Original paper

Prevalence and genotype distribution of human papillomavirus infection among HIV-infected men who have sex with men living in Lower Silesia, Poland

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Abstract

Introduction: Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide and is associated with the risk of anogenital and oropharyngeal cancers. Men who have sex with men (MSM) are at a high risk of HPV infection. However, little up-to-date data are available regarding the prevalence of HIV and HPV co-infection in MSM in Poland.

Aim: To evaluate the prevalence, genotype distribution and risk factors for HPV infection among HIV-positive MSM living in Lower Silesia.

Material and methods: A total of 54 HIV-positive and 28 HIV-negative MSM participated in the study. The polymerase chain reaction was performed to detect HPV from oral and anal swabs. A self-applied written questionnaire was conducted to collect sociodemographic and behavioural data.

Results: The prevalence rates of oral and anal HPV infection were higher in HIV-infected MSM than in HIV-negative MSM. Statistical analysis showed that the prevalence of high oncogenic genotypes, HPV 16 and HPV 18, at the anal site was significantly higher in patients with lower CD4 cell counts, in addition, HPV 18 infection was significantly more frequent in patients with higher levels of HIV RNA. Moreover, HPV 33 and HPV 52 at the anal site were significantly more common in patients with lower nadir CD4.

Conclusions: This is the first report of HPV infection among Polish HIV-infected MSM. Our results show that HIV-related immunodeficiency is associated with a higher prevalence of high-risk HPV infections, therefore early detection of HIV infection and initiation of antiretroviral therapy might reduce the risk of HPV-related diseases.

Key words: human papillomavirus, HIV, men who have sex with men (MSM), sexually transmitted infections, sexually transmitted infection.

Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection and a significant public health problem in the world. It is estimated that 80% of sexually active men and women get infected with the virus at some point in their lives [1]. HPVs belong to the Papillomaviridae family with over 200 types identified [2]. HPV genotypes are referred to as low-risk (wart-causing) and high-risk (cancer-causing) in terms of their oncogenic potential. Due to diverse morphology of the lesions and their location, the following clinical forms of warts are distinguished: common warts (*verrucae vulgares*), plantar warts (*verrucae plantares*), flat warts (*verrucae planae*) and condylomas acuminata [3]. Transmission of HPV is by direct contact (oral to genital, oral to oral or skin to skin), by touching contaminated surfaces or by autoinoculation. High-risk genotypes have carcinogenic potential and are associated with the development of cervical, anogenital and oropharyngeal cancers [4]. The most oncogenic types of papillomaviruses are HPV16 and HPV18. Early sexual initiation, a high number of sexual partners, high-risk sexual practices, lack of condom use, smoking and low economic status have been consistently associated with HPV infection [5]. Moreover, HPV prevalence among HIV-infected patients is high. The molecular

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mechanisms underlying the increased risk of HPV infection in HIV-infected individuals are poorly understood. One of the reasons can be HIV-associated tight junctions' disruption of the mucosal epithelia which may potentiate HPV infection and subsequent development of HPV-associated neoplasia [6]. Two HIV proteins *gp120* and *tat* play an important role in disruption of epithelial tight junctions and facilitate entry of HPV into cells [7]. Furthermore, studies have postulated *tat* protein to up-regulate the expression of HPV oncogenes (E6 and E7) [8, 9]. In addition, immunodeficiency associated with HIV infection limits the ability to eliminate HPV. High-risk HPV types were detected more frequently in HIV-infected patients with lower CD4 cell counts [10]. It was found that the incidence of HPV infection and anal intraepithelial neoplasia (AIN) is increased in HIV-infected men who have sex with men (MSM) [11]. It has been suggested that in HIV-infected MSM the prevalence of sexually transmitted diseases is higher than in other populations. The study showed that HPV was detected in 97.9% of the 247 anal samples (median, 5 HPV types) in HIV-infected MSM, the most common types being HPV-16 (38.2%) and HPV-6 (35.3%) [12]. Moreover, the prevalence of oral HPV infection is 3-5 fold higher in MSM compared to the general population [13]. Studies also showed that HIV-positive MSM are more likely to engage in chemsex than HIV-negative counterparts [14]. Chemsex is defined as using crystal methamphetamine, mephedrone and/or γ-hydroxybutyrate/γ-butyrolactone (GHB/GBL) to enable, enhance and/or prolong sexual contacts [15]. These substances are used before or during sex. Also the use of new psychoactive substances with often unknown chemical composition and highly addictive potential has been observed among MSM in recent years [16]. Chemsex is associated with an increased risk of having multiple sexual partners, whose serostatus is unknown. Furthermore, intercourses combined with use of these drugs are usually condomless and with higher rates of depression and anxiety, suicide and drug addiction [17]. High-risk sexual behaviour is associated with a greater risk of acquiring sexually transmitted infections, including HPV. It has been suggested that in HIV-infected MSM the prevalence of HPV infection and HPV-related diseases is higher than in other populations. However, little up-to-date data are available regarding prevalence of HIV and HPV co-infection among MSM in Poland.

Aim

The aim of this study was to evaluate prevalence, genotype distribution and risk factors for HPV infection in HIV-infected and uninfected MSM from Lower Silesia, Poland.

Material and methods

The study was performed in the HIV outpatient clinic at 2 Wszystkich Swietych Street in Wroclaw, Poland. HIV-infected MSM were invited to take part in this study, the inclusion criteria were age > 18 years and self-reported MSM status. The control group included HIV-negative MSM who reported to the HIV testing and counselling point. They were invited to take part in this study after receiving a negative HIV test result.

Data collection

At inclusion into the study, a self-applied written questionnaire was conducted to collect sociodemographic data, number of sexual partners in the last month, type of sexual intercourse (oral/anal sex), use of condoms, chemsex practice, use of substances (alcohol, cigarettes, drugs), the presence of other sexually transmitted infections (including syphilis, gonorrhoea, chlamydia, HCV). The questionnaire also included a question about HPV vaccination. Clinical information was verified and completed with information available in the HIV outpatient clinic records. We also analysed clinical data: time since HIV diagnosis, antiretroviral therapy, CD4 cells count (cells/mm^3) and level of HIV-RNA (copies/ml).

HPV detection and genotyping

For oral and anal sampling a flocked swab FLOQ-Swabs with moulded break point (Copan Flock Technologies, Brescia, Italy) were used. After sampling, its tip was placed in a plastic tube with a specific medium (Transport Medium Plus, Sacace Biotechnologies, Como, Italy) and transported to the laboratory to be kept frozen at –70°C until molecular analysis. For DNA isolation we used DNA-Sorb-A (DNA extraction kit, Sacace Biotechnologies, Como, Italy). For identification of HPV types present in the samples, we used HPV Genotypes 14 Real-TM Quant (16, 18, 31, 45, 33, 35, 39, 51, 52, 56, 58, 59, 66, 68) and HPV 6/11 Real-TM, Sacace Biotechnologies, Como, Italy. Molecular test results were analysed together with clinical parameters and data from the questionnaire.

Statistical analysis

The statistical analysis was conducted using EPIINFO Ver. 7.2.3.1. For all groups studied, the number of cases (*N*), the mean (*X*), median (*M*), range (min.–max.), lower and upper quartile (25q–75q) and standard deviation (SD) of the parameters were calculated. The verification of the hypothesis of equality of means of independent groups was performed by ANOVA or for groups with heterogeneous variance by the non-parametric Mann-Whitney *U* test. The homogeneity of variance was checked by Bartlett's test. The χ^2 test was used to discrete distribution. $P \leq 0.05$ was considered statistically significant.

Results

A total of 54 HIV-infected MSM were included in the study. Median time since HIV diagnosis was 5 years (1–19 years), the mean CD4+ cell count was 662 cells /µl, the

mean CD4+ nadir count was 397 cells/µl, the mean level of HIV RNA at the moment of HIV diagnosis was 63 770 copies/ml, 98.1% of HIV-infected MSM were receiving antiretroviral therapy (ART), 87.04% of patients had undetectable HIV RNA. The control group consisted of 28 HIV-negative MSM. The median age of HIV-infected MSM was higher compared to the control group (36.5 (22–53) vs. 29 (22–59), $p < 0.00297$). There were no significant differences in the other socio-demographic data between the two analysed groups. The statistical analysis showed that the rates of anal and oral intercourse were similar among HIV-infected and uninfected MSM (94.4% vs. 100% $p = 0.204$; 96.3% vs. 92.86% $p = 0.493$, respectively). Among HIV-positive MSM 29.41% declared condomless anal intercourse and 17.86% among HIV-negative patients ($p = 0.259$). The rates of unprotected oral sex were comparably high among the HIV-positive and uninfected groups (88.46% vs. 96.15%, $p = 0.262$). The main reasons for unprotected anal and oral intercourse were: condom-associated erection problems and decreased pleasure. Chemsex practice among HIV-infected MSM was declared by 20.37% and in HIV-negative MSM by 10.71% ($p = 0.270$). Also no significant differences were observed in the substance use between HIV-infected and uninfected MSM (alcohol: 55.56% vs. 57.14%, $p = 0.891$; cigarettes: 40.74% vs. 60.71%, $p = 0.0859$; drugs: 25.93% vs. 10.71%, $p = 0.107$). Compared to HIV-negative subjects, HIV-positive MSM more frequently heard about HPV before completing the questionnaire (68% vs. 50%, $p < 0.034$). Among all subjects included in the study only 2 HIV-infected patients declared that they were vaccinated against HPV. Statistical analysis showed no differences in the prevalence of sexually transmitted infections in the past year between the two groups of HIV-infected and uninfected MSM (syphilis: 46.3% vs. 25%, $p = 0.0608$; gonorrhoea: 18.5% vs. 10.7%, $p = 0.270$; chlamydia 11.1% vs. 0%, $p = 0.0669$, HCV 16.6% vs. 3.6%, $p = 0.0857$).

Human papillomavirus prevalence

We also evaluated the prevalence of oral and anal HPV infection. The statistical analysis showed that the prevalence of detected HPV was significantly higher in anal samples than in oral ones ($p < 0.001$). Among 54 HIV-infected MSM, 41 (76%) tested positive for anal HPV infection. High-risk HPV genotypes were detected in 39 samples, low-risk HPV genotypes in 16 samples and infections with ≥ 2 HPV types in 33 samples (Table 1). Prevalence of the oncogenic genotypes HPV 16 and HPV 18 was found in 12 and 8 anal samples of HIV-infected MSM, respectively. One patient who presented with a history of condyloma acuminata of the anal canal, was positive for low-risk HPV 6 and high-risk genotypes: HPV 16, HPV 18, HPV 39, HPV 45, HPV 66, and HPV 68 in anal samples. In HIV-negative MSM, 9 (32%) patients tested positive for anal HPV infection. High-risk HPV genotypes were detected in 9 samples, low-risk HPV genotypes in 4 samples and infections with ≥ 2 HPV types in 6 samples (Table 1). Only one anal sample tested positive for HPV 16 and one for HPV 18 among the HIV-negative group. Anal cytology was offered to MSM who tested positive for oncogenic genotypes: HPV 16 and/or HPV 18. Only 7 patients reported for this test and the results of all cytology tests were normal. The statistical analysis showed that among HIV-infected MSM compared to HIV-negative ones, the prevalence of other high-risk HPV genotypes in anal samples was significantly higher: HPV 31 ($p = 0.00951$), HPV 39 ($p = 0.00872$), HPV 68 ($p = 0.0193$), HPV 52 ($p = 0.00085$), and HPV 66 ($p = 0.0413$). Among 54 HIV-infected MSM, 10 (18.5%) tested positive for oral HPV infection, including high-risk HPV genotypes that were detected in 8 samples, low-risk HPV genotypes in 4 samples and infections with ≥ 2 HPV types in 3 samples (Table 2). Prevalent oncogenic HPV genotypes: 16 and 18 were found only in two and one oral samples of HIV-infected MSM, respectively. No oral HPV infection was detected in the HIV-negative group (Table 2). Next, we looked into possible associations between the results of molecular tests and laboratory parameters of HIV-infected MSM (CD4 cell count, CD4 nadir, level of HIV RNA at the moment of HIV diagnosis, current HIV RNA level). We also tried to find associations between the molecular test results and other parameters: co-infections with syphilis, gonorrhoea, chlamydiosis, HCV, smoking, alcohol consumption, drug use, and chemsex.

Table 1. Anal HPV types distribution by HIV serostatus (created by Martyna Biała)

HIV-positive MSM ($n = 54$)	HIV-negative MSM ($n = 28$)
HPV types:	HPV types:
Any type – 41 (76%)	Any type – 9 (32%)
Low risk – 16	Low risk – 4
High risk – 39	High risk – 9
HPV 16 – 12	HPV 16 – 1
HPV 18 – 8	HPV 18 – 1
Multiple types – 33	Multiple types – 6

Table 2. Oral HPV type distribution by HIV serostatus (created by Martyna Biała)

HIV-positive MSM ($n = 54$)	HIV-negative MSM ($n = 28$)
HPV types:	HPV types:
Any type – 10 (18,5%)	Any type – 0
Low risk – 4	Low risk – 0
High risk – 8	High risk – 0
HPV 16 – 2	HPV 16 – 0
HPV 18 – 1	HPV 18 – 0
Multiple types – 3	Multiple types – 0

Statistical analysis showed that the prevalence rates of highly oncogenic HPV genotypes, 16 and 18, at the anal site were significantly higher in patients with lower CD4 cell counts ($p = 0.0003$, $p = 0.00762$, respectively). In addition HPV 18 infection was significantly more frequent in patients with higher levels of baseline HIV RNA ($p = 0.0189$). We also found that high-risk HPV 59 infection at the anal site was significantly more frequent ($p = 0.033$) in HIV-infected MSM with a lower CD4 cell count. Moreover, HPV 33 and HPV 52 at the anal site were significantly more common in patients with lower nadir CD4 ($p = 0.0312$, $p = 0.0188$, respectively). Syphilis was more prevalent among HIV-infected MSM who tested positive for HPV 33 at the anal canal ($p = 0.0113$).

Discussion

Our study demonstrated that the prevalence of oral and anal HPV infections was higher in HIV-infected MSM than in HIV-negative ones. There were no differences in the frequency of high-risk sexual behaviour and other analysed risk factors associated with HPV infection between the two groups. However, van Aar *et al.* reported that engaging in risky sexual behaviour and drug use was more common among HIV-infected MSM compared to HIV-negative counterparts [18]. Other study indicated that the rate of drug use in MSM is higher than in other populations [19]. Across the analysed cohort, reported use of marijuana (36–46%) and/or methamphetamine (23–27%) was common [19]. Kenyon *et al.* found an increase in condomless sex associated with the use of drugs in MSM [20]. We did not observe any significant association between substance use and condomless sex, but we found high rates of unprotected anal sex among the two groups. In our study we observed that 29.41% of HIV-positive MSM and 17.86% of HIV-negative MSM had unprotected anal sexual intercourse. Crepaz *et al.* described that frequency of condomless anal sex among HIV-infected MSM was considerably higher with HIV-seropositive partners (30%) than with unknown serostatus (16%) or HIV-negative partners (13%) [21]. Unprotected sexual intercourse is associated with an increased risk of acquiring sexually transmitted infections (STI). We found no significant differences in the prevalence of sexually transmitted infections (including syphilis, gonorrhoea, chlamydia, HCV) between the two analysed groups. Moreover, many studies showed that HIV-infected MSM compared to HIV-negative MSM had higher rates of syphilis and other STIs [22]. Our analysis demonstrated that the prevalence of oral and anal HPV infection was higher in HIV-infected MSM than in HIV-negative ones. We also showed a higher rate of high-risk HPV DNA types in anal samples compared to oral specimens in MSM. Other study also found that HPV infection was significantly higher in HIV-positive MSM compared to HIV-negative MSM (60% vs. 37.8%, $p = 0.035$) [23]. Moreover, the prevalence of anal and oral HPV was: 96.3% and 21.6%, respectively in HIV-positive MSM and 70.6% and 29.4% in HIV-uninfected MSM [23]. Ren *et al.* observed that presence of positive tests for anal HPV of any type (81.0% vs. 48.2%), any high-risk type (50.6% vs. 27.1%), any low-risk type (55.7% vs. 31.8%) were all significantly more common in HIV-infected compared to HIV-negative MSM [24]. Significantly higher rates of HPV infections in the anal canal may be associated with damage of the rectal epithelium and mucosa during anal unprotected intercourse, which may facilitate the entry of the virus [25]. The molecular mechanisms underlying the increased risk of HPV infection in HIV-infected individuals are poorly understood. Studies have shown that HIV-associated tight junction disruption of mucosal epithelia may potentiate HPV infection [6]. In addition, HIV-associated immunodeficiency limits the chances to eliminate HPV infection. Moreover, our study found that infection with most oncogenic HPV genotypes: 16 and 18 was significantly associated with lower CD4 cell counts. Immunosuppression plays an important role in the development of HPV-related cancers. We observed a significantly higher prevalence of highly oncogenic HPV genotypes at the anal site compared to the oral site in HIV-infected MSM which is associated with an increased risk for anal cancer. Palefsky *et al.* showed that HIV-positive men with decreased CD4 cell counts (below 200/mm^3) had more than 3-fold increase in the risk of progression from anal low-grade squamous epithelial lesions (LSIL) to high-grade squamous intraepithelial lesions (HSIL) [26]. Guiguet *et al.* found that the risk of anal cancer increased with longer duration of immunosuppression (CD4 count < 200 cells/mm^3 and viral load > 100,000 copies/ml) [27]. In our analysis, anal cytology was offered to MSM infected with oncogenic genotypes: HPV 16 and/or HPV 18 but only 7 patients reported for the additional test. The results of all cytology tests were normal. Wu *et al.* observed that high-risk HPV infection was a significant predictor for cytological abnormality in HIV-infected and uninfected MSM – there were 15.3% of atypical squamous cells of undetermined significance, 16.6% of low-grade squamous intraepithelial lesions, 4.9% of atypical squamous cells that cannot exclude high-grade squamous intraepithelial lesions and 17% of high-grade squamous intraepithelial lesions [28]. Screening programs for HPV cytological abnormality and vaccination against HPV may reduce the risk of HPV-associated cancers in HIV-infected and uninfected MSM.

We found a significantly lower incidence of oral HPV infections compared to anal canal. A similar observation was made in another study [29]. The lower prevalence of oral compared to anal HPV infections might be associated with faster clearance from oral epithelia. The continuous flow of saliva and associated immunoglobulins allows for faster elimination of the virus. Rollo *et al.* showed oral HPV infections in 17.3 % of HIV-nega-

tive MSM and in 27.8% of HIV-positive MSM [30]. In our study oral HPV was detected in 18.5% of HIV-infected MSM, there was no oral HPV infection in the HIV-negative control group. Despite the lower prevalence of oral HPV infection, presence of highly oncogenic HPV genotypes in the oral cavity may be associated with the development of oropharyngeal cancers.

Our study had some limitations. The small size of the study groups could be associated with underpowered analysis. We did not perform anal cytology tests in all subjects. We could not verify the data from the questionnaires based on medical records in HIV-negative MSM (presence of other sexually transmitted infections, e.g. syphilis).

In conclusion, this is the first report of HPV infection among Polish HIV-infected MSM. The prevalence of oral and anal HPV infection was higher in HIV-infected MSM than in uninfected MSM. HIV-related immunodeficiency is associated with a higher prevalence of high-risk HPV infections, therefore early detection of HIV infection and initiation of antiretroviral therapy may reduce the risk of HPV-related diseases. The high prevalence of anal high-risk HPV infections especially among HIV-infected MSM calls for close observation and screening programs for anal cytology as well as vaccination against HPV.

Conflict of interest

The authors declare no conflict of interest.

References

1. Panatto D, Amicizia D, Trucchi C, et al. Sexual behaviour and risk factors for the acquisition of human papillomavirus infections in young people in Italy: suggestions for future vaccination policies. BMC Public Health 2012; 12: 623.
2. Van Doorslaer K, Tan Q, Xirasagar S, et al. The papillomavirus episteme: a central resource for papillomavirus sequence data and analysis. Nucleic Acids Res 2013; 41: 571-8.
3. Loo SK. Warts (non-genital). BMJ Clin Evid 2014; 2014: 1710.
4. Bansal A, Singh MP, Rai B. Human papillomavirus-associated cancers: a growing global problem. Int J Appl Basic Med Res 2016; 6: 84-9.
5. Rodríguez-Álvarez MI, Gómez-Urquiza JL, Husein-El Ahmed H, et al. Prevalence and risk factors of human papillomavirus in male patients: a systematic review and meta-analysis. Int J Environ Res Public Health 2018; 15: 2210.
6. Tugizov S. Human immunodeficiency virus-associated disruption of mucosal barriers and its role in HIV transmission and pathogenesis of HIV/AIDS disease. Tissue Barriers 2016; 4: e1159276.
7. Tugizov SM, Herrera R, Chin-Hong P, et al. HIV-associated disruption of mucosal epithelium facilitates paracellular penetration by human papillomavirus. Virology 2013; 446: 378-88.
8. Nyagol J, Leucci E, Onnis A, et al. The effects of HIV-1 Tat protein on cell cycle during cervical carcinogenesis. Cancer Biol Ther 2006; 5: 684-90.
9. Verma M, Erwin S, Abedi V, et al. Modeling the mechanisms by which HIV-associated immunosuppression influences HPV persistence at the oral mucosa. PLoS One 2017; 12: e0168133.
10. da Silva L, Miranda A, Batalha R, et al. High-risk human papillomavirus and cervical lesions among women living with HIV/AIDS in Brazilian Amazon. Braz J Infect Dis 2015; 19: 557-62.
11. Palefsky J. Human papillomavirus-related disease in people with HIV. Curr Opin HIV AIDS 2009; 4: 52-6.
12. de Pokomandy A, Rouleau D, Ghattas G, et al. Prevalence, clearance, and incidence of anal human papillomavirus infection in HIV-infected men: the HIPVIRG cohort study. J Infect Dis 2009; 199: 965-73.
13. King EM, Oomeer S, Gilson R, et al. Oral human papillomavirus infection in men who have sex with men: a systematic review and meta-analysis. PLoS One 2016; 11: e0157976.
14. Maxwell S, Shahmanesh M, Gafos M. Chemsex behaviours among men who have sex with men: a systematic review of the literature. Int J Drug Policy 2019; 63: 74-89.
15. Sewell J, Cambiano V, Speakman A, et al. Changes in chemsex and sexual behaviour over time, among a cohort of MSM in London and Brighton: Findings from the AURAH2 study. Int J Drug Policy 2019; 68: 54-61.
16. Donnadieu-Rigole H, Peyrière H, Benyamina A, Karila L. Complications related to sexualized drug use: what can we learn from literature? Front Neurosci 2020; 14: 548704.
17. Bohn A, Sander D, Köhler T, et al. Chemsex and mental health of men who have sex with men in Germany. Front Psychiatry 2020; 11: 542301.
18. van Aar F, Mooij SH, van der Sande MAB, et al. Twelve-month incidence and clearance of oral HPV infection in HIV-negative and HIV-infected men who have sex with men: the H2M cohort study. BMC Infect Dis 2014; 14: 668.
19. Reback CJ, Fletcher JB, Shoptaw S, Grella CE. Methamphetamine and other substance use trends among street-recruited men who have sex with men, from 2008 to 2011. Drug Alcohol Depend 2013; 133: 262-5.
20. Kenyon C, Wouters K, Platteau T, et al. Increases in condomless chemsex associated with HIV acquisition in MSM but not heterosexuals attending a HIV testing center in Antwerp, Belgium. AIDS Res Ther 2018; 15: 14.
21. Crepaz N, Marks G, Liau A, et al. Prevalence of unprotected anal intercourse among HIV-diagnosed MSM in the United States: a meta-analysis. AIDS 2009; 23: 1617-29.
22. Abara WE, Hess KL, Neblett Fanfair R, et al. Syphilis trends among men who have sex with men in the United States and Western Europe: a systematic review of trend studies published between 2004 and 2015. PLoS One 2016; 11: e0159309.
23. Ucciferri C, Tamburro M, Falasca K, et al. Prevalence of anal, oral, penile and urethral human papillomavirus in HIV infected and HIV uninfected men who have sex with men. J Med Virol 2018; 90: 358-66.
24. Ren X, Ke W, Zheng H, et al. Human papillomavirus positivity in the anal canal in HIV-infected and HIV-uninfected men who have anal sex with men in Guangzhou, China: implication for anal exams and early vaccination. Biomed Res Int 2017; 2017: 2641259.
25. Critchlow CW, Hawes SE, Kuypers JM, et al. Effect of HIV infection on the natural history of anal human papillomavirus infection. AIDS 1998; 12: 1177-84.
26. Palefsky JM, Holly EA, Hogeboom CJ, et al. Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV-positive

and HIV-negative homosexual men. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 17: 314-9.
27. Guiguet M, Boué F, Cadranel J, et al. Effect of immunodeficiency, HIV viral load, and antiretroviral therapy on the risk of individual malignancies (FHDH-ANRS CO4): a prospective cohort study. Lancet Oncol 2009; 10: 1152-9.
28. Wu PF, Hang JF, Strong C, et al. Anal human papillomavirus and its associations with abnormal anal cytology among men who have sex with men. Sci Rep 2020; 10: 3165.
29. Sirera G, Videla S, Piñol M, et al. High prevalence of human papillomavirus infection in the anus, penis and mouth in HIV-positive men. AIDS 2006; 20: 1201-4.
30. Rollo F, Latini A, Pichi B, et al. Prevalence and determinants of oral infection by Human papillomavirus in HIV-infected and uninfected men who have sex with men. PLoS One 2017; 12: e0184623.