TROPICAL DISEASES SCREENING IN IMMIGRANT PATIENTS WITH HIV INFECTION IN A EUROPEAN COUNTRY

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CERTIFICADO DEL DIRECTOR DEL TRABAJO DE INVESTIGACIÓN

El **Dr Vicenç Falcó Ferrer**, médico adjunto del Servicio de Enfermedades Infecciosas del Hospital Universitario Valle Hebrón,

HACE CONSTAR,

Que el trabajo titulado **"Tropical diseases screening in immigrant patients with HIV infection in a European country"** ha sido realizado bajo mi dirección por el licenciado **Fernando Salvador Vélez** encontrándose en condiciones de poder ser presentado como trabajo de investigación de 12 créditos, dentro del programa de doctorado en Medicina Interna/Diagnóstico por la Imagen (curso 2011-2012), en la convocatoria de junio.

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SUMMARY

Latent parasitic infections can reactivate due to immunosuppression. This is a prospective observational study of all HIV infected immigrants visited at the Infectious Diseases Department of the Hospital Universitari Vall d'Hebron (Barcelona, Spain) from June 2010 to May 2011. Screening of most prevalent tropical diseases (intestinal parasitosis, Chagas disease, leishmaniasis, malaria, schistosomiasis and strongyloidiasis) was performed according to geographical origin. 190 patients were included: 141 (74.2%) from Latin America, 41 (21.6%) from sub-Saharan Africa, 8 (4.2%) from North Africa. Overall, 36.8% (70/190) patients had at least one positive result for any parasitic disease: positive *Trypanosoma cruzi* serology in 5 patients, positive *Schistosoma mansoni* serology in 11 patients, positive *Strongyloides stercoralis* serology in 35 patients, positive *Leishmania infantum* serology in 7 patients, intestinal parasitosis detected in 37 patients. Malaria was diagnosed in one symptomatic patient. We propose a screening and management strategy of latent parasitic infections in immigrant HIV infected patients.

INTRODUCTION

In recent years, immigrant population in Spain has grown significantly, representing 12.2% of the total population in 2011, approximately 5.7 million people (*1*). On the other hand, in 2010 there were 34 million people with human immunodeficiency virus (HIV) infection around the world, and nearly 70% were concentrated in Africa and South America (*2*). These factors have changed the demographic profile of HIV-infected patients treated in Spanish hospitals, with higher proportion of immigrants, mainly from sub-Saharan Africa and Latin America.

Screening of latent infections is recommended in the initial approach of all HIV-infected patients, because of the capability to reactivate when immunosuppression is established. Tuberculin skin test (TST), chest x-ray and serologic tests (for *Toxoplasma gondii*, *Treponema pallidum*, hepatitis A, B and C viruses) should be performed (*3-5*). However, immigrant patients may have other endemic infections in their countries that can be reactivated or be manifested as severe forms because of the immunosuppression, such as *Strongyloides stercoralis* hyperinfection syndrome, or myocarditis and meningoencephalitis caused by *Trypanosoma cruzi* (*6-7*). Immune reconstitution inflammatory syndrome (IRIS) has also been related with some parasitic infections, such as leishmaniasis, schistosomiasis and strongyloidiasis (*8*).

The aim of this study was to perform a screening of prevalent tropical diseases in immigrants with HIV infection according to their geographical origin. With the results we will suggest a screening, treatment and follow-up strategy.

PATIENTS AND METHODS

Study population and data collection

Prospective observational study performed at the Infectious Diseases Department of the Hospital Universitari Vall d'Hebron, a University hospital in Barcelona (Spain). All HIV infected patients coming from Latin America, sub-Saharan Africa and North Africa visited at the Infectious Diseases Department from June 2010 to May 2011 were included. The study protocol was approved by the institutional review board of the hospital and informed consent was obtained from all patients.

The following data were collected: epidemiological data (age, gender, country and district of origin, time since arrival to our country, time since the last travel to their country, rural environment provenance), HIV infection related data (CD4+ lymphocyte cell count, HIV plasma viral load, HIV acquisition risk factor, current antiretroviral therapy, previous opportunistic infections), eosinophil count, chest x-ray, TST and serological data (*Toxoplasma gondii* serology, HBs antigen, HBc antibody, HCV antibody). Eosinophilia was defined as eosinophil cell count ≥500 cells/mm³ and/or a percentage ≥7%. TST using Mantoux method was considered positive when transversal diameter of induration was ≥5mm.

Tropical diseases screening

Intestinal parasites: Stool samples from two different days were collected in recipients containing 10% formol saline from all patients. Microscopic examination was performed using direct techniques (saline and iodine wet mounts) and after concentration techniques using formol-eter or the Ritchie's technique. Auramine stain

for *Cryptosporidium* and *Isospora* detection was also performed. Specific treatment was offered to all patients with parasite infection considered pathogenic.

Chagas disease: All patients coming from Latin America were tested for Chagas disease (unless coming from Caribbean islands). Serologic diagnosis of Chagas disease was performed using in parallel two enzyme-linked immunosorbent assays (ELISA), one with recombinant antigen (*Bioelisa Chagas, Biokit. Spain*) and the other with a crude antigen (Ortho *T.cruzi* ELISA. Jonhson & Jonhson. USA), according to WHO's diagnostic criteria. Both ELISA were performed following manufacturer's instructions. We considered a positive or negative results if both tests were concordant. All discordant sera were tested by an in-house Western Blot method using a lysate from *Trypanosoma cruzi* epimastigotes (*9*). When a positive result was obtained, chest x-ray, electrocardiogram, echocardiogram, esophagogram and barium enema were performed and specific treatment was offered.

Leishmaniasis: All patients were tested for leishmaniasis through detection of anti-*Leishmania infantum* IgG (ELISA, *Novagnost Leishmania IgG. Siemens Diagnostics. Germany*), performed according to manufacturer's instructions. Bone marrow aspiration was performed in patients with positive serology presenting pancytopenia or hepatosplenomegaly in order to diagnose visceral leishmaniasis (VL). Specific treatment was offered when confirmed VL.

Malaria: Patients coming from endemic areas (sub-Saharan Africa and some Latin American regions) were tested for malaria using a real-time polymerase chain reaction (rt-PCR) test performed in peripheral blood samples, capable to identify four different

species of *Plasmodium*. DNA extraction was carried out with automatic silica–membrane technology (NucliSENS EasyMag. BioMerieux). Primers and probe from satellite sequence were selected and used in a TaqMan-based assay as previously described by Rougemont et al (*10*). Positive rt-PCR was considered diagnostic of malaria and specific treatment was administered.

Schistosomiasis: Patients coming from endemic areas (sub-Saharan Africa and some Latin American regions) were tested for schistosomiasis by detection of anti-*Schistosoma mansoni* IgG (ELISA, *Novagnost Schistosoma mansoni IgG. Siemens Diagnostics. Germany*), performed according to manufacturer's instructions. When positive, stool and urine samples were investigated for ova detection and abdominal ultrasound was performed. Specific treatment was offered when confirmed schistosomiasis (ova detection) or suspected diagnosis (positive serology plus characteristic manifestations, such as eosinophilia, haematuria or periportal fibrosis).

Strongyloidiasis: All patients were tested for strongyloidiasis through detection of anti-*Strongyloides stercoralis* IgG (ELISA *Strongyloides IgG. DRG Diagnostics. Germany*). When positive, three more stool samples were collected and specific faecal culture for *Strongyloides stercoralis* larvae was performed. Specific treatment was offered when confirmed strongyloidiasis (larvae detection) or suspected diagnosis (positive serology plus characteristic manifestations, such as eosinophilia, skin lesions or intestinal disorders).

Statistical analysis

Categorical data are presented as absolute numbers and proportions, and continuous variables are expressed as medians and interquartile ranges (IQR). The χ^2 test or Fisher exact test, when appropriate, was used to compare the distribution of categorical variables, and the Mann-Whitney U test for continuous variables. Univariate and multivariate analysis using a forward stepwise multiple regression model were carried out to identify variables independently associated to specific parasitosis. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated. Results were considered statistically significant if the 2-tailed P value was < 0.05. SPSS software for Windows (Version 15.0; SPSS Inc, Chicago, IL, USA) was used for statistical analyses.

RESULTS

Demographic and HIV infection data

Overall, 190 patients were included in the study. Countries of origin are reported in Figure 1: 141 (74.2%) patients from Latin America, 41 (21.6%) patients from sub-Saharan Africa and 8 (4.2%) patients from North Africa (this group was excluded from statistical analysis because of its low number and considered unrepresentative). Epidemiological and HIV-related data are summarized in table 1. The median age of the patients was 37 (IQR, 32-43) years and 129 (68%) were male. The median time since arrival to Spain was 96 (IQR, 60-123) months. Regarding to HIV infection, the median of current and nadir CD4+ lymphocyte cell count were 459 (IQR, 358-625) cells/mm^3 and 223 (IQR, 118-341) cells/mm^3 respectively. At the time of study enrolment, 159 (77.9%) patients were receiving ART, and 124 (83%) of them had undetectable HIV viral load (<50 copies/mL). The sub-Saharan group compared to Latin American had significantly higher proportion of women and rural environmental provenance and lower current CD4+ lymphocyte cell count.

Latent infections screening

Data concerning latent infections screening are summarized in table 2. Nine (4.7%) patients tested positive for anti-HCV antibodies, 15 (7.9%) patients had HBV infection and 68 (35.8%) patients had past HBV infection (positive anti-HBc antibody, but negative HBs antigen). Eosinophilia was detected in 29 (15.3%) patients. TST was positive in 18 out of 179 (10%) patients. Of them, 6 patients reported previous tuberculosis disease, and a latent infection was diagnosed in the remaining 12 patients (6.7 % of the overall population). When comparing geographical areas, the prevalence

of eosinophilia, HBV and HCV infections was significantly higher among patients from Sub-Saharan Africa as compared to Latin America.

Overall, 36.8% (70/190) patients had at least one positive result for any parasitic disease.

Intestinal parasitosis: Two stool samples were collected in 139 (72%) patients; in 37 (26.6%) of them resulted positive and a total of 64 parasites were isolated (table 3).

Chagas disease: Five out of 126 (3.9%) analyzed patients were positive for Chagas disease; four from Bolivia and one from Ecuador. All of them were in the indeterminate phase of Chagas disease. Treatment with benznidazole 100mg every 8 hours (5mg/Kg/day) for 60 days was prescribed in all five patients and no adverse reaction was reported.

Leishmaniasis: Serological test for *Leishmania infantum* resulted positive in 7 out of 187 (3.7%) screened patients. None of them had clinical or analytical signs of VL and no further studies were performed.

Malaria: rt-PCR for *Plasmodium* DNA was performed in 62 patients coming from endemic countries. Only one patient tested positive for *Plasmodium falciparum*: a 32-year-old woman from Equatorial Guinea, who had arrived to our country one month before. She was asymptomatic when the screening was performed, but two days later she presented fever. Thin and thick films were positive for *Plasmodium falciparum* and specific treatment was offered.

Schistosomiasis: Eleven out of 58 (18.9%) screened patients tested positive for *Schistosoma mansoni* serology, nine from sub-Saharan Africa and two from Latin America. No patient had previously received specific treatment for schistosomiasis nor presented classic symptoms and signs, and seven of them presented eosinophilia when the screening was performed. Abdominal ultrasound was performed and urine sample was collected for ova investigation in five patients, always with normal results. Praziquantel 40mg/Kg/day during 2 days was administered to patients with eosinophilia and positive serology.

Strongyloidiasis: Thirty-five out of 190 (18.4%) patients tested positive for *Strongyloides stercoralis* serology. *Strongyloides stercoralis* larvae were detected by stool examination in one patient. Three more stool samples were obtained in eight patients and specific faecal culture resulted positive for larvae detection in one more patient. Only nine (25.7%) patients presented eosinophilia when the screening was performed. Ivermectine 200µg/Kg/day during 2 days was administered to patients with eosinophilia or confirmed diagnosis by larvae demonstration.

In the multivariate analysis, eosinophilia was significantly associated both with strongyloidiasis and schistosomiasis. Patients coming from Latin America and those arriving to our country in the last 5 years had an increased risk of having intestinal parasitosis. Results are described in table 4.

DISCUSSION

Since the relationship between HIV and some neglected tropical diseases has been described, screening for tropical diseases among HIV infected patients coming from endemic areas is becoming more relevant (*11, 12*). It is notorious the high number of asymptomatic patients with parasitological diagnosis in our study, with easily treatable diseases. Overall, we treated five patients with Chagas disease, one with malaria, seven with schistosomiasis, nine with strongyloidiasis and fourteen with intestinal parasitosis.

Immunocompromised patients may present reactivation of Chagas disease, with severe acute clinical manifestations (meningoencephalitis and myocarditis) and high parasitaemia, especially when CD4+ lymphocyte cell count is ≤200 cells/mm³ (*13-14*). Due to this consideration, active research in those patients coming from endemic areas must be taken to avoid further reactivations of Chagas disease, as it has already been done in some Spanish hospitals (*15*). Two different serological tests must be performed in all HIV-infected patients coming from Latin America (except from Caribbean islands) to screen Chagas disease; extension study will be performed and treatment with benznidazole will be offered when positive result.

Leishmania-HIV co-infection is currently reported in 2-9% of all VL cases in some endemic countries. HIV infection increases the risk of developing VL in endemic areas, reduces the therapeutic response and increases the risk of relapse; on the other hand, VL promotes the clinical progression of HIV disease (*16*). Different serological tests are available for the diagnosis of leishmaniasis; unfortunately, over 50% of co-infected patients have negative serology, and there is serological cross-reactivity between *Leishmania* and other microorganisms, such as *Trypanosome* or mycobacteria (*17*). In our study, none of the 7 patients with positive serology had neither clinical nor

analytical abnormalities, and Chagas disease was concurrently diagnosed in four of them. Therefore, positive results were most probably false positive results due to cross-reactivity. According to our results, serologic test seems to be unuseful for VL screening HIV population.

HIV infection and malaria are two of the most important health problems in developing countries, mainly in Sub-Saharan Africa. Studies about the impact of HIV infection on the risk of severe malaria differ in their findings (*18*). Although rt-PCR is more sensitive than thick/thin blood films in post-arrival screening for malaria in asymptomatic patients coming from endemic areas (*19*), this tool did not offer any advantage in our HIV population. In our experience, screening asymptomatic HIV-infected patients for malaria was not useful. This was probably due to the fact that most of analyzed patients were living in our country since more than 5 years ago at the moment of screening, reducing the risk of malaria.

Chronic schistosomiasis results from the immune response of the host to schistosome eggs and the granulomatous reaction produced by the antigens they secrete (*20*). Diminished egg excretion efficiency has been found in HIV infected patients with schistosomiasis, which difficults the diagnosis (*21*). The lack of sensitivity of classical manifestations and reduced egg excretion in HIV patients, make serology an interesting tool in schistosomiasis screening in this population; in our study, eleven patients had positive serology for *Schistosoma mansoni* and ova investigation was negative in all of them. HIV patients coming from endemic areas for schistosomiasis should be screened through serologic test; stool and urine sample must be collected when positive result in order to confirm the diagnosis. According to its efficacy and safety, praziquantel must

be offered to patients with confirmed diagnosis and those with positive serology and indirect signs of infection (eosinophilia, haematuria, periportal fibrosis, urine bladder calcification).

Strongyloides stercoralis infection is asymptomatic in most infected patients, but a fulminant fatal presentation (*Strongyloides stercoralis* hyperinfection syndrome and disseminated strongyloidiasis) may occur in situations with compromised host immunity, as HIV infection (*22*). Definitive diagnosis of strongyloidiasis is made on the basis of detection of larvae in stool samples; however, the low parasite load and irregular larval output in chronic infections (especially in immunocompromised patients) make the diagnosis very challenging (*23*). Currently serologic tests are very sensitive and specific, being useful for asymptomatic patients screening and follow-up after specific treatment (*24, 25*). Therefore, serologic test for the *Strongyloides stercoralis* infection screening in HIV population, seems to be the best strategy. Stool samples must be collected for larvae detection in positive results to confirm the diagnosis. Specific treatment with ivermectine will be offered to patients with confirmed diagnosis and patients with positive serology and other signs of infection (eosinophilia, pruritus, skin lesions or gastrointestinal disorders).

Higher prevalence of intestinal parasites in HIV infected population has been reported previously (*26*). *Cryptosporidium*, *Isospora* and other protozoan parasites have been related with advanced HIV infection, but other protozoa and helminths are increasingly recognized as a significant problem in immunocompromised individuals (*27, 28*). The higher prevalence of intestinal parasitosis among newcomers (less than 5 years living in our country) is explained because most of the intestinal parasites interrupt their life

cycle two or three years after leaving a favorable epidemiological environment. We have found no explanation for the higher prevalence of intestinal parasitosis among Latin American patients in our study. Two stool samples should be collected from all HIV infected patients coming from tropical and subtropical regions to screen for intestinal parasitosis, even if they are asymptomatic (all patients with intestinal parasitosis were asymptomatic in our study). Specific treatment must be offered when pathogenic parasites are detected or in symptomatic patients.

The low prevalence of HCV and HIV co-infection (4.7%) when comparing with the whole HIV infected population in our country, estimated in one third, could be explained by the main HIV acquisition risk factor in our study, the sexual transmission; only one patient was an intravenous drug user. As it was expected, the prevalence of HBV infection is higher in the sub-Saharan Africa group than in the Latin America group (*4*).

As it was suspected, parasitic infections among HIV infected patients coming from tropical and subtropical regions is highly prevalent, and the screening programs in HIV population coming from endemic areas are highly recommended. A similar study has been recently performed in United States; 128 immigrant HIV-infected patients were screened by stool investigation and serologic tests. Antibody detection for *Strongyloides* (26%) and *Schistosoma* (29%) antigens were higher than in our study (18.4% and 18.9% respectively). Conversely, no patient in that study tested positive for *Trypanosoma cruzi* serology, whereas 3.9% of our patients had a positive test (*29*). These differences could be explained because of the different proportions of sub-Saharian and Latin American patients in both series. Anyhow, as in our study,

eosinophilia was strongly associated with strongyloidiasis and schistosomiasis, highlighting the importance to perform a parasitic infections search in patients with high eosinophil count.

One of the limitations of our study is the use of a screening method based on serologic tests. Immunosuppression due to HIV infection may decrease the sensitivity of serologic tests and positive results may not differentiate between latent and past infections. Nevertheless, given the potential risk of reactivation and safety of most of the specific treatments, treating parasitic infections based on serological diagnosis in immunocompromised patients seems to be beneficial. Another limitation is that we have used *Leishmania infantum* and *Schistosoma mansoni* serologies to screen leishmaniasis and schistosomiasis respectively, on the basis of cross-reactivity with other species, which could drop the specificity of the test. Finally, the study population has specific social characteristics making them difficult to be followed up, requiring a greater effort by the physicians; only 139 out of 190 patients (72%) brought the stool samples and further studies after positive serologic results were difficult to perform.

CONCLUSIONS

In summary, parasitic infections are prevalent in HIV infected patients coming from tropical and sub-tropical areas. Due to the risk of reactivation and presentation as severe forms, parasitic infections screening is highly recommended in this population. According to our results and other previously reported, we propose to perform a screening of parasitic infections through stool investigation and serological tests (for Chagas disease, strongyloidiasis and schistosomiasis) in all HIV patients according to their geographical origin. Malaria screening should be individualized according the risk (newcomers from endemic areas). Screening and management strategy is summarized in Figure 2.

REFERENCES

1. Instituto nacional de Estadística (National Statistics Institute). Data available on http://www.ine.es. Last accessed on 15th March 2012.
2. World Health Organization. HIV/AIDS: Global situation and trends. Data available on http://www.who.int. Last accessed on 15th March 2012.
3. Documento de consenso de GESIDA/Plan Nacional sobre el SIDA sobre el tratamiento antirretroviral del adulto (actualización de enero 2011). Data available on http://www.gesida.seimc.org. Last accessed on 15th March 2012.
4. Recomendaciones de GESIDA/PNS/AEEH sobre tratamiento y manejo del paciente adulto coinfectado por VIH y virus de las hepatitis A, B y C (septiembre 2009).Data available on http://www.gesida.seimc.org. Last accessed on 15th March 2012.
5. González-Martín J, García-García JM, Anibarro L, Vidal R, Esteban J, Blanquer R et al. Consensus document on the diagnosis, treatment and prevention of tuberculosis. Enferm. Infecc. Microbiol. Clin, 2010;28:297 e1-20.
6. Karp CL, Auwaerter PG. Coinfection with HIV and tropical infectious diseases. I. Protozoal pathogens. Clin. Infect. Dis, 2007;45:1209-1213.
7. Karp CL, Auwaerter PG. Coinfection with HIV and tropical infectious diseases. II. Helminthic, fungal, bacterial and viral pathogens. Clin. Infect. Dis, 2007;45:1215-1220.
8. Lawn SD, Wilkinson RJ. Immune reconstitution disease associated with parasitic infections following antiretroviral treatment. Parasite. Immunol, 2006; 28: 625-633.

9. Riera C, Sulleiro E, Dopico E, Iniesta L, Tebar S, Fisa R et al. Usefulness of a western blot method for serodiagnosis of Chagas disease in cases of inconclusive serological results. In: Program and abstracts of the 7th European Congress of Tropical Medicine and International Health; Barcelona (Spain); 2011 Oct 3-6; Abstract 5.3-012.
10. Rougemont M, Van Saanen M, Sahli R, Hinrikson HP, Bille J, Jaton K. Detection of four Plasmodium species in blood from humans by 18 S rRNA gene subunit-based and species-specific real-time PCR assays. J. Clin. Microbiol, 2004; 42: 5636-5643.
11. Lillie PJ, Bazaz R, Greig JM. Screening African HIV positive patients for imported parasitic infections. J. Infect, 2008; 57: 481-484.
12. Sarner L, Fakoya AO, Tawana C, Allen E, Copas AJ, Chiodini PL et al. The utility of screening for parasitic infections in HIV-1-infected Africans with eosinophilia in London. Int. J. STD AIDS, 2007; 18: 626-629.
13. Lescure FX, le Loup G, Freilij H, Develoux M, Paris L, Brutus L et al. Chagas disease: changes in knowledge and management. Lancet Infect. Dis, 2010;10:556-70.
14. Sartori AMC, Ibrahim KY, Nunes Westphalen EV, Braz LMA, Oliveira OC, Gakiya E et al. Manifestations of Chagas disease (American trypanosomiasis) in patients with HIV/AIDS. Annals of Tropical Medicina and Parasitology, 2007;101: 31-50.
15. Rodríguez-Guardado A, Asensi-Álvarez V, Rodríguez-Pérez M, Mejuto-Álvarez P, Flores-Chávez M, Alonso-González P et al. Screening for Chagas disease in HIV-positive immigrants from endemic áreas. Epidemiol. Infect, 2011; 139:539-543.

16. Alvar J, Aparicio P, Aseffa A, Den Boer M, Cañavate C, Dedet JP et al. The relationship between leishmaniasis and AIDS: the second 10 years. Clin. Microbiol. Rev, 2008; 21: 334-359.
17. Medrano FJ, Cañavate C, Leal M, Rey C, Lissen E, Alvar J. The role of serology in the diagnosis and prognosis of visceral leishmaniasis in patients coinfected with human immunodeficiency virus type-1. Am. J. Trop. Med Hyg, 1998; 59:155-162.
18. Flateau C, Le Loup G, Pialoux G. Consequences of HIV infection on malaria and therapeutic implications: a systematic review. Lancet Infect. Dis, 2011; 11: 541-56.
19. Matisz CE, Naidu P, Shokoples SE, Grice D, Krinke V, Brown SZ et al. Post-arrival screening for malaria in assymptomatic refugees using real-time PCR. Am. J. Trop. Med. Hyg, 2011; 84: 161-165.
20. Ross AGP, Bartley PB, Sleigh AC, Olds GR, Li Y, Williams GM et al. Schistosomiasis. N. Engl. J. Med, 2002; 346: 1212-1220.
21. Karanja DM, Colley DG, Nahlen BL, Ouma JH, Secor WE. Studies on schistosomiasis in western kenia. I. Evidence for immune-facilitated excretion of schistosome eggs from patients with *Schistosoma mansoni* and human immunodeficiency virus coinfections. Am. J. Trop. Med. Hyg, 1997; 56: 515-21.
22. Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. Clinical Microbiology Reviews, 2004; 17: 208-217.
23. Siddiqui AA, Berck SL. Diagnosis of *Strongyloides stercoralis* Infection. Clin. Infect. Dis, 2001; 33:1040-7.

24. Bon B, Houze S, Talabani H, Magne D, Belkadi G, Develoux M et al. Evaluation of a rapid enzyme-linked immunosorbent assay for diagnosis of Strongyloidiasis. J. Clin. Microbiol, 2010; 48: 1716-1719.
25. Biggs B-A, Caruana S, Mihrshahi S, Jolley D, Leydon J, Chea L et al. Short report: management of chronic strongyloidiasis in immigrants and refugees: is serologic testing useful? Am. J. Trop. Med. Hyg, 2009; 80: 788-791.
26. Sanyaolu AO, Oyibo WA, Fagbenro-Beyioku AF, Gbadegeshin AH, Iriemenam NC. Comparative study of entero-parasitic infections among HIV sero-positive and sero-negative patients in Lagos, Nigeria. Acta Trop, 2011; 120: 268-72.
27. Modjarrad K, Zulu I, Redden DT, Njobvu L, Freedman DO, Vermund SH. Prevalence and predictors of intestinal helminth infections among human immunodeficiency virus type 1-infected adults in an urban African setting. Am. J. Trop. Med. Hyg, 2005; 73: 777-782.
28. Lewthwaite P, Gill GV, Hart CA, Beeching NJ. Gastrointestinal parasites in the immunocompromised. Curr. Opin. Infect. Dis, 2005; 18: 427-435.
29. Hochberg NS, Moro RN, Sheth AN, Montgomery SP, Steurer F, McAuliffe IT et al. High prevalence of persistent parasitic infections in foreign-born, HIV-infected persons in the United States. PLoS Negl. Trop. Dis, 2011; 5: e1034.
30. World Health Organization. Schistosomiasis: key points and geographical distribution. Data available on http://www.who.int. Last accessed on 15th March 2012.

Table 1. Epidemiological and HIV-related data

	Overall (n = 190)	**Latin America** (n=141)	**Sub-Saharan Africa** (n=41)	**North Africa** (n=8)	***P* value***
Male sex	129 (67.9)	108 (76.6)	15 (36.6)	6 (75)	<0.001
Age, years	37 (32-43)	37 (32-43)	36 (30-42)	39 (35-40)	0.358
Time since arrival, months	96 (60-123)	96 (60-126)	84 (60-120)	102 (43-216)	0.226
Time since last travel, months	36 (12-60)	36 (12-60)	36 (10-72)	18 (3-42)	0.809
Rural environment provenance	60 (31.6)	37 (26.2)	19 (46.3)	4 (50)	0.014
Nadir CD4+ cell count, cells/mm^3	223 (118-341)	223 (123-336)	224 (60-344)	262 (188-417)	0.501
Current CD4+ cell count, cells/mm^3	459 (358-625)	458 (369-658)	386 (274-565)	502 (453-767)	0.030
HIV RNA <50 copies/mL	124 (65.3)	97 (68.8)	24 (58.5)	3 (37.5)	0.221
HIV acquisition risk factor					
Heterosexual	112 (58.9)	65 (46.1)	40 (97.6)	7 (87.5)	<0.001
Homo/bisexual	76 (40)	75 (53.2)	1 (2.4)	0 (0)	<0.001
Intravenous drug user	1 (0.5)	0 (0)	0 (0)	1 (12.5)	-
Unknown	1 (0.5)	1 (0.7)	0 (0)	0 (0)	-
Naive patients	42 (22.1)	32 (22.7)	8 (19.5)	2 (25)	0.665
Previous opportunistic infections	37 (19.5)	30 (21.3)	6 (14.6)	1 (12.5)	0.347

NOTE. Data are reported as number (%) of patients or median value (interquartile range).

* *P* values obtained from comparison between Latin America and Sub Saharan groups.

Table 2. Infectious diseases screening.

	Overall	Latin America	Sub-Saharan Africa	North Africa	*P* value*
Eosinophilia	29/190 (15.3)	15/141 (10.6)	13/41 (31.7)	1/8 (12.5)	0.001
Latent tuberculosis infection	12/179 (6.7)	9/135 (6.6)	3/37 (8.1)	0/7 (0)	0.760
Positive *Toxoplasma gondii* serology	103/190 (54.2)	73/141 (52.5)	27/41 (65.9)	2/8 (25)	0.129
Positive anti HCV antibody	9/190 (4.7)	2/141 (1.4)	5/41 (12.2)	2/8 (25)	0.002
Positive HBs antigen	15/190 (7.9)	9/141 (6.4)	6/41 (14.6)	0/8 (0)	0.091
Past hepatitis B infection	68/190 (35.8)	44/141 (31.2)	22/41 (53.7)	2/8 (25)	0.008
Past or present HBV infection	83/190 (43.7)	53/141 (37.6)	28/41 (68.3)	2/8 (25)	<0.001
Intestinal parasitosis	37/139 (26.6)	32/102 (31.4)	4/32 (12.5)	1/5 (20)	0.036
Positive *Leishmania infantum* serology	7/187 (3.7)	6/138 (4.3)	1/41 (2.4)	0/8 (0)	0.580
Positive *Strongyloides stercoralis* serology	35/190 (18.4)	22/141 (15.6)	11/41 (26.8)	2/8 (25)	0.101
Positive *Trypanosoma cruzi* serology	5/126 (3.9)	5/126 (3.9)	0/0 (0)	0/0 (0)	-
Positive *Schistosoma mansoni* serology	11/58 (18.9)	2/17 (11.8)	9/41 (22)	0/0 (0)	0.368
Positive *Plasmodium* PCR	1/62 (1.6)	0/21 (0)	1/41 (2.4)	0/0 (0)	1.000
Any parasitological diagnosis	70/190 (36.8)	52/141 (36.9)	16/41 (39)	2/8 (25)	0.803

NOTE. Data are reported as number (%) of patients. PCR, polymerase chain reaction; HCV, hepatitis C virus; HBV, hepatitis B virus.

* *P* values obtained from comparison between Latin America and Sub Saharan groups.

Table 3. Intestinal parasites isolated.

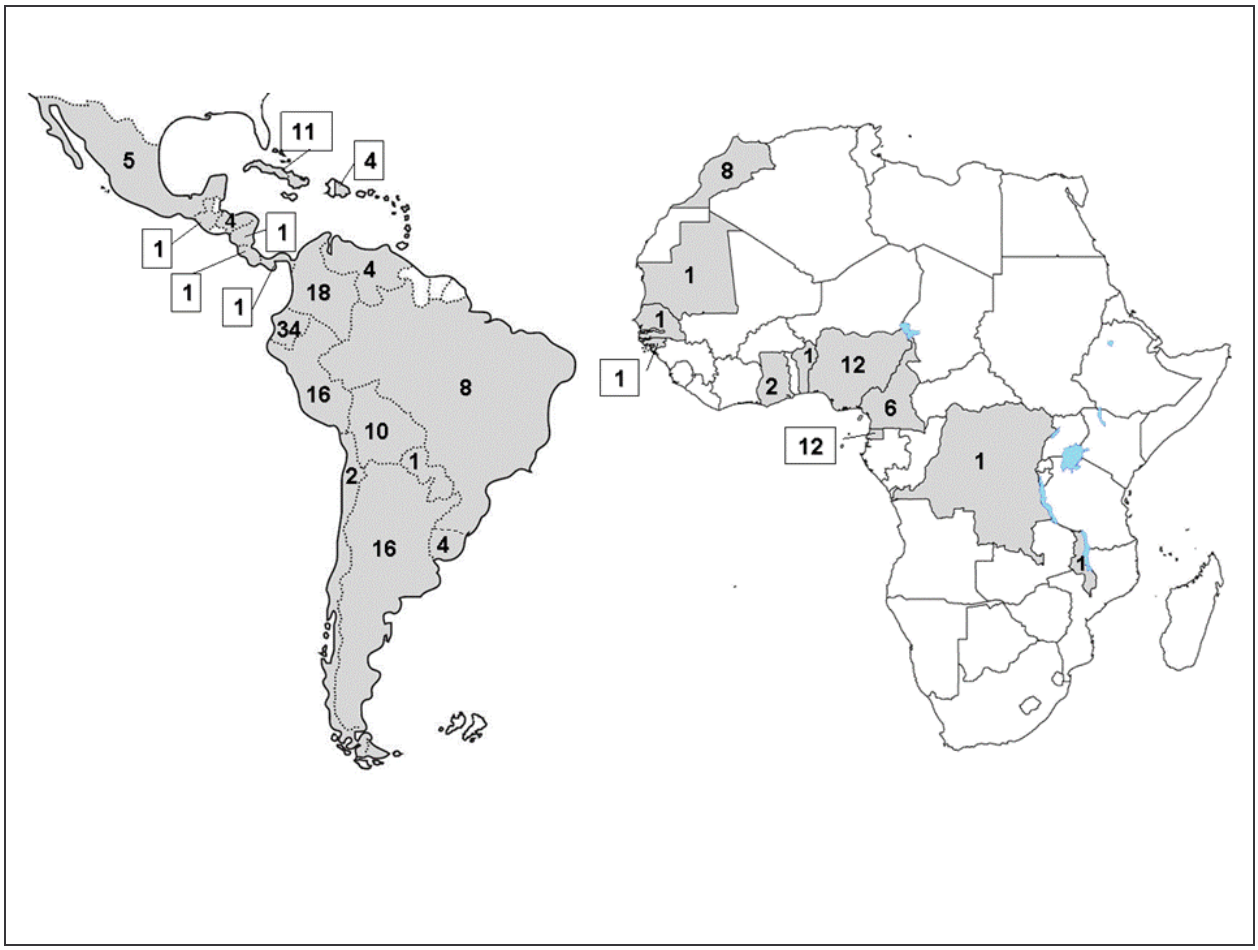
Intestinal parasite	Number of isolations
Pathogenic parasites:	
Entamoeba histolytica/dispar	4
Giardia lamblia	4
Strongyloides stercoralis	2
Trichuris trichiura	2
Ascaris lumbricoides	1
Hymenolepis nana	1
Parasites of minor medical importance:	
Blastocystis hominis	24
Dientamoeba fragilis	9
Non-pathogenic parasites:	
Entamoeba coli	9
Endolimax nana	8
OVERALL	64

Table 4. Univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
	OR (CI)	*P* value	OR (CI)	*P* value
Strongyloidiasis				
Rural environment provenance	1.15 (0.51-2.58)	0.724	-	-
Eosinophilia	2.56 (1.04-6.34)	0.036	2.56 (1.03-6.34)	0.041
Current CD4+ cell count <200 cells/mm³	3.45 (1.13-10.5)	0.022	-	-
HIV RNA ≥50 copies/mL	1.36 (0.62-2.97)	0.429	-	-
No ART	0.75 (0.28-1.97)	0.561	-	-
Previous opportunistic infection	0.88 (0.33-2.32)	0.799	-	-
Latin American origin	0.50 (0.22-1.15)	0.101	-	-
Schistosomiasis				
Rural environment provenance	4.70 (1.09-20.14)	0.028	-	-
Eosinophilia	10 (2.30-43.39)	0.001	8.74 (1.73-43.98)	0.009
Current CD4+ cell count <200 cells/mm³	12.2 (2.31-64.68)	0.001	10.3 (1.57-67.54)	0.015
HIV RNA ≥50 copies/mL	4.29 (1.01-18.34)	0.039	-	-
No ART	2.72 (0.69-10.68)	0.141	-	-
Previous opportunistic infection	1.82 (0.39-8.43)	0.435	-	-
Latin American origin	0.47 (0.09-2.47)	0.368	-	-
Intestinal parasitosis				
Time since arrival <5 years	4.16 (1.71-10.11)	0.001	4.64 (1.83-11.75)	0.001
Rural environment provenance	1.70 (0.77-3.75)	0.187	-	-
Eosinophilia	1.84 (0.72-4.69)	0.195	-	-
Current CD4+ cell count <200 cells/mm³	1.23 (0.35-4.29)	0.738	-	-
HIV RNA ≥50 copies/mL	0.72 (0.31-1.67)	0.450	-	-
No ART	0.59 (0.20-1.70)	0.328	-	-
Previous opportunistic infection	1.71 (0.65-4.51)	0.272	-	-
Latin American origin	3.2 (1.03-9.88)	0.036	3.72 (1.14-12.17)	0.001

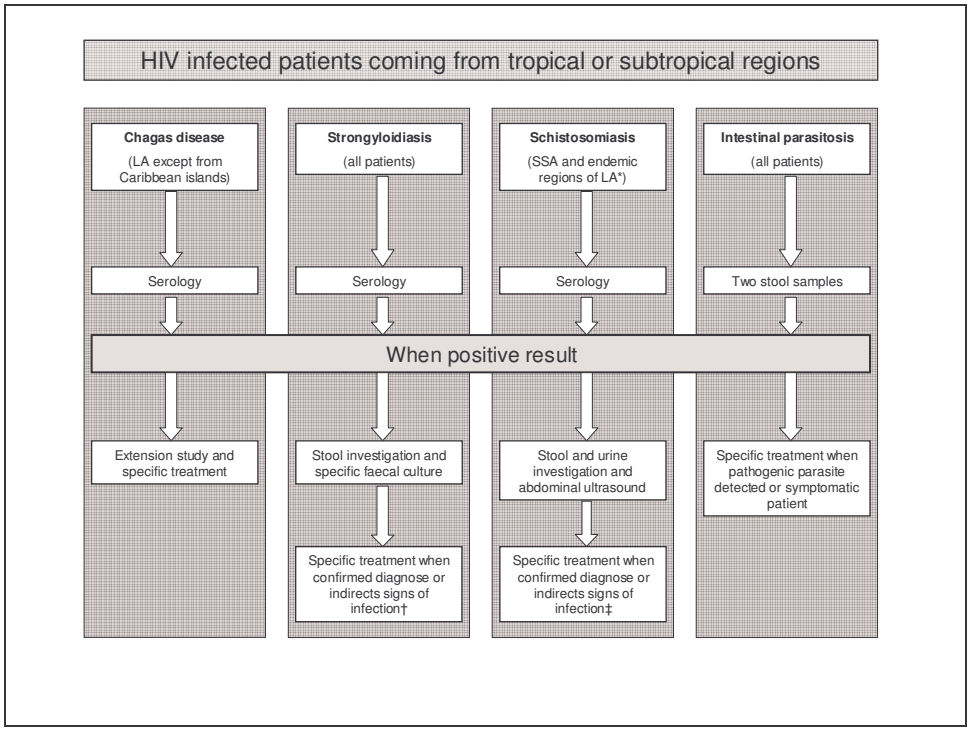
Note. OR, odds ratio; CI, confidence interval; ART, antiretroviral therapy

Figure 1. Geographical origin of patients.



Note: numbers represent number of patients coming from each country.

Figure 2. Proposal of screening and management strategy of latent parasitic infections in HIV infected patients.



NOTE: LA, Latin America; SSA, sub-Saharan Africa.

* Patients coming from Brazil, Venezuela, Surinam and Caribbean islands (*30*).

† Eosinophilia, pruritus, suggestive skin lesions, gastrointestinal disorders.

‡ Eosinophilia, haematuria, suggestive ultrasound disorders.