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HPV among Females of Reproductive Age Attending a Tertiary Institution in Port Harcourt, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author IOO designed the study, performed the statistical analysis and wrote the protocol. Authors IOO and IJA managed the analyses of the study. Authors IJA and INC managed the literature searches and wrote the first draft of the manuscript. Author IOO supervised the whole study which, author IJA used as part of her B.Sc project. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The study was aimed at determining HPV seroprevalence among females of reproductive age and identify the demographic/behavioural profile associated with the seroprevalence.
Study Design: Cross-sectional study.
Place and Duration of Study: O.B. Lulu-Briggs Health Centre, University of Port Harcourt, in Rivers State, Nigeria, from July 2013 to May 2014.
Methodology: Ninety-one females were included in this study. The age ranged from 15 to 45 years. Detection HPV infection was gotten using the ELISA and was performed according to the kit manufacturer's stipulations. The demographic characteristics of the participants were obtained with a Performa designed for the study.
Results: Higher seropositivity of anti-HPV IgG antibodies occurred in the age group 18-25 years (18.2%) than other age groups (26-35 years, 4.1% and 36-45 years, 0.0%). The highest seronegativity (100.0%) occurred in the age group 36-45 years while the age group 18-25 years

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(81.8%) had the least. Higher seropositivity occurred in females with no formal education (33.3%) than primary (9.1%) secondary (3.8%) and tertiary education (0.0%). While higher seronegativity (100.0%) occurred in tertiary education compared to secondary (96.2%), primary (90.9%) and no education (66.7%). Higher seropositivity occurred among the married (27.3%) than the singles (1.2%). Higher seronegativity occurred among singles (98.8%) than the married (72.7%). Higher seropositivity occurred among other religions (4.9%) than Christianity (4.0%). Furthermore, Christians had higher seronegativity (96.0%) compared to other religions (95.1%).

Conclusion: The study clearly shows that although the seroprevalences are higher among younger females elsewhere in Nigeria, only 4.4% of the females had IgG antibodies to HPV-6, -11, -16 and -18 vaccine genotypes. It also established a high seronegativity among the females of reproductive age in Port Harcourt, Nigeria. To the best of our knowledge, this is the first documented report of high IgG seronegativity to HPV-6, -11, -16 and -18 vaccine genotypes in a higher institution in Port Harcourt, Nigeria. These findings reveal the susceptibility of a large population of females to infections with these four HPV genotypes in the University. With these findings, early screening and clinical evaluation for HPV-related manifestations are very imperative among females of reproductive age in Nigeria.

Keywords: Antibodies; HPV infection; HPV-related manifestations; IgG; seroprevalence.

1. INTRODUCTION

HPV is the most common sexually transmitted infectious agent with a high transmission probability of about 0.6 per act and a lifetime expectance for the acquisition of 80%. Fortunately, HPV infection is transient in 90% of immunocompetent women [1,2] HPV prevalence is age-dependent, peaking after sexual debut below 25 years of age, thereafter levelling out and decreasing slightly for the next 35 to 40 years [3,4,1,2]. A second peak at about 45 years of age has been reported in some regions [5,6].

HPV infection rates are highest among young women, usually peaking soon after the age when most young women become sexually active [7]. This differs significantly between population groups and geographical regions, but it is projected that up to 79% of women worldwide will be infected with HPV at some point in their lives [8].

Several authors have raised the possibility of certain HPV types being more common in Sub-Saharan African women than elsewhere. In Ibadan, HPV 16 and 35 were the most common high-risk (HR) types, followed by HPV 31, 58, and 56. A low-risk (LR) type, HPV 42, was also common [9]. About 11.4% of women in the general population are estimated to harbour high-risk HPV infection at a given time, and 70.9% of invasive cervical cancers in the world are attributed to HPV types 16 and/or 18. The prevalence of HPV increases with the severity of the lesion. Over 70% of all cervical cancers' cases are attributable to HPV-16 and 18, while 41%-67% and 16%-32% high-grade and low-grade cervical lesions respectively are also associated with HPV-16 and 18. An additional 20% of global cervical cancers are contributed by the six most common HPV types 31, 33, 35, 45, 52 and 58 representing 13% of female cancers and are the same in all world regions. HPV-16 represents 87% of all HPV-positive tumours and it is the most commonly detected. HPV-18 which is found in approximately 99% of cases is the second type most commonly detected [10].

Since about 30 to 40% or more of human papillomavirus types are primarily sexually transmitted, prevention is an essential primary care strategy for improving reproductive health. The study is aimed at determining HPV seroprevalence among females of reproductive age in a tertiary institution in Port Harcourt, Nigeria and identify the demographic/behavioural profile associated with the prevalence.

2. MATERIALS AND METHODS

2.1 Study Area

The study was conducted among women of reproductive age in the University of Port Harcourt who carried out the medical examination at the O.B Lulu Briggs Health Center, the University of Port Harcourt in Rivers State, Nigeria.

2.2 Study Design

A cross-sectional study was carried out among females of reproductive age attending the O.B.

Lulu Brigg's Health Centre of the University of Port Harcourt, in Rivers State, Nigeria. A structured questionnaire was administered randomly to consenting pregnant women to obtain information on socio-demographic factors before sample collection.

2.3 Study Population

A total of 91 females of reproductive age of different ages and socioeconomic status who carried medical examination in the health were recruited in the study. The study was conducted by recruiting consenting females who came to the laboratory for various tests until a total of 91 patients were reached. The study was ethically approved and all samples where coded and did not contain individual identifying information. The age of the patients ranged from 18 years to 45 years (Table 1).

2.4 Specimen Collection and Preparation

About 5 ml of blood samples were aseptically collected by venipuncture technique from each woman. Each blood sample was dispensed into an appropriately labelled EDTA sample tube, screw-capped and left at room temperature for about 40 min, after which it was spun at 3,000 rpm for 10 min to separate plasma from the blood. Samples were identified with codes to avoid misinterpretation of results. Plasma was stored at -20^{O}C until ready to use.

2.5 Laboratory Analysis

Laboratory analysis was carried out at the Virus Research Unit of the Department of Microbiology, University of Port Harcourt, Choba, Rivers State, Nigeria. IgG antibodies against four specific HPV types 6/11/16/18 were analyzed *in vitro* using a commercial kit (DIA.PRO Diagnostic Bioprobes, Milano, Italy) based Enzyme-linked Immunosorbent Assay (ELISA) as described previously [11]. The efficacy of the assay concerning IgG was sensitivity (82.3%), specificity (92.0%) and accuracy (88.0%) to IgG-VLP-HPV-16, and sensitivity (100.0%), specificity (92.0%) and accuracy (94.0%) to IgG-VLP-HPV-18 [12]. The serologic test and interpretation of results were done according to instructions of the kit manufacturer. Microplates were coated with recombinant VLP's derived from HPV Type 6, 11, 16 and 18. In the first incubation, the solid phase was treated with diluted samples and anti-HPV IgG was captured, if present, by antigens. The micro-plates were washed 5 cycles with an automated washer (Biotek ELx 50, USA). After washing out all the other components of the sample, in the 2nd incubation bound anti-HPV IgG was detected by the addition of anti IgG antibody, labelled with peroxides (HRP). The enzyme captured on the solid phase, acting on the substrate/chromogen mixture, generates an optical signal that is proportional to the amount of anti-HPV IgG antibodies present in the sample. A cut-off value turns the measured optical densities into positive or negative results. The coloured reaction product was measured by using a spectrophotometric plate reader (Biotek ELx808i, USA) at an absorbance of 450-630 nm. All stages of the ELISA tests were performed according to the manufacturer's instructions. The ELISA kit manufacturer provided the formula for calculating the cut-off OD450nm (OD of negative control plus 0.250) which we used as a threshold for determining the reactive and non-reactive serum samples.

2.6 Data Analysis

The data obtained from questionnaires and laboratory analysis were entered into Microsoft Excel, analyzed using Statistical Package for Social Sciences version 21. Pearson Chi-square was calculated at 95% confidence interval and p-value < 0.05 was considered significant to determine the association between the presence of the antibodies to the virus and other parameters.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Patient characteristics

The age range of the 91 women that participated in the study was 18-45 years. Age group 26-35 had the highest frequency (53.8%), followed by the age group 36-45 years (34.1%). Age group 18-25 (12.1%) was the least and comparisons of the three age-groups were recorded to be significantly different (Table 1). The women generally had a high level of education (52.7%) had tertiary education and 28.6% had secondary education with 12.1% being married. About 54.9% of the women were Christians and others were about 45.1% and comparisons of the two religious groups were recorded to be significantly different (Table 1).

Table 1. Socio-demographic characteristics of females tested for anti-HPV 6, 11, 16 and 18 IgG antibodies

Variable	No. Tested	Percentage (%)
Age (Years)		
18-25	11	12.1
26-35	49	53.8
36-45	31	34.1
Educational Status		
Primary	11	12.1
Secondary	26	28.6
Tertiary	48	52.7
None	6	6.6
Marital Status		
Single	80	87.9
Married	11	12.1
Religion		
Christian	50	54.9
Others	41	45.1
Total	91	100.0

3.1.2 Prevalence of anti-HPV 6, 11, 16 and 18 IgG antibodies among tested women of reproductive age

Only 4 (4.4%) out of the 91 women tested had detectable antibodies to VLPs of HPV genotypes 6, 11, 16 and 18 and Group-specific seronegativity was also high (81.8-100.0%).

3.1.3 Age-Specific seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies among women of reproductive age

In term of age, higher seropositivity of anti-HPV 8, 11, 16 and 18 IgG antibodies occurred in the age group 18-25 years (18.2%) compared to age group 26-35 years (4.1%) and 36-45 years (0.0%) (Fig. 1). Fig. 1 also shows the seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies among tested women with age groups. Age group 36-45 years had the highest seronegativity frequency of 100% (n=0). This was followed by the age group 26-35 years with 95.9% (n=9) seronegativity. While the age group 18-25 years with 81.8% (n=47) seronegativity was the least and comparisons of the three age-group were recorded (Fig. 1).

3.1.4 Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to educational background

Fig. 2 shows the seropositivity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to educational background. From the 91 females of reproductive age tested, higher seropositivity was observed among females with no form of formal education (33.3%) compared to those with primary education (9.1%) and secondary education (3.8%). While zero seropositivity was observed among females with tertiary education (Fig. 2). It also shows the seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to educational background. Females with tertiary education had the highest seronegativity of 100.0% (n=48). This was followed by those with secondary education (96.2%, n=25) and those that had attained a primary level of education (90.9%, n=10). While the lowest seronegativity rate was observed among females who never had any level of education (66.7%, n=4) (Fig. 2).

3.1.5 Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to marital status

Fig. 3 shows the seropositivity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to their marital status. Higher seropositivity of anti-HPV 6, 11, 16 and 18 IgG antibodies occurred among the married (27.3%) than the singles (1.2%). Besides, higher seronegativity was observed among the singles (98.8%) compared to the married with a rate of 72.7% (Fig. 3).

3.1.6 Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to religion

Based on religion, higher seropositivity of anti-HPV 6, 11, 16 and 18 IgG antibodies occurred

among other religions (4.9%) than Christianity (4.0%). Also, females of reproductive age who were Christians had a higher seronegativity (96.0%) than those in other religions (95.1%) (Fig. 4).

4. DISCUSSION

Multiple HPV infections have been reported more in sexually active young women and among HIV-positive individuals, and are heavily dependent on HPV acquisition and persistence rates [13-16]. Determining the susceptibility and exposure of humans to HPVs would rely on the detection of HPV type-specific antibodies and the VLP ELISA has been used in achieving this. In this study, 4.4% had detectable IgG antibodies to VLPs of HPV genotypes 6, 11, 16 and 18 and 95.6% of the women had no detectable antibodies to VLPs of HPV genotypes 6,11,16 and 18.

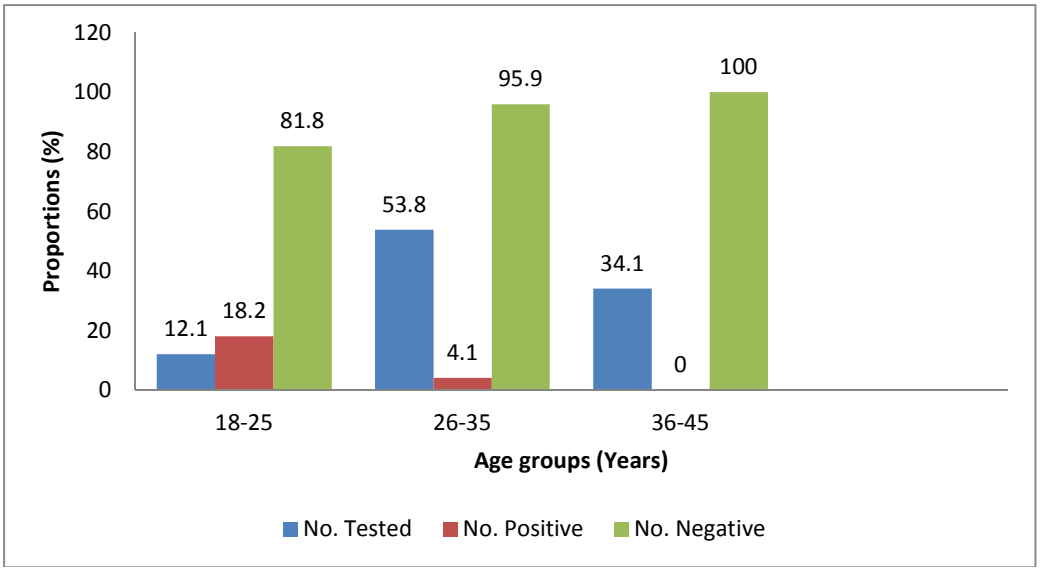

Fig. 1. Age-Specific seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in women of reproductive age

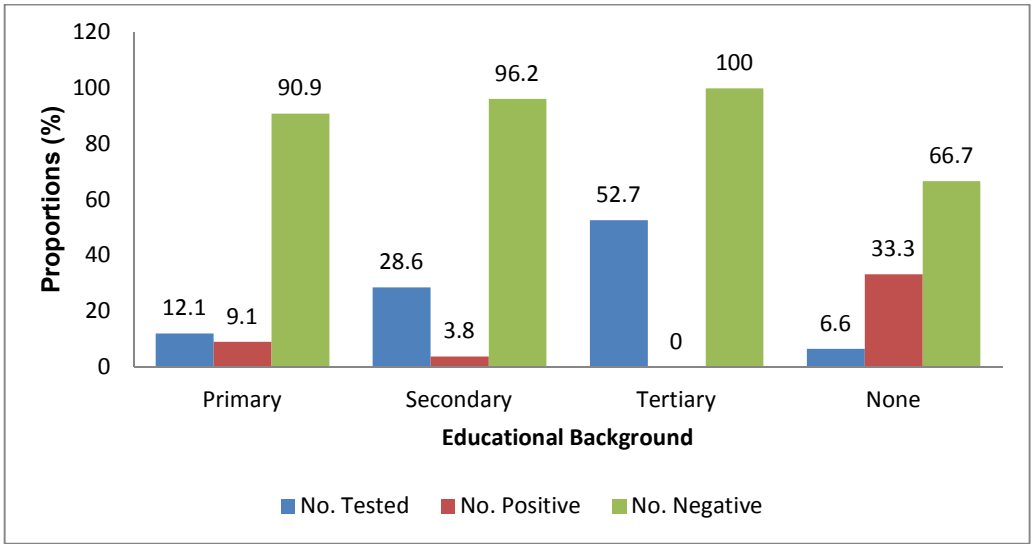

Fig. 2. Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to educational status

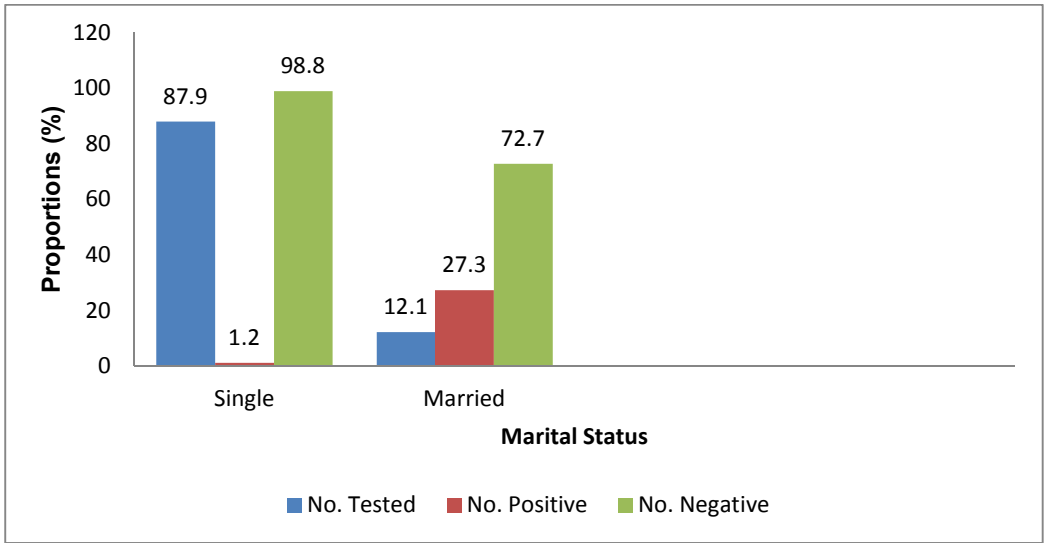

Fig. 3. Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to marital status

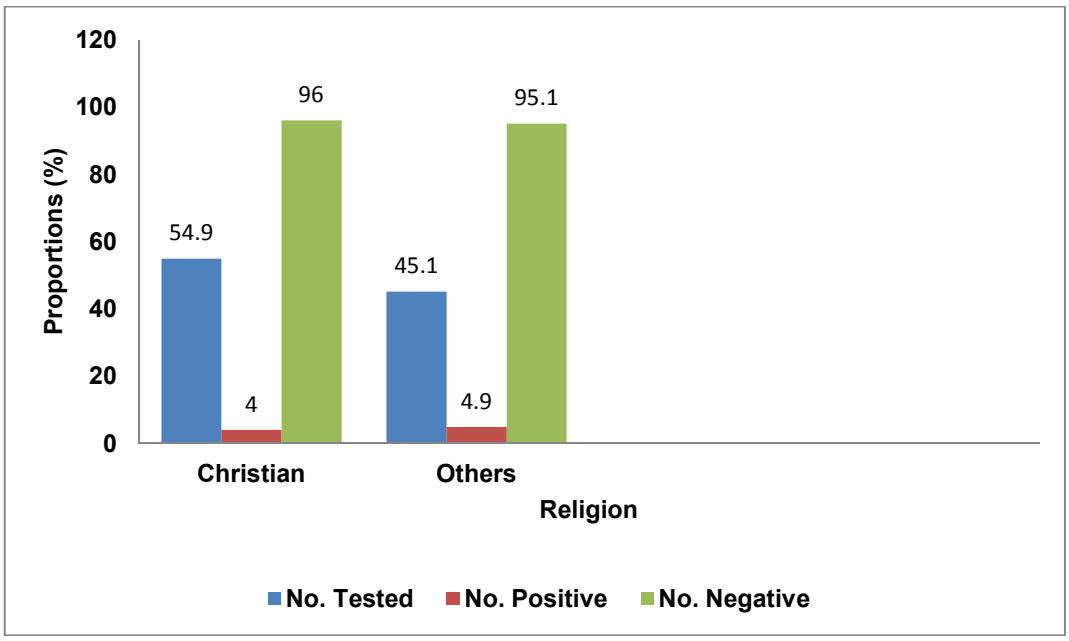

Fig. 4. Seropositivity and seronegativity of anti-HPV 6, 11, 16 and 18 IgG antibodies in relation to religion

The HPV seropositivity of 4.4% found in females of reproductive age in the University of Port Harcourt, Nigeria aligns with earlier reports of the low prevalence of HPV reported in women in Sub-Saharan Africa. The 4.4% reported in this study is a little higher than the 3.8% reported by Ogoina et al. [17] in Zaria, Nigeria. It is lower than the 4.9% reported by Okonko et al. [18,19] in Port Harcourt, Nigeria. It is also lower than the 6.6% reported by Adekunle et al. [20] in Ilesha, Nigeria.

However, the HPV seropositivity of 4.4% is in contrast to the elevated prevalence of HPV in women in Sub-Saharan Africa as reported in previous studies [21-25,17,9]. The 4.4% prevalence reported for HPV seropositivity in this study is lower than the 26.3% overall prevalence

and 24.8% among women without cervical lesions reported by Thomas et al. [9] in Ibadan, Nigeria. It is also lower than the 41.3% reported by Ogoina et al. [17] in Zaria, Nigeria. It is lower than the 17.0% prevalence of high-risk HPV types reported in rural Uganda [21] and a 25.0% prevalence reported among HIV-negative women in Harare, Zimbabwe [22]. It is also lower than the 40.0% HPV prevalence in rural Mozambique [23]; the 31.0% in Harare, Zimbabwe [24] and the 44.0% in Nairobi, Kenya [25].

The observation that 95.6% of the women tested had no detectable IgG against any of the VLPs could be because they were not exposed to any of the low- and high-risk HPV genotypes or they had undetectable antibody levels at the time sample was collected. It might also be due to the inherent sensitivity of the ELISA kit used. Thus, the high overall anti-HPV IgG seronegativity reported in this study implies that the seronegative women are susceptible to infection by any of the studied HPVs. Since the World Health Organization (WHO) reported that quadrivalent and bivalent HPV vaccines offer more than 90.0% protection against persistent infection by the vaccine genotypes in women without evidence of past or present HPV infection [26], vaccination against HPV types 6, 11, 16 and 18 is recommended for sexually active females attending the hospital without evidence of protection against the HPVs [20,18,19].

Also in this study, group-specific seronegativity was found to be high ranging from 100.0% for females with tertiary education, 96.2% for secondary education, 90.9% for females with low (primary) education to 66.7% for females who never had any level of education. This is similar to the findings reported by Okonko et al. [19] and Okonko and Ofoedu [18] Furthermore, the finding in this study of 4.0% prevalence of anti-HPV IgG antibodies among the females is very low despite having a high proportion of them with tertiary education. This is contrary to previous reports of 26.3% HPV seropositivity in Ibadan [27] ≥ 25% seropositivity for HPV-16 and -18 in Nigeria [28] 14.7% prevalence of HPV DNA in Ondo State, Nigeria [29] and 6.6% for HPV-6, 11, 16 and 18 in Osun State, Nigeria. This finding is similar to that of Thomas et al. [9] who reported that illiterate women showed increased HPV positivity in Ibadan.

The age of the females that participated in the study ranged between 18-45 years. This is similar to the age range used in previous studies [20,18,19] In this study, group-specific seronegativity was found to be high (81.8% to 100.0%) for females in all age groups. The high HPV prevalence among young age groups has been suggested to be a result of increased risk-taking sexual behaviour among young people worldwide. In Finland, seroprevalence to specific HPV types is on the increase among young females [30,11,1,2,31,32]. In Uganda, Botswana, Kenya and South Africa similar observations have been reported from both HPV DNA and/or serology studies [33,16,34,35,32].

Burd [36] reported that HPV infection is most common in sexually active young females (18-30 years old), with a sharp decrease in prevalence after 30 years of age. Adekunle et al. [20] reported in their study that 83.3% of the 6 seropositive females were in the 19-30 years age range while the remaining females were between 31-40 years of age. Okonko et al. [19] observed in their study that 66.7% of the seropositive females were in the 19-25 years age range and 22.2% of the seropositive females were in the 26-35 years age range while the remaining females were between 36-45 years of age. This is similar to the result of the present study as four of the females in all age groups was positive for HPV IgG antibodies.

In summary, earlier surveys on HPV in sub-Saharan Africa have demonstrated a relatively high prevalence of HPV with some variation depending on the selection of females for the study and how the test was carried out [9]. From the result obtained in this study, only 4 (4.4%) of the females tested had detectable IgG against any of the HPV VLPs. This is also similar to the findings in previous studies in Nigeria [27,28,29,20,18,19] who also reported high seronegativity of IgG to HPV.

One of the study limitations includes the small sample size used and the non-execution of other complementary techniques, due to the inherent sensitivity (82.3% and 100.0%) of the ELISA method. However, we believe that this limitation did not significantly affect the final interpretation of the study findings. We used 91 participants which are good and similar to the sample size used in other similar studies (18-20).

5. CONCLUSION

The present study established a high seronegativity to IgG antibodies against HPV among the females of reproductive age in Port

Harcourt, Nigeria. The study was undertaken to study the occurrence of common HPV types among females of reproductive age and to determine the risk of occurrence of HPV antibodies to infections with multiple HPV types. The study clearly shows that although the seroprevalences are higher among younger females elsewhere in Nigeria, only 4 of the females tested had antibodies to HPV. This study also showed that group-specific seronegativity was high (95.6%) for the women. To the best of our knowledge, this is the first report of high IgG seronegativity to HPV-6, -11, -16 and -18 vaccine genotypes in a higher institution (University of Port Harcourt, Nigeria). These findings reveal the susceptibility of a large population of females to infections with these four HPV genotypes in the University. The findings make routine and early screening for HPV infection very imperative for all females of reproductive age in Nigeria, as well as a routine clinical evaluation of all females of reproductive age for HPV-related manifestations.

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CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this study. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

Ethical approval was obtained from the University of Port Harcourt Research Ethics Committee.

All authors hereby declare that all experiments have been examined and approved by the Research Ethics Committee of the University of Port Harcourt and have, therefore, been performed following the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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