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Original Article

The Prevalence of Human Papillomavirus in Women Living with HIV in Mukono General Hospital, Uganda

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Abstract

Background and aims: High-risk oncogenic genotype human papillomavirus (HPV) infection induces cervical cancer (CaCx), a common cancer in women globally. Women living with human immunodeficiency virus (WLHIV) have a greater risk of hr-HPV infection and perseverance, enhancing the risk of defects in the cells of the cervix and aggressive CaCx. However, its prevalence in WLHIV is not apparent. The main objective of this research was to explore the types and prevalence of HPV infection by genotyping HPV among a cohort of WLHIV attending an antiretroviral therapy (ART) clinic in Mukono, Uganda.

Methods: A cross-sectional study was conducted among women aged 25 to 49 years attending an ART clinic in a public health facility in Mukono, Uganda. Systematic random sampling was used to select 342 WLHIV from a target population of 3000. Only participants who had an Xpert HPV test between July 2021 and December 2022 were selected and interviewed, and their responses were analyzed using descriptive statistics.

Results: Slightly more than half (56.7%) of the participants were under 35 years old, married (52.6%), and with a primary level of education (51.2%). The prevalence of hr-HPV was 39.8% (95% CI: 34.40-44.78). Of the total participants, 136 (39.8%) were high-risk HPV positive, with HPV 16, HPV18/45, and other hr-HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) being positive in 23 (6.7%), 21 (6.1%), and 110 (32.2%), respectively, while 17 (12.5%) had mixed hr-HPV infections.

Conclusion: There is a high prevalence of HPV infection among WLHIV, underscoring the need to frequently screen and diagnose CaCx pre-cancerous lesions for its effective prevention.

Keywords: High-risk human papillomavirus, Mukono, Uganda, Women living with HIV

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Introduction

Cervix cancer is a central problem and a severe threat to women's lives.[1] According to Ferlay et al, cancer of the cervix takes the fourth position in cancer globally among females, predicting new cases of 570 000 women in 2018.[2] The most significant number of patients is detected in the low- and middle-income countries (LMICs), with over 85% of Sub-Saharan Africa (SSA) having the most significant problem universally.[3] About 600 000 women are detected with cervical cancer (CaCx), and more than 300 000 deaths occur globally yearly. Nevertheless, this problem is unevenly dispersed, and out of 10 deaths, nine happen in LMICs, and 6 of these happen in only Sub-Saharan Africa.[3]

According to the Catalan Institute of Oncology (ICO)/ International Agency for Research on Cancer (IARC) report of 2021, in Uganda, the estimates showed that 6959 women are detected with CaCx, causing 4607 deaths yearly.[4] In addition, Sarah Maria et al reported that due to the great possibility of developing CaCx in women living with human immunodeficiency virus (WLHIV), the Uganda national treatment strategies for HIV and the Centers for Disease Control and Prevention recommend CaCx screening annually in WLHIV.[5] High-risk human papillomavirus (hr-HPV) is essential to CaCx progression.[6] According to Groves and Coleman, the carcinogenic forms of high-risk HPV, as categorized by the IARC, include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59.[7] Karadža et al revealed that persistent infection with one or more oncogenic HPV genotypes is the most significant important factor identified to cause cervical neoplasia.[8]

In addition, Bogale et al revealed that there is a higher positivity result with Xpert HPV assay testing as compared to the low sensitivity rate when using visual examination with acetic acid.[9] This indicates that implementing HPV DNA as a primary screening test can help reduce CaCx morbidity and mortality in Uganda.[9] The threat of cervical infection is increased by HIV infection because of hr-HPV oncogenic genotypes that bring about HSIL and invasive

cancer.[10] HIV infection changes the legal history of HPV infection because it reduces the rate at which it clears naturally and raises the development of high-grade and aggressive lesions.[11] Hence, WLHIV has a six times higher threat of developing CaCx than women without HIV.[11] However, high-risk oncogenic HPV genotype testing is not done on every woman living with HIV partly because of the limited resources. Thus, this study sought to show the burden of hr-HPV subtypes for effective vaccination strategies against CaCx and the need for consistent resources for the timely diagnosis and management to prevent fatal aggressive cancer.

Materials and Methods

Study Site

This research was conducted in Mukono General Hospital, a Government Health Facility located on the Kampala–Jinja highway in Mukono town, Uganda. It has a bed capacity of 12 and offers antiretroviral therapy (ART), cancer screening, antenatal, and postnatal deliveries as well as outpatient and in-patient services. About 3000 WLHIV regularly attend the ART clinic serving 47 lower facilities in the Mukono district.

Study Population

The women between 25-49 years attending an ART clinic in Mukono General Hospital were recruited for the study because an Xpert HPV test was done on this group. Self-collected cervical specimens were tested using a gen expert machine, polymerase chain reaction (PCR), that identifies and differentiates hr-HPV. The ART clinic was attended by 3000 WLHIV who are always advised to have an Xpert HPV test done at the start, then every 12 months. This test was conducted in Mukono General Hospital Laboratory in the Xpert HPV diagnostic section.

Study Design

This cross-sectional study was conducted in Mukono General Hospital for two months from December 2022 to January 2023. WLHIV with an Xpert HPV test were recruited using systematic random sampling and subjected to an interview guide. The study participants were selected from the target group of 3000 WLHIV between the ages of 25-49 years attending an anti-retroviral Clinic in Mukono General Hospital. The respondents' results for HPV genotypes were obtained retrospectively from respective laboratory records.

Study Procedures

Hr-HPV Diagnosis

The results from the Xpert HPV were retrieved retrospectively from the Health Management Information System (HMIS) registers and the African Laboratory Information System (ALIS). The results of 342 HIV-positive women subjected to the interview guide were obtained from the Comma Separate Values (CSV) downloaded from ALIS. Then, these results were examined for the presence and absence of hr-HPV genotypes.

Inclusion Criteria

The study participants were permanent residents of Mukono, having lived in Mukono for at least two years.

Exclusion Criteria

The study participants sampled during data collection who were found too sick to be interviewed were excluded from the sample.

Statistical Analysis

Data were entered in EpiData software (Version 4.4.2.1). Double data entry was done, and query reports were run to facilitate consistency, accuracy, and completeness. Data were cleaned and transferred to Stata software (version 17.0) for statistical analysis. In univariate analysis, continuous variables were described using measures of central tendency such as means (standard deviations) and medians (interquartile range) ranges. In contrast, categorical variables, including marital status, level of education, ever-given birth, and currently pregnant were defined using frequencies, proportions, and percentages. The prevalence of hr-HPV was determined by dividing the number of study participants with any of the mentioned hr-HPV by the total number of study participants. Furthermore, bivariate analyses were done using the modified Poisson model and the observed *P* values. This model was preferred because it assessed interaction using likelihood ratio tests that compared full models with interaction terms and reduced models without interaction terms. It also ensures that confounding was assessed for variables where the change in prevalence ratio (PR) was greater than 10%, computed as [(Crude PR – Adjusted PR)/ Crude PR] *100.

Variables with a *P* value ≤ 0.2 at bivariate analysis were considered for multivariable analysis. In the multivariable analysis, if the *P* value of a variable was statistically significant at a 5% significance level (*P* value < 0.05), it was considered a risk factor. Prevalence ratios and their 95% confidence intervals (CIs) were also reported.

Results

An overall of 342 participants were enrolled in the research. The median age was 33 years, and the youngest and the oldest were 25 years and 49 years, respectively. Three in every ten (30.4%) of the study participants were aged between 30-34 years, followed by 90 (26.3%) in the age group 25-29 years. Slightly more than half (51.2%) of the participants had primary education, and only 17 (5%) had tertiary education. More than half (52.6%) of the participants were married, and 4 in every 10(40.9%) were single. The majority (97.7%) of the participants were not pregnant at the time of the survey, and only 2.3% were pregnant. Almost universally (96.8%), they have given birth to 1 or 3 children (Table 1).

Table 1. Percent Distribution of Socio-demographic Characteristics of Study Participants

Characteristic	No. of Participants (N = 342)	%
Age (y)		
25-29	90	26.3
30-34	104	30.4
35-39	66	19.3
40-44	54	15.8
45-49	28	8.2
Education level		
Primary	175	51.2
Secondary	150	43.9
Tertiary	17	5.0
Marital status		
Single	140	40.9
Married	180	52.6
Previously married	22	6.4
Ever given birth	11	3.2
No		
Yes	331	96.8
Parity		
0	11	3.2
1-3	263	76.9
>3	68	19.9
Currently pregnant		
No	334	97.7
Yes	8	2.3

Prevalence of Human Papillomavirus by Genotypes

Out of the total participants, 136 (39.8%) were found to be high-risk HPV positive, with HPV 16, HPV 18/45, and other hr-HPV types being positive in 23 (6.7%), 21 (6.1%), and 110 (32.2%) women, respectively. In this study, 17 (12.5%) participants were infected with more than one type of hr-HPV genotype, including 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. In other words, they had mixed hr-HPV infections (Table 2).

Among those with single hr-HPV infection, HPV 18/45 (11% at 95% CI: 6.7-17.6) was prevalent compared to HPV 16 (7.4% at 95% CI: 4.0-13.2). Furthermore, amongst those with multiple hr-HPV infections, HPV 16 + other hr-HPV sequence was the most frequent (8.1% at 95% CI: 4.5-14.1) as compared with HPV 18/45 + other hr-HPV (2.9% at 95% CI: 1.1-7.6) and HPV 16 + HPV 18/45 (0.7% at 95% CI: 0.1-5.1). However, 0.7% at 95% CI: 0.1-5.1 had a mixed infection of all the hr-HPV genotypes, HPV16 + HPV18/45 + other hr-HPV (Table 3).

Table 2. Percent Distribution of Prevalence of High-risk HPV

High-risk HPV	No. of Participants (N = 342)	%
High-risk DNA	136	39.8
HPV type 16	23	6.7
HPV type 18/45	21	6.1
Other high-risk HPV	110	32.2

Note. HPV: Human papillomavirus.

Table 3. Percent Distribution of hr-HPV Types

hr-HPV Types	hr-HPV-Positive (n = 136) No. (%)	95% CI
Single test positive only		
HPV type 16 only	10 (7.4)	4.0 - 13.2
HPV type 18/45 only	15 (11.0)	6.7 - 17.6
Other high-risk HPV only	94 (69.1)	60.8 - 76.4
Multiple tests positive only		
HPV-16 + 18/45	1 (0.7)	0.1 - 5.1
HPV-16 + other hr-HPV	11 (8.1)	4.5 - 14.1
HPV-18/45 + other hr-HPV	4 (2.9)	1.1 - 7.6
HPV-16 + 18/45 + other hr-HPV	1 (0.7)	0.1 - 5.1

Note. hr-HPV: high-risk Human papillomavirus; N: Number of participants; CI: Confidence interval.

Discussion

This study indicated a relatively high hr-HPV prevalence among WLHIV (39.8%). The elevated hr-HPV prevalence with a high load of HIV in Uganda is a significant public health challenge. WLHIV are more likely to have persistent high-risk HPV and progress into cervix cancer than their counterparts. According to Monteiro et al, the occurrence of high-risk carcinogenic HPV genotypes of 39.8% reported in this study was below that of a similar study carried out in Brazil which was 63.3%.[12] The variations in the outcomes could be explained by the smaller sample size of 169 women compared to our study with 342 participants. Furthermore, the results in this study were also contrary to the 55.9% prevalence revealed by Stelzle et al in a prevalent survey on 270 WLHIV in Northeast Brazil.[11] In addition, the findings in this study differed from what Okoye et al reported, which were higher than the incidence of 28.9% reported in a 20-year systematic review of 16 237 participants in SSA.[13] Moreover, the results of the present study were contrary to what was revealed by Chachage et al at twelve hospitals, including Tanzania, Kenya, Uganda, and Nigeria, in an African cohort study on 1002 women where the prevalence was 50.9% among WLHIV and 38.8% among HIV negative women.[14]

However, the present findings were consistent with reports in research by Taku et al in rural Eastern Cape, South Africa, on 417 women, which revealed that WLHIV have a suggestively higher hr-HPV prevalence than the HIV-negative women (40.6%, 63/155 vs. 21.4%, 56/262, respectively, $P = 0.0001$).[15] Other similar studies by Nanga et al have reported higher HPV rates among women living with HIV (39.1%) than among HIV-negative women (24.1%).[16] The most prevalent were HPV 16 (20%) with multiple HPV infections among WLHIV (45.5%) than HIV-negative women (12.7%), as reported by Monteiro et al.[17] Furthermore, the prevalence for this research was more or less similar to that reported in a pilot CaCx screening program in Uganda on WLHIV attending ART

clinics in 10 high-volume hospitals by Lubega et al where the hr-HPV positivity rate was 30% (1,817), 214(12%) were HPV16 positive, 187(20%) were HPV 18/45 positive, and 66% had other hr-HPV genotypes, including HPV 31, 22, 35, 39, 51, 52, 56, 58, 59, 66, and 68. Further, 213 (12%) women had multiple infections with hr-HPV genotypes.[18] The prevalence established in this study implies that many WLHIV attending ART clinics could have a considerable burden of double disease, which needs to be given due attention. Therefore, increasing HPV vaccines and advancing vaccines with extensive action against the less common hr-HPV genotypes may improve CaCx prevention in Uganda and Africa.

Limitations of the Study

The research participants were not comfortable when asked about their sexual behavior. The results are different across the country. The direction of the association cannot be confirmed. As such, we cannot determine causality.

Conclusion

There is a high prevalence of HPV infection among women living with HIV and obtaining ART services from Mukono General Hospital, Uganda. By genotyping, HPV16 and HPV 18/45 are the most significant proportions having multiple HPV genotypes. Such findings underscore the need to frequently screen and diagnose CaCx pre-cancerous lesions for effective prevention of CaCx among WLHIV.

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Authors' Contribution

Conceptualization: Prossy Nabatte Nantale, Josephat Nyagero, Elizabeth Kemigisha.
Data collection: Prossy Nabatte Nantale.
Formal analysis: Prossy Nabatte Nantale.
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Visualization: Josephat Nyagero, Elizabeth Kemigisha.
Writing–original draft: Prossy Nabatte Nantale, Josephat Nyagero, Elizabeth Kemigisha.
Writing–review & editing: Prossy Nabatte Nantale, Josephat Nyagero, Elizabeth Kemigisha.

Competing Interests

There is no conflict of interests to declare for this study.

Ethical Approval

An approval letter from Amref International University (AMIU) graduate school was obtained, followed by ethical approval from the Uganda Christian University Research Ethical Committee with reference number: UCUREC-2022-404. A support letter was also obtained from the Medical Superintendent of Mukono General Hospital, where the research was conducted, and a national research permit was obtained from the UNCST with Reference number HS2550ES. Furthermore, the participants were explained the background and the reason for the study. The study participants had voluntary participation, with informed consent being filled out by each respondent.

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