New Microbiologica, 41, 4, 268-273, 2018, ISSN 1121-7138

FULL PAPER

HPV infection and pre-neoplastic cervical lesions among 321 HIV+ women in Florence, Italy, 2006-2016: prevalence and associated factors

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SUMMARY

Women living with HIV (WLWH) are at higher risk for HPV-related malignancies. To estimate the factors associated to HPV infection and to pre-neoplastic cervical lesions, we observed 321 WLWH in an HIV care-centre in Florence, Italy.

In 2006-2016, WLWH followed at S. Maria Annunziata Hospital underwent to gynaecological examination including HPV-test, Pap-smear, colposcopy and, if needed, cervical biopsy. Demographical and clinical information were collected and linear logistic regression was performed.

Among 321 WLWH, 161 (50.2%) resulted HPV+. Multiple genotypes were identified in 35%, and cancer high-risk genotypes in 61%. Younger age, not-caucasic origin, increasing number of partners, and shorter duration of HIV are associated with HPV infection. A colposcopy was performed in 154 HIV+/HPV+ women: histological lesions were present in 47 (30%). Among these, CIN1, CIN2 and CIN3 were present in 16, 4, and 1 patients, respectively. Being caucasic, smoking 1-20 cigarettes/day, having 2 partners in the last year, and being an injective-drug-user are associated with cervical lesions. The use of bi-valent, 4-valent and 9-valent HPV vaccines would potentially prevent lesions in 19%, 33%, and 48%.

Among WLWH efficaciously in care for HIV, demographic and behavioral factors mainly contribute to acquisition of HPV and to development of cervical lesions.

Received May 30, 2018 *Accepted* August 15, 2018

INTRODUCTION

Human papillomavirus (HPV) is the causative agent of the most common sexually transmitted infection (Markovitz *et al.,* 2014; Thorsteinsson *et al.,* 2016). More than 200 genotypes of HPV have been identified, including about 40 that can infect the uterine cervix, having in some cases a well-recognized carcinogenic role in women: it has been estimated that HPV-16 and -18 account for about 70% of all cases of invasive cervical cancer worldwide (IAS-USA, 2015).

Women living with HIV (WLWH) have a 4.2 fold higher rate of HPV infection than HIV-negative women and have significantly higher rates of persistent and recurrent infections (Luque *et al.,* 2006). Moreover, WLWH have greater diversity of HPV genotypes, higher prevalence of multiple genotype infections, and greater presence of carcinogenic high-risk genotypes other than 16 and 18 (IAS-USA, 2015). Consequently, WLWH have an higher rate of subsequent progression to high grade Cervical Intraepithelial Neoplasia 2 and 3 (CIN2-3). Overall, HIV-infected women have a 5.4-fold higher risk for cervical cancer than uninfected women (IAS-USA, 2015; Money *et al.,* 2016; Ellerbrock *et al.,* 2000). For these reasons, international guidelines recommend to vaccinate HIV-positive girls and young women against HPV, because of the heavier burden of HPV infection and associated diseases (ACIP, 2014; WHO, 2014).

Since 2006, two prophylactic vaccines (the bivalent for genotypes 16 and 18, and the 4-valent for genotypes 6, 11, 16, 18) have been licensed to prevent precancerous or dysplastic lesions and diseases caused by High Risk HPV types (HR-HPV) included in the vaccine formulation. A new 9-valent vaccine protecting against five additional HR-HPV genotypes (31/33/45/52/58) has been approved by the FDA in December 2014 and by the European Medicines Agency in June 2015 (Joura *et al.,* 2015; Konopnicki *et al.,* 2016).

The mechanisms leading to the increased burden of HPV in WLWH are poorly understood. It has been suggested that HIV-proteins enable initial HPV infection by disrupting the epithelial tight junctions. Moreover, immune deficits associated with HIV infection contribute to the HPV pathogenesis by preventing spontaneous clearance of HPV (Thorsteinsson *et al.,* 2016). Even in the combination antiretroviral therapy (cART) era, HPV impact among

Key words:
HIV/AIDS; HPV; pre-neoplastic cervical lesions; HPV vaccination.

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WLWH is still higher and harder compared with HIV-negative populations (Money *et al.,* 2016).

Among WLWH, the factors influencing the presence of HPV infection and the development of cervical lesions have been investigated in various studies in different geographic areas, and results of the these studies are contrasting (Clifford *et al.,* 2016; Delory *et al.,* 2017; Kelly *et al.,* 2017; Silva *et al.,* 2015; Thorsteinsson *et al.,* 2016; Travassos *et al.,* 2017; Volpini *et al.,* 2017). In some of these studies, behavioural factors (such as the number of sexual partners) are more significantly linked with HPV prevalence and neoplastic lesions, while in other studies HIV-related factors (such as number of CD4, being or not on cART) have a major role.

The primary objective of this study is to explore the prevalence and the associated factors for HPV infection and for neoplastic cervical lesions in a population of WLWH in care at Santa Maria Annunziata Hospital (OSMA), Florence area, Italy. As secondary objective, we will evaluate the potential impact of different vaccine formulations in our population.

MATERIAL AND METHODS

Study design

We conducted a cross-sectional study, in order to identify risk factors for HPV infection and neoplastic cervical lesions in WLWH stably in care at Santa Maria Annunziata Hospital (OSMA), area of Florence, Central Italy.

Setting and Study Population

OSMA is a tertiary hospital located in the Florence area, Tuscany, Central Italy. The Infectious Diseases Unit has an Inpatients Ward with 18 beds, and an Outpatients Service including Day-hospital and ambulatory care. The Infectious Diseases Unit has approximately 850 HIV+ patients stably in care. WLWH represent the 41% of the whole population of HIV+ patients followed up at OSMA.

All women resulted HIV+, and stably in care at OSMA in the study period 2006-2016, were prospectively enrolled in the study. We considered as stably in care a woman followed up for at least 3 years within the study period, with at least 2 outpatient visits each year. We excluded patients non stably in care (for which only few visits were available), and patients under the age of 18.

Data sources

A gynaecological screening, including HPV testing, had been proposed to all WLWH stably in care at OSMA in the study period. All WLWH who accepted, underwent to a gynaecological examination including HPV test, Pap smear, colposcopy if HPV is positive and, if needed, a cervical biopsy. This screening was practiced with variable timing, usually when the patients already had a consolidated relationship with our staff, consequently after some years of HIV care. In order to explore the role of all HPV genotypes in this population, also those considered at low risk, we decided, according to gynaecologists, to perform colposcopies in all HPV+ women. Colposcopies and cervical biopsies were performed by gynaecologists. PAP test results were classified according to 2001 Bethesda System (Solomon D *et al.,* 2001), histological lesions were classified according to WHO guidelines (WHO, 2013). Demographical and behavioural data were collected prospectively using a standardized questionnaire, and all data were included in the clinical database routinely used for follow-up visits. All HIV-related clinical data were retrospectively collected by the clinical charts.

Outcomes and study variables

We investigated the presence of HPV infection and the presence of pre-neoplastic cervical lesions. Demographical variables included age and ethnical origin; behavioural variables included tobacco exposure and number of sexual partners in the last years; HIV-related and other clinical factors included being on cART and years of cART, CD4 (at nadir and at examination), HIV viral load, risk factor for HIV acquisition, presence of other co-infections (HBV, HCV, other sexually-transmitted disease); HPV-related factors were the presence of HR and multiple genotypes.

Laboratory methods

HPV test was carried out using a system for HPV detection and genotyping by PCR and reverse line blot. Total DNA was extracted by manual (kit QIAamp DNA Mini kit, QIAGEN), or automated methods (Qiasymphony DSP with QIAsymphony DSP Virus/pathogen Midi kit, Qiagen) from cervical samples collected in specific buffer (STM, sample transport medium, Qiagen). A HPV negative sample was included in each batch of extraction to exclude any contamination and DNA was kept at -20°C until PCR amplification. All samples were then amplified and typed by Ampliquality HPV Type Express (AB Analitica, Padua Italy) able to amplify a HPV polymorphic L1 region of ~160 bp, followed by reverse Line Blot (RLB), according to manufacter's instruction. In each run a fragment of the human TST gene (thiosulfate sulfurtransferase rhodanese) was co-amplified to evaluate cell adequacy and quality of DNA extracted.

RLB strips were analyzed using an automatic software (AB Dialux) and then the results were confirmed re-reading manually the strips. In each run we included two negative controls (a HPV negative DNA sample extracted together the samples to be tested and a DNA-free sample) and one positive and already extracted DNA sample.

The test allows to detect 40 high and low risk HPV genotypes (Bouvard *et al.,* 2009): "high-risk types" (Group 1: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59), "HPV probably carcinogenic to humans" (Group 2a: HPV68a and HPV 68b), "HPV possibly carcinogenic" (Gruppo 2B: HPV 26, 53, 64, 66, 67, 69, 70, 73, 82 and "HPV not classified as to its carcinogenicity to humans" (Gruppo 3: HPV 6, 11). It can even also detect other HPV types (40, 42, 43, 44, 54, 55, 61, 62, 71, 72, 81, 83, 84, 87, 89, 90) classified usually as Low- risk HPVs.

Statistical analysis

In the analyses p-values <0.05 were considered statistically significant. Univariate and multiple logistic regression analyses were used for identifying predictive factors of HPV infection and of neoplastic cervical lesions, expressed as odds ratios (OR) and 95 % confidence intervals (CI), using SPSS version 20.0.

This article has been written according to STROBE checklists.

RESULTS

Characteristic of the Study Population

Overall, 346 WLWH are stably in care at OSMA in the study period. Among these, 321 (93%) accepted to be in-

cluded in the study. Mean age of the study population was 41 (18-76, Median 42, IQR 11). About ethnicity, 75% of WLWH were caucasic, remaining patients were from Africa (17%), South America (7%) and Asia (1%). More than half of patients (53%) have tobacco exposure at examination, most of them (58%) had a single sex partner in the last year, but a considerable part of population (27%) reported 3 or more sexual partners in the last years. The presence of other infectious diseases is common in our population: HCV infection is present in 37%, and sexually-transmitted diseases (mainly due to *Gardnerella vaginalis*, *Chlamydia trachomatis*, *Mycoplasma hominis* and *Candida spp*) are reported in 32%. About HIV, the mean duration of infection in our population was 13 years, large majority where on cART (95%), with suppressed HIV viremia in 82%. Sexual exposure and use of injective drugs where the most frequent risk factors for HIV acquisition.
Detailed characteristics of the study population are reported in *Table 1*.

Table 1 - *Characteristics of the Study Population.*

N° of patients	*321*
Demographic factors	
Age (mean, median)	41 (18-76), 42
Origin (%):	
Caucasic	75
Not caucasic	25
Behavioural factors	
Tobacco exposure (%):	
No	47
1-20 sig/day	44
>20 sig/day	9
Number of sexual partners in the last year (%):	
0	8
1	58
2	7
≥3	27
HIV-related and clinical factors	
Year of HIV infection (mean, years)	13
Patients on cART (%)	95
Years of cART (%):	
≤3	23
>3	77
CD4 count (mean, median, IQR):	
Nadir	230, 216, 200
At examination	593, 576, 395
HIV viral load (%):	
≤50	82
51-10.000	11
>10.000	7
Risk factor for HIV acquisition (%):	
Sexual exposure	54
Injective drug user	44
Other/Not determined	2
Presence of other infection/diseases (%):	
HBV	3
HCV	37
Sexually Transmitted Diseases	32

Prevalence of HPV infection

Among the 321 WLWH included, 161 (50.2%) resulted HPV+. Among the 161 HIV+/HPV+ women, high-risk (HR) genotypes for cervical cancer were present in 56%, both as single and multiple infections. Other genotypes identified were Intermediate- and Low-risk (IR and LR). Among HR genotypes, the genotype most represented was 16 (18%), followed by 58 (11%), 51 (10%) and 45 (9%). Genotype 18 has been found in 7% of cases. Multiple genotypes were identified in 56 WLWH (35%). Multiple infections were due to two or more HR genotypes in 20 patients, to a combination of HR and IR/LR in 25 patients, and to two or more IR/LR genotypes in the remaining 11 women.

Factors associated to HPV infection and to presence of HR genotypes

Data about factors associated to HPV infection and presence of HR genotypes are reported in *Table 2*. Factors associated with having HPV infection were: age (with increasing age being a protective factor, OR 0.96; IC 95% 0.93- 0.99), being not-caucasic (OR 2.0; IC 95% 1.2-3.4), having 3 or more sexual partners in the last year (OR 3.0; IC 95% 1.1-7.7), and years of HIV infection (with increasing year being a protective factor, OR 0.9; IC 95% 0.92-0.97). At multivariate analysis, increasing year of HIV infection remains the only significant protective factor.
About the presence of HR genotypes among HPV+ women, no associated factors emerged, except increasing year of HIV infection, being a protective factors (OR 0.9; IC 95% 0.88-0.98). At multivariate analysis considering age also, this factor is no longer significant.

Prevalence of cervical lesions

Among the 161 HPV+ WLWH, Pap smear citology showed ASCUS (Atypical Squamous Cells of Undetermined Significance) in 36 (22%), LSIL (Low grade Squamous Intraepithelial Lesion) in 21 (13%) and HSIL (High grade Squamous Intraepithelial Lesion) in 4 (2%). Colposcopy was proposed to all HPV+ participants and performed in 154. Histological lesions were present in 47 women (30%), who underwent to cervical biopsy, according to local gynaecologist protocols. Among these 47 women, condylomatosis was present in 26, while pre-neoplastic lesions were present in the remaining 21: CIN 1 (Cervical Intraepithelial Neoplasia) in 16, CIN 2 in 4, and CIN 3 in 1 woman.

Factors associated to presence of cervical pre-neoplastic lesions

Data about factors associated to presence of cervical pre-neoplastic lesions are reported in *Table 3*. Factors associated with having these kind of lesions were: being not caucasic (as protective factor, OR 0.2; IC 95% 0.04- 0.9), smoking 1-20 cigarettes per day (OR 3.3; IC 95% 1.1-10.0), having 2 sexual partners in the last year (OR 16; IC 95% 1.3-194.0), or having the use of injective drugs as risk factor for HIV acquisition (OR 3.4; IC 95% 1.2-9.7). At multivariate analysis, no associated factors were identified.

Potential impact of different vaccine formulation

In consideration of the distribution of HPV genotypes in our population, and also considering the presence of multiple infections including more than one HR genotypes, we speculated about the potential impact of a complete vaccination coverage with different vaccine formulations

in our study population. Assuming a complete vaccine efficacy, and an adequate timing in vaccination, the use of bi-valent, 4-valent and 9-valent formulations would have potentially prevented the pre-neoplastic lesions in 19%, 33% and 48% of WLWH in the study population, respectively. On the contrary, among the 21 patients with cervical pre-neoplastic lesions, 11 (52%) have HPV genotypes not included by any vaccine formulations.

DISCUSSION

We investigated the presence of HPV infection, and the presence of cervical pre-neoplastic lesions, in a cohort of WLWH followed up at OSMA, in the period 2006-2016.
Almost all WLWH stably in care at OSMA were recruited in the study. We did not systematically investigated the reasons why 25 women out of 346 refused to be included, but from the clinical records a recent gynaecological evaluation performed elsewhere is often reported among these patients.

Key results and interpretation

The prevalence of HPV infection among WLWH included in the study (50,2%) and the prevalence of multiple infections (35% among HPV+ patients) is higher than those reported in the general population women. A population based study performed in Italy showed an HPV prevalence in general population of 15%, and a prevalence of multiple infections among HPV+ women of 17% (Giorgi Rossi et al., 2010). On the contrary, the prevalence of HR genotypes in our study population is lower than in the general population (56% vs 71%) (Giorgi Rossi *et al.,* 2010).
Considering other studies among WLWH, the prevalence of HPV infection in our population (50.2%) is higher compared to other studies (eg 23% in Konopnicki *et al.,* 19% in Delory *et al.,* 2017), but it it is similar to that reported by Silva *et al.,* 2015 (61%). The prevalence of HR genotypes among HPV+ patients (56%) is higher in our population compared to other studies, too. As already suggested by literature (Thorsteinsson *et al.,* 2016; Konopnicki *et al.,*

Table 2 - *Associated factors to HPV infection and to presence of high-risk genotypes in 321 HIV+ women, 2006-2016.*

	HPV+/HIV+	*HPV-/HIV+*	*OR (IC 95%)*	*High-risk genotypes*	*No high-risk genotypes*	*OR (IC 95%)*
N° of patients (%)	*161 (50)*	*160 (50)*		*91 (56)**	*54 (33)**	
			Demographic factors			
Age (mean)	40.4	42.8	0.96 (0.93-0.99)	40.4	40.9	0.9 (0.9-1.0)
Origin (%):						
Caucasic	110 (68)	130 (81)	1	62 (68)	39 (72)	1
Not caucasic	51 (32)	30 (19)	2.0 (1.2-3.4)	29 (32)	15 (28)	1.2 (0.6-2.5)
			Behavioural factors			
Tobacco exposure (%):						
No	72 (45)	80 (50)	1	35 (38)	27 (50)	1
1-20 sig/day	70 (43)	71 (44)	1.1 (0.7-1.7)	46 (51)	20 (37)	1.8 (0.9-3.7)
>20 sig/day	19 (12)	9 (6)	2.3 (0.9-5.5)	10 (11)	7 (13)	1.1 (0.4-3.3)
N° of sexual partners in the last year (%):						
0	8 (5)	15 (9)	1	2 (3)	3 (5)	1
1	89 (55)	99 (63)	1.7 (0.7-4.2)	50 (55)	32 (59)	2.3 (0.4-14.8)
2	9 (6)	11 (7)	1.5 (0.4-5.2)	6 (7)	2 (4)	4.5 (0.4-49.6)
≥3	54 (34)	34 (21)	3.0 (1.1-7.7)	32 (35)	17 (32)	2.8 (0.4-18.6)
			HIV-related and clinical factors			
Year of HIV infection (mean. years)	11.6	14.8	0.9 (0.92-0.97)	10.5	13.8	0.9 (0.88-0.98)
Patients on cART (%)	153 (95)	150 (94)	0.8 (0.3-2.0)	86 (95)	51 (95)	1.2 (0.7-19.6)
Year of cART (>3) (%)	115 (75)	120 (80)	0.8 (0.2-2.7)	61 (71)	43 (84)	0.7 (0.3-2.9)
CD4 count (mean):						
Nadir	234	227	1.0 (0.99-1.01)	211	257	0.99 (0.98-1.0)
At examination	587	598	1.0 (0.99-1.01)	539	638	0.99 (0.98-1.0)
HIV viral load (%):						
≤50	128 (80)	136 (85)	1	71 (78)	45 (84)	1
51-10.000	20 (12)	14 (9)	1.5 (0.7-3.2)	10 (11)	6 (12)	1.1 (0.4- 3.1)
>10.000	13 (8)	9 6)	1.5 (0.6-3.7)	10 (11)	2 (4)	3.2 (0.7-15.1)
Risk factor for HIV acquisition (%):						
Sexual exposure	93 (58)	82 (51)	1	53 (58)	29 (53)	1
Injective drug user	65 (40)	75 (47)	0.8 (0.5-1.2)	38 (42)	22 (41)	0.9 (0.5-1.9)
Other/Not determined	3 (2)	3 (2)	0.9 (0.2-4.5)	0 (0)	3 (6)	0.7 (0.5-1.1)
Presence of co-infection (%):						
HBV	5 (3)	4 (3)	1.2 (0.3-4.7)	3 (3)	1 (2)	1.8 (0.2-17.8)
HCV	61 (38)	59 (37)	1.0 (0.7-1.6)	33 (36)	22 (41)	0.8 (0.4-1.7)
Other sexually transmitted diseases	60 (37)	44 (28)	1.5 (0.9-2.4)	38 (42)	18 (33)	1.4 (0.7-2.9)

*16 HPV-PCR positive specimens resulted as not typable.

2016; Volpini *et al.,* 2017; de Pokomandy *et al.,* 2017; Delory *et al.,* 2017) the HPV-16 genotype is the most represented, but many other genotypes other than HPV-16 are well represented in our population, with genotypes 51 and 58 being the most represented. This wide distribution of genotypes, as well as the increased prevalence of multiple infection, may be explained by the lower rate of HPV clearance among WLWH, as suggested by some authors (Thorsteinsson *et al.,* 2016; Travassos *et al.,* 2017).

In our population, the presence of HPV infection is associated with demographical factors (age and ethnicity) and to behavioural factors (having 3 or more sexual partners in the last year). Increasing year of HIV infection is a protective factor, also, but this is probably the effect of the increasing age of the population. The protective effect of age has been already reported in literature, with younger WLWH being at increased risk for HPV acquisition (Delory *et al.,* 2017; Silva *et al.,* 2015) such as the increasing number of sexual partners (Thorsteinsson *et al.,* 2016). No other HIV-related or clinical factors are linked to the risk of HPV acquisition in our population. This is probably due to the fact that the study population is stably and efficaciously in care for HIV with undetectable viremia, and both HPV+ and HPV- patients are mostly on efficacious cART since many years. On the contrary, other studies in literature suggested that having lower CD4 count, a shorter duration of cART, or a detectable HIV-RNA, are factors associated with the increased risk for HPV acquisition (Thorsteinsson *et al.,* 2016; Delory *et al.,* 2017; Silva *et al.,* 2015).

As for HPV infection, the presence of pre-neoplastic lesions in our population are associated to demographic and behavioural factors only, in particular being caucasic, smoking 1-20 cigarettes per day, having 2 sexual partners in the last years, and use of injective drugs as risk factor for HIV are factors increasing the risk. In other studies some HIV- and HPV-related factors, such as the shorter duration of cART, the lower level of CD4, and the presence of HR HPV genotypes have been associated with an higher risk of cervical lesions (Thorsteinsson *et*

Table 3 – *Associated factors to presence of pre-neoplastic lesions in 154 HPV+/HIV+ women, 2006-2016*

	Patients with pre-neoplastic lesions	*Patients without pre- neoplastic lesions*	*OR (IC 95%)*
N° of patients (%)	21 (14)	133 (86)	
Demographic factors			
Age (mean)	39.0	40.4	1.0 (0.9-1.0)
Origin (%):			
Caucasic	19 (90)	87 (65)	1
Not caucasic	2 (10)	46 (35)	0.2 (0.04-0.9)
Behavioural factors			
Tobacco exposure (%):			
No	5 (24)	63 (47)	1
1-20 sig/day	14 (66)	53 (40)	3.3 (1.1-10.0)
>20 sig/day	2 (10)	17 (13)	1.5 (0.3-8.3)
N° of sexual partners in the last year (%):			
0	1 (5)	8 (6)	1
1	12 (57)	72 (54)	1.3 (0.2-11.6)
2	6 (28)	3 (2)	16.0 (1.3-194.6)
≥3	2 (10)	49 (38)	0.3 (0.03-4.0)
HPV-related. HIV-related and clinical factors			
Presence of High-risk HPV genotypes	14 (66)	71 (53)	1.3 (0.5-3.5)
Presence of multiple HPV genotypes	8 (38)	42 (32)	1.1 (0.4-2.8)
Year of HIV infection (mean. years)	11	12	0.9 (0.9- 1.0)
Patients on cART (%)	20 (95)	127 (95)	1.0 (0.9- 1.0)
Year of cART (>3) (%)	15 (75)	96 (76)	1.0 (0.9- 1.1)
CD4 count (mean):			
Nadir	255	234	1.0 (0.9- 1.0)
At examination	642	594	1.1 (0.9- 1.1)
HIV viral load (%):			
≤50	18 (85)	105 (79)	1
51-10.000	2 (10)	16 (12)	0.7 (0.2-3.4)
>10.000	1 (5)	11 (9)	0.5 (0.1-4.4)
Risk factor for HIV acquisition (%):			
Sexual exposure	6 (29)	81 (61)	1
Injective drug user	13 (62)	51 (38)	3.4 (1.2-9.7)
Other/Not determined	2 (10)	1 (1)	27.0 (2.1-342.2)
Presence of other diseases/infetions (%):			
HBV	1 (5)	5 (4)	1.3 (0.1-11.5)
HCV	11 (52)	47 (35)	2.0 (0.8-5.1)
Sexually Transmitted Diseases	8 (38)	49 (37)	1.1 (0.4-2.7)

al., 2016; Delory *et al.,* 2017; Clifford *et al.,* 2016; Clifford *et al.,* 2017), but these associations are not present in our population. In our population, we can speculate that being stably and efficaciously in care for HIV may represent a protective factor against HPV-related cervical lesions also.

According to our limited data about the potential efficacy of the different vaccine formulation, the recently released 9-valent vaccine would have been able to prevent about 50% of pre-neoplastic lesions. On the other hand, other 50% of patients with pre-neoplastic lesions have HPV genotypes not included in any vaccine formulation. In other studies, the potential benefits of vaccination were judged to be greater, with up to 90% of women potentially protected by 9-valent formulation (Kelly *et al.,* 2017). Consequently, 9-valent HPV vaccination should be offered to these women. Another study suggests that HIV viral suppression results in higher antibody responses in WLWH vaccinated with the 4-valent HPV vaccine. Thus, planning HPV vaccination to occur when persons are virologically suppressed would be optimal strategy for maximizing immune response. Moreover, in the same study the HPV vaccination has been suggested to be highly beneficial in HIV-positive women, as 95% of women in that cohort were seronegative for at least 1 of the 4 HPV genotypes targeted by the vaccine. This study findings provided evidence that older WLWH can still benefit from HPV (Money *et al.,* 2016).

Limitations

The main limitation of our study is represented by the lack of information about HPV vaccine coverage in our population. Consequently, the impact of vaccination in HPV dynamics among these WLWH cannot be evaluated. Other limits are in generalizability of our results: as it is a monocentric study, our results are limited to similar population only, particularly women mostly caucasic, and efficaciously in care for HIV.

CONCLUSIONS

Despite these limitation, the study suggests interesting remarks. The main result of this study is that, in a population stably and efficaciously in care for HIV, some demographic and behavioural factors (in particular the smoking, the number of sexual partners and the use of injective drugs) may still contribute to the acquisition of HPV infection and to the development of cervical lesions. Specific information about these factors should be given to patients. Moreover, our results support the use of 9-valent HPV vaccine formulation in WLWH.

Conflict of interest

The Authors declare that there is no conflict of interest.

Declaration

Preliminary results of this study have been presented as abstract at 9th ICAR (Italian Congress on AIDS and Retroviral Research), Siena, 12-14 June 2017.

Ethics

It is a retrospective descriptive study. All actions described into the Study are part of the common clinical practice, and no additional activities had been performed for specific study purposes. Data about patients have been anonymized, and all findings are presented in a general manner.

Acknowledgments

We acknowledge Dr. Assunta Navarra, National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy, for her support in statistical analysis.

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