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Original

Immune status of patients with HIV/AIDS at the time of diagnosis in the Hospital San Juan de Dios

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Abstract

Aim: To compare the immune status during three years of patients diagnosed with HIV/AIDS who were treated at the San Juan de Dios Hospital.

Materials and Methods: Retrospective, descriptive study of the new cases of HIV/AIDS, older than 14 years of age, in 2003, 2006 and 2009 at the HIV Outpatient Clinic of the San Juan de Dios Hospital, Costa Rica, according to data in the clinical records. To evaluate the immune status the 160 CD4 + T lymphocytes count at moment of HIV diagnosis was used, establishing as late diagnosis <200 cells. For the analysis, an estimate of the frequency and strength of association between variables was performed.

Results: From the 282 cases studied, 46.8% of them were at an advanced stage of the illness.

Considering all cases, late diagnosis was more frequent in men (54%) than in women (26%) ($p<0.05$) and in heterosexual men (57%) than in men who have sex with men (50%) ($p<0.05$).

In regard to age, there is an increase in risk proportional to the increase in age. It was observed that the percentage of late-diagnosis patients has increased throughout the years herein studied. Even though a decrease in the group of patients who come late for the start of the ART was observed, this decrease is due to an increase in late diagnosis and not because of an increase in timely diagnosis.

Conclusions: Late diagnosis of HIV infection represents a public health problem in the geographical area covered by the services of the San Juan de Dios Hospital. It is necessary to develop strategies that allow the improvement of the resolving capacity of the primary and secondary levels of attention in order to achieve HIV diagnosis in a timely manner. In the geographical area covered by the San Juan de Dios Hospital, the populations with a greater risk of late diagnosis are heterosexual men between the ages of 25 and 64.

Key Words: HIV, AIDS, CD4-positive T lymphocytes, late diagnosis, immunodeficiency.

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Abbreviations: LD, Late Diagnosis; HSJD, San Juan de Dios Hospital; HAART, Highly Active Antirretroviral Treatment; HIV, Human Immunodeficiency Virus

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Human immunodeficiency virus (HIV) is a retrovirus that causes slow and progressive injury to the immune system; this is why people infected with the virus remain asymptomatic for several years, while continuous damage leads to severe immunosuppression, which could result in serious clinical consequences, favoring opportunistic infections and malignancies, potential causes of death for these patients.[1, 2] In fact, the disease´s natural is divided into three stages: primary infection, which occurs after HIV infection with a significant viremia, and an intense immune response, which could be a symptomatic or asymptomatic stage; the second or chronic

phase is a prolonged stage of clinical latency, characterized by continuous viral replication and progressive depletion of CD4+ T lymphocytes (TCD4+) where patients often remain asymptomatic, and a final stage or AIDS, where severe immunosuppression is achieved, which may lead to significant clinical deterioration and death.[3]

Highly Active Antiretroviral Therapy (HAART) has allowed a change in this natural history, controlling viral replication and allowing immune recovery, resulting in a lower incidence of opportunistic infections and a lower mortality from HIV-related causes.[4,5] Furthermore, scientific evidence has shown that continuous HIV replication is associated with a number of immune defects that cause irreversible immunosenescence. This is why various international guidelines recommend starting HAART at an immune status that permits a greater chance of recovering normal TCD4+ levels and better immune reconstitution, setting CD4 + <350 cells/ul counts as a parameter. Some, more recent guidelines4-5 are even more aggressive, recommending an earlier initiation of antiretroviral therapy in asymptomatic patients with TCD4 + counts between 350 and 500 cells/L, based on the damage caused by HIV infection in the untreated asymptomatic phase.[5]

These results highlight the importance of early HIV detection, so it is possible to initiate antiretroviral therapy in a timely manner, according to individual patient characteristics.

A late diagnosis (LD), defined as the detection of new infections with <200/µl TCD4+ levels, means a higher risk of developing serious opportunistic infections, drug-related adverse events and less immune recovery.[6]

Therefore, early diagnosis becomes a key issue, not just for an effective pathology approach, for the introduction of antiretroviral therapy when it could reduce virus-associated inflammation and TCD4+ count depletion, but also in preventing and stopping transmission, allowing measures to prevent risky behaviors and decrease the infection´s transmissibility.[7]

For these reasons, the immune status of patients presenting with HIV/AIDS is analyzed, for those seen at HSJD for the first time.

Materials and methods

A descriptive, retrospective study was performed, using medical records as a source of information.

All new HIV cases diagnosed in 2003, 2006 and 2009 were analyzed, for those older than 14 years-old, treated at the HIV Patient Care Clinic at San Juan de Dios Hospital.

Immune status at the time of HIV diagnosis is assessed by using the TCD4+ lymphocyte count, defining late diagnosis as having <200 TCD4+ cells/µ l.

All cases diagnosed with HIV infection are included, with two positive ELISA tests, and positive Western blot confirmatory test, in 2003, 2006 and 2009. Patients who did not have an initial TCD4+count determination were excluded.

Variables analyzed included: age, gender, nationality, sexual preference, TCD4+ lymphocyte counts.

Data analysis was performed with SPSS 14.0, by estimating the frequency and strength of association between variables.

Results

In the analyzed period, 373 patients were identified; 91 were excluded because they did not have TCD4+ records, therefore, the study included a total of 282 patients (79 in 2003, 99 in 2006 and 104 in 2009). Study population´s characteristics, by year of diagnosis are shown in Table 1.

There were more males in the study population, 74.1%; mode was in the age group of 25-34 years. Foreigners corresponded to 12%, the majority from Nicaragua. As for the sexual preference of men included, there was a similar proportion of heterosexuals and homosexuals (37.9% and 37.4%, respectively) and 7% were bisexuals.

Regarding the frequency of late diagnosis, for all cases, analyzing the ratios, it was significantly greater in males (54%) than females (26%) ($p < 0.05$), and in heterosexual men (57%) than in those who have sex with men (50%) (p

Table 1. Epidemiologic characteristics for those patients included in the study, by year of diagnosis

Characteristic		General N (%)	Year of Diagnosis		
		2003	2006	2009	
Gender		282	79	99	104
Female	73 (25,9)	23 (29.1)	32 (32.7)	19 (18.3)	
Male	209 (74,1)	56 (70.9)	66 (67.3)	85 (81.7)	
Age group (mode, years)		25,34	35-44	25-34	25-34
Nacionality	CR	241 (85,4%)	68 (86.1)	80 (81,6)	92 (88.5)
Nicarag	30 (10,6%)	5 (6.3)	14 (14.3)	11 (10.6)	
Other	4 (1,4%)	1 (1.3)	2 (2)	1 (0.9)	
Unknown	7 (2,6%	5 (6.4)	2 (2)	0	
MSM	93 (33%)	24 (30,4)	36 (36,7)	33 (31,7)	
Sexual preference					
Heterosexual male		80 (28,4%)	27 (34,2)	27 (27,6)	27 (26,0)
Female	74 (26,2%)	24 (30,4	30 (30,6)	20 (19,2)	
Unknown	35 (12,4%))	4 (5,1)	6 (6,1	24 (23,1)	
Late Diagnosis (CD4+ <200 cell/ml)		132 (46,8%)	31 (39,3)	43 (43,9)	58 (55,8)

Table 2. Late diagnosis in HIV diagnosed patients at Hospital San Juan de Dios, in 2003, 2006 and 2009

	2003 Frequency (%)	2006 Frequency (%)	2009 Frequency (%)
Late Diagnosis Advanced Disease (CD4 <200)	31 (39,3)	43 (43,4)	58 (55,8)
Late Diagnosis to start HAART (CD4 200-350)	17 (21,5)	15 (15,3)	15 (14,4)
Timely (Early) Diagnosis (CD4 >350)	31 (39,2)	40 (40,8)	31 (29,8)

<0.05). Regarding age, there is an increased risk of LD with increasing age.

Table 2 describes cases presented each year, according to their TCD4+ levels, distributed in 3 groups: LD with advanced disease (TCD4+ count <200 cells/ul), late diagnosis to start HAART (CD4 counts between 200-350 cells/ul) and early diagnosis (TCD4+ count >350 cells/µl). The percentage of patients with a late diagnosis increased over the studied years; even though the group of patients who arrived late for the start of HAART decreased, this was due to an increase in late diagnosis, not due to an increase in early diagnosis.

Figure 1 shows a more detailed distribution of patients´ percentage, according to CD4 values at time of diagnosis. It is noteworthy how this chart shows a progressive increase not just for patients with late diagnosis, but with CD4 counts below 50 throughout the 3 years, and a decrease in patients with early diagnosis.

Discussion

Early HIV/AIDS diagnosis should be a key objective in the management of this condition, as it has advantages from the public health point of view, as well as from morbidity and mortality perspectives. Still, the late entry by this population

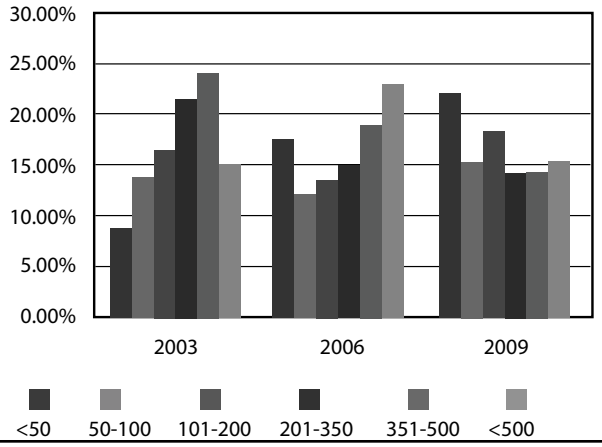

Figure 1. TCD4+ percentage at time of diagnosis, in HIV infected patients

into the health system is a global issue. In Spain,8,9 37,2% of patients presented with CD4+ lymphocyte counts <200 cells/uL; in the UK, in 2010, approximately 27% of the studied patients had a late diagnosis; 10 in France,11 about 20%, and in a multicenter study made in Europe and North America, the initial diagnosis in the AIDS stage was performed on approximately 25% of patients.12 However, Althoff et al6 and Keruly et al,13 found a decrease in the TCD4+ count at initial diagnosis, throughout a decade, in different series of the United States and Canada, and the initial worryingly low CD4+ count,6 found 41-66% of patients in the late phase. Similarly, a study in India14 reported that more than 80% of patients are diagnosed in advanced stages.

In this study, 46,8% of cases presented at a late stage, or the stage of AIDS, meaning that these patients, according to this disease´s natural history, have carried the infection approximately 8 to 10 years, making this an aggravating factor of the epidemic, as during this time they were potential infection transmitters, due to ignorance of their condition.

One important aspect, seen in this study, is that the percentage of late diagnosed cases has been increasing, mainly those with TCD4+ <50 cells/µl, resulting in a severe immune deterioration, conditioning an increased risk of opportunistic diseases for the patient, worsening their quality of life and increasing their risk of death.[1,7]

Despite the progress made in the field of HIV diagnosis, achieving a shorter window period to four weeks, and the fact that Costa Rica has a health system that with a wide population coverage and that ensures the availability of tests in general, the study shows that late diagnosis has increased over the years, and that early diagnosis has decreased, paradoxically. This could be related to a loss of awareness achieved at the beginning of the disease epidemic, both in the general population and in the health system, perhaps because "fear has been lost" to this illness and basic aspects such as promotion, prevention and diagnosis have become unattended.[15]

In the general population late diagnosis was lower in women than men, similar to those reported in other countries,16 which may be related to the obligation, in our health care system, to perform two screening tests during pregnancy; another factor that could play a role is diagnosing women as part of contact tracing, but more studies are needed to support this specific evidence. However, during 2009 this ratio was reversed, and the highest proportion corresponded to late diagnosis in women.

Late diagnosis gradually increased between ages 25 to 64, with a peak between 55 and 64, which reinforces the hypothesis of a lack of disease awareness and the absence of screening programs targeted at risky populations, because the test is performed until there is clinical evidence of the disease.[15]

In the male population there is a higher risk of late HIV diagnosis for heterosexuals than for homosexuals, given a higher risk perception among men who have sex with men, associated with the stigma that this disease is more common among them.

The delay in diagnosis may be due also to the lack of clinical suspicion by health personnel. It is not uncommon to find patients who were treated in health centers several times, months earlier, because of illnesses clearly associated with HIV / AIDS, and who have not been properly diagnosed.

Although it is not the aim of this study, it should be noted that HIV / AIDS affects mainly in our environment, young people between 25-40 years of age, who have unsafe sex with multiple partners, with homo (40%) or heterosexual (60%) behaviors, with a history of addiction to legal or illegal drugs in 40-50% of cases; 25% of these are women, 20% are commercial sex workers (Clinical HIV / AIDS HSJD, unpublished data).

Furthermore, all patients with sexually transmitted infections or tuberculosis should be studied for HIV/ AIDS. This should also be included in the differential diagnosis in patients with prolonged fever (> 15 days), unexplained weight loss, cervical lymphadenopathy, mononucleosis syndrome and cytopenias. Multiple and complex dermatologic manifestations could be seen for HIV / AIDS; for women: refractory vaginal candidiasis, cervical dysplasia, cervical cancer and pregnancy are mandatory conditions to study for HIV / AIDS. There are excellent recent reviews on this topic.[2,17]

Thus the late diagnosis of HIV infection represents a public health issue for HSJD´s area, this is why it is necessary to develop strategies to improve first and second level of care´s response capability, diagnosing HIV in a more timely manner.

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