] Walboomers, J.M., Jacobs, M.V., Manos, M.M., *et al.* (1999) Human Papillomavirus Is a Necessary Cause of Invasive Cervical Cancer Worldwide. *The Journal of Pathology*, **189**, 12-19.

https://doi.org/10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F

[32] Xi, L.F., Toure, P., Critchlow, C.W., *et al.* (2003) Prevalence of Specific Types of Human Papillomavirus and Cervical Squamous Intraepithelial Lesions in Consecutive, Previously Unscreened, West-African Women over 35 Years of Age. *International Journal of Cancer*, **103**, 803-809. https://doi.org/10.1002/ijc.10876