Published in final edited form as:

J Health Care Poor Underserved. 2013 November ; 24(4 0): 94–105. doi:10.1353/hpu.2014.0014.

HIV/AIDS in the Puerto Rican Elderly: Immunological Changes between Gender and Body Mass Index

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Abstract

Purpose—Human immunodeficiency virus (HIV) in the elderly population has serious repercussions. The elderly are underdiagnosed for HIV and the costs associated with their late-stage care represent a financial burden to the public health system. The purpose is to analyze various profiles among a cohort of elderly patients with HIV/AIDS.

Methods—This is a baseline cohort 60 years or older seen in the Retrovirus Research Center between January 2000 to December 2011. We present the profiles of our cohort stratified by gender and body mass index viewed as a covariate of interest.

Results—A total of 266 people (68% males and 32% females) seen at the Center were older than 60 years of age. Males were significantly more often overweight ($p<.05$). Females were significantly more underweight with chronic conditions ($p<.05$). Women had higher CD4 count and lower HIV viral loads ($p<.05$). Underweight elderly males were more heavily affected with the burden of HIV infection compared with women.

Keywords

Puerto Rican; HIV/AIDS; ART; elderly

Low body mass index (BMI) has been described as an independent marker of HIV disease progression and directly associated with a decrement in CD4 cell count.¹ Increments in BMI have been associated with a better tolerance of therapy, improvement in CD4 cell count, and better control of HIV viral load.² It is unclear if there is a cause and effect relationship between the low BMI and lower CD4 cell count and higher viral load. HIV/AIDS in the elderly population is an increasingly relevant issue within the epidemic due to the frequent under-diagnosis of the infection in this age group, the increasing presence and prevalence of other chronic conditions and co-morbid conditions, and the increased costs of health care needed by the elderly subject.^{3,4,5} HIV infection in the elderly population has particular repercussions in the epidemic and definite consequences for providing appropriate health care. According to the recent *2012 UNAIDS Global Epidemic Update* there is a steady improvement in the delivery of effective treatment to people with HIV across the globe.⁶ Unfortunately, the *Update* does not include data on the growing numbers who are aging with HIV. With the increasing survival of HIV-infected patients, the aging HIV patient will require recognition as a particularly vulnerable group within the HIV spectrum of patients.

Current estimates suggest there are more than three million people aged 50 and older with HIV in Africa alone, and countless more around the world.⁷ The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 34.0 million people were living with HIV at the end of 2011.⁶ The Centers for Disease Control and Prevention (CDC) reported that, in 2010, 2,500 cases of HIV infection, representing five percent (5%) of all cases of persons living with HIV/AIDS, were reported as incidence among the elderly population along the United States.⁸ In Puerto Rico in 2010, the number of cumulative cases of HIV not acquired immunodeficiency syndrome (AIDS) among the elderly was 687, representing 7% of the total number of people in PR with HIV/not-AIDS, whereas the cumulative cases of HIV/AIDS among the elderly in Puerto Rico totaled 3,180.⁸

Due to the natural biological, psychosocial, and cognitive detrimental mechanisms associated with aging, it is important to investigate in the context of the aging patients the impact of HIV infection. In this paper we present data that evaluates the role of gender as it relates to the risk profile of elderly HIV-infected patients, gender as a function of co-morbid conditions, and degree of immunological damage. In addition, we present data that highlight the role of body mass index as an important parameter associated with more advanced disease. The study aims are: 1) to describe a cohort of HIV/AIDS elderly patients aged 60 years old and over who seek health services at the Retrovirus Research Center in Hospital Universitario Ramón Ruiz Arnau in Bayamón; 2) to evaluate this population within gender as primary comparison group; 3) to assess body mass index and stage of HIV infection stratified as covariates controlled by gender.

Methods

Research design

The World Health Organization categorizes people ranging from 60 through 74 years old as elderly,⁹ although the Pan American Health Organization establishes the range of 60 through 65 years old as elderly. In this paper we have used the cutoff of 60 years as elderly.¹⁰

A multifactorial analysis was constructed stratified by gender among a baseline cohort of HIV-infected elderly patients admitted to the Retrovirus Research Center (RRC) in Bayamón, Puerto Rico between January 2000 and December 2011. The RRC of the Universidad Central del Caribe hosts an HIV registry of adult patients that receive health care at the Ramón Ruiz Arnau University Hospital with its ambulatory immunologic clinic facility. The registry has been operational since 1992. These health facilities provide the majority of the HIV care services to 650,000 inhabitants of the northeastern region of the Island.

As the patients are diagnosed, they are referred to the RRC; the data from the HIV/AIDS registry is collected at first contact and every six months thereafter. After an informed consent is obtained, an enrollment questionnaire is completed. Variables included in the analyses were obtained from the enrollment questionnaire which gathered information on HIV risk behaviors, socio-demographic characteristics, and the use of alcohol during a 30-minute face-to-face interview. Laboratory testing is performed and includes CD4 cell count and PCR HIV viral load. Data abstraction of clinical data and laboratory findings were from the 12 months prior to study entry.

Variables studied include body mass index variables (underweight, normal weight and overweight/obese); sociodemographic variables: sex, education (categorized as <6th grade until master's or doctoral degree) and civil status (single through separated). Risk behavior variables (use of drugs and/or alcohol in the last six months); psychosocial variables (suicide attempt in the last six months, among others); clinical manifestations (mental disorders, among others); AIDS stratified by type, laboratory findings (CD4 count and viral load) and treatment. The BMI at study entry was calculated using the following formula $BMI = mass (lb)/height^2 \times 703$, then categorized into three groups, as follows: underweight (BMI 18.4–18.49), normal (BMI 18.5–24.99) and overweight/obese (BMI >25). The alcohol abuse variable was abstracted from the patient's medical record and was defined as follows: consuming an average of more than two drinks per day or more than 14 drinks per week, or attendance at Alcoholics Anonymous in the last 12 months.¹¹ Furthermore, the alcohol use variable was defined as the consumption of any quantity of alcoholic beverages in the last 12 months. Clinical manifestations included mental disorders (schizophrenia, bipolar state, psychosis and anxiety), renal insufficiency, anemia, diabetes mellitus Type II, and cardiovascular disease.

The AIDS stratified by type included the variable Clinical AIDS which was defined after 1977 by the presence of at least one of the following: *Pneumocystis jirovecii* pneumonia (PJP), cerebral toxoplasmosis (CT), wasting syndrome, recurrent bacterial pneumonia (RP), pulmonary tuberculosis (PTb) and Kaposi's sarcoma (KS). The variable Immunological AIDS which was defined as a CD4 count below 200 cells per cubic millimeter of blood in the last year and HIV alone which was defined as a CD4 count above 200 cells per cubic millimeter of blood without any opportunistic infections.¹²

The prescriptions of antiretroviral therapies (ART) in the last year were collected dichotomously at baseline. A non-probabilistic (by availability) sample of the HIV registry in the Retrovirus Research Center was used, taking into account all patients equal to or greater

than sixty years old enrolled between January 2000 through December 2011. This results in a sample of 266 patients.

Statistical analysis

The Statistical Package of Social Sciences (IBM-SPSS) program version 17.0.1 was used to perform univariate, bivariate and multivariate analyses. Univariate analyses included frequencies, percentages, central tendency measures (mean and median) and dispersion measures (standard deviation measures and quartiles) (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0.1. Chicago: SPSS Inc).¹³ A normality test using the Shapiro-Wilk estimate was performed in all variables in order to select the correct parametric or non-parametric test. Differences between genders including enrollment findings were analyzed with the chi-square distribution or Fisher-exact test. Differences among medians between were evaluated using the independent samples Mann-Whitney test.

The general linear model (GLM) is a statistical linear model derived from the multiple regression model: $Y = XB + U$; where Y is a matrix with series of multivariate measurements; X is a matrix in the form of a design matrix; B is a matrix containing parameters that are usually to be estimated and U is a matrix containing errors or noise.¹⁴ In this study two Multivariate General Linear (MGL) Models were constructed to assess two possible scenarios: First, the relationship of gender as fixed factor and body mass index (BMI) as covariate with CD4 count and PCR HIV viral load as dependent variables, controlled by use of antiretroviral therapy and type of AIDS. Second, the relationship of BMI as fixed factor and type of AIDS as covariate with CD4 count and viral load as dependent variables, controlled by use of antiretroviral therapy and gender. A Box's M test of equality of covariances matrices was performed to assess if our models have the assumption of covariance homogeneity ($p > .05$). The Pillai's Trace estimator was used in order to know if the fixed factors contribute in the variability of the dependent variables. Note that for both models the covariates were seen as direct interest rather than possible confounders.

A test of Between-Subjects Effect with a Pairwise Comparisons using a Bonferroni adjustment for multiple comparisons was applied to perceive statistical differences between and within the groups. The significance level (α) was set at .05.

Results

Gender stratification profile

There were 266 patients 60 years or over which were enrolled during the baseline study period. The elderly women in our group were significantly widowed, more often underweight, had a higher rate of diabetes mellitus, renal insufficiency, and reported mental disorder more often. ($p < .05$) The illicit drug profile was similar to men, with the exception of a small tendency towards less heroin use and less alcohol abuse. ($p < .05$) The self-reported event of suicide attempts was significantly lower among women. ($p < .05$) The remainder of the psychosocial profile was analogous to that of men. The stage of HIV disease was similar across genders although the rate of clinical AIDS at presentation was lower, along with a

higher mean CD4 cell count and lower HIV viral load in women. A significantly lower number of women were ART naïve at study entry (see Tables 1 and 2). The profile of men over the age of 60 years revealed a larger number of normal weight and a substantially higher number of self-reported suicide attempts compared with women 60 and older. Alcohol abuse was significantly higher in men than in women. The presence of anemia along with a higher number presenting with clinical AIDS was higher in men. In addition, a lower CD4 cell median count and a higher PCR HIV median viral load were evident in men than in women. Men had a lower baseline ART therapy history at study entry. (Tables 1 and 2)

Immunological profile with BMI and stage of HIV infection as covariates

In Table 3 we present the multivariate general linear models. The first model proves to be appropriate (Box's $M=34.77$; $p>.05$). Fixed factors contribute to the model (Pillai's trace F for gender = 2.88; $p<.0001$ / Pillai's trace F for BMI = 4.06; $p<.0001$). The female spectrum was as follows: Underweight women have an estimated marginal mean CD4+ T-cell count of 203.75, normal weight women have an estimated marginal mean CD4+ T-cell count of 252.43 and overweight women have an estimated marginal mean CD4+ T-cell count of 397. In terms of HIV PCR viral load: underweight women have an estimated marginal mean of 250,697, normal weight women have an estimated marginal mean of 118,943, and overweight women have an estimated marginal mean of 120,050. The pairwise comparisons in CD4+ T-cell count proved to be significant ($p<.05$) as well in HIV PCR viral load ($p<.05$).

Underweight men have an estimated marginal mean CD4+ T-cell count of 183.70, normal weight men have an estimated marginal mean CD4+ T-cell count of 194.76, and overweight men have an estimated marginal mean CD4+ T-cell count of 264.12. For HIV PCR viral load, we found the following: underweight men have an estimated marginal mean of 247,052, normal weight men have an estimated marginal mean of 203,115, and overweight men have an estimated marginal mean of 142,619. The pairwise comparisons in CD4+ T-cell count proved to be significant ($p<.05$) as well in HIV PCR viral load (normal weight vs. overweight) ($p<.05$). No interactions were significant ($p>.05$).

The second model proves to be adequate (Box's $M=70.103$; $p>.05$). Fixed factors contribute to the variability of the model as well (Pillai's trace F for BMI = 3.84; $p<.05$ / Pillai's trace F for type of AIDS = 0.508; $p<.05$). Underweight with Clinical AIDS has an estimated marginal mean CD4+ T-cell count of 240.75; underweight with Immunological AIDS has an estimated marginal mean CD4+ T-cell count of 153.20; and underweight with HIV only has an estimated marginal mean CD4+ T-cell count of 223.38.

Normal weight with Clinical AIDS has an estimated marginal mean CD4+ T-cell count of 191; normal weight with Immunological AIDS has an estimated marginal mean CD4+ T-cell count of 189.79; and normal weight with HIV only has an estimated marginal mean CD4+ T-cell count of 236.97. Overweight with Clinical AIDS has an estimated marginal mean CD4+ T-cell count of 372.75; overweight with Immunological AIDS has an estimated marginal mean CD4+ T-cell count of 282.17; overweight with HIV only has an estimated marginal mean CD4+ T-cell count of 302. The HIV PCR viral load shows: Underweight

with Clinical AIDS has an estimated marginal mean of 345, 67.05; underweight with Immunological AIDS has an estimated marginal mean of 222,348; underweight with HIV only has an estimated marginal mean of 130,466.25. Normal weight with Clinical AIDS has an estimated marginal mean of 47,815; normal weight with Immunological AIDS has an estimated marginal mean of 245,642.45; and normal weight with HIV only has an estimated marginal mean of 199,933.81. Overweight with Clinical AIDS has an estimated marginal mean of 89,462.50; overweight with Immunological AIDS has an estimated marginal mean of 128,396.09; and overweight with HIV only has an estimated marginal mean of 150,226.09. The pairwise comparisons in CD4+ T-cell count proved to be significant ($p < .05$) as well in HIV PCR viral load ($p < .05$). No interactions were significant ($p > .05$). (Table 3)

Discussion

Our research adds new information for understanding the HIV epidemic in the island.⁸ The need to understand the socio-demographic profiles present in the geriatric HIV-infected patients is fundamental in order to address relevant interventions strategies. Our studies suggest that the risk scenario and socio-demographic profile of the elderly people with HIV is similar in men and women. In addition we present data that reveals a different immunological scenario for the elderly HIV-infected patient which is more favorable for women than men. The large number of ART-naïve elderly men with HIV adds credibility to the reported presence of a late diagnosis and or late testing in the elderly HIV-infected patient. Our cohort is predominantly composed of medical indigent patients, thus our study adds an additional dimension of vulnerability in the population studied which is most likely affected by disparities in health care delivery and access.^{6,7,15} It is recognized that despite the elderly being the new at-risk group for HIV, little research is devoted to addressing the specific issues affecting diagnosis, prevention and treatment of AIDS in this specific cohort.^{16,17}

Previous studies have demonstrated that having low and high BMI in combination with aging and HIV/AIDS is a real challenge for the future of health services delivery, co-morbidities, planning of health education programs, ageism stigma, and immunosenescence.^{2,3,18–22}

Older individuals are increasingly becoming a new at-risk group for HIV infection, together with those surviving longer due to the introduction of ART. It is predicted that more than half of all HIV-1-infected individuals in the U.S. will be older than 60 years of age in the year 2015.^{8,23} This trend is similar in Puerto Rico where the population pyramid is suffering a shift due to the rapid decline of its younger elements.¹⁰

The present study provides the first in depth assessment of the association of gender, BMI, and stage of HIV infections in a cohort of elderly Hispanics. Our data suggest that BMI is significantly associated with degree of deterioration of the CD4 cell count and the HIV viral load. This association is found in both men and women. Nevertheless, the complexity of providing HIV care in this group (given the issues of medication tolerance and adherence, the concomitant presence of co-morbid conditions, and the need for a diverse spectrum of

medications required for these co morbid conditions) suggests that body weight and BMI is a relevant marker to follow in the management of these patients. Our cohort data do not measure changes in body weight as a variable at baseline; future longitudinal studies addressing changes in BMI as a prognostic marker are planned.^{24–26}

Generally, elderly men tend to have lower CD4 cell count and a high HIV viral load count compared with women; in contrast, elderly women were more willing to take antiretroviral treatment than men.^{14,20,27} We have found that being obese/overweight with clinical AIDS has an incremental effect in CD4 count and a lessening repercussion in PCR HIV viral load count (as obesity and overweight were not distinguished from one another in the present study). At this time we are uncertain whether these effects are related solely to being obese/overweight or are the sum of a multifactorial spectrum. Further studies are needed in order to completely explore this association. Our study reveals that underweight men tend to have a lower CD4 cell count and higher PCR viral load count than underweight women. Our observation expands upon those of Avelino-Silva who reported that in general, older HIV-infected patients have lower CD4 cell counts and higher viral loads than younger cohorts.⁵

The literature highlights the fact that the process of aging affects the complex interaction between HIV infection and the immune system, and that both conditions contribute to the dysfunction of immune cells, including a decrease in the phagocytes' microbicidal capability, natural killer cells' cytolytic function.^{5,15,21,28,30} Our studies introduce the additional variable of BMI as an element that may be synergistically detrimental in the natural history of HIV infection in this cohort of patients.^{1,29,31}

In conclusion, we found a steady difference in CD4 cell count and PCR HIV viral load count with a significant association with being underweight and presence of clinical AIDS. It is advised an immediate process for planning and implementing educational and interventional prevention strategies such as those affecting BMI focused especially in the Puerto Rican elderly.

Our study data were collected at the time of the participants' enrollment, without evaluating the time related variation of the study variables. Despite this limitation, the study highlights the role gender and body mass index amongst elderly HIV-infected patients in Puerto Rico and the need to reassess culturally adapted approaches and health protocols to target this population.

Acknowledgments

The authors would like to deeply thank the support and the unconditional help of the following key people: Mrs. Magaly Torres, Mrs. Yolanda Rodríguez, Mrs. Wanda I. Marín, Miss Miriam Velázquez, Mrs. Lesbia Rodríguez, Mrs. Gisela I. Cestero, and Miss Glenda L. Ortiz.

The project described above was supported by Award Number 8G12MD007583 and from the National Center for Research Resources and 8U54MD 007587-03 from the National Institute on Minority Health and Health Disparities. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources of the National Institutes of Health

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Table 1

SOCIODEMOGRAPHIC, BODY MASS INDEX, RISK BEHAVIORS AND PSYCHOSOCIAL PROFILE
AMONG HIV PATIENTS AGE D 60 Y/O + AT ENROLLMENT (N=266)

Variables	♂ N= 180 ^a N (%)	♀ N= 86 ^a N (%)	p value* —
Sex	180 (68)	86 (32)	
Education			>.05
<6th grade	38 (24)	16 (20)	
7–9th grade	33 (21)	18 (23)	
10–12th grade	56 (35)	29 (36)	
Baccalaureate degree	32 (20)	14 (18)	
Master; MD; PhD	0 (0)	1 (3)	
Civil status			.00
Single	57 (35)	14 (18)	
Married	28 (17)	15 (19)	
Consensual union	15 (9)	16 (20)	
Widow	10 (6)	19 (24)	
Divorced	40 (25)	14 (18)	
Separated	11 (8)	1 (1)	
Body Mass Index			.02
Underweight	15 (9)	13 (16)	
Normal (healthy) weight	84 (51)	33 (40)	
Overweight / Obese	67 (40)	36 (44)	
Risk Behaviors ^b			
Use of Heroin in the last six months?	66 (36.9)	28 (32.6)	.00
Use of Cocaine in the last six months?	92 (51.4)	42 (48.8)	>.05
Use of Crack in the last six months?	52 (29.1)	25 (29.1)	>.05
Use of Cannabis in the last six months?	89 (49.7)	37 (43)	>.05
Alcohol use in the last six months?			.04
Use	61 (33.9)	27 (35.1)	
Abuse	43 (23.9)	11 (14.3)	
Psychosocial Variables ^b			
Suicide Attempt in the last six months?	37 (20.7)	11 (12.8)	.04
Isolation in the last six months?	73 (40.8)	30 (34.9)	>.05
Antisocial Behavior in the last six months?	72 (40.2)	26 (30.2)	>.05
Loss of Work in the last six months?	27 (15)	12 (14)	>.05
Economic Problems in the last six months?	43 (25)	22 (27.5)	>.05

* Chi-square distribution test

^a Numeric discordances represents missing values

^b Not mutually excluded data

♂=Men

♀=Women

Table 2

CLINICAL MANIFESTATIONS, LABORATORY FINDINGS AND TREATMENT PROFILE AMONG HIV PATIENTS AGED 60 Y/O + AT ENROLLMENT (N=266)

Variables	♂ N= 180 ^a n (%)	♀ N= 86 ^a n (%)	P value*
Clinical Manifestations ^b			
Mental Disorders	8 (4.4)	12 (14.1)	.01**
Renal Insufficiency	3 (1.7)	7 (8.2)	.01**
Anemia	89 (49.7)	32 (37.2)	.03
Diabetes Mellitus	14 (8)	13 (15.3)	.04**
Cardiovascular Disease	51 (28.7)	26 (30.6)	>.05
AIDS stratified by type			
Clinical AIDS	28 (15.6)	10 (11.6)	.04**
Immunological AIDS	60 (33.3)	31 (36)	>.05
HIV alone	86 (47.8)	40 (46.5)	>.05
Laboratory findings	Median (IQR) ♂	Median (IQR) ♀	
CD4+ T cell median	201 (86–445)	337.6 (99.75–497.50)	.01***
HIV viral load	189,456.82 (11,000–19,7730)	163,876.86 (7,800–19,3000)	.04***
Treatment			
Basal antiretroviral treatment	98 (54.7)	58 (69)	.02

* Chi-square distribution test

** Fisher's Exact Test

*** Mann-Whitney test statistic

^a Numeric discordances represents missing values

^b Not mutually excluded data

♂=Men

♀=Women

IQR = Interquartile Rate

Table 3**a.****FIRST MGL MODEL (THE RELATIONSHIP OF SEX AND BODY MASS INDEX (BMI) WITH CD4 COUNT AND VIRAL LOAD VARIABLES, CONTROLLED BY USE OF ANTIRETROVIRAL THERAPY AND TYPE OF AIDS)**

ManCOVa model 1 ^a	sex	BMI	Estimated Marginal Mean	p ^b
CD4 count ^d	Masculine	Underweight	183.70 ^c	<.05
		Normal weight	194.76	
		Overweight	264.12 ^c	
	Feminine	Underweight	203.75 ^c	
		Normal weight	252.43	
		Overweight	397.00 ^c	
PCR Viral Load count ^d	Masculine	Underweight	247,052.30	<.05
		Normal weight	203,115.00 ^c	
		Overweight	142,619.12 ^c	
	Feminine	Underweight	118,943.33	
		Normal weight	250,697.78 ^c	
		Overweight	120,050.00 ^c	

3b.**SECOND MGL MODEL (THE RELATIONSHIP OF BMI AND TYPE OF AIDS WITH CD4 COUNT AND VIRAL LOAD VARIABLES, CONTROLLED BY USE OF ANTIRETROVIRAL THERAPY AND SEX)**

MANCOVA model 2 ^a	BMI	Type of AIDS	Estimated Marginal Mean	p ^b
CD4 count ^d	Underweight	Clinical AIDS	240.75 ^c	<.05
		Immunological AIDS	153.20 ^c	
		HIV only	223.38	
	Normal weight	Clinical AIDS	191.00 ^c	
		Immunological AIDS	189.79	
		HIV only	236.97 ^c	
	Overweight	Clinical AIDS	372.75 ^c	
		Immunological AIDS	282.17 ^c	
		HIV only	302.00	
PCR Viral Load count ^d	Underweight	Clinical AIDS	345,671.05 ^c	<.05
		Immunological AIDS	222,348.00	
		HIV only	130,466.25 ^c	
	Normal weight	Clinical AIDS	47,815.00 ^c	
		Immunological AIDS	245,642.42 ^c	
		HIV only	199,933.81 ^c	

3b.

SECOND MGL MODEL (THE RELATIONSHIP OF BMI AND TYPE OF AIDS WITH CD4 COUNT AND VIRAL LOAD VARIABLES, CONTROLLED BY USE OF ANTIRETROVIRAL THERAPY AND SEX)

MANCOVA model 2 ^a	BMI	Type of AIDS	Estimated Marginal Mean	p ^b
	Overweight	Clinical AIDS	89,462.50 ^c	
		Immunological AIDS	128,396.09 ^c	
		HIV only	150,226.09 ^c	

^a Pillai's trace F for sex= 1.88; $p < .0001$ / Pillai's trace F for BMI= 4.06; $p < .0001$

^b Test of Between-Subjects Effects

^c Bonferroni adjustment for multiple comparisons

^d Dependent variable