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Research Article

Oncogenic human papilloma virus infection among women attending the cytology clinic of a tertiary hospital in Lagos, South-West Nigeria

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ABSTRACT

Background: Cervical cancer is the most common gynaecological cancer and a leading cause of cancer death in women in Nigeria. Persistence infection with high risk or oncogenic Human Papillomavirus (HPV) types is now known to be a necessary cause of cervical cancer.
Methods: This study is a descriptive cross-sectional study carried out to determine the prevalence and distribution of oncogenic HPV infection among women seen at the cytology clinic of a tertiary hospital in Lagos South-west Nigeria and then identify the likely predisposing factors to this infection. Eligible women were selected by consecutive sampling method for the study. Pap smear and endocervical swab samples were collected from each participant. The endocervical swab samples were screened for HPV types 16, 16A, 31, 33 and 35 by the multiplex Polymerase Chain Reaction (PCR) using the specific primers for the HPV types.
Results: Twenty-four (30.4%) of the 79 tested swab samples were positive for viral DNA of high risk HPV 16. There was a statistically significant difference in the mean ages of participants with positive cervical HPV and those without the infection respectively (34.8 ± 9.9 vs. 46.2 ± 10.1 years; P = 0.028). However, there were no significant differences found between the women with HPV positivity and those without with respect to marital status (P = 0.074), tribe (P = 1.009), religion (P = 0.681) and educational status (P = 0.552). Other identified risk factors that showed statistically significant differences for oncogenic HPV infection were age at sexual debut (P = 0.009), parity (P = 0.003), number of lifetime sexual partner(s) (P = 0.000), use of combined oral contraceptives (P = 0.044), HIV seropositivity (P = 0.000) and smoking (P = 0.033).
Conclusion: Cumulative high risk HPV infection is high in Lagos, Nigeria. This thus support the need for routine and early screening of all identified high risk sexually active women for HPV infection in Nigeria, as well as emphasising further the importance of sex education for the girl child in schools and increased awareness for parents towards HPV vaccination for their generally healthy adolescent girls.

Keywords: Cervical cancer, HPV, Nigeria, Oncogenic human papilloma virus, PCR

INTRODUCTION

Cervical cancer is the second most common cancer among women in the developing countries and the seventh most common cancer in the developed countries.[1] Over 500,000 new cases are seen yearly with over 80% of them being from the developing countries.[1-3] Worldwide, it claims the lives of 300,000 women annually with over 80% coming from the developing countries.[1] It is the most common gynecological cancer and a leading cause of cancer death in women in Nigeria.[4]

Persistence infection with high risk or oncogenic human papillomavirus (HPV) types is now known to be a

necessary cause of cervical cancer.[5,6] HPV is the most common sexually transmitted virus and it is estimated that about 75% of sexually active women and men will acquire a genital HPV infection at some time.[7] Approximately 20 million women are infected with the virus worldwide.[8]

HPV infection is an epitheliotropic infection.[9] Most infections are subclinical and will cause no physical symptoms; however, in some people subclinical infections will become clinical and may cause benign papillomas (such as warts [verrucae] or squamous cell papilloma), or cancers of the cervix, vulva, vagina, penis, oropharynx and anus.[10] HPV has also been linked with an increased risk of cardiovascular disease.[11]

The prevalence of cervical human papillomavirus (HPV) infection in sub-Saharan Africa is among the highest in the world just like cervical cancer[12] while a pooled analysis of the International Agency for Research on Cancer (IARC) on HPV Prevalence Surveys also observed that the highest HPV prevalence was seen in Nigeria.[13,14]

Factors that increase an individual's chance of acquiring cervical oncogenic HPV infection include: multiple sexual partners smoking, multiparity, early onset of sexual intercourse, oral contraceptive usage and HIV infection.[12,15-17]

In Nigeria, like most other under-developed black nations, there is paucity of data on the strength of the association between these identified factors and the prevalence of HPV infection and thus this study will therefore aim at determining the prevalence and distribution of oncogenic HPV infection among women seen at the cytology clinic of a tertiary hospital in Lagos South-west Nigeria and then identify the likely predisposing factors to this infection.

METHODS

This is a descriptive cross-sectional study carried out among women attending the cytology clinic of a tertiary hospital in Lagos, South-west, Nigeria over a period of 6 months.

A total number of 79 eligible women were selected by consecutive sampling method for the study. These participants were counseled appropriately and consents were taken to be enrolled in the study.

Excluded from the study were pregnant women, those who have undergone hysterectomy, women with obvious cervical lesions and those who were mentally or physically unable to undergo a pelvic examination.

Questionnaires were administered to collect relevant information. Pap smear and endocervical swab samples were collected from each participant. The endocervical swab samples were transported in a viral transport medium (VTM) to the central research laboratory of the College of Medicine and were stored in a -20°C freezer.

The samples were screened in pools of 5 for HPV types 16, 16A, 31, 33 and 35 following which individual samples from the pools that flagged positive were further screened.

Deoxyribonucleic acid (DNA) extraction of the high risk HPV types was carried out on the samples using the diatomaceous earth DNA extraction protocol followed by amplification of the extracted DNA by the multiplex Polymerase Chain Reaction (PCR) using the specific primers for the HPV types. Detection of amplified viral DNA was done by agarose gel electrophoresis using 1.5% agarose.

All quantitative data were entered in computer and analyzed using SPSS version 17 for windows.[18] Descriptive statistics were computed for all relevant data. Association between anaemia and pregnancy was tested using chi-square. All significance were reported at $P < 0.05$.

Ethical approval for the study was obtained from the hospital's health research and ethics committee and written consent obtained from each participant prior to involvement in the study.

RESULTS

A total of 79 women with the age range of 22-78 years were screened in the study for high risk HPV types 16, 16A, 31, 33 and 35 by multiplex PCR.

Twenty-four (30.4%) of the swab samples were clearly positive for viral DNA of high risk HPV 16 which was the only HPV type detected on further analysis.

When maternal socio-demographic characteristics were examined according to cervical high risk HPV positivity (Table 1), there was a statistically significant difference in the mean ages of participants with positive cervical HPV and those without the infection respectively (34.8 ± 9.9 vs. 46.2 ± 10.1 years; $P = 0.028$).

However, there were no significant differences found between the women with HPV positivity and those without with respect to marital status ($P = 0.074$), tribe ($P = 1.009$), religion ($P = 0.681$) and educational status ($P = 0.552$).

In Table 2, 38.2% of participants with age of menarche before 14 years were positive for HPV compared to 31.4% of those whose menarche was at 14 years and above ($P = 1.088$).

Out of the participants who had their sexual debut (coitarche) before the age of 16 years, 43.8% were

positive for high risk HPV while only 27.0% were positive among those with age at sexual debut being 16 years and above (P = 0.009). There were also statistically significant differences recorded in the parity (P = 0.003), number of lifetime sexual partner(s) (P = 0.000), use of combined oral contraceptives (P = 0.044) and HIV seropositivity (P = 0.000) among women with cervical high risk HPV positivity and those without respectively.

Table 1: Socio-demographic characteristics of the study population (n=79).

	HPV positive N (%)	HPV negative N (%)	*P value
Age of respondents			
<25	0 (0.0)	2 (100.0)	0.028
25-34	11 (30.6)	25 (69.4)	
35-44	7 (26.9)	19 (73.1)	
45-54	4 (33.3)	8 (66.7)	
≥55	2 (66.7)	1 (33.7)	
Mean ± SD	34.8 ± 9.9	46.2 ± 10.1	
Marital Status			
Single	5 (26.3)	14 (73.7)	0.074
Married	15 (31.9)	32 (68.1)	
Divorced/separated	3 (37.5)	5 (62.5)	
Widowed	1 (20.0)	4 (80.0)	
Tribe			
Yoruba	10 (29.4)	24 (70.6)	1.009
Hausa	5 (26.3)	14 (73.7)	
Ibo	7 (43.8)	9 (56.2)	
Others	2 (20.0)	8 (80.0)	
Religion			
Christianity	15 (31.9)	32 (68.1)	0.681
Islam	9 (30.0)	21 (70.0)	
Others	0 (0.0)	2 (100.0)	
Educational status			
None	1 (100.0)	0 (0.0)	0.552
Primary	5 (29.4)	12 (70.6)	
Secondary	11 (33.3)	22 (66.7)	
Tertiary	6 (24.0)	19 (76.0)	
Postgraduate	1 (33.3)	2 (66.7)	
Total	24 (30.4)	55 (69.6)	

Five (41.7%) of the participant who had a history of smoking compared to only 28.4% who had never smoked were positive for oncogenic HPV infection in this study (Table 3).

This difference was statistically significant (P = 0.033). History of alcohol intake was however, not shown in the study to impact significantly on cervical high risk HPV positivity in the participants as 33.3% and 27.7% of women with history of alcohol consumption and those without were positive for HPV type 16 respectively (P = 0.775).

Table 2: Sexual and reproductive history of the study population (n=79).

	HPV positive N (%)	HPV negative N (%)	*P value
Age at menarche			
<14 years	13 (38.2)	21 (61.8)	1.088
≥14 years	11 (31.4)	24 (68.6)	
Age at coitarche			
<16 years	7 (43.8)	9 (56.2)	0.009
≥16 years	17 (27.0)	46 (73.0)	
Parity			
<2	8 (17.4)	38 (82.6)	0.003
≥2	16 (48.5)	17 (51.5)	
Lifetime sexual partner(s)			
<1	11 (19.6)	45 (80.4)	0.000
≥2	23 (69.7)	10 (30.3)	
Oral contraceptive pills			
Yes	8 (42.1)	11 (57.9)	0.044
No	16 (26.7)	44 (63.3)	
HIV seropositivity			
Yes	4 (40.0)	6 (60.0)	0.000
No	20 (29.0)	49 (71.0)	
Total	24 (30.4%)	55 (69.6%)	

Table 3: Social history of the study population (n=79).

	HPV positive N (%)	HPV negative N (%)	*P value
History of smoking			
Yes	5 (41.7)	7 (59.3)	0.033
No	19 (28.4)	48 (71.6)	
History of alcohol intake			
Yes	11 (33.3)	21 (66.7)	0.775
No	13 (27.7)	34 (72.3)	
Total	24 (30.4)	55 (69.6)	

DISCUSSION

The prevalence of HPV in this study was 30.4%. This is much lower than the worldwide prevalence of 10.4%[19] and that of other studies done in Asia[20,21] and North-America.[22] However, this is similar to the reported prevalence by Bao et al.[23] in a study carried out among Asian women. Previous HPV surveys in Sub-Saharan Africa had also generally shown high HPV prevalence, with some variation depending on how the participants were selected, the screening methods and the strains of HPV that were tested for.[24] A prevalence of 66.1% was reported in a study carried out in Burkina-Faso.[25] Similar studies also carried out in other parts of Africa showed a prevalence of as high as 97.2%.[26] These variations in figures may be attributable to the exhaustive nature of the HPV detection strategy used in the various studies especially those carried out in Asia and America.

The commonest high risk HPV detected in our study was type 16 (100.0% of tested smear samples). This is similar to the reported worldwide commonest oncogenic HPV type[27] which is also in concordance with the predominant HPV types reported by Munoz[28] and Clifford.[29] HPV 16 and 18 are the two most frequently detected types among invasive cervical cancer in Nigeria, and that they account for 78% of HPV-positive invasive cervical cancer, which is very similar to the proportion estimated in other world regions by published case series.[30] This finding has important implications in the eventual implementation of prophylactic HPV vaccines based on the high risk types 16 and 18.[27]

Older females above the age of 25 years were more likely to be infected with high risk HPVs than those less than 25 years in this study with the peak prevalence seen above at age 55 years and above. This picture is almost similar to the finding in a study carried out among the general population of Ibadan, Nigeria which showed a modest peak in HPV prevalence among women in the <25 years age range and a high prevalence among the middle aged and old women.[31] Part of the reasons that was adduced for this trend was that a fraction of the spouses or partners of these women may continue to have multiple sexual contacts throughout their lives thereby re-infecting themselves and these women.[13] Other studies carried out in other West-African countries showed an increased prevalence of HPV among women who were less than 25 years of age.[32,33]

There was no statistical relationship between lower educational level and prevalence of high risk.

HPV as most of the participants had at least attained some level of education. This finding suggests that acquisition of HPV infection which is related to sexual lifestyle may not necessary be influenced by education as tendency to engage in unprotected sexual cut across all categories of respondents irrespective of educational status. This notion also corroborates the less likelihood of acquisition of the high risk HPV based on marital status, tribe and religion as discovered in the study.

Our study also showed that lower age of sexual debut, parity, increased number of lifetime sexual partners, use of oral combined oral contraceptive pills, smoking as well as HIV co-infection which are all directly or indirectly related to increased sexual activities coupled with acquisition of HPV infection and its persistence as reliable predictors of high risk HPV infection. These findings confirm the report of previous studies done within and outside the African continent.[12,15,16,19,22,34]

Limitations of the study

The study is hospital based and the findings may not be representative of the general population. In view of the high rates of HPV infection in Nigeria, it is necessary for future prospective studies to be undertaken in Nigeria using larger sample sizes and even more specific assays of other high risk HPV serotypes to shed further light on the associations between HPV and these identified major risk factors.

CONCLUSION

Cumulative high risk HPV infection is high in Lagos, Nigeria. These findings thus support the need for routine and early screening of all identified high risk sexually active women for HPV infection in Nigeria, as well as emphasising further the importance of sex education for the girl child in school and increased awareness for parents towards HPV vaccination for their generally healthy adolescent girls.

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