Clinical-epidemiological characterization of women who received post-exposure HIV prophylaxis in a public hospital in Porto Alegre, Rio Grande do Sul

Caracterização clínico-epidemiológica de mulheres que receberam a profilaxia pós-exposição ao HIV em um hospital público de Porto Alegre, Rio Grande do Sul

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ABSTRACT

Introduction: Prevention strategies are key to combating the epidemic of infections such as HIV and syphilis. The epidemiological scenario of Porto Alegre/RS for these infections shows the need for greater efforts in the area of prevention, seeking to characterize both the population that uses these strategies and the services involved in the care of exposed people. **Objective:** This study aimed to characterize the clinical and epidemiological profile of patients who received post-exposure prophylaxis (PEP) to HIV treated in a public hospital in Porto Alegre/RS. **Methods:** This is a retrospective, research, descriptive study based on the Clinical Protocol and Therapeutic Guidelines for PEP, updated in 2018 by the Ministry of Health. Prophylaxis request forms and medical records of patients treated were analyzed. **Results:** The population consisted of 87 women who received PEP from January to September 2019. There was a predominance of women aged between 20 and 29 years old (55.2%). The most frequent sexual exposure was consensual (69.0%) followed by sexual assault (31.0%). Porto Alegre was the place of residence of most patients (73.6%). The most frequently used therapeutic regimen was the combination of atazanavir, ritonavir, and tenofovir plus lamivudine. On the first visit, 8.0% of the patients showed reactive results for the treponemal syphilis test. Only 23.0% and 14.9% of patients returned for anti-HIV tests in the first and third months after exposure, respectively, and the results were non-reactive. Only 19 patients (21.8%) attended the consultations between 0 and 28 days after PEP. **Conclusion:** It was identified that a considerable percentage of women already had reactive serology for syphilis, most women did not return for follow-up within 28 and 90 days after the first consultation, more than half of the women were aged between 20 and 29 years old, and the most frequent sexual exposure was consensual. In this sense, efforts are needed, such as adequate counseling, adoption of interventions such as sending messages by cell phone, telephone calls, and preparation of educational materials, seeking to improve adherence to treatment and follow-up in the service, which is important given the scenario of epidemiology in Porto Alegre.

Keywords: HIV. Sexually transmitted diseases. Post-exposure prophylaxis. Disease prevention.

RESUMO

Introdução: Estratégias de prevenção são fundamentais para o combate à epidemia de infecções como o vírus da imunodeficiência humana (HIV) e sífilis. O cenário epidemiológico de Porto Alegre/RS para essas infecções mostra a necessidade de maiores esforços na área de prevenção, buscando caracterizar tanto a população que utiliza essas estratégias quanto os serviços envolvidos no atendimento das pessoas expostas. **Objetivo:** Caracterizar o perfil clínico-epidemiológico das pacientes que receberam a profilaxia pós-exposição (PEP) ao HIV atendidas em um hospital público de Porto Alegre/RS. **Métodos:** Trata-se de um estudo retrospectivo, documental, descritivo e baseado no Protocolo Clínico e Diretrizes Terapêuticas para PEP, atualizado em 2021 pelo Ministério da Saúde. Foram analisados os formulários de solicitação da profilaxia e prontuários das pacientes atendidas. **Resultados:** A população foi composta de 87 mulheres que receberam a PEP no período de janeiro a setembro de 2019. Predominaram mulheres com idades entre 20 e 29 anos (55,2%). A exposição sexual mais frequente foi a consentida (69,0%), seguida pela violência sexual (31,0%). Porto Alegre foi o local de residência da maioria das pacientes (73,6%). O esquema terapêutico utilizado com maior frequência foi a combinação com atazanavir, ritonavir e tenofovir associado à lamivudina. No primeiro atendimento, 8,0% das pacientes demonstraram resultados reagentes para o teste treponêmico de sífilis. Retornaram para a realização dos testes anti-HIV no primeiro e terceiro mês após a exposição apenas 23,0 e 14,9% das pacientes, respectivamente, e os resultados foram não reagentes. Apenas 19 delas (21,8%) compareceram às consultas entre zero e 28 dias posteriores à PEP. **Conclusão:** Foi identificado que um percentual considerável de mulheres já apresentava sorologia reagente para sífilis, a maioria das mulheres não retornou para o seguimento no período de 28 e 90 dias após o primeiro atendimento, mais da metade delas tinha idade entre 20 e 29 anos e a exposição sexual mais frequente foi a consentida. Nesse sentido, são necessários esforços como aconselhamento adequado, adoção de intervenções como o envio de mensagens pelo celular, ligações telefônicas e elaboração de materiais educativos, buscando a melhoria da adesão ao tratamento e do acompanhamento no serviço, o que é importante diante do cenário epidemiológico de Porto Alegre.

Palavras-chave: HIV. Infecções sexualmente transmissíveis. Profilaxia pós-exposição. Prevenção.

INTRODUCTION

In Brazil, the incidence of infections caused by the Human Immunodeficiency Virus (HIV) has remained high. In the last three years alone, approximately 40,000 new cases of HIV were reported in the country. Despite the decline in the number of deaths related to Acquired Immunodeficiency Syndrome (AIDS), Rio Grande do Sul (RS) had the highest number of deaths (7.2 cases per 100,000 inhabitants) when compared to other Brazilian states according to the last bulletin published in 2021. Additionally, the highest death rate was also recorded in Porto Alegre (24.1 deaths per 100,000 inhabitants), which is the second Brazilian capital with the highest number of new AIDS cases (41.9 cases per 100,000 inhabitants)[1].

As a response to the epidemic, the Brazilian Ministry of Health promoted a strategy called 'Combined HIV Prevention,' which refers to biomedical, behavioral, and structural approaches to HIV prevention, and the combination of different actions centered on

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individuals, leading to considering their specificities[2]. As for biomedical approaches, the first prevention measures are the most classic ones, such as the use of male and female condoms as a physical barrier to the virus. Second, there are interventions using antiretrovirals, drugs that act by preventing the virus from multiplying. The biomedical strategies that include the use of antiretrovirals, indicated for individuals who are not infected by HIV, are pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP), which differ according to the moment in which they are used, that is, before exposure and after exposure, respectively. The first with continuous treatment and the second with a 28-day prescription. In addition to these strategies, treatment as prevention contributes to a significant reduction in virus transmission[3].

The PEP is part of the Brazilian Ministry of Health and has been widely used since 1998. Initially, it was recommended only in situations of accidents with biological material and, later, it was also included in situations of sexual assault. As of 2010, it began to be used in cases of unprotected sexual intercourse with an HIV-infected partner of unknown serology or who has a high probability of being infected[4].

A case-control study that evaluated the effectiveness of PEP against HIV showed that prophylaxis with zidovudine (AZT) reduces the probability of infection by 81% in health professionals exposed to HIV via the percutaneous route, whereas prophylaxis with this antiretroviral (ARV) was the first to demonstrate the effectiveness of PEP[5]. In addition, a meta-analysis identified 25 studies that evaluated PEP in non-human primate models, where the risk of seroconversion was reduced by 89% in those who received prophylaxis[6].

In Brazil, the Clinical Protocol and Therapeutic Guidelines (PCDT) for Post-Exposure Prophylaxis of Risk for HIV Infection, Sexually Transmitted Infections (STIs), and Viral Hepatitis was developed by the Ministry of Health (and updated in 2021), providing the main recommendations to professionals and services involved in the care of exposed people. The risk situations for HIV infection that are part of this protocol are exposure to circumstances in which sexual assault events occur, consensual sexual exposure, and accidents with biological material, that is, situations involving percutaneous exposure, exposure through mucous membranes, cutaneous membranes (involving non-intact skin) and bite with the presence of blood[7].

For the indication of whether PEP should take place for HIV, the exposed individual must undergo a rapid test for HIV, and the result must be non-reactive for the initiation of prophylaxis. If reactive, it must be confirmed by another rapid test, and then be referred for clinical follow-up and antiretroviral treatment (ART). Knowledge of the source person is not mandatory. It is also recommended to know the serological status of hepatitis B (HBV) and hepatitis C (HCV) of the exposed person through rapid or laboratory tests with collection in the first consultation and verification of immunizations. For sexual exposures, rapid or laboratory tests must also be requested for the diagnosis of syphilis in the first consultation and the patient must continue with clinical follow-up for the repetition of the tests[7]. Every woman exposed to sex should be investigated for symptoms of pregnancy, the indication of emergency contraception and, if necessary, a pregnancy test should be requested. Any women victims of sexual assault, in addition to the other tests already mentioned, whenever possible, should be evaluated for the occurrence of infection by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*[7,8].

The preferred regimen for PEP in adults and adolescents older than 12 consists of a 300 mg tenofovir (TDF) co-formulated tablet associated with 300 mg lamivudine (3TC) and a 50 mg dolutegravir (DTG) tablet. It is a scheme with a high genetic barrier, reducing the possibility of resistance and a lower incidence of adverse reactions[7,9]. Dolutegravir is also indicated for women who are likely to become pregnant, who use a contraceptive method, or who have other conditions that prevent pregnancy[10] According to experimental studies in non-human primates, prophylaxis should be initiated within 72 hours after exposure[11-13], the ideal time being the first two hours after possible contact with the virus[6].

Despite the time that PEP for HIV has been offered and the increase in the number of dispensations in recent years, knowledge of PEP is still low among users and health professionals[14]. Another problem, a consequence of lack of knowledge about PEP, occurs when individuals exposed to HIV miss the 72-hour window for starting prophylaxis, sometimes because they do not know the time limit in which PEP is still effective[15]. In addition, the low perception of risk can mean that many individuals undergoing HIV PEP do not complete the 28-day treatment cycle and do not return to follow-up appointments to carry out the necessary tests and, mainly, to know their serological status for HIV[16]. Studies have already shown that it is difficult for professionals and services to properly adhere to PEP, due to a lack of knowledge about this strategy and limited technologies in services[4].

OBJECTIVE

Thus, the objective of this study was to characterize the profile of patients who received PEP for HIV treated by the Medication Dispensing Unit (MDU) of a public hospital and to evaluate the clinical and laboratory follow-up of prophylaxis. In addition to describing the clinical and sociodemographic profile of patients in this hospital service, we aimed to determine the HIV seroconversion rate and identify the frequency of repeated exposure to prophylaxis.

METHODS

Characterization of the study

A retrospective, documentary, and descriptive analysis was carried out at MDU Hospital Fêmina, in Porto Alegre (RS), located in the Pharmacy Service of this Hospital, where PEP for HIV is dispensed. The standardized forms for requesting prophylaxis filed at the MDU, the records of these dispensations in the *Sistema de Controle Logístico de Medicamentos* (SICLOM), and the electronic medical records of patients treated at Hospital Fêmina were analyzed.

Study location

Hospital Fêmina is a reference service for women who were victims of sexual assault, and has an Infectious Diseases Day Hospital service to assist women living with HIV/AIDS. In addition, the Hospital has a 24-hour Gynecological and Obstetric Emergency

Service, which is also one of the gateways to PEP. Based on the PCDT of PEP[7], a pre-established flow is followed and includes the application of rapid HIV and syphilis tests, a request for laboratory tests, and the prescription of medication according to an institutional form, which includes, in addition to antiretrovirals, emergency contraception, antimicrobials, vaccine, and immunoglobulin for hepatitis B (the latter only for cases of sexual assault).

The requested laboratory tests are performed to detect HIV (anti-HIV-1/2), hepatitis B (HBsAg), hepatitis C (anti-HCV), HTLV (anti-HTLV), treponemal test (chemiluminescence – CMIA) and non-treponemal (VDRL) for the diagnosis of syphilis. Checking for hepatitis B immunization (anti-HBs), and liver enzyme (AST/ALT), as well as a pregnancy test (β-HCG), may be asked. About 30 days after exposure, anti-HIV, treponemal/VDRL, and anti-HTLV tests are repeated. In 90 days, the tests are once again repeated, without the need for syphilis follow-up, which must be monitored until the fourth week. The assessment regarding the toxicity of antiretrovirals is carried out around two weeks after receiving the prophylaxis, and includes the measurement of liver enzymes (AST/ALT), in addition to other tests that may be requested according to the clinical situation of each patient.

For patients eligible for HIV prophylaxis, the prescribed medications are provided along with the first copy of the institutional form, which contains guidance on the correct use of medications, in addition to other information, such as a request for return to schedule follow-up appointments in the infectology service (when the results of laboratory tests are evaluated). If necessary, the patient can also seek psychological care and social assistance available at that location.

Study population

The study population consisted of women treated in MDU Hospital Fêmina, who received PEP for HIV. The inclusion criteria were: patients aged 18 years or over, treated from January to September 2019, who received the standardized institutional form for dispensing HIV post-exposure prophylaxis. The exclusion criteria are: forms with illegible patient identification, accident with any biological material, patients who collected antiretrovirals in another place, and those who were referred to another service.

Data extraction and analysis

Sociodemographic data, as well as the date of prescription, dispensation and exposure, exposure circumstances, characteristics of the exposed person, and information about the prescribed therapeutic scheme, were extracted from the prophylaxis dispensation forms. Other information related to the clinical and laboratory profile, such as the performance of specific laboratory tests, information on adverse reactions, follow-up appointments, and the occurrence of HIV seroconversion, were obtained by checking the electronic medical record of each patient.

The analysis was performed through descriptive statistics using the "Statistical Package for Social Sciences" software (SPSS, version 20.0, Chicago, IL, USA). Sociodemographic and clinical-laboratory characteristics were described using frequency distribution, mean, minimum and maximum values, median and interquartile ranges (IQR).

RESULTS

From January to September 2019, 99 HIV PEP consultations were carried out at the Gynecological and Obstetric Emergency Service of Hospital Fêmina. Of these, two cases had a positive result for HIV and, consequently, were referred for HAART, and not for PEP. Out of these consultations, four patients were seen twice during the study period, and one of them was referred for PrEP during clinical follow-up. To characterize care and analyze the profile of patients treated, only their first occurrence of PEP during this period was analyzed. Of these 93 patients, six arrived at the service after 72 hours of exposure, not being candidates to receive PEP antiretrovirals, totaling the inclusion of 87 patients in this study.

Of the 87 patients evaluated in this research, the majority resided in Porto Alegre (73.6%) when they accessed the service, and the most frequently observed age group was 20 to 29 years (55.2%). The most frequent exposure circumstance was consensual sexual exposure (n = 60; 69.0%), followed by sexual assault (n = 27; 31.0%) (**Table 1**). The central region of Porto Alegre was the place of residence of most patients treated (45.3%), as shown in **Table 2**.

The most frequently used therapeutic scheme was the combination of atazanavir (1 tablet/day), ritonavir (1 tablet/day), and tenofovir

Table 1 – City of residence and age group of patients evaluated in the study by circumstances of exposure

	Total (n=87)		Consensual Sexual exposure (n=60)		Sexual Assault (n=27)	
	n	%	n	%	n	%
City						
Alvorada	3	3.4	1	1.7	2	7.4
Canoas	5	5.7	4	6.7	1	3.7
Gravataí	4	4.6	4	6.7	0	0.0
Porto Alegre	64	73.6	42	70.0	22	81.5
Viamão	7	8.0	6	10.0	1	3.7
Other cities	4	4.6	3	5.0	1	3.7
Age range (years)						
18–19	7	8.0	4	6.7	3	11.1
20–29	48	55.2	32	53.3	16	59.3
30–39	23	26.4	18	30.0	5	18.5
40–49	8	9.2	5	8.3	3	11.1
≥50	1	1.1	1	1.7	0	0.0

Table 2 – Regions where patients residing in Porto Alegre evaluated in the present study came from.

Regions*	Total (n=64)	
	n	%
Center	29	45.3
Northwest/Humaitá/Navegantes/Ilhas	9	14.1
Partenon/Lomba do Pinheiro	9	14.1
South/Center-South	6	9.4
North/Baltazar axis	4	6.3
East/Northeast	4	6.3
Restinga/Extreme South	2	3.1
Glória/Cruzeiro/Cristal	1	1.6

*Territorial regions covered by the district managements of the Municipal Health Secretariat of Porto Alegre.

associated with lamivudine (co-formulated tablet – 1 tablet/day) (**Table 3**). Only two patients received the regimen with dolutegravir together with tenofovir/lamivudine (co-formulated tablet – 1 tablet/day). Most patients also received the other prophylaxis in this first visit: penicillin G benzathine (for penicillin allergy sufferers: azithromycin 2g), azithromycin 1g, ceftriaxone, metronidazole and vaccine for hepatitis B (first dose). Emergency contraception was dispensed to 57.5% of the patients treated (**Table 3**).

Another way of evaluating the patients was through carrying out tests to detect pregnancy (β-HCG), which were requested mainly in cases of sexual assault (n=25; 92.6%), and less frequently in cases of consented exposure to sex (n=11; 18.3%). Only one case, related to exposure due to sexual assault, presented a value of 7.89 lU/mL in the first consultation, which is a result suggesting a previous pregnancy.

In the first consultation, in many cases, measurements of the liver enzymes ALT (n=81; 93.1%) and AST (n=55; 63.2%) were requested, which is important to check for any liver alterations, especially to evaluate the indication of PEP antiretrovirals. The values were: ALT (median=14 U/L; IQR=8 U/L) and AST (median=17 U/L; IQR=6 U/L). It was also observed that 4 (4.7%) of the patients who had withdrawn from the regimen containing atazanavir (n=85) returned to the service due to drug intolerance. The most frequent symptoms were jaundice (n=3; 3.5%) and skin lesions in one case. These patients returned to the service an average of 8 days after withdrawal of antiretrovirals, a period that varied between 3 and 13 days.

The serological follow-up of the 87 patients was observed from the results obtained from the samples collected in the first visit to their sequence approximately 90 days after exposure (**Table 4**). The frequency of serologies in the first visit was high. In this sense, it was possible to identify that, in the first consultation, 8.0% of the patients who attended showed reactive results for the treponemal test for syphilis (6.7% of those who reported consensual sexual exposure and 11.1% of those who reported sexual assault) (**Table 4**). Of these reagent results, for only three diagnostic confirmations, non-treponemal tests were requested, and the results were 1:2, 1:4, and 1:128. In addition, a patient exposed to sexual assault presented a positive result for the non-treponemal test, with a value of 1:2; however, a confirmatory treponemal test was not found. In general, the frequency of performing non-treponemal tests was lower than for treponemal tests, and the highest number of requests was in the first consultation (n=51; 58.6%). Of the patients who had a confirmatory test, only one had a repeat test, which occurred in a period longer than 90 days, and showed a non-reagent result. All patients who had positive test results received penicillin G benzathine, 2.4 million IU (a single dose), as the treatment on the first visit. However, as we have already mentioned, in only one case serological follow-up was performed.

Still, regarding the first visit, tests for anti-HIV-1/2, HbsAg, and anti-HCV were performed in 97.7% of patients, while the test for anti-HTLV-1/2 was performed in 11.5% of the patients assisted, and all had non-reagent results (**Table 4**). The number of patients who returned for repeat exams in the first month after exposure was low (n=20). Treponemal tests for syphilis were used in 11.5% of the patients, the anti-HIV – ½ test in 23.0%, the HbsAg test in 17.2%, the anti-HCV test in 19.5%, and the anti-HTLV test – ½ in 16.1%, all of which had non-reactive results. Finally, in the assessment of the third month after exposure, the following tests were performed and showed non-reagent results: 14.9% for anti-HIV – ½, 14.9% for anti-HCV, and 9.2% for anti-HTLV – ½ (**Table 4**). The laboratory follow-up of the patients could continue until the sixth month; however, it usually occurs at the physician's discretion and especially in cases where the source person is known to be positive for hepatitis C. Nevertheless, it is difficult to know the serological status of the source person in consensual and non-consensual sexual exposures.

The evaluation of the profile of antibodies to hepatitis B (anti-HBs) was requested during laboratory follow-up for 29 patients (where 17 reported consensual sexual exposure and 12 reported sexual assault). Of the patients who underwent the test and had protective antibody titers greater than or equal to 10 IU/mL, 12 (70.6%) were for consensual sexual exposure and 8 (66.7%) for sexual assault. Out of these patients, only 2 vaccine data were not obtained at the hospital. The rest of the patients were given the hepatitis B vaccine on the day they received the PEP. The serological follow-up test

Table 3 – Frequency of prescription of prophylaxis for HIV infection, STIs, emergency contraception and vaccination for hepatitis B according to the circumstances of exposure

Variables	Total (n=87)		Consensual Sexual Exposure (n=60)		Sexual Assault (n=27)	
	n	%	n	%	n	%
HIV prophylaxis						
DTG (50 mg) + TDF/3TC (300 mg/300 mg)	2	2.3	1	1.7	1	3.7
ATV (300 mg) + RTV (100 mg) + TDF/3TC (300 mg/300 mg)	85	97.7	59	98.3	26	96.3
Prophylaxis of sexually transmitted infections (STIs)						
Penicillin G Benzathine 2.4 million IU (IM, single dose)	79	90.8	57	95.0	22	81.5
Azithromycin 2g (PO, single dose)	4	4.6	1	1.7	3	11.1
Azithromycin 1g (PO, single dose)	77	88.5	57	95.0	20	74.1
Ceftriaxone 500 mg (IM, single dose)	80	92.0	57	95.0	23	85.2
Metronidazole 2g (PO, single dose)	81	93.1	57	95.0	24	88.9
Hepatitis B vaccine						
Received the first dose	69	79.3	45	75.0	24	88.9
Emergency contraception						
Levonorgestrel 0.75mg (2 tablets, PO, single dose)	50	57.5	35	58.3	15	55.6

ATV: Atazanavir; DTG: Dolutegravir; IM: Intramuscular; 3(TC): Lamivudine; RTV: Ritonavir; TDF: Tenofovir; IU: International Units; PO: Oral.

Table 4 – Laboratory follow-up of patients assisted due to exposure circumstances.

	Total (n=87)		Consensual Sexual Exposure (n=60)		Sexual Assault (n=27)	
	N	%	n	%	n	%
First Service						
Treponemal Test for Syphilis						
Reagent	7	8.0	4	6.7	3	11.1
Non-reagent	54	62.1	42	70.0	12	44.4
Anti-HIV - 1/2						
Non-reagent	85	97.7	58	96.7	27	100.0
HBsAg						
Non-reagent	85	97.7	58	96.7	27	100.0
Anti-HCV						
Non-reagent	85	97.7	58	96.7	27	100.0
Anti-HTLV - 1/2						
Non-reagent	10	11.5	5	8.3	5	18.5
1st month post-exposure						
Treponemal Test for Syphilis						
Non-reagent	10	11.5	8	13.3	2	7.4
Anti-HIV - 1/2						
Non-reagent	20	23.0	10	16.7	10	37.0
HBsAg						
Non-reagent	15	17.2	10	16.7	5	18.5
Anti-HCV						
Non-reagent	17	19.5	10	16.7	7	25.9
Anti-HTLV - 1/2						
Non-reagent	14	16.1	8	13.3	6	22.2
3rd month post-exposure						
Anti-HIV - 1/2						
Non-reagent	13	14.9	8	13.3	5	18.5
Anti-HCV						
Non-reagent	13	14.9	8	13.3	5	18.5
Anti-HTLV - 1/2						
Non-reagent	8	9.2	5	8.3	3	11.1

Anti-HIV: Human Immunodeficiency Virus antibody; HBsAg: Hepatitis B virus surface antigen; Anti-HCV: Hepatitis C antibody; Anti-HTLV: Human T-lymphotropic virus antibody.

for antibodies to hepatitis B was only requested for patients who returned for follow-up appointments.

When the follow-up was analyzed only by attending consultations at the infectology service (Hospital-Dia), it was observed that the number of patients who attended the consultations was even lower than the serological tests performed. This difference between the number of patients consulted and the number of patients who underwent the test(s) can be explained by the fact that some patients returned only for the emergency, and may not have scheduled appointments with the infectologist. In cases where there was more than one consultation in the same period, only the last consultation was considered. Only 19 patients attended consultations between 0 and 28 days after the PEP (**Table 5**), with the mean time taken to attend consultations being 6 days, varying between 1 and 17 days. Although it was observed that patients with both types of exposure had low adherence to serological follow-up and consultations with the infectology service, a greater demand for care occurred in cases of sexual assault, especially during the period from 0 to 28 days.

Table 5 – Frequency of pre-scheduled follow-up appointments

	Total (n=87)		Consensual Sexual Exposure (n=60)		Sexual Assault (n=27)	
	n	%	n	%	n	%
Post-PEP medical appointments						
0–28 days	19	21.8	11	18.3	8	29.6
29–45 days	11	12.6	5	8.3	6	22.2
46–60 days	3	3.4	3	5.0	0	0
61–90 days	0	0	0	0	0	0
>90 days	9	10.3	6	10.0	3	11.1

DISCUSSION

The present study analyzed the attendance records of women who accessed the emergency service of Hospital Fêmina for evaluation after situations of sexual assault and consensual sexual exposure to HIV infection. Most PEP prescriptions were related to consensual sexual exposure (69.0%), with the most frequent age group for both exposures being 20 to 29 years. Most patients from Porto Alegre lived in the Center region, which suggests that they chose this service due to its proximity to their places of residence. This region ranks seventh in the incidence of AIDS cases in Porto Alegre, with 44 cases per 100,000 inhabitants, according to the 2017 indicator. From 2012 to October 2018,12,971 cases of people infected with HIV were reported. Of these, 40% were represented by women, mainly aged between 25 and 34 years[17], corroborating the importance of the existence of 24-hour services that can accommodate on-time situations of exposure to HIV for this population.

The return of patients to the service within 28 days after exposure would be important to assess possible adverse effects related to the use of antiretrovirals and reinforce measures of treatment adherence, but only 21.8% of the patients included in the study returned to the infectology health care service during this period, with 18.3% related to cases of consensual sexual exposure and 29.6% to cases of sexual assault. Among the 85 patients who received the regimen containing atazanavir, 4.7% returned to the service due to an adverse reaction, mainly jaundice. Due to the low rate of return of patients to the service in the period up to 28 days after the start of prophylaxis, as previously reported, it is possible to suggest that the number of patients who had adverse reactions was even higher than that found in this study. A study carried out in Fortaleza, Ceará, showed that only 25.7% of individuals completed the 28-day course of treatment and the occurrence of an adverse reaction was reported in 23.4% of patients who underwent PEP[18]. Another retrospective study conducted in a hospital in Barcelona, Spain, showed that 46.3% of patients who received atazanavir had adverse reactions, with gastrointestinal reactions being the most frequent. Furthermore, in that same study, of the patients who had received the regimen with atazanavir and returned to the service, 12% did not complete the 28-day course of prophylaxis[19]. Scannell and Guthrie[20], through a meta-analysis that evaluated 19 studies on PEP for victims of sexual assault in the United States of America, showed that only 25.7% of the victims complied with the course of treatment and that one of the reasons for discontinuing it would be the adverse reactions to antiretrovirals. These studies show the low adherence of patients who received

PEP and, therefore, the importance of clinical follow-up to reinforce adherence measures and monitor the adverse effects of the prescribed antiretroviral therapy.

In the present study, it was observed that only 14.9% of patients returned to the service to undergo the anti-HIV test in a period equal to or greater than 90 days, and a smaller number of patients consulted the infectology service in that period (n = 9; 10.3%). Inciarte et al.[19] also demonstrated a low rate of return for carrying out the test for HIV detection in the same period, observing a return rate of 33.0%. Another retrospective study, which evaluated the PEP in five reference health centers for the treatment of HIV in Brazil, identified that only 27.2% of the patients completed the PEP follow-up and, of these patients, all were non-reactive for HIV[21]. Additionally, the study conducted in Fortaleza, which evaluated the clinical follow-up of 858 patients undergoing PEP, showed that only 30.8% of the patients attended the first follow-up consultation and only 9.8% attended the last consultation[18], the same situation that was observed in our study. In addition, other serological tests to detect infections such as syphilis, hepatitis B, and hepatitis C, especially from the first month after exposure, were performed in a low frequency. Of the patients who returned during this period to carry out the tests, all had non-reagent results. However, we did not obtain data on performing tests on another service.

In this study, it was not possible to identify the reason for discontinuing clinical and laboratory follow-up. In the first consultation, the patients received written instructions through the first copy of the standardized institutional form for requesting the PEP, which described the guidelines for returning and scheduling consultations with the infectious diseases service. However, the adopted methodology did not allow evaluation of the quality of verbal information passed on by health professionals in this first consultation. A better understanding of the information passed on to patients at that time is needed to understand possible flaws in guidance or referrals.

The low return for follow-up also made it impossible to assess the HIV seroconversion rate of the women assisted. In this perspective, a systematic review followed by a meta-analysis, which evaluated studies related to PEP in different populations and exposure circumstances, identified 37 seroconversions for HIV in a total of 8007 patients, and in only three of them the cause was reportedly the failure in the effectiveness of PEP. Furthermore, in most cases seroconversion was attributed to continuous high-risk exposures[22]. In the period evaluated by this study, four patients were seen more than once due to repeated exposure, which increases the risk of infection. According to a meta-analysis, the rate of sexual transmission of HIV per sexual act is 0.08% (95%CI 0.06–0.11) from male to female in high-income countries and 0.38% (95%CI 0. 13–1.10) in low-income countries. In receptive anal exposures, the risk was increased to 1.7% (95%CI 0.3–8.9) per act. Another reason that could increase the infection rate is the presence of genital lesions, a fact that increases the risk to 5.3% (95%CI 1.4–19.5)[23].

In the epidemiological bulletin made available by the Secretariat for Health Surveillance in 2021, 120 cases of acquired syphilis were recorded for every 100,000 inhabitants in Porto Alegre. This configures Porto Alegre as the third Brazilian capital with the highest rate of detection of acquired syphilis and with high coefficients of detection of syphilis, in pregnant women, and congenital syphilis[24]. Analyzing the data obtained in our study, we identified seven patients who had a positive result on the treponemal tests and one patient who had a positive result on a non-treponemal test. Only three of these patients underwent a confirmatory test. Confirmation of the result for syphilis is not mandatory for starting treatment in cases where there is a risk of loss of follow-up, such as pregnant women or cases of sexual assault[7]. Although all patients received a dose of benzathine penicillin G, only one case had confirmation of the patient's cure. In the other seven cases, no returns were found. Monitoring and treatment of acquired syphilis with benzathine penicillin G depends on the stage of infection. If the infection is recent, the treatment is administered in a single dose, but if the infection is late, three doses should be administered with an interval of seven days for each dose[8,25].

It is important to emphasize that health professionals should guide patients who have access to PEP regarding the other measures included in the Combined Prevention aimed at preventing HIV, syphilis, viral hepatitis, and other STIs, such as the use of condoms[2,25], regular testing[26] or even referral to other strategies such as PrEP[3,27], seeking to reduce these new infections. The World Health Organization guidelines for 2014 on PEP provided recommendations for the adoption of counseling measures to improve adherence rates to this prophylaxis, but emphasizes that, even in the impossibility of adequate initial counseling, often due to lack of resources and trained professionals, the start of PEP[28] should not be delayed. These counseling measures are interventions that aim to improve the user's risk perception concerning exposure to HIV[29]. However, some studies have identified that the effects of these measures are still inconclusive in terms of improving adherence to PEP[3,29] and as a preventive measure against HIV[30].

The professional training fpr emergency services, familiarizing these providers with HIV prevention technologies as well as with the improvement of institutional protocols, can bring benefits such as an increase in the uptake and rate of prescription of PEP to patients with risk exposure, in addition to training these professionals to provide more adequate and comprehensive guidance during care[31,32], also promoting greater dissemination of other prevention strategies[4].

Other interventions may be promising for improving adherence to prophylaxis and clinical-laboratory follow-ups of patients who access the PEP, such as those used to improve compliance with the antiretroviral treatment prescribed for people living with HIV, which are: sending messages via cell phone, reminders, phone calls[33,34] and the preparation and supply of educational materials that allow greater knowledge about this strategy[35].

Strengths

We emphasize that consensual sexual exposure was the most prevalent (69.0%), followed by sexual assault (31.0%). In this study, it was possible to demonstrate a low rate of return to follow-up consultations, as only 19 patients (21.8%) attended consultations between 0 and 28 days after PEP. Returning to consultations is important to check for adverse reactions, adherence to treatment, laboratory follow-up, and assessment of the HIV seroconversion rate. Of the patients who received the PEP, only 14.9% returned to the service to undergo the anti-HIV test in a period equal to or greater than 90 days.

Limitations

A limitation of this study was the impossibility of evaluating the performance of rapid tests (HIV and syphilis) since we could not find records in the specific control spreadsheets of most patients who received PEP. According to the PCDT of the PEP, the rapid test for HIV is important for evaluating whether prophylaxis is indicated, meaning an emergency care in which one should not wait for the results of laboratory tests to indicate prophylaxis. Rapid tests for syphilis are also important in the first consultation to screen for this infection. If it were possible to evaluate the results of these tests, especially those used for diagnosing syphilis, the number of patients with positive results could be even greater than that described in this study. We know that the procedure of carrying out rapid tests is adopted and that the result information can change the flow of care for patients in this service.

CONCLUSION

The present study showed low adherence to follow-up consultations, most patients did not return for clinical and laboratory follow-up and laboratory tests, which are important for the clinical evaluation of patients who received PEP. Only 19 patients attended the 28-day follow-up appointments, and 10 patients returned for the 90-day appointments after exposure. In addition, the study indicated missed opportunities to reduce the number of infections, especially for HIV and syphilis. Reactive results for syphilis were detected in a significant percentage of patients (8%), only considering the first consultation. No HIV seroconversion was found, but only 13 patients returned for the test at the end of the 90 days of exposure. Consensual sexual exposure was found to be the most frequent type of exposure, and more than half of the patients were aged between 20 and 29 years. About 2/3 of the patients resided in Porto Alegre. Adequate and comprehensive counseling for this population to adopt preventive measures is essential to reduce the number of these infections and promote sexual and reproductive health. In this sense, more efforts are needed, in a multidisciplinary scope and at the different levels of SUS care, to link the patients attended to the health services, which becomes even more relevant in the epidemic context of the city of Porto Alegre. Some measures can be adopted by the services to improve adherence, such as adequate counseling, especially in the first consultation, in addition to other measures, such as the training of professionals involved in caring for exposed people. Moreover, some interventions to improve adherence to prophylaxis and monitoring of PEP, such as sending messages by cell phone, making phone calls, and preparing educational materials for this population, may contribute substantially.

Approval by the Human Research Ethics Committee

This research was approved by the Human Beings Research Ethics Committee (CEP) of *Universidade Luterana do Brasil* (ULBRA), case No. 3.577.974, and by the CEP of the co-participating institution, Grupo Hospitalar Conceição (GHC), under case No. 3.637.304.

Participation of each author

PPF: Conceptualization, Data curation, Writing – original draft. KGS: Conceptualization. CBM: Conceptualization, Writing – review & editing.

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Conflict of interest

The authors declare no conflicts of interest.

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