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Intestinal Parasitic Infections in Adult Living with HIV in Cochabamba, Bolivia

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Abstract

Background: Thanks to the widespread use of Antiretroviral Therapy (ART), Human Immunodeficiency Virus (HIV) infection is becoming a chronic manageable disease. In low resources settings where ART is available, but not widely, opportunistic infections such as parasites diseases remain common. These conditions represent a public health problem in the world due to the high prevalence in developing countries and particularly for patients with HIV/AIDS. To date there have been no systematic study on the prevalence of intestinal parasites in people living with HIV/AIDS (PLWHIV) in Bolivia. The study aimed to evaluate the occurrence of intestinal parasitic infections in PLWHIV who attended routine controls at the reference center for HIV control and prevention in Cochabamba (CDVIR) between January 2011 and December 2015.

Methods: Ethical approval was obtained prior to the commencement of this study from the Ethics Committees of the Department of Cochabamba-Bolivia and the Universidad Mayor de San Simón, Institute of Biomedical Research (IIBISMED/UMSS). Code: CB-2016-015.

A Retrospective Analysis was carried out Based on the reports of the reference laboratory in the city of Cochabamba (LABIMED) using direct parasitological methods founded on the macroscopic and microscopic identification of parasitic elements present in the stool. Data was collected in an Excel spreadsheet, based on reports from the parasitology laboratory, which was transferred for statistical analysis to SPSS 24.0 (SPSS Inc., Chicago IL, USA). The characteristics of the study participants are reported as mean, range and percentage, as appropriate. The test of X^2 or Fisher's exact test was used for all categorical variables. Logistic regression analysis was used to test the associations. A given statistical test was reported significant if it resulted in a p-value <0.05.

Results: During the 5-years of the study, a number varying between 313 and 620 patients were assessed each year, and 12 parasitic species were identified. The highest prevalence was 33.2% in 2011 and there was 9.9% of polyparasitism. In 2012, the prevalence was 28.6%, with 8.3% of polyparasitism, in 2013 it reached 30.4% with a polyparasitosis of 7.7%, while in 2014 it was 24. 5%, the lowest in the period, with a polyparasitism rate of 8.5%. Finally, in 2015 the prevalence reached 27.1% with a polyparasitism rate of 7.3%. The most prevalent species in order of frequency were *Blastocystis Homminis, Entamoeba coli* (non-Pathogen), *Giardia Lamblia* and *Entamoeba histolytica/dispar,* respectively. Regression analysis showed no significant association with sex or with consistence of stool sample but prevalence was higher in people under 30 years of age.

Conclusion: Taking into account the epidemiological and geographical context, the frequency of presentation of these infections reach practically one third of these population and thus remains a high problem in Bolivia. So, further studies are required to clarify the epidemiology of these infectious diseases in this endemic region.

Keywords: HIV; Parasites; Prevalence; Reference laboratory for HIV

List of abbreviations

ART	:	Anti-Retroviral Therapy
CDVIR	:	Reference center for HIV control and prevention in Cochabamba
CI	:	Confidence intervals
HAART	:	Highly active antiretroviral therapy
HIV/AIDS	:	Human Immunodeficiency Virus
IIBISMED	:	Institute of Biomedical Research
LABIMED	:	Biomedical Research Laboratory / Reference laboratory for HIV
PLWHIV	:	People living with HIV/AIDS
PNC/VS	:	National HIV/AIDS Control Program
UMSS	:	Universidad Mayor de San Simón
UNAIDS	:	Joint United Nations Program on HIV/AIDS
SPSS	:	Statistical Package for Social Science

Background

In December 2013, the Joint United Nations Program on HIV/AIDS (UNAIDS) supported the efforts led by countries and regions to set new targets for increasing HIV treatment beyond 2015. A powerful momentum is now being built towards a new narrative on the treatment of HIV and AIDS. A new, final, ambitious but achievable goal: by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people diagnosed will receive antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have viral suppression [1].

At the end of 2015, there were 2.1 million [1.8 million–2.4 million] new HIV infections worldwide, adding up to a total of 36.7 million [34.0 million–39.8 million] PLWHIV. Global coverage of ART reached 46% [43–50%], and in Latin America and the Caribbean, treatment coverage reached 55% [47-64%] [1].

Because rates of new HIV infections in adults are relatively static, epidemics in Latin America are generally stable even with a steady decrease in the number of people newly infected with HIV since early 2000s. The total number of people living with HIV in this region continued to grow and reach 1.8 million [1.5 million-2.1 million] in 2010, up from 2.0 million [1.7 million-2.3 million] in 2015 [1].

Advances in ART allow considering infection by HIV as a disease of chronic course compatible with a good quality of life when adequately monitored, and therapy has been instituted. Thanks to ART, HIV infection is now a chronic manageable disease but the management of comorbidities such as cardiovascular, renal, liver, co-infections with hepatitis B or C are now the greatest challenges. In low resources settings where ART is now available, but not widely, Opportunistic Infections (OIs) such as parasites diseases remain common and continue to be a leading cause of morbidity and mortality in PLWHIV, because of a severe immunosuppression caused by either a lack of knowledge of serological status in patients presenting late with an opportunistic infection as an or late manifestation of AIDS, a lack of adherence to antiretroviral treatment, or a therapeutic failure due to resistance to ART [2].

Parasitic diseases represent a medical, economic and social problem in the world due to its high prevalence in developing countries and particularly for PLWHIV. It is estimated that worldwide, about two billion people are affected by soil transmitted helminthes such as *Ascaris lumbricoides*, *Ancylostoma/Necator* spp. and *Trichuris trichiura*, 50 million by *Entamoeba histolytica* and 2.8 million by *Giardia duodenalis* (synonymous *G. lamblia* and *G. intestinalis*) [3]. The clinical importance of these infections continues to be debated, especially in the case of Blastocystis Homminis.

Parasitic infections are common among patients with HIV/AIDS. These infections are responsible of frequent complications in this population such as chronic diarrhea that contributes to the development of malabsorption and malnutrition in AIDS patient; its lifetime incidence among HIV-infected patients is estimated to be 30-70% [4]. Intestinal parasites are therefore an important cause of morbidity and mortality in PLWHIV. Frequent pathogenic parasites who infect HIV patients are rarely involved agents before the epidemic of HIV/AIDS with prevalence varying considerably according to the geographic context and the epidemiological profile of each country.

In developing countries, rates as high as 60 to 80% are reported [5-7], with concomitant infections by multiple parasites. Several diagnostic studies in AIDS patients without antiretroviral therapy indicate that opportunistic infections account for a large proportion of cases of chronic diarrhea (75-80%) [1]. The most common pathogens are usually enteric parasites including some that are unusual and have not been implicated in human disease until the advent of AIDS [8], such as *Cryptosporidium* spp., *Microsporidium* or *Isospora belli*, for which there are no effective primary prophylaxis guidelines. There is no specific treatment for cryptosporidiosis, whose cure depends on the immunological recovery related to ART [9]. The treatment of microsporidiosis also depends on ART, but there are effective complementary drugs. In intestinal or disseminated infections produced by *Enterocytozoon bieneusi,* the treatment of choice is fumagillin. If other species are involved, albendazole is recommended and the treatment of choice for isosporosis is cotrimoxazole [5,9,10].

There are currently no epidemiological estimates the prevalence of intestinal parasites in PLWHIV in Bolivia. The data provided comes from a national HIV treatment program and, therefore, can be expected to be representative. This study aimed to evaluate the occurrence of intestinal parasitic infections that occur most frequently in patients who attended in routine checkups for HIV infection (PLWHIV) at the reference center for HIV control and prevention in Cochabamba (CDVIR) between January 2011 and December 2015, and thus provides elements for building strategies for prevention and control.

Methods

Settings

In Bolivia 16.640 confirmed cases of HIV were reported since June 2016 in the health care system and 1.015 deaths related to AIDS diseases. Official data indicate that the estimated HIV prevalence is 0.15% with an annual incidence of approximately 0.01% (1000 new cases per year), meaning that approximately 10 out of every 10,000 people in the country would have been notified as HIV cases, of which about 2.400 would be on ART in the public health care system. In Cochabamba, the HIV / AIDS program of the Department Health Service (SEDES) registered 408 new infections in 2015. The surveillance system shows a predominantly young epidemic, with 67% of cases being aged less than 40 years [2].

In this context, all patients confirmed to be HIV infected are registered and treated free of charge in the National HIV/AIDS Control Program (PNC/VS) and periodically monitored at the CDVIR in every department of Bolivia. In Cochabamba until 2016, approximately 1.400 PLWHIV were cared for at the center were clinical checkups and routine laboratories are performed in the Medical Research Laboratory (LABIMED) of the Universidad Mayor de San Simón (UMSS). These checkups are subsidized and include direct corproparasitological test, determination of viral load and flow cytometry to measure CD4, CD8 and the ratio CD4/CD8, once a year.

The CDVIR has limitations regarding infrastructure and personnel, infections are empirically handled due to a lack of dedicated laboratories and also because these additional test represent a cost for the patient who often cannot pay. Therefore, there is a lack of etiologic diagnoses and patients are treated based on therapeutic tests. Many patients do not respond adequately to these therapies generating complications such as chronic diarrhea, malnutrition, or wasting syndrome.

Study population

The present study was conducted in Cochabamba according to an analytical design carried out retrospectively with the reports of the LABIMED on HIV-infected outpatients followed in the CDVIR, from January 2011 to December 2015. Considering only one sample per patient-year, all the results of the participants were obtained from the parasitology laboratory registry, correspond to routine stool tests performed on all fecal samples using simple wet/saline and iodine mounts, in addition to concentration technique by the formol-ether sedimentation method performed simultaneously on all stool samples and the presence of parasites was analyzed.

Methods such as specific staining for detection of parasites like as *cryptosporidium* or microsporidium are not routinely performed and the patient has to pay for other tests if required, since the national program does not subsidize them. Polyparasitism was defined as at least two different species identified in one stool sample.

Selection criteria were to be a patient with confirmed HIV infection, who is followed and treated at the HIV reference center, and to be at least 18 years of age. Records that did not have complete data were excluded; but the numbers were low: 6 (1.9%) in 2011, 5 (1%) in 2012, 10 (1.9%) in 2013, 8 (1.4%) in 2014, and 10 (1.6%) in 2015.

Statistical analysis

Data were collected on a specially designed Excel spreadsheet, based on the paperback reports of the parasitology laboratory, which was transferred for statistical analysis to SPSS 24.0 (SPSS Inc., Chicago IL, USA). Characteristics of study participants are reported as mean, range and percentage as appropriate. The $\chi 2$ test or Fisher's exact p-value was used for all categorical variables. Frequency of parasitic infections were computed for grouped data according to sex, age and the consistence of the stool sample. Logistic regression analysis was used for testing associations, subsequently, with variables that showed a significant association, a multivariate model was built to estimate adjusted odds ratios. A p-value <0.05 was considered as significant and 95% Confidence Intervals (CI) were computed. We developed separate models per year because a single patient can be in several years.

Results

A total of 2510 fecal samples were received between 2011 and 2015 from patients with a confirmed diagnosis of HIV infection and who attended laboratory tests in the CDVIR. During this period a number varying between 313 and 620 was assessed each year. The global distribution of patients attending LABIMED was predominantly male (Table 1), with a men/women ratio close to the 1.7 masculinity index stated in the report on progress in the HIV response in Bolivia 2014 by UNAIDS [4]. This ratio does not vary during the entire study period. The age distributions showed a greater proportion of people in age over 40 years and was homogeneous across years. Liquid feces occurred at a frequency of up to 48% in 2011 and remained close to 40% across years.

	2011	2012	2013	2014	2015	
	(n=313)	(n=493)	(n=520)	(n=564)	(n=620)	P Value
Characteristic						
sex						0.37
Man –no. (%)	197 (62.9)	316 (64.1)	329 (63.3)	334 (59.2)	400 (64.5)	
Men/Women Ratio	1.69	1.78	1.72	1.45	1.82	
Age-yr-no. (%)	36±12	37±12	37±12	38±13	37±13	0.67*
<30	116 (37.1)	160 (32.5)	162 (31.2)	157 (27.8)	193 (31.1)	
30 – 39	89 (28.4)	155 (31.4)	163 (31.3)	180 (31.9)	196 (31.6)	
≥40	108 (34.5)	178 (36.1)	195 (37.5)	227 (40.2)	231 (37.3)	
Aspect of feces (Liquid)-no. (%)						<0.001
Yes	151 (48.2)	210 (42.6)	188 (36.2)	222 (39.4)	292 (47.1)	
Lienteric feces-no. (%)						0.002
yes	28(8.9)	24(4.9)	37(7.1)	44(7.8)	70(11.3)	
a*ANOVA F test, no.: number						

Table 1: Characteristics of all participants by year.

During the review of laboratory reports of stool samples, twelve types of parasites genera were identified. The proportion of parasitic infection, defined as positive for at least one intestinal parasite, was 33.2%, the highest in 2011 (Table 2), and it was the lowest in 2014 with a prevalence of 24.5%. The highest polyparasitism rate was detected in 2011 with 9.9% and the lowest in 2015 (7.3%).

Outcomes /Year	2011	2012	2013	2014	2015
Parasite Infection – n (%)	**(n=313)**	**(n=493)**	**(n=520)**	**(n=564)**	**(n=620)**
Any	104 (33.2)	141 (28.6)	158 (30.4)	138 (24.5)	168 (27.1)
Polyparasitism	31 (9.9)	41 (8.3)	40 (7.7)	48 (8.5)	45 (7.3)
Parasites species – n (%)					
Blastocystis hominis	32 (10.2)	47 (9.5)	66 (12.7)	56 (9.9)	44 (7.1)
Entamoeba coli	38 (12.1)	47 (9.5)	38 (7.3)	21 (3.7)	59 (9.5)
Giardia lamblia	15 (4.8)	15 (3.0)	26 (5.0)	37 (6.6)	30 (4.8)
Entamoeba histolytica/dispar	9 (2.9)	11 (2.2)	13 (2.5)	17 (3.0)	16 (2.6)
Hymenolepis nana	3 (1.0)	9 (1.8)	4 (0.8)	2 (0.4)	8 (1.3)
Chilomastix mesnili	4 (1.3)	5 (1.0)	4 (0.8)	1 (0.2)	4 (0.6)
Strongyloides stercoralis	1 (0.3)	4 (0.8)	1 (0.2)	3 (0.5)	4 (0.6)
Entamoeba hartmanni	0	2 (0.4)	3 (0.6)	0 (0.0)	1 (0.2)
Trychomona hominis	1 (0.3)	1 (0.2)	3 (0.6)	2 (0.4)	0
Iodoameba butschili	0	0	0	0	2 (0.3)
Isospora belli	1 (0.3)	0	0	0	0
Taenia sp	0	1 (0.2)	0	0	0

Table 2: Prevalence of Intestinal parasitic infections by year in adult patients of a reference laboratory (LABIMED), Cochabamba-Bolivia.

Throughout the course of the study period, there was a clear predominance of parasites classified as protozoa in fecal samples processed in the reference laboratory. In 2011, the infection rate was 33.2%, the highest prevalence observed in the study, while in 2014 it was 24. 5%, the lowest in the period. The parasitic species mostly found were *Blastocystis homminis, Entamoeba coli* (No pathogen)*, Giardia lamblia and Entamoeba histolytica/dispar* (Table 2). *B. homminis* was the most frequently detected parasitic specie, reaching 12.7%, the highest rates in 2013 and decreasing to 7.1% in 2015. The prevalence of parasite infections and polyparasitism according to age, sex and stool consistence is presented in (Table 3), within each year.

Association with age, sex and stool consistence was not significant, but each year, there was a predominant proportion of parasite infections in age under 30. In all years but 2011, there was a greater proportion of women with parasitic infections. Similarly, polyparasitism was also higher in women than in man. The age group mostly affected was under 30 years of age, with also higher frequencies of polyparasitism in this age group. This association was significant, except in 2011. Liquid feces were significantly associated with a higher presence of parasites in direct microscopic examination each year (Table 3).

			Parasite Infection			**Polyparasitism**		
Year / Characteristic			**Yes** no. /N. (%)	**OR (95% IC)**	**P value**	**Yes** no. /N. (%)	**OR (95% IC)**	**P value**
2011 (n=313)	Sex				0.53			0.31
		F	36/116(31.0)	1		13/36(36.1)	1	
		M	68/197(34.5)	1.17(0.71-1.91)		18/68(26.5)	0.64(0.27-1.52)	
	Age				0.11			0.27
		<30	46/116(39.7)	2.30(1.28-4.14)		16/46(34.8)	2.67(0.78-9.15)	
		30 – 39	34/89(38.2)	2.16(1.16-4.00)		11/34(32.4)	2.39(0.66-8.70)	
		≥40	24/108(22.2)	1		4/24(16.7)	1	
	Liquid feces				0.16			0.77
		Yes	56/151(37.1)	1.4 (0.87-2.24)		15/48(31.3)	1	
		No	48/162(29.6)	1		16/56(28.6)	0.88(0.38-2.04)	
	Lienteric feces				0.9			0.32
		Yes	9/28(32.1)	0.95(0.41-2.17)		4/9(44.4)	2.02(0.50-8.08)	
		No	95/285(33.3)	1		27/95(28.4)	1	

2012 (n=493)	Sex				0.08			0.03
		F	59/177(33.3)	1		23/59(39.0)	1	
		M	82/316(25.9)	0.70 (0.47-1.05)		18/83(21.7)	0.43(0.20-0.91)	
	Age				<0.001			0.04
		<30	64/160(40.0)	2.82(1.73-4.60)		21/65(32.3)	3.58(1.12-11.48)	
		30 – 39	43/155(27.7)	1.62(0.97-2.71)		16/43(37.2)	4.44(1.32-14.94)	
		≥40	34/178(19.1)	1		4/34(11.8)	1	
	Liquid feces				<0.001			0.66
		Yes	78/210(37.1)	2.06(1.39-3.07)		17/63(27.0)	1	
		No	63/283(22.3)	1		24/79(30.4)	1.18(0.57-2.46)	
	Lienteric feces				0.001			0.22
		Yes	14/24(58.3)	3.7(1.6-8.70)		6/14(42.9)	1.99(0.65-6.15)	
		No	127/469(27.1)	1		35/128(27.3)	1	
2013 (n=520)	Sex				0.24			0.3
		F	64/191(33.5)	1		19/64(29.7)	1	
		M	94/329(28.6)	0.79(0.54-1.17)		21/94(22.3)	0.68(0.33-1.40)	
	Age				0.003			0.69
		<30	60/162(37.0)	2.14(1.34-3.41)		16/60(26.7)	0.91(0.38-2.19)	
		30 – 39	56/163(34.4)	1.90(1.91-3.05)		12/56(21.4)	0.68(0.27-1.71)	
		≥40	42/195(21.5)	1		12/42(28.6)	1	
	Liquid feces				0.002			0.04
		Yes	73/188(38.8)	1.85 (1.26-2.71)		16/85(18.8)	1	
		No	85/332(25.6)	1		24/73(32.9)	2.11(1.02-4.39)	
	Lienteric feces				0.16			0.05
		Yes	15/37(40.5)	1		7/15(46.7)	2.91(0.98-8.64)	
		No	143/483(29.6)	1.62(0.82-3.22)		33/143(23.1)	1	

2014 (n=564)	Sex				0.18			0.04
		F	63/230(27.4)	1		28/64(43.8)	1	
		M	75/334(22.5)	0.77(0,52-1.13)		20/75(26.7)	0.47(0.23-0.95)	
	Age				<0.001			0.68
		<30	53/157(33.8)	2.70(1.66-4.40)		18/53(34.0)	1.21(0.49-3.00)	
		30 – 39	49/180(27.2)	1.99(1.22-3.22)		19/49(38.8)	1.49(0.60-3.71)	
		≥40	36/227(15.9)	1		11/37(29.7)	1	
	Liquid feces				0.02			0.06
		Yes	66/222(29.7)	1.59(1.08-2.34)		20/73(27.4)	1	
		No	72/342(21.1)	1		28/66(42.4)	1.95(0.96-3.97)	
	Lienteric feces				<0.001			0.49
		Yes	22/44(50.0)	3.48(1.86-6.51)		9/22(40.9)	1.39(0.55-3.52)	
		No	116/520(22.3)	1		39/117(33.3)	1	
2015 (n=620)	Sex				0.41			0.68
		F	64/220(29.1)	1		16/64(25.0)	1	
		M	104/400(26.0)	0.86(0.59-1.24)		29/104(27.9)	1.16(0.57-2.36)	
	Age				<0.001			0.39
		<30	76/193(39.4)	2.76(1.78-4.27)		24/76(31.6)	1.80(0.75-4.32)	
		30 – 39	48/196(24.5)	1.38(0.86-2.19)		12/48(25.0)	1.30(0.49-3.46)	
		≥40	44/231(19.0)	1		9/44(20.5)	1	
	Liquid feces				0.002			0.25
		Yes	96/292(32.9)	1.74(1.22-2.50)		16/72(22.2)	1	
		No	72/328(22.0)	1		29/96(30.2)	1.51(0.75-3.07)	
	Lienteric feces				0.77			0.16
		Yes	20/70(28.6)	1.09(0.63-1.89)		8/20(40.0)	2.00(0.76-5.27)	
		No	148/550(26.9)	1		37/148(25.0)	1	

Table 3: Parasitic infections according to characteristics of adult patients in a reference laboratory (LABIMED), by year.

In these multivariate analyses, liquid feces remained significantly associated with higher prevalence of parasitic infections each year but in 2011(Table 4). There was a non-significant association of parasitic infection with gender, but a significant decrease with age; infections remained significantly higher in patients under 30 years. The association of parasitic infection with stool consistence and lientery were not significant each year, but adjusted OR were similar.

Year / Characteristic	OR (95% IC).	P value
2011		
Men (yes=1)	1.22(0.74-2.00)	0.44
Age		0.38
<30 yrs (yes=1)	2.51(1.38-4.60)	
30 - 39 yrs (yes=1)	2.34(1.24-4.41)	
≥40 yrs (yes=1)	1	
Liquid feces (yes =1)	1.46(0.90-2.38)	0.13
Lienteria (yes=1)	0.78(0.33-1.84)	0.57
2012		
Men (yes=1)	0.70(0.47-1.06)	0.09
Age		0.2
<30 yrs (yes=1)	2.75(1.66-4.54)	
30 - 39 yrs (yes=1)	1.53(0.90-2.60)	
≥40 yrs (yes=1)	1	
Liquid feces (yes =1)	1.90(1.27-2.86)	0.002
Lienteria (yes=1)	3.25(1.36-7.77)	0.008
2013		
Men (yes=1)	0.81(0.55-1.20)	0.29
Age		0.03
<30 yrs (yes=1)	2.12(1.32-3.42)	
30 - 39 yrs (yes=1)	2.02(1.25-3.25)	
≥40 yrs (yes=1)	1	
Liquid feces (yes =1)	1.84(1.25-2.73)	0.002
Lienteria (yes=1)	1.37(0.68-2.77)	0.38
2014		
Men (yes=1)	0.84(0.56-1.25)	0.39
Age		0.18
<30 yrs (yes=1)	2.63(1.60-4.33)	
30 - 39 yrs (yes=1)	1.89(1.15-3.09)	
≥40 yrs (yes=1)	1	
Liquid feces (yes =1)	1.34(0.89-2.02)	0.15
Lienteria (yes=1)	2.84(1.48-5.46)	0.002
2015		
Men (yes=1)	0.91(0.63-1.33)	0.64
Age		0.01

<30 yrs (yes=1)	2.65(1.70-4.12)	
30 - 39 yrs (yes=1)	1.32(0.83-2.11)	
≥40 yrs (yes=1)	1	
Liquid feces (yes =1)	1.70(1.18-2.47)	0.004
Lienteria (yes=1)	0.89(0.50-1.57)	0.69

Table 4: Multivariate logistic regression analysis of factors associated with intestinal parasitic infections in adult HIV patients.

Discussion

The countries in Latin America are adopting the continuous model of HIV care, and are monitoring the milestones of the so-called cascade of attention and treatment of HIV infection. One of the most important barriers identified is the retention of attention. During the study period, percentages of linkage and retention towards CDVIR services can be estimated around 40%. Ministry of Health in Bolivia reported in 2017 that only 42% of the PLWHIV in Cochabamba are linked and retained in the health system [11,12]. It is however difficult to know the number of PLWHIV and it is usually an estimate.

HIV / AIDS is currently a public health problem in Bolivia due to the constant and continuous spread of the disease. The available information for the year 2016 allows us to determine that approximately 1 in 4 PLWHIV would be receiving antiretroviral treatment, even if new notifications and new initiations are considered, the percentage does not exceed 37% (6128/16640). OIs represent a cause of morbidity and mortality in PLWHIV, although there is a high degree of uncertainty due to coverage of the mortality system in Bolivia [2]. According to the 2014 report of UNAIDS, the knowledge of serologic status among all people living with HIV reached 79%, 82% of people living with HIV and who know their status are on treatment, and 77% on treatment who are virally suppressed [2].

Considering the rates of retention, the proportion of patients attending the CDVIR can be estimated to: 64% in 2011, 82% in 2012, 71% in 2013, 65% in 2014, and 60% in 2015. In the present series, diagnosis of new cases and deaths or migrations can explain the increase in the number of PLWHIV tested for parasitic infections in the study period.

Variations in the prevalence of intestinal parasites can be attributed to geographical characteristics of the region, socioeconomic characteristics, health system, or nutritional aspects of persons enrolled.

The rationale for repeated analysis in successive years responds to fluctuations related to new diagnoses of PLWHIV who enter and perform controls at the reference center and patients who for various reasons are lost to the service that cannot be analyzed in time series.

The results in our series show that *Blastocystis hominis* is the more frequent parasite in patients attending CDVIR, as in most studies conducted in PLWHIV. In Peru, it was reported with 24.6% [13]. In patients with HIV, as in other patients as well, there is a great controversy regarding its pathogenicity [14]. Some studies did not find a correlation between diarrhea or other nonspecific digestive symptoms, and *B. Hominis*, but in Brazil cases associated with symptomatology have been reported [5,14].

In our study, the highest prevalence of intestinal parasites infection in our series was reached in 2011 (33.2%), lower than in published studies. In the study of Omayra Chincha conducted in Peru, a prevalence of 39.8% was found in PLWHIV and, *B. Hominis* was the most prevalent specie with 24.6%.

Species reported in Peru include: *I. belli* was 8.4%, *Cryptosporidium Sp*. was 4.5%, *Cyclospora cayetanensis* was 3.3%, and, *E. histolytica and H. nana* were 1.2%. [13] But, all these parasites were not found in Bolivia, where species such as *Entamoeba coli, Giardia lamblia* and *E. histolytica/dispar* are the most prevalent.

Opportunistic agents such as *Cryptosporidium spp., microsporidium, and Isospora belli* were less frequent among patients with HIV in Cochabamba [14].

The reasons may be the geographical context and may also be the methods used for the detection of intestinal parasites. There are differences between studies in detection methods [16]. It is obvious that the use of direct microbiological tests for detection of intestinal parasites is insufficient especially for detection of agents such as cryptosporidium and microsporidium reported as highly prevalent in people with AIDS. Within a clinical setting, the search for Cryptosporidium in stool specimens relies on the use of different techniques: acid-fast staining, Direct Fluorescent Antibody (DFA), and/or enzyme immunoassays for detection of Cryptosporidium sp. antigens. Molecular methods (e.g., polymerase chain reaction - PCR) are increasingly used in reference diagnostic labs, since they can identify Cryptosporidium at the species level [16], and PCR are the reference method.

For *microsporidium*, the most common diagnostic methods are based on stains, such as Calcofluor White M2R, Uvitex 2B, or Fungi Fluor, and by using Weber's modified trichrome staining or other modifications [16]. Tests for *Cryptosporidium, Microsporidium*, and *Isospora belli* are not routinely done in most reference laboratories for routine controls; they are performed

only when; healthcare providers should specifically request testing for such parasites.

Identify the different species of microsporidium is important because some of them do not respond adequately to the specific treatment. Low efficacy of albendazole has been described against *Enterocytozoon bieneusi,* since it yields only to decline in the parasite load and degenerative alterations of the spores. Clinically, stool frequency and volume decrease in infected patients having a stable body weight [17-21].

In the study conducted in Peru, authors used four different techniques in addition to direct examination, to detect a broad spectrum of parasites, including coccidia oocysts. Direct corproparasitological methods do also not allow to detect coccidia as C*ryptosporidium* and *I. belli.*

Bachur et al in 2008 in Brazil studied enteric parasites in PLWHIV by comparing before HAART and after HAART, using two different techniques, Baermann-Moraes and modified Ziehl-Neelsen methods for fecal parasitological examinations. They found a significant reduction of the infection rates of *S. stercoralis* from 30.1% to 11%, of *Ascaris lumbricoides* from 15.6% to 2%, of *Hookworms* from 13.7% to 2%, of *Trichuris trichiura* from 13.1% to 1%, *of Giardia duodenalis* from 7.9% to 1%, of *I. belli* from 4.8% to 1%, of *Cryptosporidium sp.* from 8.1% to 0, and no significant reduction of *E. histolytica/ dispar* from 3.3% to 1%, [13]. The overall prevalence of enteric parasites decreased from 63.9% to 24%. When the coverage with HAART is high with a reduced number of people with AIDS related diseases, the prevalence of opportunistic parasites is low [8].

Bachur et al performed a study in Brazil comparing the period before and after introduction of Highly Active Antiretroviral Therapy (HAART). The findings showed a significant difference between these two periods in terms of a reduction of the prevalence of Strongyloides *stercoralis – Ascaris lumbricoides, hookworms, Trichuris trichiura, Hymenolepis nana, Giardia duodenalis, Entamoeba histolytica/dispar, Isospora belli, Cryptosporidium* sp, and non-pathogenic protozoans as well; thus the prevalence of enteric parasites decreased from 63.9% to 24% ($p<0.001$) [8].

In the absence of statistics related to the prevalence of intestinal parasites in PLHIV in Bolivia, taking into account the growth in the number of newly diagnosed patients each year who are admitted and retained by the national HIV/AIDS control program and the reported number of deaths, considering the prevalence reported by Bachur in Brazil before and after HAART [8].

The symptomatology of the patient and the CD4 count at the time of the study were not reported to the CDVIR and it did not appear in the records of the LABIMED. Also we had no information about the treatment.

Within the limitations of the study, the demographic and clinical variables included in the analysis are very abridged due to limitations in the registration system and lack of linkage between the databases of the different laboratories, making it difficult to link the information on the count of CD4, virologic status, staging / performance status, along with sociodemographic[Rodriguez-Perez, 2019 #38] data (e.g. rural versus urban, area of residence), for this reason are not available or included in this study. However, our results point that there is still a huge number of cases of intestinal parasites in Bolivia and therefore.

Conclusions

There is a need for an adequate management to avoid the morbidity and mortality complications in PLWHIV in Bolivia. The present results highlights that it is crucial to strengthen surveillance of HIV patients. The diagnostic methods currently available in the LABIMED do not allow for the diagnosis of a wide spectrum of parasites for which direct methods are not sensitive such as cryptosporidium, microsporidium and isospores. This study highlights the importance of reinforcing the routine testing for opportunistic infections in people living with HIV in the country, the diagnoses must be determined by the use of appropriate parasitological methods. The HIV control strategies should consider routinely investigate the presence of intestinal parasites and generate detection protocols to facilitate the diagnosis and treatment of patients with HIV.

One aspect that should be highlighted is that in the absence of Bolivian national or sub-national estimates regarding the prevalence of intestinal parasites in PLWHIV, it is difficult to relate the prevalence of enteric parasites with the background population.

Although multivariable regression has been used to control confusion, the very limited number of variables included in the reference laboratory records limits the analysis of the many possible confounding factors not measured.

Absolute prevalence estimates in the context of care, follow-up and monitoring performed at the referral center show a high prevalence of parasitic infection. It is reasonable to consider that the patient monitoring and report system should be evaluated.

There is also a need for low-cost diagnostic tools to identify intestinal parasites and monitor HIV, especially in patients without ART who have a deteriorated general health status and function (fragility), with an increased risk of morbidity and mortality. In this population, it is necessary to establish diagnostic protocols for the detection of intestinal parasites that cannot be diagnosed with the currently available methods.

Finally, it is necessary to establish a data collection system and network that allows concentrate the data of the PLWHIV at the departmental and national levels, since the reports of hospitalization, laboratory of parasitology and immunology (CD4 and viral load) are not linked in the reference laboratories.

Trial registration

Ethical approval for the study was obtained from the Ethics Committees of the Department of Cochabamba-Bolivia and the

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Authors' contributions

JA, CE, MR, DI, AR, analyzed and interpreted the patient data regarding the parasitological disease and the epidemiological factors. MT and RY performed the microbiological and molecular examination of the stool samples; JA, JY and AR realized statistical analysis and were a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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