

GREATER SURVIVAL AMONG PATIENTS WITH IMMUNOGENETIC MARKERS ASSOCIATED WITH RAPID PROGRESSION TO AIDS: IMPLICATIONS FOR NURSING CARE^I

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ABSTRACT

Objective: This study sought to verify the influence of changes in sexual behavior after HIV-infection diagnosis, including the adoption of safe sex practices, among AIDS patients with immunogenetic markers of rapid disease progression.

Methods: Twenty-seven AIDS patients, genetically predisposed to rapid AIDS progression, were interviewed. DRB1 and DQB1 alleles were characterized using PCR-amplified DNA hybridized with sequence specific oligonucleotide probes or by sequence-specific primer analysis. HLA class I antigens were typed using a microlymphocytotoxicity assay.

Results: In spite of the presence of immunogenetic factors associated with individual predisposition to a rapid evolution of the disease, changes in sexual behavior combined with the use of antiretroviral therapy, may result in greater survival.

Conclusion: This suggests that counseling, detection of unsafe sexual practices and health education focusing on positive healthy behavior are tools nursing must use with HIV-positive patients. These tools may help to lead to a greater survival among these individuals, even among those with genetic predisposition to rapid disease progression, with implications for improvement of nursing care programs for HIV-infected patients.

Descriptors: AIDS, HIV, HLA, behavior, survival rate, nursing.

INTRODUCTION

The AIDS epidemic is characterized by extreme heterogeneity in the clinical course as well as in the incidence of HIV-1 infection among exposed individuals and has stimulated

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longitudinal cohort studies designed to document heterogeneity as well as to mitigate factors that regulate HIV-1 infection, disease progression, and immune defenses⁽¹⁾.

Individuals have been identified who demonstrate disparate abilities to control HIV-1 infection. Although the average time to develop AIDS in people with untreated infection is ten years. A subset of infected persons (1-5%) has been identified who maintain low to undetectable HIV-1 viral loads, normal CD4⁺ T cell counts, and no manifestations of HIV-1 clinical immunocompromise or disease despite documented infection with HIV-1. This group of individuals, who are considered long-term nonprogressors presenting with slow progression to AIDS, manifest a unique ability to successfully control HIV-1 viremia in the absence of antiretroviral therapy, in some cases for up to 20 years. On the other hand, individuals that develop AIDS 2-3 years after infection with the virus were considered to have rapid progression to AIDS⁽²⁾.

Host genetic factors, such as HLA alleles which have an extraordinary degree of polymorphism and have a major role in the HLA locus in controlling the immune response, have associations with different rates of progression to AIDS and have been extensively studied⁽³⁾. Various cohort studies have identified associations between HLA genes (class I and class II) and progression to AIDS. In this respect, the HLA-B14, -B27, -B57, and -B44 were found to be associated with slow progression to AIDS, while the rapid progression from HIV-1 infection to AIDS has been strongly associated with HLA-A1-Cw7-B8-DR3-DQ2 and HLA-A11-Cw4-B35-DR1-DQ1 haplotypes, conferring a high risk of rapid progression to AIDS⁽⁴⁾.

In a previous study, when we compared the frequencies of HLA markers that have been associated with rapid progression to AIDS in several populations. These markers in AIDS patients presenting with cytomegalovirus retinitis (CMV-R) were overrepresented (75% in patients with and 46.2% in those without CMV-R), indicating that with the development of CMV-R, the frequency of HLA-B35 and -DQ2 markers associated with rapid progression to AIDS is increased⁽⁵⁾.

In Brazil, the period of survival after AIDS diagnosis has changed. Median survival was 5 months for cases of AIDS diagnosed in the 1980s, 18 months for those diagnosed in 1995, 58 months for those diagnosed in 1996⁽⁶⁻⁷⁾, and finally, in 2002 the mean was seven years⁽⁸⁾. The amount of these gains and the analysis of the predictors of survival both indicate there are several factors that may be associated with prolonged life expectancy, such as early diagnosis and antiretroviral treatment⁽⁸⁾.

However, other factors may also be associated with the disease progression and life expectancy, namely, sexual behavior associated with the disease. In this study, we

evaluated the influence of sexual behavior, before and after HIV-infection diagnosis, on the survival of AIDS patients who have HLA antigens associated with rapid progression to AIDS.

MATERIALS AND METHODS

Subjects

This study was conducted by analyzing data collected in 1997-1999, that was based on the two patient groups evaluated in Dr Rodrigues' thesis⁽⁹⁾. This study determined the HLA class I and II alleles frequency among AIDS patients exhibiting or not exhibiting cytomegalovirus retinitis (CMV-R), and additionally, identified the association between the HLA markers and CMV-R development among AIDS patients.

Group I was composed of AIDS⁽¹⁰⁾ patients with CMV-R (n=44) confirmed by retinal examination by a trained ophthalmologist using indirect binocular ophthalmoscopy. These sample was selected from the Outpatient Ophthalmology Clinic of the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil. Group II patients without CMV-R (n=80) were selected from the Outpatient Special Unit for Treatment of Infectious Diseases of the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil; a regional center for this type of care.

DNA extracted from peripheral blood leukocytes using a salting-out procedure was performed for the typification of the HLA alleles. DRB1 and DQB1 alleles were identified using PCR-amplified DNA, hybridized with sequence specific oligonucleotide probes or by sequence-specific primer analysis using commercial kits (One Lambda, Canoga Park, CA, and Ruprecht-Karls-Universität, Heidelberg, Germany or One Lambda, Canoga Park, CA), as described by Fernandes et al.⁽¹¹⁾. The HLA class I antigens were typed using a microlymphocytotoxicity assay, using peripheral blood lymphomononuclear cells⁽¹²⁾.

To perform this study, the only patients selected were those who were identified as having_HLA antigens associated with rapid progression to AIDS, namely, HLA-A1-Cw7-B8-DR3-DQ2 and HLA-A11-Cw4-B35-DR1-DQ1, and that also displayed a healthy mentality in the interview process.

From the 124 patients initially included in this study, and who under went HLA allele typification, 70 (56.5%) patients were found have HLA antigens associated with rapid progression to AIDS. After reviewing each patient's medical history, 30 patients were found have died and 13 patients could not be interviewed due to cognitive impairment and major psychiatric disorders. Therefore, the present study involved 27 AIDS patients presenting with HLA antigens associated with rapid progression to AIDS. The interviews were conducted, after informed consent had been obtained from all individuals, in a reserved

room in the health facility previously described, when the patients were waiting for their followup appointment.

Data Collection

Data collection was conducted using a semistructured interview guide to elicit information from the participants based on our goal of identifying sexual practices, characteristics of past and present situations which have placed persons in high-risk sexual situations, and demographic information such as age, marital status, gender and duration of AIDS.

Ethical aspects

The Medical Ethics Committee of the University Hospital of the Faculty of Medicine of Ribeirão Preto, Brazil, approved the study protocol (process number 7679/2001). Participants were informed that involvement was voluntary, that they could refuse to answer any questions, and that they could cease participation at any time without penalty. Prior to the start of each interview, written informed consent was obtained.

Statistical analysis

Fisher's exact test and the GraphPad software (InStat program, CA, USA) were used for all analyzes. In a 95% confidence interval, *P* values less than or equal to 0.05 were considered to be significant.

RESULTS

Participant characteristics

The study sample was comprised of 27 participants. The majority of individuals were male (55.6%), caucasians (77.8%), single (37.1%). The mean age of the sample was between the ages of 35 and 39 (40.7%), and AIDS diagnosis time was over six years (51.8%).

Antiretroviral use

During the interview, the majority of patients (24 of 27 or 88.9%) reported taking the antiretroviral therapy. In addition, it was found that the majority of deceased patients (20 of 30 patients) and patients with cognitive impairment (8 of 13 patients) were also undergoing antiretroviral therapy, based on their medical records.

Upon evaluation of the antiretroviral use among AIDS patients presenting with HLA antigens associated with rapid progression to AIDS of the initial sample (70 patients), the patients interviewed showed antiretroviral use was significantly increased in relation to deceased patients ($p=0.04$).

HIV infection characteristics

Diagnosis time

Among the 27 patients selected in this study, 13 of 27 (48.2%) were HIV infected for 2-5 years, 8 of 27 (29.6%) for 6-9 years and 6 of 27 (22.2%) for over 10 years.

Risk situations for HIV transmission

The major risk situation for HIV infection was sexual, stated by 18 of 27 patients (66.7%). Of these, 6 of 27 (33.3%) patients indicated marital relations as the transmission agent and 5 of 27 (27.8%) acquired HIV infection from casual sexual intercourse.

Sexual behavior before and after HIV infection

The major changes of sexual behavior, in relation to number of sexual partners, unsafe sex practices including having sex with multiple partners and failure to use condoms, frequency and characteristics of past and present situations which have placed persons at risk for HIV infection are shown in Table 1.

Sexual partners

Before HIV infection, 13 of 27 (48.1%) patients had more than four previous sexual partners, after diagnosis this number had significantly decreased, namely, no patient had as many partners as before the diagnosis ($p=0.0001$). Additionally, 14 of 27 (51.9%) patients stated that they have had only one sexual partner ($p=0.02$) and 12 of 27 (44.4%) patients related having no sexual partner after HIV infection ($p=0.0001$).

Frequency of sexual intercourse

Frequency of sexual intercourse changed after HIV infection as well. It was found that 22 of 27 (81.5%) patients decreased the frequency of sexual intercourse after infection ($p=0.0001$), of those 5 of 27 (18.5%) patients stated sexual abstinence ($p=0.05$), 10 of 27 (37%) patients last had their sexual intercourse over six months ago ($p=0.001$) and 7 of 27 (25.9%) patients last had sexual intercourse one month ago.

Sexual practice

Among the 10 of 27 (37%) patients that stated having had anal sex before HIV infection, only 3 of 27 (11.1%) patients continued this practice, which is a significant decrease ($p=0.05$).

Condom use

Significant decrease in unprotected sex was seen after HIV infection ($p=0.0008$). In addition, after infection, an increase in the number of patients that practiced condom use during vaginal intercourse was found ($p=0.05$). These results are shown in Table 1.

TABLE 1- Comparison of sexual behavior before and after HIV-infection individuals presenting with HLA antigens associated with rapid progression to AIDS.

SEXUAL BEHAVIOR	BEFORE HIV-INFECTION (n=27) p=* [*]		AFTER HIV-INFECTION (n=27) p=* [*]	
	n ^o	%	n ^o	%
Number of sexual partners				
None	-	-	12	44.4
			p=0.0001 *	
One	05	18.6	14	51.9
Two-three	09	33.3	01	3.7
			p=0.01* *	
Over four	13	48.1	0	0
			p=0.0001 *	
Sexual practice	n ^o	%	n ^o	%
None	-	-	05	18.5
			p=0.05* *	
Vaginal	17	63	19	70.4
Anal	10	37	03	11.1
			p=0.05* *	
Condom use	n ^o	%	n ^o	%
Never	18	66.7	05	18.5
			p=0.0008 *	
Sometimes	06	22.2	03	11.1
Always	03	11.1	17	63.0
			p=0.0002 *	
No sexual intercourse	-	-	02	7.4
Sexual practice and condom use	n ^o	%	n ^o	%
None	18	66.7	05	18.5
			p=0.0008 *	
Vaginal	07	25.9	15	55.6
			p=0.05* *	
Anal	01	3.7	01	3.7
No sexual intercourse	-	-	02	7.4
Sexual orientation	n ^o	%	n ^o	%
Homosexual	01	3.7	02	7.4
Heterosexual	24	88.9	25	92.6
Bisexual	02	7.4	-	-

* Fisher's exact test.

DISCUSSION

Several genetic markers are associated with progression to AIDS and, to a lesser extent, others are associated with resistance to HIV infection. AIDS epidemicity is characterized by extreme heterogeneity in terms of the course of the disease and incidence of HIV-1 infection among exposed individuals^(2,3). These findings probably reflect the genetic variants of HIV-1 strains and host genetic polymorphic genes, including chemokine and chemokine receptor structural genes and HLA alleles⁽¹⁾. The progression from HIV-1 infection to AIDS has been strongly associated with HLA-A1-Cw7-B8-DR3-DQ2 and HLA-A11-Cw4-B35-DR1-DQ1 haplotypes, conferring a high risk of rapid progression to AIDS⁽⁴⁾.

It has been assumed that associations between the progression to AIDS and particular HLA alleles reflect differential antigen presentation by class I or II molecules exhibiting particular motifs in the peptide binding groove⁽⁵⁾. A direct effect of HLA allele products on progression to AIDS is plausible, given their role in antigen presentation to T

cells and the evidence indicating that cytotoxic T cells (CTLs) play an important role in protection against HIV-1. Another mechanism to explain rapid progression to AIDS in individuals with certain HLA genotypes may involve the regulation of natural killer (NK) cell activity. A number of studies have indicated that rapid disease progression after HIV-1 infection is correlated with decreased NK cell activity. Like CTLs, NK cells are involved in surveillance and killing of foreign or infected cells through a mechanism involving HLA molecules⁽¹³⁾.

Studies of survival among adult Brazilian AIDS patients demonstrates a substantial increase in life expectancy. This improvement coincides with the widespread availability of antiretroviral treatment in Brazil^(8,14). In this study, about 1/3 (38.6%) of HIV-infected individuals presenting with HLA antigens associated with rapid progression to AIDS were available to participate. These patients had AIDS for six years (51.8%) and the majority of participants were taking the antiretroviral therapy (88.9%) and prophylactic medication against opportunistic infections (37%). Both contributed to increased life expectancy of HIV-infected patients and also their quality of life improved⁽¹⁵⁾.

Analisis about antiretroviral therapy use revealed that the majority of HIV-infected individuals who were exhibiting HLA antigens associated with rapid progression to AIDS, both those eligible and not eligible, were taking the highly active antiretroviral therapy, suggesting that others factors may be associated with survival of patients included in the study. As well, studies have shown that level of educational, gender⁽¹⁶⁾ and opportunistic infections⁽¹⁷⁾ have an effect on AIDS patients' survival. Moreover, factors such as changes of sexual behavior focusing on risk reduction may be associated too.

To evaluate changes of sexual behavior in these patients, comparative analisis on unsafe sexual practices before and after HIV-infection showed a significant increased of condom use ($p=0.0001$), decreased number of sexual partners ($p=0.0001$), decreased frequency of sexual intercourse ($p=0.0001$) and a decrease of anal practices ($p=0.05$) after HIV-infection.

This study has focused on exploratory and descriptive goals. The findings suggest a change in sexual behavior, namely, the number of sexual partners, specifically casual partners, decreased after HIV-infection and the majority of patients stated that they had only one or no sexual partner. Additionally, a significant decrease of frequency of sexual intercourse was also observed ($p=0.0001$). As well, 1/3 of patients related last having sexual intercourse over six months ago ($p=0.001$) or sexual abstinence ($p=0.05$) after HIV-infection.

Changes in sexual behavior along with safe sex practices together with antiretroviral therapy may contribute to and improve life expectancy of AIDS patients.

Finally, these results suggests that counseling, detection of unsafe sexual practices and health education focusing on healthy behavior are tools nursing must use with HIV-positive patients. These tools may help to lead to a greater survival among these individuals, even among those with genetic predisposition to rapid disease progression, with implications for improvement of nursing care programs for HIV-infected patients.

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