ORIGINAL PAPER

Prevalence and genotypic characteristics of cervical papillomaviruses in a cohort of HIV-positive women in Peru

Jaime A. Collins[1,2], Miriam L. Soria[3], Rosa E. Borchane[4]

[1]Infectious Diseases Service, Department of Internal Medicine, Almenara General Hospital, EsSalud, Lima, Peru
[2]Vice-Rectorate of Research, Faculty of Medicine, Federico Villarreal National University, Lima, Peru
[3]Cytopathology and Genetics Service, Department of Clinical Pathology, Almenara General Hospital, EsSalud, Lima, Peru
[4]Gynecology and Obstetrics Service, Aurelio Diaz Ufano y Peral Hospital, Almenara Health Network, EsSalud, Lima, Peru

Abstract

Introduction: Papillomaviruses are the main causes of cervical cancer. Objective of the study was to determine the prevalence and genotypic characteristics of cervical papillomaviruses in HIV (human immunodeficiency virus)-positive women.

Material and methods: Prospective cross-sectional observational study among HIV-positive women at Almenara General Hospital in Peru, between November 2017 and December 2018, was conducted. HPV detection and typing was performed using a polymerase chain reaction technique that evaluated 21 genotypes, stratified according to oncogenic risk, i.e., six low-risk or non-oncogenic (6, 11, 42, 43, 44, and 81), and fifteen high-risk or truly oncogenic (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, and 68).

Results: We evaluated 148 HIV-positive women. The overall prevalence of papillomavirus infection of the cervix was 41% (61/148). Of these infections, 75% (46/61) were caused by oncogenic genotypes, and in this risk group, 57% (26/46) of women were affected by a single papillomavirus genotype. The most frequent non-oncogenic genotypes detected were human papillomavirus (HPV)-6 in 26% (16/61) and HPV-11 in 23% (14/61) of women. The most frequent oncogenic genotypes were HPV-16 (16%; 10/61), HPV-52 (13%; 8/61), HPV-58 (13%; 8/61), HPV-53 (12%; 7/61), HPV-31 (10%; 6/61), and HPV-45 (10%; 6/61). The frequency of HPV-18 reached 5% (3/61), while concurrent infection with HPV-16/18 was detected in 3% (2/61) of patients.

Conclusions: The prevalence of papillomavirus infection of the cervix in HIV-positive women is high in our center, with three quarters caused by oncogenic genotypes. Genotype 16 was the most frequent high-risk papillomavirus.

HIV AIDS Rev 2026; 25, 1: 70-75
DOI: https://doi.org/10.5114/hivar/186817

Key words: HIV, genotype, HPV, cervix uteri, Peru.

Introduction

Papillomaviruses are the main causes of cervical cancer [1]. Most women in low- and middle-income regions have this malignant neoplasms. Moreover, HIV (human immunodeficiency virus)-positive women have a higher occurrence of papillomavirus infections and cervical cancer than HIV-negative women [2].

Address for correspondence: Jaime A. Collins, Infectious Diseases Service, Department of Internal Medicine, Almenara General Hospital, EsSalud, Lima, Peru, e-mail: jcollinslp@gmail.com

Article history:
Received: 28.09.2023
Revised: 08.01.2024
Accepted: 04.04.2024
Available online: 13.01.2026

International Journal of HIV-Related Problems
HIV & AIDS Review

A few systematic reviews have addressed the genotypic characteristics of cervical papillomaviruses and their clinical consequences in HIV-positive women, including studies from Latin America [3-5]. However, publications on this topic are practically unknown in Peru. Therefore, the objective of the study was to determine the prevalence and genotypic characteristics of cervical papillomaviruses in HIV-positive women in a national hospital. This study will be used as a basis to implement preventive measures against cervical cancer in HIV-positive women.

Material and methods

Design and population

A prospective observational cross-sectional study was carried out.

All HIV-positive women who had a consecutive molecular test for cervical papillomaviruses between November 2017 and December 2018, in an outpatient clinic of the Division of Infectious Diseases, Guillermo Almenara Irigoyen National Hospital, EsSalud (Peruvian Social Health Insurance), were considered for enrollment. During that period, the initial stage of a systematic screening for papillomaviruses in HIV-positive women in the hospital was carried out. Physicians were free to provide their HIV-positive female patients a gynecological evaluation formally implemented in the division; this evaluation included screening for papillomaviruses. There were no exclusion criteria, except that the cervical specimen was not suitable for molecular evaluation of papillomaviruses.

Data collection

In this study, the following variables were included: age at the time of the study, duration of HIV infection (from serological evidence of HIV infection to the time of the study), CD4+ T lymphocyte count in cells per microliter, antiretroviral therapy (ART) at the time of the study (yes versus no), virological response to ART (success versus failure), and cervical papillomavirus infection according to a molecular test (negative versus positive oncogenic or non-oncogenic). Both data on CD4+ T lymphocytes and HIV viral load (maximum six months before the study) were collected. For the purposes of this research, virological success of ART was an HIV viral load of less than 200 copies per milliliter, and failure was considered a viral load greater than this cut-off point. Cervical papillomavirus infection was evaluated as single or multiple according to the number of genotypes found. Therefore, infection with a single papillomavirus genotype was considered a single infection, while infection with two or more papillomavirus genotypes was deemed a multiple infection.

All data were collected from an electronic platform of the Division of Infectious Diseases (CB01), which was used for the care of HIV-positive patients in the hospital. Also, data on cervical papillomavirus genotype were re-collected from a folder with printed laboratory reports in chronological order, which is kept by the Division of Infectious Diseases.

Uterine cervix cell sampling

Cervix cell samples for papillomavirus analysis were collected using a cyto-brush, and then placed in a liquid transport medium in a collection tube. This was carried out as part of the outpatient consultation by a gynecologist (RB). All women were placed in a lithotomy position on a gurney, with a vaginal speculum. In addition, patients came for scheduled visit appointment as part of the hospital management system.

Papillomavirus investigation

This was carried out using a polymerase chain reaction technique [GenoArray diagnostic kit for human papillomavirus (HPV) 21-HBGA-21, Hybribio®] that detects 21 genotypes, stratified according to oncogenic risk: six low-risk or non-oncogenic (HPV-6, HPV-11, HPV-42, HPV-43, HPV-44, and HPV-81), and fifteen high-risk or truly oncogenic (HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-51, HPV-52, HPV-53, HPV-56, HPV-58, HPV-59, HPV-66, and HPV-68). The test was performed in the Division of Cytopathology and Genetics of the hospital, under the supervision, interpretation, and validation of a member of the research team (MS).

Statistical analysis

The study results were presented and analyzed by means of descriptive statistics.

Ethical issues

All cases were analyzed anonymously for the proposed study, and only the authors had access to the database of these patients. There was no additional risk to the women evaluated in the study, as cervical papillomavirus genotype screening is part of the international standard of evaluation in both HIV-positive and HIV-negative women.

Results

A total of 148 women were included in the study, which covered nearly half of all HIV-positive women treated at the Almenara Hospital. The general characteristics of the studied population are presented in Table 1. Based on average, the cohort was composed of middle-aged women, with eleven-year as documented time of retroviral infection. In addition, vast majority of the patients were on ART, with a successful virologic response and high level of CD4+ T lymphocytes on average.

Table 1. General characteristics (*N* = 148)

Characteristic	
Mean age in years (SD)	46 (12)
Mean time of HIV infection in years (SD)	11 (7)
Median CD4+ T lymphocyte count in cell per milliliter (SD)	489 (283)
Number of people on antiretroviral therapy[a] (%)	145 (98)
Number of virological successes with antiretroviral therapy (%)	135 (93)

[a]Including three people who were about start therapy at the time of evaluation.
SD – standard deviation

Cervical papillomavirus infection prevalence in the entire cohort was 41% (61/148), which refers to the total number of papillomavirus infections of both non-oncogenic and truly oncogenic genotypes. In the last group only, the prevalence was 31% (46/148). The spectrum of these infections is shown in Figure 1. In the oncogenic group, 33% (15/46) of the patients were also infected with non-oncogenic genotypes. Similarly, multiple papillomavirus infection was six times higher in the oncogenic group than in the non-oncogenic group, in relative terms.

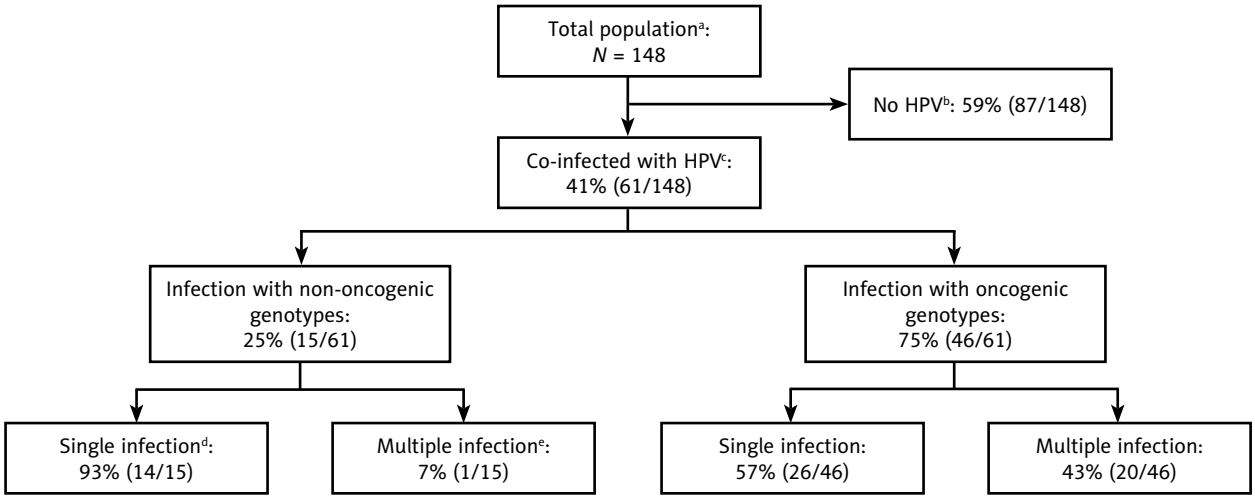
The individual frequencies of papillomavirus genotypes are shown in Table 2, stratified by the risk they imply. HPV-6 and HPV-11 were the most frequent non-oncogenic genotypes. There were no cases of infection with HPV-42 and HPV-43 genotypes. The six most frequent oncogenic genotypes detected were as follows: HPV-16 (16%), HPV-52 (13%), HPV-58 (13%), HPV-53 (12%), HPV-31 (10%), and HPV-45 (10%). HPV-18 genotype frequency was lower (5%), and there were no cases of HPV-35 genotype infection.

Table 2. Frequency of papillomavirus genotypes in the cervix (*n* = 61)

Genotypes	*n* (%)
Low oncogenic risk[a]	
HPV-6	16 (26)
HPV-11	14 (23)
HPV-44	1 (2)
HPV-81	7 (12)
High oncogenic risk[b]	
HPV-16	10 (16)
HPV-18	3 (5)
HPV-31	6 (10)
HPV-33	3 (5)
HPV-39	3 (5)
HPV-45	6 (10)
HPV-51	2 (3)
HPV-52	8 (13)
HPV-53	7 (12)
HPV-56	2 (3)
HPV-58	8 (13)
HPV-59	3 (5)
HPV-66	2 (3)
HPV-68	2 (3)

[a]Here were no cases of HPV-42 and HPV-43.
[b]There were no cases of HPV-35.

Additionally, two women had concurrent infection with HPV-16 and HPV-18 (or HPV-16/18) genotypes, recognized as the highest oncogenic risk genotypes (3%; 2/61).



[a]Total number of HIV-positive women included in the study. [b]HIV infection only. [c]HPV/HIV co-infection. [d]Infection with a single papillomavirus genotype. [e]Infection with two or more papillomavirus genotypes.

Figure 1. Spectrum of cervical papillomavirus infection

Table 3. Frequency of oncogenic papillomaviruses in HIV-positive women by region [4]

Genotype/Region	Cervical cytology	
HPV-16		
Local[a], 16% (10/61)	Normal	Low-grade
Africa	13%	22%
Asia	22%	22%
Europe and North America	18%	16%
Latin America	24%	25%
HPV-18		
Local[a], 5% (3/61)	Normal	Low-grade
Africa	10%	14%
Asia	15%	11%
Europe and North America	9%	10%
Latin America	9%	14%
HPV-31		
Local[a], 10% (6/61)	Normal	Low-grade
Africa	7%	8%
Asia	15%	11%
Europe and North America	12%	10%
Latin America	11%	15%
HPV-45		
Local[a], 10% (6/61)	Normal	Low-grade
Africa	6%	11%
Asia	5%	5%
Europe and North America	6%	9%
Latin America	4%	7%
HPV-52		
Local[a], 13% (8/61)	Normal	Low-grade
Africa	13%	17%
Asia	13%	13%
Europe and North America	13%	13%
Latin America	3%	15%
HPV-58		
Local[a], 13% (8/61)	Normal	Low-grade
Africa	11%	15%
Asia	12%	11%
Europe and North America	14%	12%
Latin America	12%	19%

[a]*Findings of the current study.*

Discussion

This study shows molecular evidence on the magnitude and diversity of HPV infection in the cervix of HIV-positive women on ART in Peru. To the authors' knowledge, this is the first study of its type at the national level. Cervical infection prevalence of both non-oncogenic and oncogenic papillomavirus genotypes was high. Additionally, three-quarters of these infections were caused by oncogenic genotypes.

The prevalence of cervical infection with oncogenic papillomavirus genotypes in the current study is similar to that described in Asia (33%; 1,005/3,003), but lower than in Europe and North America (50%; 3,958/7,984), Africa (74%; 4,896/6,578), and Latin America (69%; 1,606/2,318), according to a systematic review published in 2017 [4]. However, differences are more noticeable with the rates reported from Africa and Latin America, whereas in the current study, the prevalence was less than half of that reported from Africa and Latin America.

A more recent systematic review on a selection of studies between June 2016 and January 2020 showed lower rates of co-infection with oncogenic genotypes in all regions, except Latin America, where the opposite is true [5]. Therefore, in Asia, the rates ranged from 33% to 26% (58/216), in Africa, from 74% to 66% (2,542/3,870), in Europe and North America, from 50% to 40% (862/2,174), and in Latin America, from 69% to 74% (490/668), which may be a warning sign for the region. Nevertheless, in this review, the added population was smaller than the previous one, due to a limited number of studies accumulated in the last few years.

Another systematic review from Latin America only, demonstrated a weighted cervical infection prevalence of oncogenic papillomavirus of 51% (95% CI: 42-60%) [3], which is in accordance with what has been mentioned so far.

From a country-by-country perspective, comparing recent data, cervical infection prevalence with oncogenic papillomavirus genotypes is similar to Manaus in northwestern Brazil [6], but lower than in southeastern Brazil (seven of eight studies) [7] as well as in Kenya [8] and urban Burundi [9] in Africa. In comparison with Belgium [10] and Denmark [11], the prevalence is higher (Table 4). These results seem to reinforce the trend of a higher prevalence in Africa, while considering that each reality is different, with possible significant variations within the same country.

On the other hand, in this study, the individual frequencies of the oncogenic genotypes revealed variable behavior in comparison with those of other regions of the world [4]. However, the HPV-16 and HPV-18 genotype frequencies, recognized as having the highest oncogenic risk, were lower. The comparison was made among women who had normal and low-grade cervical cytology. Frequencies of the other oncogenic genotypes with a higher presence in the current study were similar or, in some cases, higher than data from other regions of the globe (Table 3).

The HPV-53 prevalence reached 12% (7/61) in the present study. However, it could not be compared with the other regions, because it was not part of the list of oncogenic genotypes for the review [4]. In contrast, it is interesting that there were no cases of HPV-35 infection in our study. In other regions, this genotype was shown not marginal: in Africa (10% and 16%), in Asia (6.6% and 7.3%), in Europe and North America (7% in each case), and in Latin America (9% and 8%) for normal and low-grade cervical cytology, respectively [4].

Table 4. Prevalence of cervical papillomaviruses in HIV-positive women in selected countries

Authors	City or region	Country	No. of patients	Prevalence according to oncogenic risk, %	
				Non-oncogenic HPV	Oncogenic HPV
Present study	Lima	Peru	148	10	31
Texeira *et al.* [6]	Amazonas	Brazil	299	NR	31
Freitas *et al.* [7]	Southeast	Brazil	2,166	12-71	17-88
Menon *et al.* [8]	SR	Kenia	2,116	NR	64[a]
Ndizeye *et al.* [9]	Urban	Burundi	151	0	46
	Rural	Burundi	150	11	19
Konopnicki *et al.* [10]	Brussels	Belgium	508	NR	23
Thorsteinsson *et al.* [11]	NR	Dinamarca	295	NR	26

[a]95% CI: 50-77%.
NR – not reported, SR – systematic review

Several factors may be related to the lower occurrence of co-infection observed in the study. Firstly, the patients evaluated represent HIV-positive women from the general population rather than high-risk sub-groups, such as women engaged in sex work, which has been extensively documented in a systematic review [12]. Secondly, the protective effect of ART was reported in another systematic review [13]. Women on ART had a lower cervical infection prevalence with oncogenic papillomaviruses compared with women who were not on antiretrovirals. Nearly all women in this study were receiving ART. Based on the review, the administration of such therapy may result in a reduced occurrence of high-grade lesions (or cancer) in the cervix. Apart from taking ART, evidence of a successful virologic response was observed in the vast majority of women in the current study. Thirdly, a high level of CD4+ T lymphocyte count is also associated with better outcomes [13], which was confirmed in our study with an average CD4+ T lymphocyte count close to normal, although with a wide standard deviation. The protective effect attributable to ART may be mediated, among others, by the restoration in the level and functionality of CD4+ T lymphocytes. However, a high basal level of these lymphocytes also supports the protective response against papillomavirus infection. For this reason, the best clinical scenario is early diagnosis of HIV infection and prompt initiation of ART.

The results of this study are important, because they can be translated into concrete prevention measures, especially against cervical cancer, which is the most frequent malignant neoplasm in Peruvian women [14, 15]. A measure against papillomaviruses is immunization with vaccines [16-18]. This study found seven components of the oncogenic genotypes, which are part of the locally available 9-valent vaccine against papillomaviruses [19]. These genotypes include HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58. Out of these seven, five were among the most frequent: HPV-16, HPV-31, HPV-45, HPV-52, and HPV-58, as shown in Table 2. Therefore, our study support systematic vaccination against papillomaviruses in HIV-positive women who are one of the highest risk groups for cervical cancer development. This approach is even more relevant if we consider that the patients evaluated in the research did not have acquired immunity by vaccination against papillomaviruses, as it is probably the case with the rest of HIV-positive women at the national level. In fact, vaccination against papillomavirus in women or people in general, should be given before starting sexual life. However, this does not happen in real life, especially in regions with lower incomes.

There are two important limitations of the study to acknowledge. First, is its cross-sectional design; the evaluation of papillomavirus infection could also be done in a longitudinal manner, allowing to determine more accurately the persistence of infection by these viruses and therefore, to better define the risk of cervical cancer, among other major outcomes. Second, it does not include cytology of the cervix; changes in cytology or histology of the cervix could be used to measure the effect of papillomavirus infection. Furthermore, a relationship between these could be established. However, the limitations are relative, given that the main objective of the study was to determine the prevalence and genotypic characteristics of cervical papillomavirus infection. In addition, such limitations do not detract from the validity of the present study, which on the one hand, is pioneering in the focused population, and on the other hand, has been carried out systematically and accurately with a significant size of sample. Hence, the study can serve as a basis for other research in the directions proposed.

Conclusions

At the Guillermo Almenara Irigoyen National Hospital, EsSalud, the overall prevalence of cervical papillomavirus infection in HIV-positive women is high. Three quarters of these infections are caused by oncogenic genotypes. Infection pattern with a single papillomavirus genotype is more frequent than the multiple infection pattern. Papillomavirus-16 is the most frequent high oncogenic risk genotype. Concurrent infection with papillomaviruses 16 and 18

is low. A comparative perspective demonstrates that the results are similar or better than other regions. However, the situation could improve with the implementation of concrete measures, including vaccination against papillomaviruses in HIV-positive women and application of such vaccinations in the general population.

Disclosures

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

References

1. Crosbie EJ, Einstein MH, Franceschi S, Kitchener HC. Human papillomavirus and cervical cancer. Lancet 2013; 382: 889-899.
2. Liu G, Sharma M, Tan N, Barnabas RV. HIV-positive women have higher risk of human papilloma virus infection, precancerous lesions, and cervical cancer. AIDS 2018; 32: 795-808.
3. Caicedo-Martínez M, Fernández-Deaza G, Ordóñez-Reyes C, Olejua P, Nuche-Berenguer B, Mello MB, Murillo R. High-risk human papillomavirus infection among women living with HIV in Latin America and the Caribbean: a systematic review and meta-analysis. Int J STD AIDS 2021; 32: 1278-1289.
4. Clifford GM, Tully S, Franceschi S. Carcinogenicity of human papillomavirus (HPV) types in HIV-positive women: a meta-analysis from HPV infection to cervical cancer. Clin Infect Dis 2017; 64: 1228-1235.
5. Dickey BL, Coghill AE, Ellsworth GB, Wilkin TJ, Villa LL, Giulia-no AR. An updated systematic review of human papillomavirus genotype distribution by cervical disease grade in women living with human immunodeficiency virus highlights limited findings from Latin America. Sex Transm Dis 2021; 48: e248-e254. DOI: 10.1097/OLQ.0000000000001412.
6. Teixeira MF, Sabidó M, Leturiondo AL, de Oliveira Ferreira C, Torres KL, Benzaken AS. High risk human papillomavirus prevalence and genotype distribution among women infected with HIV in Manaus, Amazonas. Virol J 2018; 15: 36. DOI: 10.1186/s12985-018-0942-6.
7. Freitas BC, Suehiro TT, Consolaro ME, Silva VR. HPV infection and cervical abnormalities in HIV positive women in different regions of Brazil, a middle-income country. Asian Pac J Cancer Prev 2015; 16: 8085-8091.
8. Menon S, Wusiman A, Boily MC, Kariisa M, Mabeya H, Luchters S, et al. Epidemiology of HPV genotypes among HIV positive women in Kenya: a systematic review and meta-analysis. PLoS One 2016; 11: e0163965. DOI: 10.1371/journal.pone.0163965.
9. Ndizeye Z, Vanden Broeck D, Lebelo RL, Bogers J, Benoy I, Van Geertruyden JP. Prevalence and genotype-specific distribution of human papillomavirus in Burundi according to HIV status and urban or rural residence and its implications for control. PLoS One 2019; 14: e0209303. DOI: 10.1371/journal.pone.0209303.
10. Konopnicki D, Manigart Y, Gilles C, Barlow P, De Marchin J, Feoli F, et al. High-risk human papillomavirus genotypes distribution in a cohort of HIV-positive women living in Europe: epidemiological implication for vaccination against human papillomavirus. AIDS 2016; 30: 425-433.
11. Thorsteinsson K, Storgaard M, Katzenstein TL, Ladelund S, Rønsholt FF, Johansen IS, et al. Prevalence and distribution of cervical high-risk human papillomavirus and cytological abnormalities in women living with HIV in Denmark – the SHADE. BMC Cancer 2016; 16: 866. DOI: 10.1186/s12885-016-2881-1.
12. Soohoo M, Blas M, Byraiah G, Carcamo C, Brown B. Cervical HPV infection in female sex workers: a global perspective. Open AIDS J 2013; 7: 58-66.
13. Kelly H, Weiss HA, Benavente Y, de Sanjose S, Mayaud P; ART and HPV Review Group. Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis. Lancet HIV 2018; 5: e45-e58. DOI: 10.1016/S2352-3018(17)30149-2.
14. Ministry of Health of Peru. Cancer situation room in Peru (January-April, 2022). Lima: National Centre for Epidemiology, Disease Prevention and Control; 2022.
15. Ministry of Health of Peru. Clinical practice guidelines for the prevention and management of cervical cancer. Lima; 2017.
16. Venegas-Rodríguez G, Jorges-Nimer A, Galdos-Kajatt O. Papillomavirus vaccine in Peru. Rev Peru Ginecol Obstet 2020; 66. DOI: https://doi. org/10.31403/rpgo. v66i2286.
17. Ghebre RG, Grover S, Xu MJ, Chuang LT, Simonds H. Cervical cancer control in HIV-infected women: past, present, and future. Gynecol Oncol Rep 2017; 21: 101-108.
18. Tan N, Sharma M, Winer R, Galloway D, Rees H, Barnabas RV. Model-estimated effectiveness of single dose 9-valent HPV vaccination for HIV-positive and HIV-negative females in South Africa. Vaccine 2018; 36 (32 Pt A): 4830-4836.
19. Ministry of Health of Peru, General Directorate of Medicines, Supplies and Drugs. Sanitary Registration of Pharmaceutical Products. Gardasil 9, recombinant nonavalent human papillomavirus vaccine – Sanitary Registration: BE01039 [Internet]. Lima: Minsa; 2023. Available at: https://www.digemid.minsa.gob.pe/rsProductosFarmaceuticos/ (Accessed: 20.04.2023).