The Journal of Medical Research

Research Article

JMR 2019; 5(3): 120-126
May- June
ISSN: 2395-7565

www.medicinearticle.com
Received: 27-05-2019
Published: 17-06-2019

The Cytopathological and Molecular Aspects of Dysplasic Lesions of the Cervix: Particularities to Patients Living with Hiv Followed at Panzi General Reference Hospital

Nyakio Olivier[1,2,5], Kibukila Fabrice[3], Chasinga Tchass[4], Gad Murenzi[8], Bwami Joyeux[1], Kasongo Bertin[6], Tambwe[7], Albert[7], Kakudji Prosper[7], Kalenga Prosper[7], Kakoma Jean Baptiste[7]

1 Gynecology and Obstetrics Service, Panzi General Reference Hospital
2 Department of Gynecology and Obstetrics, Evangelical University in Africa (UEA)
3 Department of Gynecology and Obstetrics, Bukavu State University (UOB)
4 Anatomopathology Service, Panzi General Reference Hospital
5 International Advanced Center for Research and Training (ICART)
6 Provincial Division of Health (South Kivu)
7 Department of Gynecology and Obstetrics, School of Medecine, University of Lubumbashi
8 Rwanda Military Hospital

Abstract

Introduction: Cervical cancer is one of the most common cancers and takes the second place among women's cancers in terms of incidence and the first place in terms of breast cancer mortality. Its incidence and mortality are significantly increased in patients living with HIV / AIDS. The purpose of this work is to describe the cytopathological and molecular aspects of cervical dysplasia in HIV-positive women in our environment and to look for some associated factors, in particular the degree of immunosuppression and the clinical stage. **Methodology**: This was a cross-sectional, descriptive, and analytical study of cervical-uterine smears (n = 111) and human papillomavirus genotyping (n = 73) in HIV-infected patients received from January 2018 to December 2018 at Panzi GRH (South Kivu, DR Congo). The data analysis was done using SPSS statistics 20 software. **Results**: The average age of the patients was 42.25 ± 10.42 years. The cervical-uterine smear (CUS) was normal in 82.9% of cases and cytological abnormalities were found in 13.5% of cases. The majority of patients were in WHO stages I (45.9%) and II (45.0%) of HIV infection and had a CD4 count greater than 500 cells / mm3 in 47.9% of patients. Among the 73 patients who had been tested for HPV infection, 35 (47.9%) were positive. The most common carcinogenic genotype among HPV positive patients was 18-45 (17.1%). There was not a significant difference in carcinogenic genotypes and intraepithelial lesions as a function of WHO clinical stages (p = 0.3819 and p = 0.7945). **Conclusion**: The coexistence between HIV and HPV infections seems to be strongly associated with the occurrence of cervical cytological abnormalities in our sample study. Hence the need, on the one hand, for a national policy for early detection of cervical cancer in all patients living with HIV / AIDS, and on the other hand, for deepened studies at the international level for the tuning of a plurigenic vaccine containing all oncogenic genotypes, those one that are geographically widespread (genotypes 16 and 18) are not more common to HIV-positive patients in our study environment.

Keywords: dysplastic lesions, cervical cancer, HIV / AIDS, HPV, Panzi GRH.

***Corresponding author:**
Nyakio Olivier
Head of Gynecology and Obstetrics Department at Panzi GRH, Teacher at the Faculty of Medicine of Evangelical University in Africa
Email: oliviernyakio[at]yahoo.fr

INTRODUCTION

Currently, it has been found that the risk of developing a malignant tumor is higher in HIV-infected people than in the general population. Malignant tumors associated with HIV infection include AIDS-class tumors including Kaposi's sarcoma, non-Hodgkin's malignant lymphomas and, since 1993, invasive cervical cancer and non-AIDS cancers [1-3]. A significant proportion of HIV-associated tumors are related to infection with an oncogenic virus such as Epstein-Barr virus, herpes virus type 8 or papillomavirus [4-5].

Cervical cancer is one of the most common cancers worldwide and takes the second place among women's cancers in terms of incidence and first in terms of mortality [5-6]. Every year it affects more than 500,000 women, 80% of whom are in developing countries [6].

In Africa, the incidence increased from 80,419 cases in 2008 to 99,038 cases in 2012 with 57,400 deaths. However, these statistics can be largely underestimated because only 8% of the population in sub-Saharan Africa is covered by cancer registries [7-8]. In the Democratic Republic of Congo (DRC), these cancer registries exist but sometimes are not operational.

The incidence of cervical cancer is significantly higher in seropositive patients than in seronegative patients; it can even reach 50% in some populations [9].

In a study conducted in Brazil on cervical dysplasia and cervical cancer in 114 women, 37 (32.46%) of whom had cervical cancer, 7 (19%) were HIV positive [10]. It has also been reported that several studies have been carried out showing the importance of the increasing risk of cervical cancer occurrence in cases of HIV / AIDS [10].

Therefore, it is recommended to systematically offer HIV / AIDS infected women screening for HPV-induced lesions (human papillomavirus) by performing a cervical smear during the discovery of seropositivity. To achieve this goal, multidisciplinary care, including the general practitioner, the specialist physician and the paramedical health professionals are necessary.

Therefore, this study aims to describe the cytopathological and molecular aspects of cervical dysplasia in HIV-positive women in our environment and to look for certain associated factors, including the degree of immunodepression and the clinical stage of HIV infection.

METHODOLOGY

Type and study framework

This is a cross-sectional, descriptive and analytical study performed on HIV-infected patients received from January to December 2018 at Panzi GRH (South Kivu, DR Congo). In total, we enrolled 111 patients, all of whom having benefited a cervical-uterine smear (n = 111) while HPV genotyping was performed in 73 patients (n = 73).

Sampling

We used a comprehensive technique including HIV-positive patients (unigold and determined tests), regardless of the clinical stage, hospitalized at Panzi GRH who underwent the cervical-uterine smear screening. The sampling was carried out after sensitization by a qualified medical staff and in respect of all ethical considerations.

Patients were ineligible for study if they were pregnant, had a sexually transmitted disease other than HIV, were already received a treatment for cervical cancer and also those who were not willing to the study.

Variables

The following variables were studied:

- **Dependent variables:**
  a) The genotype: we analyzed the following genotypes according to the configuration of the Gene xpert device: genotype 16, genotypes 16-18, 16-18-45, 16-18-45 and others, 16 and others, 18-45, 18-45 and others and finally other genotypes. All these genotypes were dichotomized into high-risk carcinogenic genotypes (genotype 16, genotypes 16-18, 16-18-45, 16-18-45 and others, 16 and others, 18-45, 18-45 and others) and other carcinogens (other genotypes).
  b) Cytopathological results: The cytopathological examination of the smear allowed us to identify the following aspects: normal smear, inflammatory smear, Atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesions (HSIL). These results were grouped into two classes: atypical, low-grade and high-grade intraepithelial lesions (ASC-US + LSIL + HSIL) that are precancerous lesions and those related to normal smear (normal + inflammatory smear, these are non-precancerous lesions).
- **Independent variables:** The age of patients were divided in five different age groups, the CD4 count, HIV clinical stages according to WHO and HPV test results

Data collection and analysis

Data collection included cytopathic and genotyping results following a cervical-uterine smear. This was done at Panzi GRH and described the different cytopathic aspects of the cervical lesions. Genotyping was performed at Kigali Military Hospital (Rwanda), and for the missing genotypes, the samples were sent to the United States in a laboratory partnered with that one of Kigali Military Hospital.

The analysis of the data was done using SPSS statistics 20. The Chi-2 test (Pearson test) and Fisher's exact test allowed to compare the observed proportions with a significance threshold set at p. <0.05. Ethical considerations were taken into account, as mentioned above, after favorable opinion of the local ethics committee.

RESULTS

The Age of patients

Table 1: The Age of patients

Effective age	range (n =111)	Percentage
15 - 24 years	3	2,7
25 - 34 years	28	25,2
35 - 44 years	33	29,7
45 - 54 years	33	29,7
>or=55 years	14	12,6
Total	111	100,0

The average age of the patients was 42.25 ± 10.42 years with the extremes of 19 and 65 years, the modal classes being the age groups of 35-44 years and 45-54 years which by It self represented 59.4% of the patients.

Cervical cytopathology

Table 2: Cytopathological results

Cytopathological results	Effective	Percentage
Normal smear	92	82,9
Inflammatory	4	3,6
ASC-US*	8	7,2
LSIL**	5	4,5
HSIL***	2	1,8
Total	111	100,0

* Atypical squamous cells of undetermined significance
** Low grade squamous intraepithelial lesion
*** High grade squamous intraepithelial lesion

The cervical-uterine smear (CUS) was normal in 82.9% and inflammatory in 3.6% of cases, while cytological abnormalities, which were found in 13.51% of cases, included 7.20% atypical (ASC-US), 4.50% low-grade lesions (LSIL) and 1.80% high-grade lesions (HSIL).

Clinical and biological symptomatology of HIV / AIDS

Table 3: WHO clinical stage

WHO stadiums	Effective	Percentage
Stage I	51	45.9
Stage II	50	45.0
Stage III	8	7.2
Stage IV	2	1.8
Total	111	100.0

The majority of patients were in stage I (45.9%) and II (45.0%) WHO.

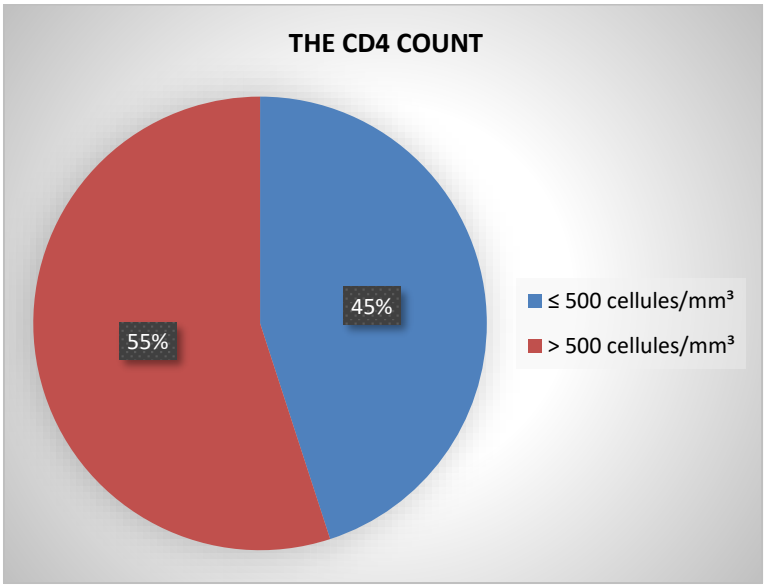

Figure 1: The CD4 count

More than half of the patients, 55%, had a CD4 count greater than 500 cells / mm3

HPV Testing and HPV Genotyping

Table 4: HPV test and HIV + patients

HPV	Effective	Percentage
Positive	35	47.9
Negative	38	52.1
Total	73	100.0

Among 73 patients who had been tested for HPV, 35 (47.9%) were tested positive, while 38 (52.1%) of them were free from the infection.

Table 5: HPV Genotypes and HIV + Patients

Genotypes	Effective Test HPV (n =73)	Percentage	Genotypes	Effective HPV+ (n = 35)	Percentage
Genotype 16	4	5.47%	Genotype 16	4	11.4%
Genotypes 18 – 45	6	8.21%	Genotypes 18-45	6	17,1%
Genotypes 16 - 18 - 45 and others	3	4.1%	Genotypes 16 - 18 - 45 and others	3	8.6%
Genotypes 16 - 18 – 45	1	1.36%	Genotypes 16 - 18 – 45	1	2.9%
Genotypes 16 and others	3	4.1%	Genotypes 16 and others	3	8.6%
Genotypes 18 - 45 and others	3	4.1%	Genotypes 18 - 45 and others	3	8.6%
Others	**15**	**23.28%**	**Others**	**15**	**42.9%**
Negative HPV	38	52.05%			
Total	73	100%	Total	35	100%

Among 73 patients tested for HPV, high-risk carcinogenic genotypes represented 27.34% (8.21% for 18-45 genotypes and 5.47% for genotype 16); while with 35 cases tested for HPV positive, high-risk carcinogenic genotypes represented 57.2% (17.1% for genotypes 18-45 and 11.4% for genotype 16).

Table 6: HPV Test Results and WHO Clinical Stages of HIV Infection

WHO Stage	HPV		Total
	Positive	Negative	
Stage I	15 (45.5%)	18 (54.5%)	33 (100%)
	42.9%	47.4%	45.2%
Stage II	16 (50%)	16 (50%)	32 (100%)
	45.7%	42.1%	43.8%
Stage III et IV	4 (50%)	4 (50%)	8 (100%)
	11.4%	10.5%	11%
Total	35 (47.9%)	38 (52.1%)	73 (100%)
	100%	100%	100%

The proportion of HPV positive patients was higher in stage II (50.0%), III and IV (50.0%) than in stage I (45.0%), but that difference was not statistically significant (p = 0.1497).

Table 7: HPV genotypes and WHO clinical stages of HIV infection

WHO Stage	Genotypes		Total
	High risk carcinogens	Others	
Stage I	9 (60.0%)	6 (40.0%)	15 (100%)
Stage II	10 (62.5%)	6 (37.5%)	16 (100%)
Stage III et IV	1 (25.0%)	3 (75.0%)	4 (100%)
Total	20 (57.1%)	15 (42.9%)	35 (100%)

High-risk carcinogenic genotypes were relatively more common in clinical stages I (60.0%) and II (62.5%) than in stages III and IV (25.0%); but that difference was not statistically significant (p = 0.3819).

Table 8: Cytopathological results and HPV test in HIV + patients

Cytopathological results						
HPV	**Normal smear**	**ASC-US**	**LSIL**	**HSIL**	**Inflammatory**	**Total**
Positive	28 (80.0%)	3 (8.5%)	2 (5.7%)	1 (2.9%)	1 (2.9%)	35 (100%)
	47.5%	60.0%	40.0%	50.0%	50.0%	47.9%
Negative	31	2	3	1	1	38
	52.5%	40.0%	60.0%	50.0%	50.0%	52.1%
Total	59	5	5	2	2	73
	100%	100%	100%	100%	100%	100%

Among 73 HPV-tested patients, 47.5% with normal smear had a positive HPV test compared to 60.0% with ASC-US, 40.0% with LSIL and 50.0% with HSIL. The difference observed was not statistically significant (p = 0.430).

Table 9: Cytopathological results and genotypes of HPV

HPV genotypes	Cytopathological results		Total
	ASC-US+ LSIL+HSIL	Normal + Inflammatory smear	
Highrisk carcinogenic genotypes	3 (15.0%)	17 (85.0%)	20 (100%)
Others	3 (20.0%)	12 (80.0%)	15 (100%)
Total	6 (17.1%)	29 (82.9%)	35 (100%)

The proportion of atypical, low and high-grade lesions was relatively low in patients with high-risk carcinogenic genotypes (15.0%) compared to patients with other genotypes (20.0%), but that difference was not significant. not statistically significant (p = 0.519).

Table 10: Cytopathological results and WHO clinical stages of HIV infection

WHO Stages	Cytopathological results		Total
	ASC-US+ LSIL+HSIL	Normal + inflammatory smear	
Stage I	7 (13.7%)	44 (86.3%)	51 (100%)
Stage II	6 (12.0%)	44 (88.0%)	50 (100%)
Stage III et IV	2 (20.0%)	8 (80.0%)	10 (100%)
Total	**15 (13.5%)**	**96 (86.5%)**	**111 (100%)**

The proportion of atypical, low and high grade lesions was higher at WHO clinical stages III and IV (20.0%) compared with stage I (13.7%) and stage II (12.0%), but the difference was not statistically significant (p = 0.7945).

DISCUSSION

The Age range

In our study, the average age is 42.25 ± 10.42 years with the extremes of 19 and 65 years. This result is similar to that found by Fatuma Bintou [11] in Mali (38.9 ± 7.86 years), that of Boukili Khaoula [12] in Morocco (46.08 ± 8.7 years with extremes of 28 and 60 years) and that of Hasnoui Radhia [13] in France (43.5 years with extreme of 22 and 75 years). A similar study was conducted in Sweden by Söderlund-Strand [14] who found an average age of 33 years with extremes of 23 and 61 years. Massad Stewart [15] found an average age of 35 years in the United States and Joshi S. [16] 34.9 years in India.

Thus, we notice in our study that 59.4% of patients were 35 to 54 years; this would be explained in our environment by the precocity and the multiplicity of sexual relations, the consequence of a precarious socio-economic level.

Cytopathology

Cervical-uterine smear remains the most common used tool for cervical cytopathology because of its low cost and its ease of realization. In our series, the CUS was normal in 82.9% of cases and inflammatory in 3.6%. The cytologic abnormalities which were found in 13.5% of cases, included 7.20% cellular atypical (ASC-US), 4.50% low-grade lesion (LSIL), and 1.80% high grade lesions (HSIL). Thomas C. [17] found a normal CUS in Athens in 42.62% of the cases, compared to 4.1% of atypical, 2.3% of LSIL and 0.3% of HSIL.

Several authors conducted similar studies, among others, Jia-Jiang Wang *et al*. [18] in China who found: normal CUS in 71.7% of cases compared to 14.8% of ASC-US; 8.7% of LSIL and 2.3% of HSIL. Kasap B. *et al*. [19] found in their study in Turkey: a rate of 84.9% of normal CUS; 1.55% of ASC-US; 5.3% of LSIL and 4.0% of HSIL. Garbuglia A.R. *et al*. [20] had the following results in Italy: normal CSU in 76.4% of cases; ASCUS, LSIL and HSIL in 24.4% of cases while Correa *et al*. [21] obtained a normal CUS of 63.2% in Brazil. Agaba *et al*. [22] noted in their study in Nigeria: 31.7% normal CUS; 39.3% of ASC-US; 15.2% of LSIL and 13.8% of HSIL.

Among 73 HPV-tested patients (Table 8), 47.5% of them with normal smear had a positive HPV test compared to 60.0% with ASC-US, 40.0% with LSIL and 50.0% with HSIL. Thus, the difference observed was not statistically significant (X2 = 0.980, df = 4, p = 0.430). By making a horizontal reading of this table (3rd line not in bold, a result taking into account only the HPV test positive), it is noticed that the smear was normal in 80% of the cases in the HPV positive patients, versus 8.5 % of ASC-US and 8.6% of LSIL-HSIL. These results are almost similar to those of Aggarwal R *et al*. [24] in India who found 7.6% LSIL and HSIL grade abnormalities.

We observe from the above studies that cervical cytopathology is normal in the majority of cases. This normality of the CUS is explained by the sensitivity of this exam which is about 70 to 80%.

WHO HIV/AIDS Clinic

The WHO classification stage of HIV infection indicates the most common clinic manifestations observed and groups them into 4 stages of increasing severity. The occurrence of these manifestations, together with the CD4 lymphocyte count (when it is available), makes it possible to define the evolutionary stage of the immunodeficiency and to guide the therapeutic management [23].

The majority of patients in our work were in WHO stages I (45.9%) and II (45.0%). R. Aggarwal *et al*. [24], in their HPV genotype study in India, found that the majority of patients (81.5%) were WHO stage I compared to 6.9% stage II, 10% and 1.5% at stages III and IV respectively. A comparable study was conducted by Fridmann *et al*. [25] in Paris and showed that 18% of patients were in WHO stage I.

In a vertical reading of Table 6, we find a positive HPV level in 42.9% in WHO clinical stage I to patients of HIV / AIDS infection; this rate increases slightly in stage II (45.7%) to fall in stages III and IV (11.4%). This observation is different from that conducted by Aggarwal R *et al*. [24] in India who concluded in their study the following results: 76.1% positivity of the HPV test in patients with clinical stage I of the WHO compared to 7.7% in stage II and 15.3% in stages III and IV. In our series, the clinical stage of the WHO HIV / AIDS infection does not appear to have influenced the HPV test because the difference was not significant (X2= 0.928, df=2, p= 0.1497). The high-risk carcinogenic genotypes (Table 7) were relatively more frequent at clinical stages I (60.0%) and II (62.5%) than at stages III and IV (25.0%); but the difference was not statistically significant (X2 = 1.925, df = 2, p = 0.3819).

This high, optimistic and reassuring frequency of patients clinically admitted to WHO stages I and II in our study series would be linked to the very meticulous follow-up of HIV patients at Panzi General Hospital who strives for strict compliance antiretroviral therapeutic requirements.

CD4 count

Knowledge of CD4 count is an excellent indicator for therapeutic follow-up and prognosis in HIV-positive patients. In our study, the frequency of CD4 count greater than 500 cells / mm3 was 55%. A study by Kadhel [26] in the French West Indies showed a frequency of CD4 count greater than 500 cells / mm3 in about 31.4% of cases in HIV-positive patients with dysplastic lesions of the cervix. Many other studies were conducted in the same context, with nevertheless disparate results. Thus, Massad LS *et al*. [27] found in the United States a lower frequency of CD4 count greater than 500 cells / mm3 (36% and 16% in their respective two studies); this frequency was however different from that obtained by M.A.G. Gonçalves *et al*. [10] in Brazil as well as Garbuglia A.R. *et al*. [20] in Italy who respectively reported a frequency of CD4 count greater than 500 cells / mm3 of the order of 66.67% and 69.0% respectively.

This frequency of CD4 count greater than 500 cells / mm3 found in our series would be related to the early initiation of antiretroviral therapy when the seropositivity was discovered.

HPV genotypes

Several recognized carcinogenic HPV genotypes were found in our study. Among 35 patients tested positive for HPV, the high-risk of carcinogenic genotypes (16 and 18), which are recognized as the most widespread [6-28], were found in 57,1% of the cases whereas the other genotypes were found in 42.9% of cases (Table 7). But in isolation, the serotype 16 represented only 11.4% of cases (Table 5).

Several other similar studies were conducted out:

- Josh *et al*. [16] found in India an HPV 16 frequency of 11.5%, followed by HPV 31 (9.5%) and HPV 18 (6.8%);
- Söderlund *et al*. [14] found a 23.8% incidence of HPV 16 in their study conducted in Sweden;
- Massid LS *et al*. [27] in a study comparing the prevalence of HPV genotype 16 in HIV-negative and seronegative women, concluded that HPV 16 is more common in HIV-infected women (62%), whereas in HIV-positive women, it is the oncogenic serotypes other than HPV 16 which are the most common;
- Gonçalves M.AG. *et al*. [10] did a similar study to that one of Massid in Brazil and also found that HPV16 was the most common genotype in seronegative patients (63.9%) while it represented 22.73% of genotypes in seronegative patients;
- Mukanyangezi *et al*. [29] obtained in their work in Rwanda 21.8% of HPV16, 21.8% of HPV52 and 5.1% of HPV18;
- Nina Jancar *et al*. [30] found in their study in Slovenia an excessively high frequency of HPV16 (64.9%) while HPV18 represented 12.2%;
- Dongmei Wu *et al*. [31], in their study in China, found that the serotype HPV16 was 14.4%, followed by HPV52 (10.8%), finally HPV18 (8.0%);
- Philippe Simon and al. [32], in their study in France, found a frequency of 21% of HPV16;
- P. Nicolau *et al*. [33] had in their study in Italy a high frequency of serotype 16 HPV (53,85%).

In the light of the foregoing, it is worth noting that the most common type of HPV differs from one region to another, although it must be recognized that HPV16 is the most widely spread [34].

It is also noteworthy that the incidence of HPV16, examined in isolation, is low compared to other oncogenic genotypes in HIV-positive patients with cervical dysplasia, compared to HIV-negative patients; which is also the case in our study. This would be explained by a hypothetical independent relationship of HPV16 to the effects of HIV that may reflect an innate ability to avoid immune control of the host, and corollary, other oncogenic HPV, most affected by immunity impaired, would be more prevalent in HIV-positive patients than HIV-negative patients with dysplastic lesions of the cervix [27].

It should be noted that the combination of serotypes was found in 88.6% in patients with a positive HPV test (Table 5). This notion of multiplicity has been reported by many authors [21-35]. High-risk

carcinogenic genotypes (HPV 16 and 18) were found in 57.1% of the cases in this study. Our observations are not far from the results of Ramogola-Masire D *et al*. [35] who found in their study in Botswana a multiplicity rate of 82% with a high-risk carcinogenic serotypes found in 51% of cases.

The proportion of atypical, low and high grade lesions (Table 9) is relatively low for patients with high-risk carcinogenic genotypes (15.0%) compared to patients with other genotypes (20.0%), but the difference is not statistically significant (X2 = 0.1509, df = 1, p = 0.519).

CONCLUSION

The coexistence between HIV and HPV infections seems to be strongly associated with the occurrence of cervical cytological abnormalities in our sample study. Hence the need, on the one hand, for a national policy for early detection of cervical cancer in all patients living with HIV / AIDS, and on the other hand, for deepened studies at the international level for the tuning of a plurigenic vaccine containing all oncogenic genotypes, those one that are geographically widespread (genotypes 16 and 18) are not more common to HIV-positive patients in our study environment.

Conflict of Interest

All authors acknowledge having contributed to the realization of the latter and declare that there is no conflict of interest between them.

Contribution of the Authors

All authors claim to have contributed to the design of this article

Acknowledgments

Special thanks to our mentor and school teacher, Professor Emeritus Jean Baptiste SAKATOLO KAKOMA ZAMBEZE. Master, please find in this work the fruit of your supervision.

REFERENCES

1. Dal Maso L, Serraino D et Franceshi S. Epidemiology of AIDS-Related, Tumors in developed and developing countries. European Journal of cancer. 2001; 37(10):1188-1201.
2. Ghebre RG, Grover S, Xie MJ, Chuang LT, Simonds H. Cervical cancer control in HIV-infected women: past, present and future. Gynecologic Oncologic Reports. 2017; 21:101-108.
3. Spano JP. Aids-Related malignancies: state of the art therapeutic challenges. Journal of clinical oncology. 2008; 26(29):4834-42.
4. Bodartha SA, Varma S, Rosith AF. Gynecologic cancer in HIV-women: a systemic review and meta-analysis. American Journal of Obstetrics and Gynecology, 2019. doi: http://doi.org/10.1016/j.ajog.2019.02.022
5. Castle PE, Giuliano AR. Genital tract infections, cervical inflammation, and antioxydant nutrients assessing their roles as human papillomavirus cofactors. J Natl Cancer InstMonogr. 2003; 31:29-34.
6. Lansac J, Lecompte P, Marret H. Gynécologie pour le praticien. Elsevier Masson. 8ème Edition, 2019, 89-107.
7. Bruni LB, Albero G, Aldea M, Serrano B, Valencia S. ICO Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary report, 2014.
8. Moussavou PB, Koumakpayi IH, Nkili-Meyong AA. Molecular analysis of human Papillomavirus detected among women positive for cervical lesions by visual inspection with acetic acid/Lugol's iodine (VIA/VILI) in Libreville, Gabon. Infect Agent Cancer [Internet]. 2016; 11(1). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5015258/ [PubMed]
9. Smith JS, Sanusi B, Swarts A, Faesen M, Levin S, Goeieman B, *et al*. A randomized clinical trial comparing cervical dysplasia treatment with cryotherapy vs loop electrosurgical excision procedure in HIV-seropositive women from Johannesburg, South Africa. Am J Obst Gynecol. 2017; 217(183):e1-11.
10. Gonçalves MAG, Soares EG, Fernandes APM, Fonseca BAL, Bettini JSR, Simoes RTS, *et al*. Langerhan's cell count and HLA class II profile in cervical intraepithelial neoplasia in the presence or absence of HIV infection. Eur J Obstet Gynecol Reprod Biol. 2004; 114:221-227.
11. Fatouma BS. Etude des facteurs de risques des lesions dysplasiques et cancéreuses du col de l'utérus diagnostiquées au Mali. Thèse de Médecine. Univer de Bamako, 2007.
12. Boukili K. les lésions du haut grade du col utérin. Thèse de médecine. Univer Sidi Mohammed Ben Abdellah, 2016.
13. Hasnoui R. frottis cervico-utérin de dépistage: la prise en charge des patientes vivant avec le VIH est-elle optimale sur le territoire de la COREVIH Ile de France Nord ? Thèse de médecine. Univer Paris Diderot Paris 7, 2017.
14. Söderlund-strand A, Eklund C, Kemetli L, Grillner T, Törnberg S, Dillner J, *et al*. Genotyping of human papillomavirus in triaging of low-grade cervical cytology. Am J Obst Gynecol. 2011; 205(145):e1-6.
15. Massad LS, Xie X, D'Souza G, Darragah TM, Minkoff H, Wright R, *et al*. Incidence of cervical precancers among HIV-seropositive women. Am J Obstet Gynecol. 2015; 212(606):e1-8.
16. Josh S, Babu JM, Jayalakshmi D, Kulkarni V, Divate U, Muwonge R, *et al*. Human papillomavirus infection among human immunodeficiency virus-infected women in Maharashta, India. DElsevier. Vaccine, 2014; 32:1079-1085.
17. Wright TC, Stoler MH, Behrens CM, Apple R, Derion T, Wright TL, *et al*. The ATHENA human papillomavirus study: design, methods, and bareline results. Am J Obst Gynecol. 2012; 206(46):e1-11.
18. Wang JJ, Li-Ping L, Qinz-wei H, Wang ZQ, Dong J, Shen WW, *et al*. A proper triage for detecting women with high-risk human papillomavirus genotypes other than HPV16/18. Eur J Obstet Gynecol Reprod Biol. 2017; 219:113-118.
19. Kasap B, Yetimalar H, Keklik A, Yildiz A, Cukurova K, Soylu F. Prevalence and risk factors for human papillomavirus DNA in cervical cytology. Eur J Obstet Gynecol Reprod Biol. 2011; 159:168-171.
20. Garbuglia AR, Piselli P, Lapa D, Sias C, Del Nonno F, Baiocchini L, *et al*. Frequency and multiplicity of human papilomavirus infection in HIV-1 positive women in Italy. Journal of Clinical Virology. 2012; 54:141-146.
21. Correa CM, Teixera NC, De Araujo AC, Carvalho NO, DelCastillo DM, Campos RR, *et al*. Prevalence and multiplicity of HPV in HIV women in Minas Gerais, Brazil. Rev Assoc Med Bras. 2011; 57(4):418:423.
22. Agaba AP, Tracher TD, Ekwempu CC, Idoko JA. Cervical dysplasia in Nigeria women infected with HIV. Int J Gynecol Obstet. 2009; 107:99-102.
23. Collège des Universités de Maladies Infectieuses et Tropicales. ePILLY trop. Maladies infectieuses tropicales. Ed alinéa plus. 2016, 583p.
24. Aggarwal R, Sachdeva RK, Naru J, Suri V, Sharman A, Nijhawan R. HPV genotyping in North India women infected with HIV. Int J Gynecol Pathol. 2012; 31(5):475-481.
25. Fridmann S, Boufassa F, Cartier S, Peretti D, Lazure T, Mole M, *et al*. Facteurs de risqué d'acquisition des lésions du col utérin dans une population de femmes infectées par le VIH. J Gynecol Obstet Biol Reprod. 2006; 35(cahier1):490-496.
26. Kadhel P, Multigner L, Bardinet F, Goerger-Sow MT, Janky E. Cervical intraepithelial neoplasia and invasive cancer nike in women infected with HIV in the French West Indies. British HIV Association HIV Medecine, 2012; 13:79-89.
27. Massad LS, Xie X, Burk RD, D'Souza G, Darragah TM, Minkoff H, *et al*. Association of cervical precancer with human papillomavirus types other than 16 among HIV co-infected women. Am J Obstet Gynecol. 2016; 214(354):e1-6.
28. Cubie HA, Seagar AL, Beattie QJ. A longitudinal study of HPV detection and cervical pathology in HIV infected women. Sex Transm Inf. 2000; 76:257-261.
29. Mukanyangezi MF, Sengpiel V, Manzi D, Tobin G, Rulisa S, Bienvenu E, *et al*. Screening for human papillomavirus, cervical cytopathological abnormalities and associated risk factors in HIV-positive and HIV-negative women in Rwanda. British HIV Association HIV Medecine. 2018; 19:152-166.
30. Nina J, Bostjan J, Poljak M, Lunar MM, Bokal EV. Distribution of human papillomavirus genotypes in women with cervical cancer in Slovenia. Eur J Obstet Gynecol Reprod Biol. 2009; 145:184-188.
31. Dongmei W, Cai L, Huang M, Zengh Y, Yu J. Prevalence of genital human papillomavirus infection and genotypes among women from Fujian Province, PR China. Eur J Obstet Gynecol Reprod Biol. 2010; 151:86-90.
32. Simon P, Roumegere T, Nöel C, et Nöel CJ. Human papillomavirus infection in couples with female low-grade intraepithelial cervical lesion. Eur J Obstet Gynecol Reprod Biol. 2010; 153:8-11.
33. Nicolau P, Mancebo G, Agramunt S, Sole-Sodeno JM, Bellosillo B, Muset MM, *et al*. Urine human papillomavirus prevalence in women with high-grade cervical lesions. Eur J Obstet Gynecol Reprod Biol. 2014; 183:12-15.

34. Alibegashvili T, Clifford GM, Vaccarella S, Baidosvili A, Gogiashvili L, Tsagareli Z, *et al*. Human papillomavirus infection in women with and without cervical cancer in Tbilisi, Georgia. Cancer Epidemiology. 2011; 35:465-470.
35. Ramogola-Masire D, McGrath CM, Banhart KT, Friedman HM, Zetola NM. Subtype distribution of human papillomavirus in HIV-infected women with cervical intraepithelial neoplasia stages 2 and 3 in Botswana. Int J Gynecol Path. 2011; 30:591-596.