

# Seroprevalence of High-Risk Human Papilloma virus type 18 (Hr-HPV-18) Infections among Women with HIV-1 Infection on Long Term Suppressive Anti-Retroviral Therapy in a Tertiary Hospital in Jos, Nigeria.

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**Abstract:** We aimed to determine the sero-prevalence of Hr-HPV-18 among cohort of women with HIV-1 infection on follow up at a Tertiary Hospital, Jos, Nigeria. A cross sectional hospital-based study involving 100 women with confirmed HIV-1-infection from a HIV treatment cohort. The blood samples of 91 participants were analyzed using ELISA kit. The mean age of the participants was 37.2±8.7 years. Of the 91 tested samples, 13.2% were positive to anti-HPV antibodies. The prevalence of anti-HPV 18 antibodies was highest (15.6%) among women aged 31-44 years and women who were married (16.7%). Majority of the women were self-employed 49.4%. Antibodies detected were highest among women with non-formal education (33.3%). There was statistically significant antibody detection among women who had had at least 3 deliveries. Majority of infection was among those with low CD4. A test of association of all other factors showed no significant association except parity, P=0.044. The proportion of Anti-HPV-18 IgG was low compared with most recent studies. There is the need for larger studies with emphasis on cervical cancer screening programs as well as the introduction of a subsidized vaccine in national immunization scheme which are strategies that can curb the increasing burden of cervical cancer in Nigeria.

**Keywords:** HPV, High-risk, Seroprevalence, Women, HIV, Cervical Cancer

## 1. Background

Human papillomavirus (HPV) is a sexually transmitted infection (STI) and commonly acquired shortly after sexual initiation with an infected person [1]. HPVs are small DNA viruses and their infection is mostly associated with benign and malignant neoplasms of the genital tract in both men and women such as genital warts, penile intraepithelial neoplasia, invasive penile carcinoma, cervical intraepithelial neoplasia and cervical cancer as well as head and neck cancers [2-4]. The infection is common among sexually active individuals with approximately 75- 80% of sexually active individuals will become infected in their life time [5]. In Africa, the age-specific prevalence of HPV varies across countries being highest in younger women with a steady decline in prevalence with increasing age in Kenya, Uganda and Zimbabwe but generally reaches a plateau at approximately 40 years of age in Nigeria and Mozambique. The reason for these different age prevalence patterns in Africa remains unclear [3]. Cervical cancer is the second most common cancer among women worldwide, and ranking first in many developing countries<sup>[6]</sup>. Cervical cancer is the second most common cancer in women aged 15-44 years in Nigeria with an incidence rate of 27/100,000 and its estimated that every year, 14,089 women are diagnosed with cervical cancer and 8,240 die from the disease in Nigeria<sup>[7]</sup>. Studies have reported the prevalence

rates of 20%-86.5% of HPV infection both in Southern and Northern Nigeria in hospital settings and general population [8-10]. The risk factors associated with HPV infection include: early sexual debut, high parity, prolonged use of contraceptives, multiple sexual partners, smoking, infection with other sexually transmitted diseases including HIV [11, 12].

Women who are immunosuppressed have been said to have higher rates of HPV infection, resistant to treatment of HPV-related diseases and also prone to accelerated development of HPV-associated cancer [13]. The interaction between the two sexually transmitted infections (HPV and HIV) appears to be related to the alteration in cell-mediated immunity in HIV infected persons, increased susceptibility and possible reactivation of latent HPV infection [14]. The biological interaction between HPV and HIV needs further elucidation, although there is some evidence that the presence of HPV infection may be associated with increased HIV transmission [13]. Nearly 130 types of HPV are known to occur and are categorized into three (3) broad categories based on their potential to causing cancer: high risk type-HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82; intermediate type-HPV 26, 53, 66, and low risk type-HPV 6, 11, 40, 42, 43, 44, 54, 61, 72, 81, and CP6108<sup>[15]</sup>. HPV types 16 and 18 are implicated in approximately 70% of cervical cancers worldwide [5].

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The available DNA based assays are highly sensitive and specific for measuring current infections but do not provide information on lifetime cumulative HPV exposure. Serological assays with different properties are available to measure a wide range of anti-HPV antibodies for epidemiologic and clinical research purposes in measuring immune exposure or protection from subsequent infections [16]. The pre-coated antibody of Human HPV monoclonal antibody detects polyclonal antibody with biotin labels. Seroprevalence surveys are useful for establishing the rates of infection in the general population and for identifying groups at highest risk for targeting prevention; this also serves as epidemiologic research tools and can also be used in clinical services. In this study, we aimed to determine the sero-prevalence of HPV 18 infection among women with HIV-1 infection who are on long term suppressive anti-retroviral therapy in a tertiary hospital in Jos.

## 2. Materials and Methods

### Study Area and Population

This was a cross-sectional study carried out between February-April 2017. The study population comprised 100 consenting women (18–50 years) with confirmed HIV-1 infection on follow up at the HIV treatment Centre of Bingham University Teaching hospital (BHUTH) Jos, Nigeria. After obtaining ethical approval from the hospitals' "Ethics Committee", the women were recruited and counseled and only those who consented were enrolled in the study. Exclusion criteria were women who refused to give consent and those below 18 year.

### Sample Collection and Laboratory Procedures

A 5 mL blood sample was collected into plain tubes by venipuncture from each of the enrolled women with the assistance of a phlebotomist. The blood samples were transported immediately to APIN JUTH laboratory for processing and storage. The blood samples were allowed to clot for 30 minutes and then centrifuged at  $1,000\times g$  for 10 minutes to separate the serum. The serum samples were stored at  $-20^{\circ}\text{C}$  until analysis. An enzyme-linked immunosorbent assay (MyBioSource, Inc, San Diego, CA USA) was used to screen for HPV immunoglobulin G (IgG) antibodies in the serum samples. The assay was carried out and cutoff value calculated according to manufacturer's instructions and specifications. The average optical density (OD) value of the negative control wells plus 0.15 were taken as the cutoff value. A negative HPV result was interpreted as any sample with an OD value less than the calculated cutoff value, and samples with an OD greater than the calculated cutoff value were reported as positive for anti-HPV-IgG.

## 3. Statistical Analyses

The obtained results and data from the questionnaires were reported in an excel sheet and analyzed as presented in the tables. The Statistical Package for the Social Sciences software version 20.0 (SPSS Inc., IL) was used for the analyses. The associations between variables were

identified by Pearson's chi-square. All tests were two-sided and a P-value of  $\leq 0.05$  was considered significant.

## 4. Results

Of the 100 samples collected only 91 were analyzed as 9 of the samples were inadequate. The overall prevalence of HPV-18 infection in the study population was 13.2% (12/91). The mean age of the study participants was  $37.2 \pm 8.7$  years. Women aged 31-44 years (70.3%) had a significantly higher prevalence of HPV 18 ( $X^2 = 1.454$ ;  $P = 0.693$ ) with an infection rate of 10(15.6%), while those aged 18–30 years had a prevalence 15.4%, and those aged  $\geq 45$  had a prevalence of 14.3%, with the least infection rate being (7.7%). Also, majority of the women were married (46.2%). The presence of antibodies was highest (16.7%) among the married women, though not statistically significant ( $X^2 = 1.454$ ;  $P = 0.693$ ). Majority of the participants were self-employed 49.4%, employed 26.4%, while those unemployed were 24.2%. The proportion of observed antibodies was highest (13.2%) among those self-employed, ( $X^2 = 0.631$ ;  $P = 0.889$ ). Majority had primary education 28.6%, while those with secondary or tertiary education were 25.3%. Women with non-formal education had the highest antibody detection rate in this study (33.3%), while those with primary education had a detection rate of 19.2%, and lowest prevalence was in those with  $\geq$ secondary education 13.0% ( $X^2 = 0.358$ ;  $P = 0.949$ ). The majority of the participants were Christians 90.1%, but more antibodies were found among the Muslims 14.3%, with no statistical significance, ( $X^2 = 2.445$ ;  $P = 0.294$ ), (table 1).

The reproductive and clinical characteristics of the women are shown in Tables 2. The data showed that high parity  $>3$  was strongly associated with the possibility of HPV infection 8(17.4%), Test of association between parity and HPV infection showed a significant association ( $X^2 = 8.116$ ;  $P = 0.044$ ). Women who had vaginal discharge were 38(42.0%), those without vagina discharge were 59(65.0) --- Please review. It doesn't add up, with highest antibodies detection recorded among the latter group 8(15.4%). Complaints of urinary disturbance was 36.3% with the highest HPV infection rate recorded in this group being 18.2% ( $X^2 = 7.981$ ;  $P = 0.460$ ); 64.0% had no complaints. Majority of women were  $>2$  years on ART (84.6%) and HPV antibodies detection in this group was 13.0%. Majority of patients (94.5%) had CD4  $>200$ , but the infection was highest among those with CD4 of  $\leq 200$  with an infection rate of 2(40.0%) ( $X^2 = 0.804$ ;  $P = 0.180$ ). The majority of women had no smoking experience(99.0%), ( $X^2 = 0.154$ ;  $P = 0.695$ ), and those not taking alcohol were 86.8% ( $X^2 = 0.146$ ;  $P = 0.702$ ). Those with 1 sexual partner were 89.0% with an infection rate of 13.6%, and those with multiple ( $\geq 2$ ) sexual partners (11.0%) had a 10.0% prevalence rate ( $X^2 = 0.197$ ;  $P = 0.906$ ). The percentage of women with oral contraceptive was lower (35.2%) but with higher rate of HPV antibodies detection (18.8%). The tests of associations of all other factors (vaginal discharge, complaint of urination, duration on ART, CD4 cells, smoking, alcohol consumption, unprotected sex, number of sexual partners, and oral contraception) showed no significant association except parity,  $P = 0.044$  (table 2).

**Table 1:** Distribution of HPV infection according to age and socio-demographic characteristics

Variables	No of Samples (%)	No of positive (%)	P-value
<b>Age</b>			0.571
18-30	14(15.4)	1(7.1)	
31-44	64(70.3)	10(15.6)	
≥45	13(14.3)	1(7.7)	
<b>Marital status</b>			0.693
Single/separated	24(26.4)	2(8.3)	
Married	42(46.2)	7(16.7)	
Widow	25(27.5)	3(12.0)	
<b>Occupation</b>			0.889
Unemployed	22(24.2)	2(9.1)	
Self-employed (Business)	45(49.4)	6(13.2)	
Employed	24(26.4)	4(16.7)	
<b>Education</b>			0.949
No formal education	12(13.2)	4(33.3)	
Primary	26(28.6)	5(19.2)	
Secondary and above	23(25.3)	3(13.0)	
<b>Religion</b>			0.294
Christianity	82(90.1)	10(12.2)	
Islam	9(9.9)	2(14.3)	

**Table 2:** Distribution of HPV infection according to reproductive and clinical characteristics

Variables	No of Samples	No of positive (%)	P-value
<b>Parity</b>			0.044
None	24(26.4)	2(8.3)	
≤2	21(23.1)	2(9.5)	
>3	46(50.5)	8(17.4)	
<b>Vaginal discharge</b>			0.739
Yes	38(42.0)	4(10.5)	
No	59(65.0)	8(15.4)	
<b>Complaint of urination</b>			0.288
Yes	33(36.3)	6(18.2)	
No	58(64.0)	6(10.2)	
<b>Duration on ART</b>			0.756
< 1	14(15.4)	2(14.3)	
>2	77(84.6)	10(13.0)	
<b>CD4</b>			0.180
≤200	5(5.5)	2(40.0)	
>200	86(94.5)	10(11.6)	
<b>Smoking</b>			0.695
Yes	1(1.1)	0(0.0)	
No	90(99.0)	12(13.3)	
<b>Alcohol consumption</b>			0.702
Yes	12(13.2)	2(16.7)	
No	79(86.8)	10(12.7)	
<b>Unprotected sex</b>			0.695
Yes	86(94.5)	11(12.8)	
No	5(5.5)	1(20.0)	
<b>No of sexual partners</b>			0.906
1	81(89.0)	11(13.6)	
≥2	10(11.0)	1(10.0)	
<b>Oral contraceptive</b>			0.248
Yes	32(35.2)	6(18.8)	
No	59(64.8)	6(10.2)	

## 5. Discussion

HIV infection increases the risk of acquisition and transmission of HPV infection; however, oncogenic HPV types such as 18, 35, 52, 56 and 68 may be more important

risk factors for pre-cancerous cervical lesions particularly among HIV infected women in Africa population. In this study, the prevalence of hrHPV type 18 infections was 13.2%. This percentage is lower than the general HPV antibodies reported in Ibadan (26.3% and 23.7%), Zaria (43.0%) in Western and Northern Nigeria respectively [17-19]. Other studies, have found higher prevalence among HIV infected women [3,19]. Studies have also reported contrary seroprevalence rates of hr-HPV infections including type 18 in South Africa women: 46% HPV-16, 2% HPV-18, 6% HPV-31, and 6% HPV-33 [20]; while Pegoraro reported the prevalence of 47% HPV-16, 14% HPV-18 and 25% for other HPV types [21]. However, the prevalence of HPV-18 and other types are expected to be lower [22]. Our results are contrary to earlier findings which showed that women with HIV infection were more likely to be infected with non-16 and non-18 hrHPV types [3]. An earlier study in Jos found a 45% prevalence of hrHPV among HIV+ women [23]. Factors such as sociocultural: nutritional, environmental, sexual behavior, parity and hygiene, co-infections with other sexually transmitted infections (STIs) and genetic factors, along with specific geographic distribution of hrHPV types may explain the variation in prevalence rates of hrHPV and cervical cancer incidence across populations. However, the incidence of cervical cancer in Zambia is higher than in Nigeria where the incidence is <50%, and these differences in distribution of hrHPV in West and East Africa, may explain these regional variations in cervical cancer incidences [3, 24]. The current high prevalence of hrHPV-18 strain infection among HIV positive women in Nigeria and other African countries may thus have negative impact in the era of ART.

In this study, anti-HPV-18 IgG sero-positivity was not significantly associated with lower age group, marital status, occupation, educational level, religion, clinical symptoms, duration of ART, CD4, smoking, alcohol consumption, unprotected sexual behavior, number of sexual partners and oral contraception; however there was a significant association with parity. It has been speculated that women using hormonal contraception, multiple sexual partner and vaginosis might be at a higher risk of acquiring to HPV infection. However, Hugo, in a study conducted in 2013 did not find such an association [11] which was similar to an earlier study in Nigeria [3].

## 6. Conclusion

The prevalence of anti-HPV-18 IgG was low among the study population as compared to most recent studies, although the sample size was small. This suggests that there may be a high distribution of this infection among HIV positive women and is a major risk factor to the development of cervical cancer. Women aged 31-44 years, married women and those with no formal education had high rates of seroprevalence of HPV, though covariate associations did not show significant levels except for parity. Further larger prospective studies are required to shed more light on the pathogenesis and transmission of the virus and the associated risk factors. This will also play a key role in cervical cancer screening programs and in the introduction of a subsidized HPV vaccine in our national immunization programs are required in other to prevent the current

epidemic of cervical cancer in Nigeria. Furthermore, longitudinal investigations of HPV genotype-specific risks and other attitudinal factors such as sexual behavior, healthcare seeking behavior to STIs, personal hygiene, smoking, and alcohol consumption that enhance pre-cervical cancer outcomes should be conducted in Nigeria and across Africa.

## 7. Acknowledgement

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## 8. Conflicts of Interest

The authors declare that they have no conflict of interests.

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