REVISTA DO INSTITUTO DE MEDICINA TROPICAL DE SÃO PAULO
JOURNAL OF THE SÃO PAULO INSTITUTE OF TROPICAL MEDICINE

ORIGINAL ARTICLE

http://dx.doi.org/10.1590/S1678-9946201860034

Epidemiological and clinical profile of HIV-infected patients from Southwestern Goias State, Brazil

Regyane Ferreira Guimarães Dias[1,2], Luciana Oliveira Bento[1,2], Camila Tavares[1], Hélio Ranes Filho[1,2,3], Melisia Adelaide Cesário da Silva[2], Luciene Carneiro Moraes[2], Ana Amélia Freitas-Vilela[3], Marcos Lázaro Moreli[1], Ludimila Paula Vaz Cardoso[1,3,4]

ABSTRACT

Knowledge about epidemiological distribution patterns of HIV infection in different geographic regions is relevant to understand the dynamics of the disease in Brazil. This study aims to characterize the epidemiological and clinical profile of HIV-infected patients from Southwestern Goias State, from 2005 to 2015. A standardized questionnaire was used to collect clinical-epidemiological, virological, and immunological data from the medical records of all HIV-infected patients (n=539) who were followed at the regional reference center of Jatai, Goias State, Brazil, from 2005 to 2015. We detected the prevalence of male patients and the heterosexual route of transmission, as well as an expressive number of young women infected with HIV. The HIV infection was more prevalent in reproductive ages (55.3%). Most patients presented clinical manifestations related to HIV infection at the time of diagnosis. Twenty-four patients presented coinfection with hepatitis C virus, syphilis, hepatitis B virus, leprosy or Chagas disease. Pneumonia caused by *Pneumocystis jirovecii* was the most common opportunistic infection, followed by neurotoxoplasmosis, tuberculosis, and neurocryptococcosis. Combined antiretroviral therapy improved CD4$^+$ T-cell counts: the mean CD4$^+$ T-cell counts after treatment was twice as high as those found at the first medical appointment; and highly active antiretroviral therapy promoted viral suppression in a significant number of patients. Considering the increasing distribution of HIV infection to the interior of Brazil, this descriptive study outlines the clinical-epidemiological characteristics of HIV infection in Southwestern Goias and contributes to develop local prevention strategies and public service plans.

KEYWORDS: HIV/AIDS. Epidemiology. Midwest Brazil.

INTRODUCTION

The Joint United Nations Program on HIV/AIDS (UNAIDS) estimates that there are about 36.7 million people living with HIV/AIDS around the world[1]. In Brazil, 842,710 HIV/AIDS cases were reported from the beginning of the epidemic up to June 2016. Although high, the incidence rate stabilized at 19.1 cases/100,000 inhabitants in Brazil in 2015[2]. The incidence rate of HIV/AIDS markedly differs among Brazilian regions: it has been growing linearly in the North, Northeast and South regions; it has been declining in the Southeast region; and it is stable in the Midwest region. In the latter region, the incidence rate varied from 17.3 in 2005 to 18.5 cases per 100,000 inhabitants in 2015[2].

The scenario has changed over the last years because the incidence of HIV

[1]Universidade Federal de Goiás, Programa de Pós-Graduação em Ciências Aplicadas à Saúde, Jataí, Goiás, Brazil

[2]Secretaria Municipal de Saúde, Serviço de Assistência Especializada, Jataí, Goiás, Brazil

[3]Universidade Federal de Goiás, Curso de Medicina, Unidade Acadêmica Especial de Ciências da Saúde, Jataí, Goiás, Brazil

[4]Universidade Federal de Goiás, Programa de Pós-Graduação em Biologia da Relação Parasito-Hospedeiro, Goiânia, Goiás, Brazil

Correspondence to: Ludimila Paula Vaz Cardoso
Universidade Federal de Goiás, Regional Jataí (REJ), R. Riachuelo, CP 03, nº 1530, Setor Samuel Graham, CEP 75804-020, Jataí, GO, Brazil
Tel: +55 64 3606-8130, +55 62 98405-0042

E-mail: ludimilacardoso@gmail.com

Received: 4 December 2017

Accepted: 16 May 2018

infection has shifted from metropolitan centers to the interior of the country and has become more prevalent among individuals with low income and poor education level. In other words, the current scenario reflects interiorization and pauperization of the disease[3-6]. Several studies have described the epidemiological profile of HIV infection in patients living in the main Brazilian urban centers, but there are limited data about its incidence rate in inner cities of the country, especially in Midwestern Brazil[7-9]. In this region, Goias State holds the highest number of cases of HIV infection: 1,004 cases were recorded in 2015, with an incidence rate of 15.2 cases/100,000 inhabitants. Although prevalent in heterosexual males, HIV infection among men who have sex with men (MSM) and heterosexual females is increasing[2,10].

Goias State is divided into five macroregions (Northeast, Midwest, North-central, Southeast and Southwest); each one has a regional reference center responsible for providing diagnosis, treatment, and care to local HIV-infected patients. The regional center from Southwestern Goias is located in Jatai, a medium-sized city with 94,890 inhabitants that is 320 km far from the capital, Goiania. Jatai hold one of the first four positions in the ranking of number of HIV-infected individuals in cities with more than 50,000 inhabitants in the Goias State from 2009 to 2012. The incidence rate is greater than the national rate, ranging from 20.5 to 21.1 infected individuals per 100,000 inhabitants, and the number of deaths associated with AIDS has increased since 2010[11-13].

Considering the interiorization and pauperization of the HIV epidemic, the knowledge of epidemiological distribution patterns of the disease in different Brazilian regions is relevant to understand the dynamics of the HIV epidemic, as well as to develop prevention strategies and public service plans. In this sense, the present study aims to characterize the clinical and epidemiological profile of HIV-infected patients who were assisted at the regional health center of Jatai, a city from Southwestern Goias State, in the Midwest region of Brazil, from 2005 to 2015.

MATERIAL AND METHODS

This is a descriptive study of HIV-infected outpatients followed-up at the Clinical Hospital Doutor Serafim de Carvalho (Jatai, Goias State, Brazil), which is the main public hospital from Southwestern Goias and a regional reference center for treatment of patients with infectious diseases. The local Research Ethics Committee approved the study protocol (UFG Nº 926.441 and 1.009.763).

Data were collected from medical records of patients diagnosed with HIV from 2005 to 2015, who were assisted at the aforementioned hospital. The researchers used a standardized questionnaire to collect the following information from the records: sociodemographic [age, gender, race/ethnicity (black, white, and mixed ethnicity); sociobehavioral (possible HIV exposure and sexual orientation - heterosexual, homosexual or bisexual); and clinical information (clinical manifestations at diagnosis, opportunistic infections, coinfections, deaths and the use of combined antiretroviral therapy - cART)].

The baseline $CD4^+$ T-cell count and plasma viral load (PVL) quantification were the outcomes of interest to examine the immunological and virological status, respectively, of the patients at the moment of their first medical appointment at the hospital. The first and last $CD4^+$ T-cell counts and PVL quantification were selected only for those patients undergoing cART. The lower and upper limits of detection of PVL were 50 and 500,000 copies/mL, respectively (Versant HIV-1 RNA 3.0 Assay, branched-chain DNA, Bayer, Tarrytown, NY, USA).

Data were analyzed using the Stata Data Analysis and Statistical Software version 12.0 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX, USA). The profile description of the parameters was reported by using mean and standard deviation (SD) to continuous variables, as well as frequency and percentage of categorical variables. Selected variables were compared between subjects with and without medical records using the chi-square test and the Student's t test for categorical and continuous variables, respectively. Values of $p < 0.05$ were considered statistically significant.

RESULTS

We examined the medical records of 539 patients with positive serology for HIV, who were assisted at a regional reference hospital in Jatai from 2005 to 2015. Analysis of the epidemiological profile (Table 1) revealed that the patients' mean age was 39.5 years (SD: 11), with the predominance of men (57.9%), age group from 20 to 40 years (54.2%), and the mixed self-declared ethnicity (57.1%). Stratification of the groups by gender confirmed the highest incidence rate among 20-40 year-old male and female patients: 55.1% and 50%, respectively. Only 6.7% of the patients were diagnosed before 2000; most of them (70%) were diagnosed within the last ten years (2006-2015).

Regarding the possible route(s) of HIV infection, 494 patients (97.4%) reported unprotected sex; 4 patients reported unprotected sex and/or sharing syringes during intravenous drug use; 3 patients reported unprotected sex and/or blood transfusion and 6 patients reported mother-to-child transmission. Most patients (82.4%) informed heterosexual orientation among male and female patients

Table 1 - Sociodemographic, behavioral, and laboratory data of HIV-infected patients from Jatai, Goias State, Brazil[a]

Parameter	Total records (n= 539)	Incomplete records (n= 170)	Complete records (n= 369)	
Categorical variables	**n (%)**	**n (%)**	**n (%)**	***p*-value[1]**
Gender				0.293
Female	227 (42.1)	66 (38.8)	161 (43.6)	
Male	312 (57.9)	104 (61.2)	208 (56.4)	
Age (years)[b]				0.965
< 20	5 (1.1)	1 (1.1)	4 (1.1)	
20 - 40	247 (54.2)	45 (51.7)	202 (54.7)	
41- 60	190 (41.7)	38 (43.7)	152 (41.2)	
>60	14 (3.1)	3 (3.5)	11 (3)	
Race/Ethnicity[c]				0.544
White	160 (30.6)	49 (31.8)	111 (30.2)	
Mixed ethnicity	298 (57.1)	83 (53.9)	215 (58.4)	
Black	64 (12.3)	22 (14.3)	42 (11.4)	
Route of Infection[d]				0.159
Sexual	494 (97.4)	138 (96.5)	356 (97.8)	
Sexual + IDU	4 (0.8)	0 (0)	4 (1.1)	
Sexual + Hemotransfusion	3 (0.6)	2 (1.4)	1 (0.3)	
Vertical Transmission	6 (1.2)	3 (2.1)	3 (0.8)	
Sexual Orientation[e]				0.647
Heterosexual	413 (82.4)	114 (81.4)	297 (82.3)	
Homosexual	64 (12.8)	18 (12.9)	46 (12.7)	
Bisexual	26 (5.2)	8 (5.7)	18 (5.0)	
HIV Diagnosis[f]				0.157
1984 - 2000	35 (6.7)	14 (8.9)	21 (5.7)	
2001 - 2005	115 (21.9)	37 (23.4)	78 (21.2)	
2006 - 2010	167 (31.8)	55 (34.8)	112 (30.4)	
2011 - 2015	209 (39.7)	52 (32.9)	157 (42.7)	
cART use[g]				0.001*
cART	400 (76.6)	102 (66.7)	298 (80.8)	
Naïve	122 (23.4)	51 (33.3)	71 (19.2)	
Follow-up				<0.001§
Followed-up	395 (73.3)	27 (15.9)	368 (99.7)	
Death	84 (15.6)	83 (48.8)	1 (0.3)	
Transference	20 (3.7)	20 (11.8)	0 (0)	
Abandonment	40 (7.4)	40 (23.5)	0 (0)	
Continuous variables	**mean (SD)**	**mean (SD)**	**mean (SD)**	***p*-value[2]**
Age (years)[b]	39.5 (11.0)	40.4 (11.2)	39.3 (11.0)	0.793
CD4⁺ T-cell count (cells/mm³)				0.01**
Baseline[h]	408.2 (354.3)	329.4 (298.8)	436.4 (368.4)	0.001#†
Last[i]	625.2 (386)	421.4 (382.8)	677.9 (369.4)	0.03##
PVL (copies/mL)				
Baseline[j]	1,471,537 (2.91e+07)	118,361.5 (189,930.3)	1,918,899 (3.36e+07)	0.002¥
Last[k]	27,984.2 (95,037.1)	62,753 (139,879.5)	19,092.2 (77441.78)	<0.001¥¥

Abbreviations: cART, combined antiretroviral therapy; IDU, intravenous drug use; PVL, plasma viral load. [a]The patients were divided into the groups "complete records" and "incomplete records" according to the completeness of their medical records. Total records = complete records + incomplete records. There are missing data for: [b]83 patients; [c]17 patients; [d]32 patients; [e]38 patients; [f]13 patients; [g]17 patients; [h]38 patients with total and incomplete medical records; [i]101 and 80 patients with total and incomplete medical records, respectively; [j]52 and 49 patients with total and incomplete medical records, respectively; [k]102 and 81 patients with total and incomplete medical records, respectively. [1]*p*-values refers to the chi-square test. [2]*p*-values refers to the Student's t test. *Statistically significant difference between the following groups: *cART use:* * incomplete *vs.* complete. *Baseline CD4⁺ T-cell count:* **total *vs.* complete; #incomplete *vs* complete. *Last CD4⁺ T-cell count:* ##total *vs.* complete; †total *vs.* incomplete; †incomplete *vs.* complete. *Baseline PVL:* ¥total *vs.* incomplete. *Last PVL:* ¥¥incomplete *vs.* complete. *Follow-up:* §total *vs.* incomplete; ¥¥incomplete *vs.* complete.

followed by homosexual (12.8%) and male bisexual (5.2%) orientation. At the time of evaluation, 400 patients were taking cART drugs and 122 patients were not (naïve patients); in the first group, seven women were undergoing or had completed the prophylactic therapy during pregnancy to prevent vertical transmission.

The most frequent complaint of HIV-infected patients was weight loss (18.4%), followed by fever (13.4%), diarrhea (11.1%), lymphadenomegaly (8.3%), oral moniliasis (6.3%), neurological disorders (3.5%), headache (2.8%), recurrent bacterial infection (2.6%), seborrheic dermatitis (2.4%), fatigue and oral lesions (2%), herpes zoster (1.8%). In a few cases, there were night sweats, genital and anal lesions, pneumonia, hepatomegaly, condilomatosis, viral meningitis and prurigo nodularis. Twenty-four patients presented coinfection with hepatitis C virus (n=9), syphilis (n=8), hepatitis B virus (n=3), leprosy (n=3), and Chagas disease (n=1). There was no information regarding the signs and symptoms for 131 patients (24.3%) (data not shown).

During the clinical course of the disease, 203 patients (37.7%) were admitted to the hospital due to opportunistic infections, especially pneumonia caused by *Pneumocystis jirovecii* (10.6%), neurotoxoplasmosis (9.3%), tuberculosis (5.2%), neoplasia and neurocryptococcosis (2.6%), oral moniliasis (2.4%), and histoplasmosis (1.3%). Other opportunistic infections such as atypical mycobacteriosis, disseminated cytomegalovirus infection, peripheral neuropathies, herpetic encephalitis, cutaneous and visceral leishmaniosis, isosporiasis and ocular toxoplasmosis were registered at lower frequencies.

Eighty-four out of the 539 patients (15.6%) died; most of them were male (n=51). The cause of death of 50 patients (60%) were related to HIV infection, including pneumonia (caused by *P. jirovecii*), neurotoxoplasmosis, cryptococcosis, lymphoma, uterine cancer, Kaposi's sarcoma, fulminant hepatitis, visceral leishmaniosis and tuberculosis. The death of 34 patients (40%) were attributed to other causes non-related to HIV infection, such as acute myocardial infarction, renal insufficiency, breast cancer, esophagus cancer, lung cancer, and external causes.

A total of 170 out of 539 patients (31.5%) did not present complete medical records at the end of this study, because they died during the study period (n=83), were transferred to health care centers located in other cities (n=20), abandoned the treatment or were lost from the follow-up (n=67). These records reported only the baseline laboratory data collected during the first medical appointment at the health assistance service under study, or some laboratory data collected during the medical follow-up.

However, it was observed that these subjects had similar characteristics to those who presented the medical records. Most of the parameters, (gender, age/stratified age, race/ethnicity, route of infection, sexual orientation, and time of diagnosis) was not statistically significant between groups without and with medical records (Table 1)

Analysis of the immunological and virological status of the patients stratified by exposure to cART (Table 2) evidenced that the mean baseline CD4$^+$ T-cell counts and PVL in cART-naïve patients were 773.1 cells/mm^3 and 61,107.85 copies/mL, respectively. The PVL ranged from 1,000 to 100,000 copies/mL (62%) in most cART-naïve patients; was undetectable (< 40 copies/mL) in 4 patients

Table 2 - Laboratory data of HIV-infected patients from Jatai, Goias State, Brazil, stratified by the use of combined antiretroviral therapy (cART)

Parameter		**cART** n= 298 (80.8%)	**Naive** n= 71 (19.2%)	
Continuous variables		**mean (SD)**	**mean (SD)**	***p*-value[1]**
CD4$^+$ T-cell count (cells/mm^3)				
	Baseline	356.2 (291.7)	773.1 (458.6)	<0.001*
	Last	664.5 (369.9)	n/a	
PVL (copies/mL)				
	Baseline	2,366,028 (3.74e+07)	61,107.85 (142,672.2)	0.140
	Last	14,229.25 (63,681.05)	n/a	
Categorical variable		**n (%)**	**n (%)**	**n (%)**
PVL stratification (copies/mL)		**First**	**Last**	
	< 1,000	63 (21.1)	243 (81.6)	17 (23.9)
	1,001-10,000	57 (19.1)	19 (6.4)	21 (29.6)
	10,001-100,000	95 (31.9)	21 (7.0)	23 (32.4)
	> 100,000	83 (27.9)	15 (5.0)	10 (14.1)

Abbreviations: cART, combined antiretroviral therapy; n/a, not applicable; PVL, plasma viral load. *Statistically significant difference between the mean of baseline and last CD4$^+$ T-cell count in the group of patients undergoing cART. [1] *p*-values refers to the Student's t test.

(5.6%); and was > 100,000 copies/mL in 10 patients (14.1%).

In the group of patients undergoing cART, the mean baseline levels of CD4+ T-cell count and PVL were 356.2 cells/mm^3 and 2,366,028 copies/mL, respectively. One hundred and seven patients (35.9%) presented CD4+ T-cell counts <500 cells/mm^3. The mean last CD4+ T-cell counts and PVL were 664.5 cells/mm^3 and 14,229.25 copies/mL, respectively. Only the baseline and the last mean CD4+ T-cell counts in patients undergoing cART were significantly different from each other ($p < 0.001$). Thirty-three (11.1%) out of the 63 (21.1%) patients with the first PVL <1,000 copies/mL had viremia below the limit of detection, and 83 patients (27.9%) had the first PVL >100,000 copies/mL. After taking cART, 218 (73.2%) out of the 243 (81.6%) patients with the last PVL <1,000 copies/mL had undetectable viremia, and only 15 patients (5%) remained with PVL >100,000 copies/mL.

Most patients (n=297; 97.4%) were taking cART consisting of two classes of antiretroviral drugs: a nucleoside reverse transcriptase inhibitor (NRTI) in combination with a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a boosted protease inhibitor (PI). Three patients (1%) were receiving highly active antiretroviral therapy (HAART); two of them had already taken salvage therapy with integrase inhibitor.

DISCUSSION

Southwestern Goias is an economically rich region with high gross domestic product. Its suitable relief, hydrography, and climate for agriculture and livestock make this region one of the main soybean, corn, sorghum, and sugarcane producers, as well as one of the main areas of livestock management in Brazil. These features have attracted several multinational companies, ethanol, biodiesel and ecodiesel industries, and many migrants from all over the country[14].

The epidemiological and clinical profiles of HIV-infected patients living in small and medium-sized municipalities are poorly described, contrasting with national studies that cover mostly the population living in large urban centers[7-9]. Considering the AIDS epidemic spreading to the interior of Brazil and the attractive prospect of Southwestern Goiás, it is important to better understand the HIV infection dynamics in this region to prevent and monitor its dissemination.

In Jatai, a medium-sized city from Southwestern Goias, the first case of HIV infection was reported in 1997 in a male patient. This city presented the highest incidence rate of HIV infection in the Goias State between 2009 and 2012[11-13]. In line with data reported by the Brazilian Ministry of Health, the present study found the predominance of male patients infected with HIV through the heterosexual route due to unprotected intercourse[2]. We also detected an expressive incidence of HIV infection among young women (58.6%). The national rate of HIV infection among women increased from the beginning of the AIDS epidemic up to 2008, after which it decreased among women but raised among men. In Jatai, the male/female ratio was 0.9:1 in 2008 and 1.4:1 during the study period[15]. In contrast to the national trend, the incidence of HIV infection among women is increasing in some cities of the interior of Brazil[4,10,16].

Regarding the age group, the HIV infection was more prevalent in the reproductive ages (up to 40 years-old; 55.3%), with few cases among males older than 60 years-old (3.1%). Other studies and the Brazilian Ministry of Health have also reported that the reproductive age group was the most commonly involved[2,9,17,18].

The elevated HIV infection rate among Brazilian 60-69 year-old individuals is partially due to their increased sexual activity, which probably occur without protection[19].

Our study reported the predominance of the heterosexual route of HIV transmission, followed by the homosexual route. Heterosexual route has markedly grown in almost all regions of Brazil, confirming the potential role that wedding plays in the transmission of HIV infection to heterosexual women. In addition, the incidence of HIV infection among MSM increased in Midwestern Brazil from 36.1% in 2004 to 45.8% in 2013[3,9,20,21]. However, the prevalence of HIV infection may be under- and overestimated among MSM/bisexual and heterosexual patients, respectively, in the present study. The individuals tend to emphasize their heterosexual relationships due to fear of the persistent stigma and discrimination.

The incidence rate of HIV infection among intravenous drug users (IDU) in Southwestern Goias may also be underestimated. A previous study has reported expressive rates of HIV infection in this group of patients from the Midwest, Southeast, and South regions of Brazil, which support the idea that the supply and access to illicit drugs in these regions are common[22]. The prevalence of HIV infection among IDU in the Goias State is 2%[9,18].

The geographic location of Jatai facilitates the access to illicit drugs and may directly influence the epidemiological profile of HIV infection in Southwestern Goias. Jatai is an important route of drug traffic because it is near the main highway from Southwestern Goias (BR-364) that reaches the States of Mato Grosso and Mato Grosso do Sul, which in turn border with Paraguay and Bolivia.

Despite the advances in HAART, HIV infection still causes hospitalization and death due to opportunistic infections and difficulties in diagnosing them. Opportunistic

infections affect the immune system of HIV-infected patients, impair the treatment, favor the disease progress to AIDS, and cause death[23,24]. Pneumonia caused by *P. jirovecii* was the most prevalent opportunistic infection identified in HIV-infected patients studied herein, followed by neurotoxoplasmosis, tuberculosis, and neurocryptococcosis; this finding corroborates literature reports[25-29]. Toxoplasmosis is the most common cause of focal neurological injuries in Brazilian HIV-infected patients[25,26]. Cryptococcosis, the main systemic mycosis in immunosuppressed patients, especially in the form of meningoencephalitis and tuberculosis are important causes of morbidity and mortality among HIV-infected patients[27-29].

As the opportunistic infection primarily affects individuals with $CD4^+$ T-cell counts lower than 200 cells/mm^3, the mean $CD4^+$ T-cell counts of patients with and without opportunistic infection (255 and 423 cells/mm^3, respectively) were significantly different.

The mortality rate identified in this study (15.6%) was greater than that reported for Midwestern Brazil in 2015 (4.7%). The gender-specific mortality rate was higher among men (60.7%), in agreement with national data[2]. The fact that nearly 60% of the deaths were associated with HIV infection demonstrates that the availability of ART alone is not sufficient to provide survival of HIV-infected patients; other factors such as late diagnosis, clinical manifestations that confuse the diagnosis of opportunistic infections and poor adherence to treatment may negatively impact the incidence of deaths associated with AIDS[30,31].

Although the regional reference center for HIV care in Jatai complies with the goals of the National Program on Sexually Transmitted Infection from the Brazilian Ministry of Health,which recommends early diagnosis, universal cART prophylaxis/therapy and routine laboratory tests for monitoring HIV infection, the morbidity and mortality rates associated with HIV infection remain high, indicating the need to develop actions to prevent evolution of the disease to severe immunodeficiency and death. Several studies have reported that cART promotes immune status recovery and viremia reduction[32,33]. In our study, the mean $CD4^+$ T-cell count after cART was twice as high as those detected in the first medical appointment. In addition, HAART promoted viral suppression in a significant number of patients.

The limiting factor of this study was that the method used to collect data from medical records failed to address the geographic and temporal profile of HIV infection in patients living in Southwestern Goias, during the study period (2005-2015). However, the present study had an important strength, the large sample size that represented all HIV-infected patients who were assisted at the regional health center of Southwestern region of Goias State, from 2005 to 2015.

Considering the current scenario of interiorization of HIV infection in Brazil, this descriptive study outlined the clinical and epidemiological profile of HIV-infected patients from the interior of Goias State. Altogether, our findings help to understand the epidemiology of the disease and develop specific actions and plans to address the priority needs of HIV-infected patients.

CONFLICT OF INTERESTS

All authors declare that they have no conflicts of interest.

ACKNOWLEDGMENTS

The authors thank the medical staff from the Clinical Hospital Doutor Serafim de Carvalho, Jatai, Goias State, Brazil. This study was supported by the National Council for Scientific and Technological Development (CNPq, grant Nº 462150/2014-3).

AUTHORS' CONTRIBUTIONS

Regyane Ferreira Guimarães Dias participated in the study designs and in the field work, performed the statistical analysis and drafted the manuscript; Luciana Oliveira Bento and Camila Tavares participated in the study designs and in the field work and drafted the manuscript; Hélio Ranes Filho and Luciene Carneiro Moraes participated in the study designs and drafted the manuscript; Melisia Adelaide Cesário da Silva participated in the field work, and drafted the manuscript; Ana Amélia Freitas-Vilela analyzed the data, performed the statistical analyses and drafted the manuscript; Marcos Lázaro Moreli conceived, participated in the study designs and drafted the manuscript; Ludimila Paula Vaz Cardoso conceived, designed the study, coordinated the field work, analyzed the data, performed the statistical analysis and drafted the manuscript. All authors read and approved the final manuscript.

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