



Human Papillomavirus Infection Among HIV-positive Women in Lubumbashi, Democratic Republic of the Congo

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Abstract: *Background:* Human Papillomavirus (HPV) infection is the most common sexually transmitted infection in the world, particularly affecting people living with human immunodeficiency virus (HIV). A synergy between the two viruses is however described by several authors but very little is known in women living with HIV-HPV co-infection in Lubumbashi in the South of the Democratic Republic of Congo (DRC). *Objective:* The purpose of this study was to determine the prevalence of HPV infection in women living with HIV, to define the socio-demographic profile of HPV infection and to analyze certain clinical and paraclinical parameters. *Methodology:* A total of 77 women, including 58 HIV-infected women (group 1) and 19 HIV-free women (group 2), were included in a cross-sectional descriptive study that was conducted from November 01 to 30, 2019 at the HIV-AIDS Mother-Child Transmission Prevention Unit (MCTPU) of the Lubumbashi University Clinics (LUC). HPV was tested on cervical-vaginal secretions obtained either by self-sampling or by a sample taken by a previously trained examiner. HPV was investigated by the INNO-LIPA (PCR) method at the Microbiology, Bioorganic Chemistry and Macromolecular Unit laboratory of the Free University of Brussels in Belgium (FUB) while the diagnosis of HIV infection (PCR), viral load determination and CD4 level assay was performed in the LUC laboratory. *Results:* The overall frequency of HPV infection was 74.03%. It was significantly higher in HIV-infected women than in non-HIV-infected women (81.08% vs. 52.63%). The socio-demographic profile of the HPV-infected patient was made up of predominantly married, multi-parented women, aged on average 35, with a secondary education level and an average socio-economic level. Low monthly incomes and HIV infection were almost 4 times at risk for HPV infection (OR 4.2 [1,439-12,262] and OR 3.75 [1,269-11,080] respectively). Finally, HIV-positive patients infected with HPV had overall low levels of Lymphocyte T CD4 compared to those not infected with HPV. *Conclusion:* Our study shows that in Lubumbashi, HPV infection is present in both HIV-positive and negative women but its prevalence is distinctly higher in HIV-positive patients than those without HIV infection. It is interesting to determine in subsequent studies the different genotypes of HPV circulating in Lubumbashi and to define the proportion of genotypes at high carcinogenic risk.

Keywords: Human Papillomavirus, HIV, Lubumbashi

1. Introduction

Human Papillomavirus (HPV) is a group of viruses that are extremely and variously spread around the world, with over a hundred different genotypes identified. HPV infection is, far beyond that of human immunodeficiency virus (HIV), the most common viral sexually transmitted infection (STI) in the world with about 290 million women infected in the world in 2019. HPV-HIV co-infection is common and has been sufficiently documented [1-4].

HPV is a small DNA virus with a strong epithelial tropism, infecting basal epithelial cells and causing benign and malignant lesions of the skin, anogenital mucosa and upper gastrointestinal tract [3]. Several taxonomic classifications of HPV exist, as a function of their oncogenic potency thus, 3 types have been described, namely HPV with high carcinogenic risk (HR-HPV) such as 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68; potentially carcinogenic HPV such as 26, 53, 66, 67, 70, 73 and 82, and low carcinogenic risk HPV such as 6 and 11 [5, 6].

Outside of condylomatosis, the major disease caused by HPV infection is cervical cancer, the fourth most common cancer in the world, with 570,000 new cases in 2018, including 311,000 deaths [1]. According to the World Health Organization (WHO), more than 85% of women are young, poorly educated and live in countries with limited resources, and without effective intervention the number of new cervical cancer cases and deaths could reach 700,000 and 400,000 respectively by 2030 [7-9].

The prevalence of HPV infection, the risk of developing cervical intraepithelial (CIN) lesions, and the risk of persistent HPV infection increase in HIV-infected women compared to those without HIV infection. A low level of CD4 lymphocytes is also observed in case of co-infection of HPV-HIV. Several evidences showed a synergistic interaction between the two infections. HIV promotes the persistence of HPV and modulates the HPV E6 and E7 genes expression, that are responsible for oncogenic transformation. HIV also leads to impaired host immune responses, resulting in reduced ability to control infection and thus allows for easy development of HPV infection [4, 10-12].

In the Democratic Republic of the Congo (DRC) in general and in Lubumbashi in particular, few studies have focused on HPV infection, let alone HPV-HIV co-infection. The purpose of this study was to determine the prevalence of HPV infection in women living with HIV, to define the socio-demographic profile of HPV infection and to analyze certain clinical and paraclinical parameters.

2. Methodology

This is a descriptive cross-sectional study with an analytical component that involved 77 women recruited in Lubumbashi from 01 to 31 October 2019, including 58 women infected with HIV (group 1) and 19 women without HIV infection (group 2). They were recruited in the HIV-AIDS Mother-Child Transmission Prevention Unit (MCTPU) of the Lubumbashi University Clinics (LUC).

Socio-demographic, clinical and obstetric data were collected through a directed interview and a clinical examination conducted by previously trained investigators. For HPV analyzes, the samples were obtained by cervical-vaginal sampling using a single use sterile cotton swab, either by self-sampling made by the patients themselves or by a trained investigator. Once taken, the sample was spread on a glass slide and then dried in the open area and then packaged and sent to the Microbiology, Bioorganic Chemistry and Macromolecular Unit laboratory of the Free University of Brussels in Belgium for the HPV research, which was carried out by the INNO LiPA polymerase chain reaction (PCR) method.

The diagnosis of HIV infection was made by extracting and amplifying viral RNA by PCR followed by the determination of HIV viral load and CD4 T cell count at the LUC laboratory, respectively, with the Cobas® amplirep and Cobas Taq Man 98 devices from Roche.

The data collected was analyzed using Microsoft Excel 2010 and SPSS 20 software. First, a univariate analysis was performed and described the overall characteristics of the study population using descriptive statistics. The position and dispersion indices were calculated for the quantitative variables. In a bivariate analysis, statistically significant associations between the occurrence of HPV infection and HPV-HIV co-infection and independent variables were performed by calculating the Odds ratio (OR) and its 95% confidence interval by crossing the dependent variable (HPV infection) with each independent dichotomized variable.

To compare the averages, the Kolmogorow-Smirnov test was carried out to test the normality. The Student t-test used for the Ghaussian distributions and wilcoxon for non-Ghaussian one. The confidence interval (CI) was set at 95% and the significance threshold was $p < 0.05$. Approval for the conduct of the study was obtained from the Medical Ethics Committee of the University of Lubumbashi (UNILU/CEM/114/2018). The principles of respect for the person, charity and justice were observed and patients freely agreed to participate to the study.

3. Results

3.1. Frequency of HPV infection in HIV-positive Women

Table 1. Frequency of HPV infection in target population and 2 study groups.

Parameters studied	number (n)	percentage (%)
Overall frequency of HPV infection (n=77)	57	74,03
Frequency of HPV infection in HIV-positive patients (group 1) (n=58)	47	81,03
Frequency of HPV infection in the absence of HIV infection (group 2) (n=19)	10	52,63

The overall frequency of HPV infection is 76.3%. It is higher in HIV-infected women (81.03%) than in non-HIV-infected women (52.63%).

3.2. Socio-demographic Characteristics

3.2.1. Age and Parity of Patients Examined

Table 2. Age and parity of patients examined.

Average age of the overall population studied (average \pm SD) (years)	35,87 \pm 6,91		Min-Max	p
Average age of population in the 2 study groups (years)	HPV+ average \pm SD (years)	HPV- average \pm SD (years)		
Group2 (n=19)	37,70 \pm 6,129	37,56 \pm 5,434	29-50	0,957
Group 1 (n=58)	35,34 \pm 6,390	35,09 \pm 10,473	21-59	0,919
Mean parity of the overall population studied (average \pm SD, Min-Max)	4,45 + 3,021		0-12	
Mean population parity in both study groups	HPV+ average \pm SD	HPV- average \pm SD		
Group 2 (n=19)	3,70 + 1,703	3,33 + 1,657	0-6	0,641
Group 1 (n=58)	4,53 + 3,154	4,09 + 2,468	0-12	0,667

The above table shows that there are no statistically significant differences in mean age and parity between HPV and non-HPV infected patients.

3.2.2. Marital Status, Education, Occupation, Socio-economic Status and Parity

Table 3. Socio-demographic characteristics of HPV infected patients (n=57).

Marital status	n (%)
Single	9 (15,8)
Divorced	5 (8,8)
Married	40 (70,1)
Widows	3 (5,3)
Educational level	
Primary	17 (29,8)
Secondary	26 (45,6)
University	14 (24,6)
Occupation	
Employee	5 (8,8)
Official	8 (14)
Liberal	23 (40,4)
Household	21 (36,8)
Socio-economic level	
lower	8 (14)
average	39 (68,4)
High	10 (17,5)
Parity	
Nulliparous	1 (1,8)
Primiparous	6 (10,5)
Pauciparous	23 (40,4)
Multiparous	27 (47,5)

Table 3 shows that the socio-demographic profile of the HPV-infected patient consists of women who are predominantly married (70.1%), with a secondary education level (45.6%) in a professional occupation (40.4%) with a middle socio-economic level and who are multiparous in

47.5% of cases.

Analyzing the relationship between HPV infection and the socio-demographic level of patients, it was noted that the low monthly income exposed the risk of HPV infection four times (OR=4.2; 95% CI [1.439-12.262]) (Table 4).

Table 4. Relationship between monthly income level and HPV infection.

Monthly income level	HPV+n (%)	HPV-n (%)	OR [IC à 95%]
Low	42 (84)	8 (16)	4,2 [1,439-12,262]
High	12 (44,4)	15 (55,6)	1

3.3. Relationship Between HPV and HIV Infections

3.3.1. Frequency of HPV Infection in HIV-positive Women

The frequency of HPV infection is significantly higher in HIV-positive women compared to HIV-negative women as shown

in Table 1 above (81.03% vs 52.63%). It was also found that patients with HIV infection were three-fold susceptible to HPV infection.

Table 5. Relationship between HIV and HPV infections.

HIV infection	HPV+ n (%)	HPV-n (%)	OR [IC à 95%]
HIV positive patients	45 (81,8)	10 (18,2)	3,75 [1,269-11,080]
HIV negative patients	12 (54,5)	10 (45,5)	1

3.3.2. Distribution of CD4 Cell Counts in HIV-positive Patients with HPV Infection

Analyzing CD4 cell counts in the overall HIV-positive population, it was noted that those infected with HPV had lower CD4 counts than those without HPV, regardless of the type of mean used (Table 6).

Table 6. CD4 cell counts in HIV positive patients with or without HPV infection.

TCD4 cell	Average	Median	Geometric mean	Harmonic mean	Total
HPV +	793,28	910	739,28	654,59	32
HPV -	876	917	870,14	863,78	8
Total					40

4. Discussion

4.1. Frequency of HPV Infection

In this study, the frequency of HPV infection is estimated to be 52.63% in women who are not infected with HIV. This frequency is very close to that of 51.5% reported in Guinea Conakry [13]. And 54.9% reported in China [14], but it remains lower than that of 60% observed in Equatorial Guinea [15]. However, it is significantly higher than the 28% reported in Burkina Faso [16], in Kinshasa, the capital of the DRC [17] and 47.9% reported recently in South Kivu in eastern DRC [18].

In the overall population examined in this study, the overall prevalence of HPV infection is 74.03%, an extremely high frequency given the statistics published elsewhere. This is explained by the majority of the at-risk population included in this study, which was composed mainly of HIV-positive women who had a frequency of 81.03%. In the face of impaired immune defense associated with HIV infection, latent HPV infections may be reactivated [19, 20]. In addition, HPV infection and its persistence are more common in people living with HIV due to the common acquisition risk factors between HPV and HIV and an increased susceptibility to HPV infection from the beginning of the decrease in cellular immunity. HPV infections are characterized in people living with HIV by higher local HPV viral loads, concomitant presence of several HR genotypes, and more frequent reactivation of latent infections [21].

4.2. HPV Infection and Patient Age

In our series, the average age of the population studied was 35.87 ± 6.91 years. This age falls within the age limits reported by Sainei *et al* in 2018 [22] in a study conducted in Malaysia where the highest prevalence of HPV infection was between 35 and 44 years of age and by Taghizadeh *et al* [23] in Iran in 2017 where the highest proportion of HPV infection was found to be between 34 and 40 years old. In contrast, Wang J *et al* [14], Yuan *et al* [24] and Nyakio *et al* [18]

reported lower age limits in women with high HPV infection, ranging from 26 to 30 years, 21 to 30 years, and 15 to 24 years, respectively, while the Assoumou team at the Gabon [25] reported significantly higher age limits ranging from 45 to 54 years. In Algeria, in a similar study, Masdou *et al* also described a high frequency of high-oncogenic HPV genotypes in patients with an average age of 40.2 years [26].

It should also be noted that in our study, there were no significant differences between the average age of HPV-infected and non-HPV-infected patients in either HIV-infected woman (group 1) or non-HIV-infected women (group 2).

4.3. HPV Infection and Socio-economic and Cultural Profile of Patients

With respect to marital status, our study noted that the highest number of cases of HPV infection were among married women with 75%. This is in line with figures previously published in Iran of up to 77.6% [23]. But Nigeria and the DRC later reported relatively lower proportions than ours - 61% [27] and 64.1% [17], respectively. Other authors found lower frequencies among married women infected with HPV, 19% in South Kivu (DRC) [18] and 11.0% in Tunisia [28]. Married women are among those at risk from HPV infection, but their proportion varies from region to region, considering the socio-cultural background.

Relative to education and socio-economic level, we found that the majority of women infected with HPV were high school (45.6%) and middle socio-economic (68.4%). In analyzing our results, it was noted that having low monthly earnings put patients at risk of HPV infection nearly four times (OR: 3.75 [1.269-11.080]). These findings support the observations of Ardhaoui *et al* [28], who reported a large proportion of middle-class women infected with HPV, a class known to be marked by multiple sexual partners and unstable conjugal relationships. HPV infection is usually linked to sexual intercourse. However, it remains transient and the virus is eliminated in most women. HPV will become undetectable in 70% of cases at one year and in 90% of cases at two years. In other women, HPV will persist in a latent or

quiescent form for several years. Other studies indicated that overall, the prevalence of HPV infection hovers around 30% in women before age 35 [18, 29].

4.4. HIV/HPV Co-infection

Our study showed that the prevalence of HPV infection was significantly higher in HIV-positive women than in HIV-negative women (81.03 versus 52.63%). It has also shown that HIV infection exposes patients to HPV infection almost 4 times. In addition, by analyzing TCD4 cell counts in the overall HIV-positive population, it was noted that those infected with HPV had lower CD4 counts than those without HPV infection.

These observations support some previous work having shown that HIV infection increased the risk of infections such as HPV infection through alteration of cell-mediated immunity. In women living with HIV, HPV infection and HPV-associated diseases such as genital warts are very common. It has been argued that latent or persistent HPV infections that are generally due to the long-term maintenance of the viral genome in the form of autonomous plasmids may activate especially after an episode of immunosuppression (19). The prevalence of HPV infection among HIV-positive women varies between 40 and 95%, according to numerous studies, while it ranges between 23 and 55% among HIV-negative women [30].

5. Conclusion

In Lubumbashi, the prevalence of HPV infection in HIV-positive women is 81.03%, compared to 52.63% in HIV-negative patients examined. The socio-demographic profile of the HPV-infected HIV-positive patient in Lubumbashi is made up of a married, multiparous woman of secondary and middle socioeconomic status. HIV-positive patients with low monthly incomes are at four times the risk of acquiring HPV infection. Furthermore, the study showed that CD4 cell counts are relatively low in HIV-positive HPV-infected patients compared to non-HIV-infected patients and that HIV infection exposes HIV-positive patients to HPV infection 3 times over. It is interesting to determine in subsequent studies the different genotypes of HPV circulating in Lubumbashi and to define the proportion of genotypes at high carcinogenic risk.

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