Original Article

Analyzing the prevalence of proctological diseases in HIV-positive and -negative patients

Thiago da Silveira Manzione [a,b,*], *Luiza Mello Ayres Morgado* [a,b], *Sidney Roberto Nadal* [a,b]

[a] *Irmandade Santa Casa de Misericórdia de São Paulo, Departamento de Cirurgia, Disciplina de Coloproctologia, São Paulo, SP, Brazil*
[b] *Instituto de Infectologia Emílio Ribas, São Paulo, SP, Brazil*

ABSTRACT

Objective: To compare proctological diseases in HIV-positive and -negative patients.
Method: Prospective study conducted in the proctology outpatient clinic at *Instituto de Infectologia Emílio Ribas* from 2013 through 2019. All of them underwent anamnesis and proctological examination and were divided into two groups (HIV+ and HIV−). The groups were then compared with regard to age, sex, diagnosis, and whether or not there was any indication for surgery.
Results: 485 HIV + patients (41.9%) (Group I) and 672 HIV− (58.1%) (Group II). The mean age in Group I was 42.8 years, and 404 (83.3%) of the patients were males. In Group II, the mean age was 48.3 years, and 396 (59%) patients were females. In comparing the groups, a statistically significant difference was found regarding sex, age, and diagnosis. The incidence of hemorrhoid and anal skin tags was higher in group II and that of condyloma acuminata was higher in in Group I (p < 0.001). In Group I, condyloma acuminata was more prevalent, but in those with CD4 levels above 500 cells/mm³, the diagnoses were more similar to those in the population without HIV.
Conclusions: Proctological diseases were found to be similar but have different incidences. The incidences of diseases in HIV− and + patients tend to approach each other as CD4 level increases.

Análise da prevalência de doenças proctológicas em pacientes HIV positivo e negativo

RESUMO

Objetivo: Comparar as doenças proctológicas nos pacientes HIV positivos e negativos.
Método: Estudo prospectivo realizado no ambulatório de proctologia do Instituto de Infectologia Emílio Ribas de 2013 a 2019. Todos foram submetidos a anamnese e exame

* Corresponding author.
  E-mail: thiagomanzione@hotmail.com (T.S. Manzione).

Hemorróidas
Fissura anal
Fístula anal

proctológico, e divididos em dois grupos (HIV+ e HIV−) sendo comparados em relação a idade, sexo, diagnóstico e se havia ou não indicação cirúrgica.
Resultados: 485 pacientes HIV+ (41.9%) (Grupo I) e 672 HIV negativos (58.1%) (Grupo II). A média de idade do Grupo I foi 42.8 anos sendo 404 (83.3%) do masculino. No grupo II, a média de idade foi de 48.3 anos, sendo 396 (59%) do sexo feminino. Comparando os grupos, houve diferença estatisticamente significante em relação ao sexo, idade e diagnóstico. Houve maior incidência de hemorróida e plicoma no Grupo II e condilomas acuminados no Grupo I (p < 0.001). No Grupo I, o condiloma acuminado foi mais prevalente, porém naqueles com CD4 acima de 500 células/mm^3, os diagnósticos se aproximaram da população sem HIV.
Conclusão: As doenças proctológicas foram semelhantes, com incidências diferentes. A incidências das doenças de pacientes HIV− e + tendem a se aproximar na medida que o nível do CD4 aumenta.

Introduction

According to UNAIDS, there were 36.9 million people infected with HIV in the world in 2017, 1.8 million of whom in Latin America. Approximately 21.7 million people had access to antiretroviral therapy in 2017, and mortality from HIV-related illnesses dropped from 1.4 million in 2010 to 940 thousand in 2017.[1] However, there are still many diseases for which the immunosuppression caused by the virus is a gateway. Hence, understanding how this process takes place in different organs of the body is of fundamental importance.

Anorectal diseases afflict 5.9%–34% of HIV-positive patients and are usually the reason that leads the patient to seek a physician.[2] Although classic AIDS-defining diseases, such as non-Hodgkin's lymphoma and Kaposi's sarcoma, have declined mainly due to antiretroviral therapy, the prevalence[3] of some tumors, such as anal carcinoma, has increased and remains more common in the population carrying the virus.[4]

Benign anorectal diseases, in turn, are a constant in the general population: the average incidence of hemorrhoidal disease for instance ranges from 4.4% to 86%,[5] but there are few studies on the prevalence of this type of pathology in the Brazilian population and even a smaller number thereof in the HIV-positive population.

This study aims to compare the HIV population with the non-HIV population with respect to the prevalence of proctological diseases as a whole.

Method

Prospective study conducted in the coloproctology outpatient clinic at *Instituto de Infectologia Emílio Ribas* from 2013 through 2019. Non-HIV patients were referred from Basic Health Units maintained by the Municipal Health Department of the City of São Paulo between 2015 and 2016, whereas HIV-positive patients were referred from the hospital itself.

Name, age, sex, main diagnosis, and whether or not there was any indication for surgery for the 1157 patients included in the study were recorded. Patients with incomplete data were excluded, and if there was more than one diagnosis, only their main complaint, i.e. that which had brought the patient to seek care, was considered. These patients were then divided into two groups: HIV-positive (HIV+) and non-HIV patients. The analysis results were compared between the two groups.

All patients treated at the coloproctology outpatient clinic underwent general anamnesis in order to identify what their main complaint was; general and proctological examination (inspection of the anal, perianal and perineal regions) were then conducted by experienced doctors.

For data evaluation we used the SPSS 13.0 statistical analysis software. The descriptive analysis was performed by means of frequency tables and calculating summary measures such as mean, median and standard deviation. To test the study objectives/hypotheses, chi–squared tests were used for comparing qualitative variables. Student's *t*-test was used for comparing quantitative variables. A level of significance (p) of 5% was adopted in the study.

Results

Of the 1157 patients selected for the study, 35 were excluded due to incomplete data. Of the total, 485 were HIV+ (41.9%) (group I–HIV+), and 672 were seronegative for HIV (58.1%) (group II–HIV−). The mean age in group I was 42.8 years (17–80 years). Of these patients, 81 (16.7%) were females and 404 (83.3%) were males. The CD4 levels were up to 250 cells/mm^3 in 54 patients (11.6%), between 251 and 500 cells/mm^3 in 135 (29.1%), and above 500 cells/mm^3 in 275 (59.3%) (Fig. 1).

Viral burden was undetectable in 398 patients (84.5%), up to 1000 copies in 30 (6.4%); between 1000 and 10,000 copies in 10 (2.1%); from 10,000 to 100,000 in 22 (4.7%); and over 100,000 copies in 11 (2.3%) (Fig. 2).

The minimum HIV-time in the sample ranged from zero (i.e. newly diagnosed) to 31 years of illness, with an average of 12.7 years. The average ART-time was 10.6 years, with a minimum of zero years, i.e. when there was no indication for it, and a maximum of 31 years.

In group II, the mean age was 48.3 years (12–90), 396 (59%) patients were females and 275 (41%) were males.

In comparing the two groups, there was a statistically significant difference in relation to sex with a predominance of males in the group with HIV. (p < 0.01) (Fig. 3). There was also
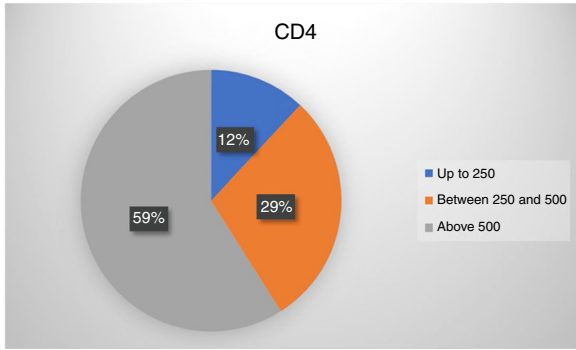
Fig. 1 – Distribution of HIV-patients according to CD4 counts, in cells/mm³.

Fig. 2 – Distribution of HIV patients according to viral burden, in number of copies.

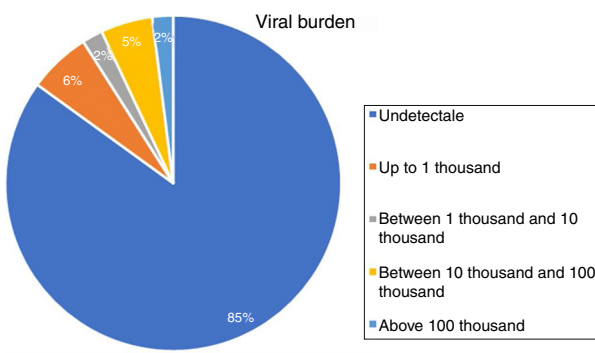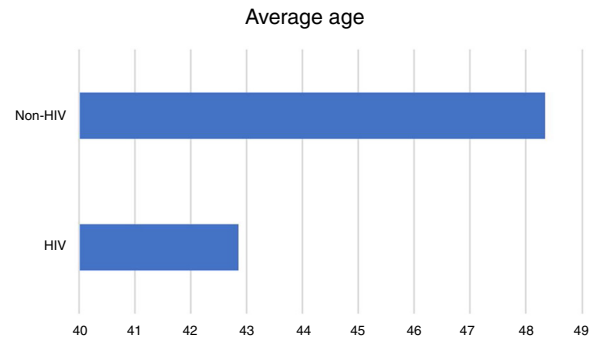**Fig. 3 – Prevalence of each sex in the studied groups.**

Fig. 4 – Average age, in years, in the two groups.

a difference in ages, with group II having a higher average age (p < 0.01) (Fig. 4).

We found 32 diagnostic possibilities in the two groups (Fig. 5), namely: hemorrhoids, condyloma acuminata, anal skin tags, fissure, polyp, fistula, rectitis, constipation, abdominal pain, anal incontinence, abscess, squamous cell carcinoma (SCC), colon tumor, bowenoid papulosis, hypertrophic papilla, herpes, rectal prolapse, pilonidal cyst, diverticular disease of the colon, anal syphilis, hemorrhoidal thrombosis, Buschke-Löwenstein tumor, colitis, intestinal tuberculosis, and others (cystocele, diarrhea, pruritus, dermatitis, nevus, ulcer, irritable bowel syndrome, vaginitis, proctalgia fugax, IUC, fecaloma,

gonorrhea/chlamydia, pain in the coccyx, foreign body, low back pain, and Chagas disease). In addition, some patients were also referred for HPV screening and follow-up, due to positive occult blood test (PSO+) results, and for bowel cancer screening.

After comparing the groups (Fig. 6), we found a difference regarding the prevalence of diseases and reasons that led the patients to seek medical care. In group I, we observed more cases of condyloma acuminata (33.2%), hemorrhoids (13.4%), HPV screening, fissures, and anal skin tags. In group II, in turn, we found a prevalence of hemorrhoids (20.5%), followed by anal skin tags (19%), other diagnoses, physical examination with no changes or fissures.
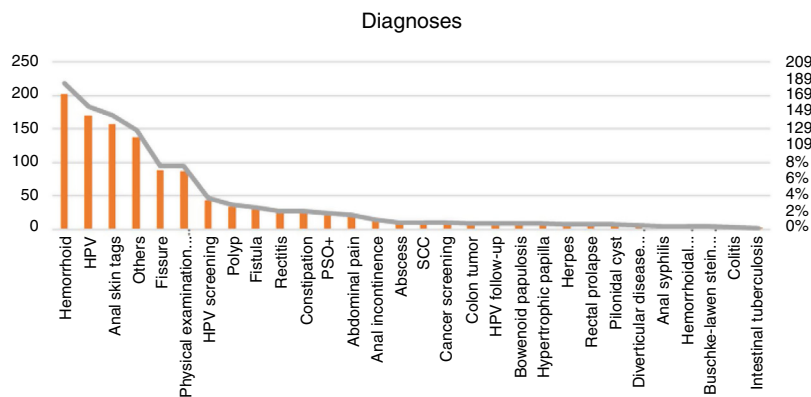
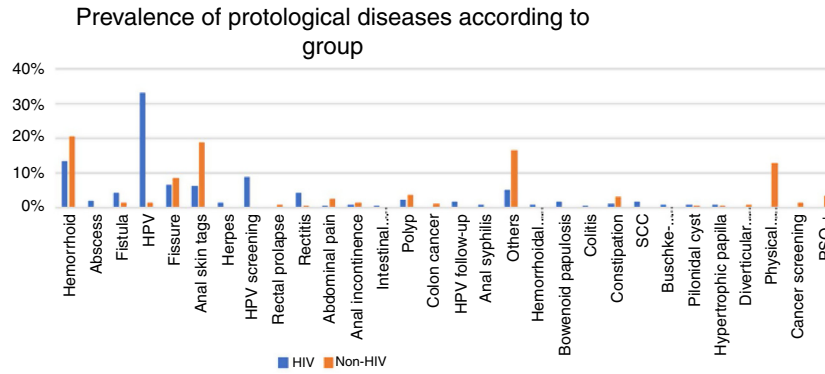**Fig. 5 – Diagnoses found in the patients evaluated.**

Fig. 6 – Comparison of the prevalence of proctological diseases between the groups.
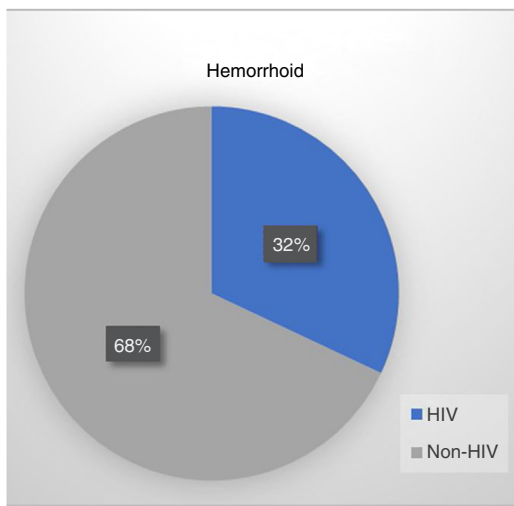

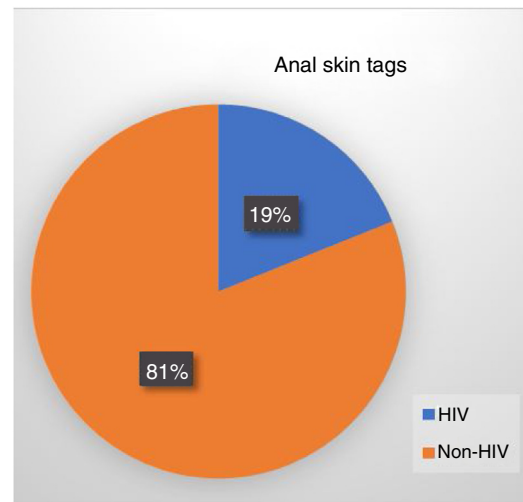**Fig. 7 – Hemorrhoid prevalence in the groups.**

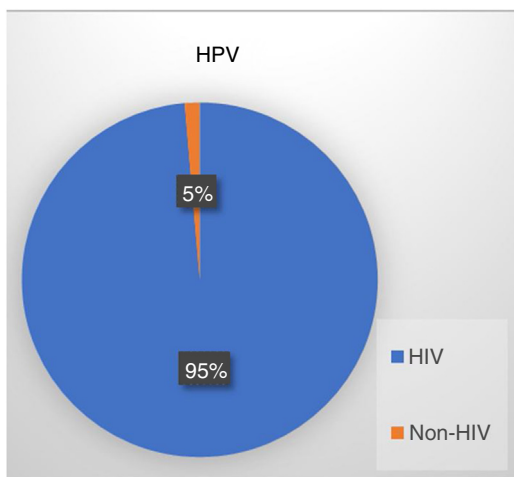**Fig. 9 – Prevalence of anal skin tags in the groups.**

Fig. 8 – HPV prevalence in the groups.

Subsequently, when comparing the findings from the two groups, we observed a greater number of hemorrhoids cases (p = 0.002) (Fig. 7) and a greater number of anal skin tags cases (p < 0.001) (Fig. 8) in group II. Condyloma acuminata, in turn,

was predominant in group I (p < 0.001) (Fig. 9). The number of fissure cases showed no statistical difference (p = 0.186).

In group I, we observed that condyloma acuminata was the most prevalent condition irrespective of CD4 counts (Fig. 10A, B and C). In patients with CD4 up to 250 cells/mm^3, besides condyloma acuminata, the other most commonly found conditions were hemorrhoids, abscesses, herpes, and anal skin tags. In those with CD4 counts between 251 and 500 cells/mm^3, condyloma and hemorrhoid were also present, but were followed by rectitis, fissure, and anal skin tags. With CD4 counts above 500 cells/mm^3, the diagnoses were more similar those in the population without HIV, namely: condyloma acuminata, hemorrhoid, fissure, anal skin tags, and rectitis, in addition to the cases referred for HPV screening.

When we specifically compared the HIV population having CD4 counts above 500 cells/mm^3 with non-HIV patients for the most prevalent diseases, such as hemorrhoidal disease, we see that the difference between the groups decreased by 2.2% and is no longer statistically significant (Table 1).

However, condyloma acuminata, despite its difference having decreased by 7% and thus approaching the non-HIV group, still remained more prevalent in the population with HIV

A

CD4 UP TO 250 CELLS

B

CD4 BETWEEN 250 AND 500 CELLS

C
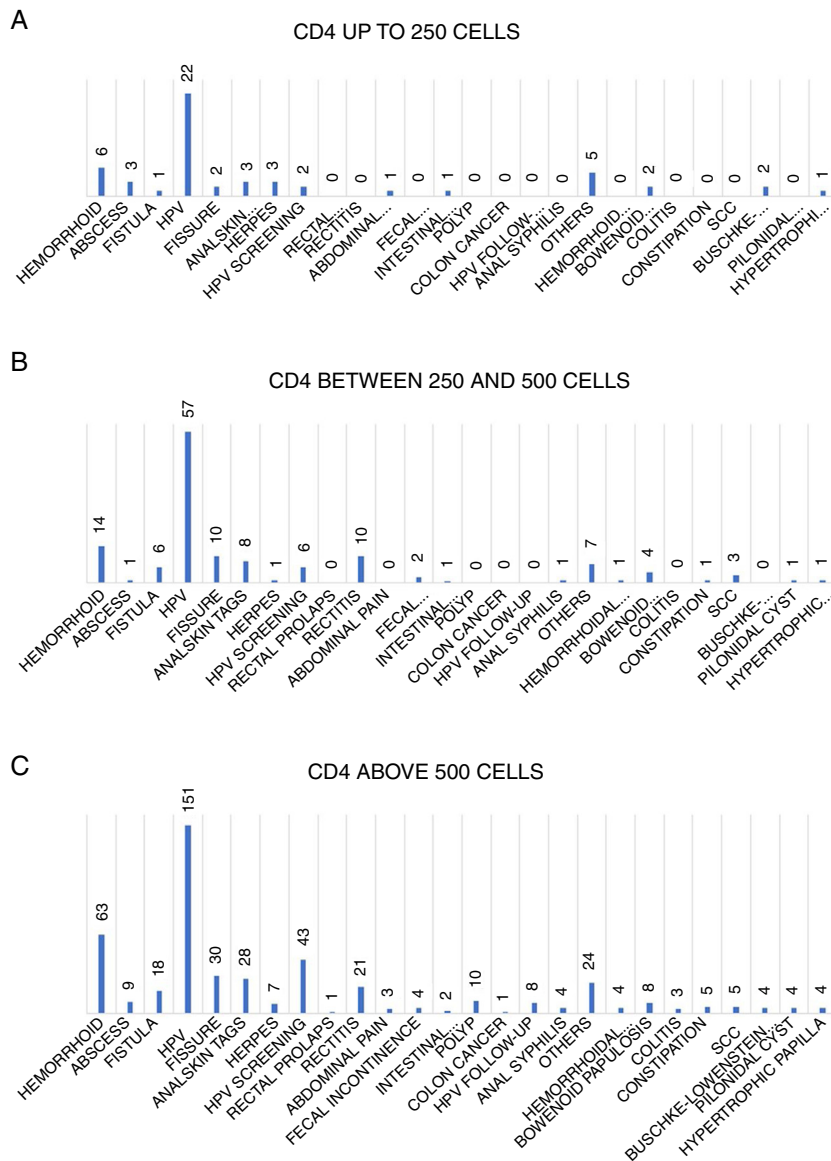
CD4 ABOVE 500 CELLS

Fig. 10 – Diagnoses in patients with CD4 counts: (A) CD4 counts below 250 cells/mm^3; (B) CD4 counts between 250 and 500 cells/mm^3; (C) CD4 counts above 500 cells/mm^3.

Table 1 – Comparison between groups for hemorrhoidal disease.

Hemorrhoid					
	No. of cases	%		No. of cases	%
HIV	65	13.40%	HIV CD4 > 500 cells/mm^3	43	15.60%
Non-HIV	138	20.50%	Non-HIV	138	20.50%
Difference between groups		7.10%	Difference between groups		4.90%
p = 0.02			p = 0.082		

Table 2 – Comparison between groups for condiloma acuminata.

Condiloma acuminata					
	No. of cases	%		No. of cases	%
HIV	161	33.20%	HIV CD4 > 500 cells/mm^3	72	26.20%
Non-HIV	9	1.30%	Non-HIV	9	1.34%
Difference between groups		31.90%	Difference between groups		24.80%
p < 0.001			p < 0.001		

Table 3 – Comparison between groups for anal skin tags.

Anal skin tags					
	No. of cases	%		No. of cases	%
HIV	30	6.20%	HIV CD4 > 500 cells/mm^3	17	6.18%
Non-HIV	128	19.05%	Non-HIV	128	19.05%
Difference between groups		12.80%	Difference between groups		12.87%
p < 0.001			p < 0.001		

Table 4 – Comparison between groups for fissure.

Fissure					
	No. of cases	%		No. of cases	%
HIV	31	6.40%	HIV CD4 > 500 cells/mm^3	18	6.55%
Non-HIV	57	8.48%	Non-HIV	57	8.48%
Difference between groups		2.10%	Difference between groups		1.94%
p = 0.186			p = 0.316		
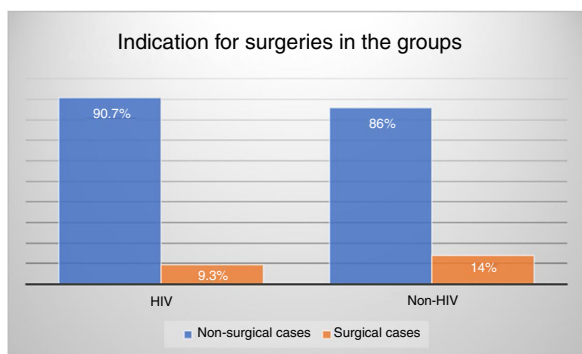
Fig. 11 – Comparison of the prevalence of proctological diseases between the groups.

(p < 0.001) (Table 2). Some diagnoses have not changed, such as those of anal skin tags (Table 3) and fissures (Table 4).

Of all patients in this study, 139 (12%) had an indication for surgery. Of these, 45 belonged to group I (9.3%) and 94 to group II (14%). When comparing them, we found more indications for surgery in group II (p = 0.015) (Fig. 11).

Discussion

Hemorrhoidal disease is the most commonly seen anorectal disorder in coloproctology, affecting more than 75% of individuals at least once in their lifetimes, with about a third of the cases being symptomatic and requiring medical assistance.[6,7] However, the actual prevalence is very difficult to determine, as the vast majority of patients either do not seek medical assistance or mistakenly attribute to hemorrhoidal disease the symptoms of other anorectal pathologies. In the United States, the prevalence was estimated at 4.4% or 8.5 million patients.[8] A Spanish study carried out between 2010 and 2011, in turn, revealed a 14.7% prevalence of hemorrhoidal disease in the population.[9] In 2004, the National Institutes of Health in the United States (NIH) linked the diagnosis of hemorrhoids to 3.2 million outpatient visits, 306 thousand hospitalizations, and 2 million medical prescriptions. In 2012, the term

"hemorrhoid" was the most searched among health-related topics on Google.[10]

We also found a study with the non-HIV population, conducted by Cruz et al.,[11] that reviewed 34,000 patients with coloproctological complaints and having hemorrhoidal disease as the main diagnosis in 27.3% of cases. In 2002, Pinho et al.[12] prospectively evaluated 2323 patients at a coloproctology outpatient clinic and found anorectal diagnoses (hemorrhoids, perianal thrombosis, fissures, fistulas, and anal skin tags) in 44% of them.

Our sample also confirmed the high prevalence of hemorrhoidal disease, with 947 patients having a global 19.1% prevalence (181 cases). When grouping the data into different subsets, we found hemorrhoids in 13.4% of the HIV population and in 20.5% of the non-HIV population.

A study carried out at Doula Hospital, in Cameroon, Africa, a service with characteristics similar to ours, such as the fact that it is a tertiary referral hospital specializing in the treatment of HIV patients, located in that country's financial capital and having a large multidisciplinary team and great flow of patients, evaluated 390 patients for the prevalence of symptoms and signs of macroscopic anorectal diseases. They found a 10.3% prevalence of hemorrhoidal disease, followed by proctitis (10%), and anal fissure, results that are similar to ours when neoplasms were excluded.[2]

Sexually transmitted diseases are also a public health problem with an estimated incidence of 333 million cases per year. Anorectal involvement is common; however, the exact prevalence of these pathologies remains unknown due to the numerous asymptomatic cases and the lack of accurate epidemiological data.[13]

HPV is the most common sexually transmitted viral infection worldwide, and its typical lesion is condyloma acuminata. Over 120 types of HPV have been identified; serotypes 6 and 11 are more commonly found in benign verrucous lesions while serotypes 16 and 18 are the most commonly seen in dysplasia and malignant lesions.[13,14] More than 80% of men and women contract HPV before the age of 45, and this number increases to 92.6% in the population of HIV positive patients (men who have sex with men) and over 70% among HIV-positive women. In HIV-negative individuals, in this same group of men who

have sex with men, the prevalence of HPV drops to 63.9%.[15] When compared to the heterosexual population, the prevalence of HPV is 2–6 times higher in the high-risk population.[16] Antiretroviral therapy does not appear to reduce the risk of developing condylomas; still, in patients with higher CD4 counts and lower viral burden, the risk for that decreases[17]. Our results corroborate this study: even though the group with the highest CD4 counts is quite similar to the HIV-negative group, there was still a prevalence of condyloma in this population.

A study carried out in 2018 by Tosato Boldrini et al.[18] shows that a CD4 count above 500 cells/mm^3 was a protective factor against HPV 16 and 18 and multiple infections. An undetectable viral burden was also a protective factor against any type of HPV, high-risk HPV, and multiple infections. The fact that they were not making use of an antiretroviral therapy was a risk factor for any HPV. The antiretroviral therapy is responsible for improving the immune system by increasing the amount of CD4+ T lymphocytes. Nevertheless, even patients with cell levels close to those in the non-HIV population still have a higher prevalence of HPV infection. A possible explanation for this is that the anorectal region depends more on local immunity[4] or that new reinfections by different serotypes occur due to the sexual behavior of individuals,[14,19] but there are insufficient data to confirm these hypotheses.

We assume that the population in our study is representative of the group of patients being treated for HIV at *Hospital Emílio Ribas*. Still, we can interpret as a limitation to the study the fact that this is a referral center specializing in the treatment of these patients and that it is not possible to prevent geographic variations from having an impact on the results herein presented. Just as the lack of some patients' data resulted in reduced sample size.

Since its introduction in 1995, retroviral therapy has changed the life expectancy of HIV patients and they are now living longer, with an American perspective of 25% of individuals living with HIV being aged 50 years or older. The increase in life expectancy makes them more susceptible to the development of malignant or benign colorectal pathologies that generally affect the elderly. There is an estimate that 20%–25 % of these patients will need elective or emergency surgery over the course of the disease, whether related to it or not.[20–22] Although there are numerous studies describing the results of anorectal surgery in patients with HIV or AIDS, little is known about the characteristics and results in other colorectal pathologies, such as cancer, diverticular or inflammatory disease.[22] In our sample, 12% of patients had indication for surgery, 9.3% in the HIV group and 14% in the non-HIV group, with a statistical difference between them (p = 0.015). However, data focusing on this subject are still lacking and are insufficient for further conclusions.

Conclusion

The results we obtained in the conditions this study was conducted have allowed us to conclude that anorectal diseases are the same in HIV-positive and -negative patients, despite exhibiting different incidences and with hemorrhoidal disease remaining the most prevalent condition, irrespective of the group. In HIV-patients with CD4 T lymphocytes counts above 500 cells/mm^3, the diseases resemble those found in non-HIV patients, except for condyloma acuminata, which remains higher in the chronically immunosuppressed group.

Conflict of interest

The authors declare no conflicts of interest.

Financial support

REFERENCES

1. UNAIDS https://unaids.org.br/estatisticas/.
2. Luma HN, Eloumou SAFB, Fualefeh-Morfaw EA, Malongue A, Temfack E, Lekpa FK, et al. Anorectal pathology amongst HIV infected patients attending the Douala General Hospital: a cross-sectional study. Int. J. STD AIDS. 2016;28:389–96.
3. Oette M, Mosthaf FA, Sautter-Bihl ML, Esser S. HIV-associated anal dysplasia and anal carcinoma. Oncol. Res. Treat. 2017;40:100–5.
4. Nadal SR, Manzione CR, Horta SH. Comparison of perianal diseases in HIV-positive patients during periods before and after protease inhibitors use: what changed in the 21st century. Dis. Colon. Rectum. 2008;51:1491–4.
5. Cruz GMG, Ferreira RMRS, Neves PM. Doença hemorroidária–aspectos epidemiológicos e diagnósticos de 9.289 pacientes portadores de doença hemorroidária. Rev. Bras. Coloproctol. 2006;26:6–23.
6. Tsang YP, Fok KL, Cheung YS, Li KW, Tang CN. Comparasion of transanal haemorrhoidal dearterialisation and stapled haemorrhoidopexy in management of haemorrhoidal disease: a retrospective study and literature review. Tech. Coloproctol. 2014;18:1017–22.
7. Marsicovetere P. Examining, diagnosing, and treating benign anorectal conditions. JAAPA. 2018;31:32–7.
8. Bastawrous AL. Hemorrhoids. In: Beck DE, Wexner SD, Saclarides TJ, Senagore AJ, Stamos MJ, Wexner SD, editors. The ASCRS Textbook Of Colon And Rectal Surgery, 11, 2nd ed. New York: Springer; 2011. p. 176–7.
9. Estalella L, Lopez-Negre JL, David Parés D. Enfermedad hemorroidal. Med. Clín. (Barcelona). 2013;140:38–41.
10. Guttenplan M. The evaluation and office management of hemorrhoids for the gastroenterologist. Curr. Gastroenterol. Rep. 2017;19:30.
11. Cruz GMG, Santana JL, Santana SKA, Ferreira RMR, Neves PM, Faria MNZ. Doenças anais concomitantes à doença hemorroidária: revisão de 1.122 pacientes. Rev. bras. Coloproct. 2006;26:369–76.
12. Pinho MS, Ferreira LC, Vasconcelos ECG, Souza Filho NA, Reis MC. Análise da prevalência por sexo e idade nas doenças anorretais freqüentes. Rev. bras. Coloproc. 2002;3:158–63.
13. Assi R, Hashim PW, Reddy VB, Einarsdottir H, Longo WE. Sexually transmitted infections of the anus and rectum. World J. Gastroenterol. 2014;20:15262–8.
14. Blas MM, Brown B, Menacho L, Alva IE, Silva-Santisteban A, Carcamo C. HPV prevalence in multiple anatomical sites among men who have sex with men in Peru. PLoS One. 2015;10:e0139524.
15. Albuquerque A, Medeiros R. New insights into the role of human papillomavirus in anal cancer and a anal wart development. Acta Cytol. 2019;63:118–23.

16. Lu B, Viscidi RP, Lee JH, Wu Y, Villa LL, Lazcano-Ponce E, et al. Human papillomavirus (HPV)6, 11, 16, and 18 seroprevalence is associated with sexual practice and age: results from the multinational HPV Infection in Men Study (HIM Study). Cancer Epidemiol. Biomarkers Prev. 2011;20:990–1002.

17. Dolev JC, Maurer T, Springer G, Glesby MJ, Minkoff H, Connell C, et al. Incidence and risk factors for verrucae in women. AIDS. 2008;22:1213–9, http://dx.doi.org/10.1097/QAD.0b013e3283021aa3.

18. Tosato Boldrini NA, Bondi Volpini LP, de Freitas LB, Musso C, Merçon de Vargas PR, Spano LC, et al. Anal HPV infection and correlates in HIV-infected patients attending a Sexually Transmitted Infection clinic in Brazil. PLoS One. 2018;13:e0199058.

19. Sadlier C, Rowley D, Morley D, Surah S, O'Dea S, Delamere S, et al. Prevalence of human papillomavirus in men who have sex with men in the era of na effective vaccine;a call to act. HIV Med. 2014;15:499–504.

20. Martin CP, Fain MJ, Klotz SA. The older HIV-positive adult: a critical review of the medical literature. Am. J. Med. 2008;121:1032–7.

21. Dua RS, Wajed SA, Winslet MC. Impact of HIV and AIDS on surgical practice. Ann. R. Coll. Surg. Engl. 2007;89:354–8.

22. Gahagan JV, Halabi WJ, Nguyen VQ, Carmichael JC, Pigazzi A, et al. Colorectl surgery in patients with HIV and AIDS: trends and outcomes over a 10-year period in the USA. J. Gastrointest. Surg. 2016;20:1239–46.