Changes In The Socio-Demographics, Risk Behaviors, Clinical And Immunological Profile Of A Cohort Of The Puerto Rican Population Living With Hiv: An Update Of The Retrovirus Research Center (1992–2008)

Christine Miranda, MPHE, **Diana M. Fernandez, EdD**, **Geronimo Maldonado, MPH**, **Raul O. Ramon, MS**, **Miriam Velázquez, MS**, **Angel M. Mayor, MD**, and **Robert F. Hunter-Mellado, MD**
Retrovirus Research Center and the Internal Medicine Department, Universidad Central del Caribe, School of Medicine, Call Box 60-327, Bayamon, PR 00960-6032

Abstract

Objectives—We describe the changes in the socio demographic, risk behavior, immunological and clinical trends profiles of a cohort HIV patients followed at the Retrovirus Research Center, at baseline and study periods interval by periods intervals: 1992–1997, 1998–2003, and 2004–2008.

Methods—This is a cross-sectional study of a longitudinal cohort comprised of 4016 HIV/AIDS patients admitted to the RRC since January 1992. Data collected include socio-demographic variables; risk related variables; psychological variables; and clinical variable by periods of study.

Results—The most common AIDS defining conditions observed in patients were: Pneumocistis Cariini pneumonia (PCP), toxoplasmosis of brain (TP), and wasting syndrome (WS). Chronic conditions are more prevalent than AIDS-defining conditions in the cohort of patients.

Conclusions—Understanding the socio demographic, HIV risk behavior profile; and the immunological and clinical trends among HIV patients is critical for redesigning services and programs oriented in HIV patient care.

Index words

socio-demographic; risk; clinical; immunological; profile; HIV/AIDS; patients; Puerto Rico

INTRODUCTION

The prevalence of the most critical clinical presentations associated to the Acquired Immunodeficiency Syndrome (AIDS) infection has decreased over the last 20 years (1). The fundamental explanation for this change in the epidemiology of the HIV infection from an often-lethal disease to a highly treatable chronic condition can be attributed almost exclusively to the availability of antiretroviral therapy (2). Despite improvements in the therapeutic index for HIV infection, the persistence of racial and ethnic disparities are still evident which result in disparities in the access of effective HIV therapy and as a consequence an increase in the rate of new infections in this part of society (3). Similar to other infectious processes the success of prevention and treatment efforts will depend on the accurate and complete identification of the infected population as well as those at high risk

Address reprints requests to: Christine Miranda, MPHE - Retrovirus Research Center, Internal Medicine Department, Universidad Central del Caribe, School of Medicine, Call Box 60-327, Bayamon, PR 00960-6032. christine.miranda@uccaribe.edu.

for acquiring the infection. The collection, analysis, and interpretation of surveillance data remain critical for keeping abreast of the evolving nature of the epidemic (4–5).

Hariri & McKenna have indicated that the first decade of the HIV epidemic was characterized by an increase in the incidence of AIDS cases as a direct consequence of improved diagnostic and therapeutic milestones that facilitated the process of identifying and monitoring the clinical manifestations of the infection (6). In 1993, AIDS was the eighth leading cause of death in men and women aged 25 to 44 years, and accounted for 2% of all deaths in the United States (U.S.) (7). The numbers of reported AIDS cases and deaths in the United States declined between 1995 and 1998 with rates of 28%, 45%, and 18% each year, remaining relatively stable, at approximately 40,000 infections each year up until 2004 (8). This decline has been explained by the widespread use of improved antiretroviral therapy in the mid-1990s (9); the increased use of prophylaxis for opportunistic infections; and primary prevention interventions (10). In the early years of the epidemic, HIV/AIDS was characterized as a disease of white men who had sex with men (MSM) (8). Twenty percent of cases were related to injection drug use, while heterosexuals and females from all transmission categories accounted for about 5% and 8% of all reported cases, respectively (11).

According to the mandatory HIV reporting system, Puerto Rico had the second highest rate of HIV infection among 33 U.S. states and 5 territories in 2006 (12). For that same year, the incidence rate of HIV was 45.0 cases per 100,000 population in Puerto Rico which was twice the rate for the 50 U.S. states and District of Columbia (DC) (22.8 per 100,000) and 1.5 times the estimated rate for Hispanics in the U.S. (29.4 per 100,000) (12). According to the CDC, the incidence rate among males in Puerto Rico was 1.8 times the rate among U.S. males (34.3 per 100,000) and 1.4 times the rate among U.S. Hispanic males (43.1 per 100,000). In addition, the incidence rate among females in Puerto Rico was 2.5 times the rate among U.S. females (11.9 per 100,000) and 2.0 times the rate in U.S. Hispanic females (14.4 per 100,000). The overall incidence of HIV was twice as high in males than in females (62.0 vs. 29.8 per 100,000). In 2006, Puerto Ricans aged 30–39 years accounted for 38% of new HIV infections; with 39% of new infections associated to illicit-drug injection risk behavior, 37% associated to high-risk heterosexual contact, and 24% to male-to-male sexual contact (12). In the continental United States, male-to-male sexual contact represented 72% of new infections among males, including 72% among Hispanics living in the US. Among U.S. females, high-risk heterosexual contact was the predominant transmission category (80%) (12).

The number of people living with HIV worldwide continued to grow in 2008, reaching an estimated 33.4 million which was more than 20% higher than in the year 2000 (13). In 2008, an estimated 2.7 million new HIV infections were reported and an estimated death of 2 million individuals death due to AIDS-related illnesses (13).

In the Caribbean HIV/AIDS claimed an estimated 12,000 lives in 2008 making HIV one of the leading causes of mortality amongst adults between 15–44 years. A total of 240,000 individuals are currently living with HIV in this region, which represents the second highest level of adult HIV prevalence in the world (13). In 2008, 20,000 newly infected patients were estimated to have occurred in this region with unprotected heterosexual intercourse as the main risk factor. Although national adult HIV prevalence has been stabilized in several Caribbean countries, AIDS still remains one of the leading causes of death among people between 25 to 44 years old. In the Caribbean, women account for approximately half of all HIV infections with a prevalence particularly elevated among adolescent and young women, who tend to have infection rates significantly higher than males of their own age (13).

As of April 30, 2009, the Puerto Rico AIDS Surveillance Program has reported a cumulative total of 33,373 AIDS (including HIV diagnosis) cases (14). In males, 87.0% were aged between 25 to 54 years old at diagnosis with females representing 24.5% of all AIDS cases (14). The main modes of transmission for males was injection drug use (53.0%) followed by male to male sexual contact (22.0%). In females, the most common modes of transmission were heterosexual contact (62.0%) and illicit-drug injection (36.0%). Since the establishment of mandatory HIV case reporting on April 2003, a total of 7,548 new HIV cases have been reported as of April 2009. Of these 33.0% were female and 67.0% were males. In the cohort of 25 to 44 years old the mean age at HIV diagnosis was similar in males and females (64.0% vs. 60.0%). The most common modes of transmission for new infections were similar to those reported with AIDS; illicit-drug injection and male to male sexual contact for males (44.0% vs. 22.0%) and heterosexual contact and illicit-drug injection for females (63.0% vs. 24.0%) (14).

The Retrovirus Research Center (RRC) is located in the Bayamon Health Region of the Commonwealth of Puerto Rico. This health region is composed by 11 municipalities which include: Barranquitas, Comerio, Corozal, Naranjito, Orocovis, Bayamon, Toa Alta, Vega Alta, Cataño, Dorado, and Toa Baja. In 2008, the Bayamon Health Region population was estimated at 642,516 inhabitants (15). This corresponds to 16.2% of the estimated population of Puerto Rico. As of april 2009 a total of 5,630 cumulative AIDS cases had been reported in this health region, supersded only by San Juan with 7,840 cumulative AIDS cases (14).

The RRC is a multidisciplinary research center for the study of HIV/AIDS, which has been operating since 1992. It has grown and has become more efficient in integrating the resources and capabilities of the investigators interested in HIV research within and external to our institution. The goal of the RRC is to promote and stimulate the study of HIV infection as a multidisciplinary research arena that incorporates the clinical features of the infection including the immunological, virological, psychological and behavioral variables relevant to the study of this disease. The longitudinal nature of the HIV/AIDS database of our Center allow studies on factors which influence survival and mortality including medication compliance, health care access, and changing patterns of risk behavior amongst our predominantly Hispanic cohort. The RRC works closely with the Data Management and Statistical Research Support Unit (DMSRSU) who helps in the integration of the variables of the databank, the quality control process, implementation of analytical strategies and appropriate study methodology. The HIV Registry had over 4,000 registered patients between 1992 and 2009.

The objectives of this research paper are to: 1) describe the sociodemographic, HIV risk behavior, immunological and clinical profile of HIV/AIDS patients who have enrolled in the Registry, 2) report on variables through three defined periods of time 1992–1997, 1998–2003, and 2004–2008, and 3) assess changes in the clinical and laboratory presentation of our patients in the pre HAART and post HAART era.

RESEARCH DESIGN AND METHODS

Methods

This is a cross-sectional study of a longitudinal cohort comprised of a non-probabilistic sample of 4016 HIV/AIDS patients admitted to the RRC since January 1992. Patients who arrive to our inpatient or outpatient HIV health care facilities are invited to participate in the registry. Prior to enrollment an informed consent is discussed and signed. An initial interview and a comprehensive evaluation of relevant variables pertaining to the HIV diagnoses are administered to all patients that agree to participate. Medical record

abstraction is performed to complement the interview information. The methods for data collection have been described previously (16).

Measurement Instruments

The HIV Registry Initial and Follow-up Questionnaire (interview and data abstraction) were created by researchers of the RRC and have been in use since 1992. New modules and new variables are continually assessed and incorporated in both instruments as the knowledge base of HIV increases. The HIV Registry initial questionnaire currently includes a total of 336 variables. The data collected includes socio-demographic variables (e.g. age, gender, education, employment status, civil status, and housing); risk related variables (e.g. sexual risk practices and drug, tobacco and alcohol use profiles); clinical variables (e.g. medical history, the presence of AIDS defining conditions, the presences of other conditions or other non-AIDS opportunistic infections, the presence of constitutional signs and symptoms); therapeutic variables (e.g. therapeutic and prophylactic drugs related to AIDS conditions); and laboratory data (e.g. immunological and hematological parameters) (16). Complementary instruments are also used in our patients and kept as a separate databank. These include the Adult Spectrum of Disease (ASD) Questionnaire that was created by the Centers for Disease Control and Prevention, the health disparity questionnaire and the mortality evaluation instrument. Follow-up interviews are scheduled at six-month intervals after the initial visit.

Variables

Highly active antiretroviral therapy (HAART) in Puerto Rico became available in 1996; coinciding with the introduction of Puerto Rico's last major health reform movement (18). For the purpose of this article, we have grouped the reported patients population according to the year of entry to the registry. Study periods were defined as follows: Period 1; 1992–1997; Period 2: 1998–2003; and Period 3: 2004–2008. These periods were selected since the first period includes patients four years before the introduction of HAART and one year after its implementation (1992–1997), the second period represents the implementation phase of HAART therapy (1998–2003), and the third interval is one in which HAART was generally available (2004–2008). A descriptive analysis using frequencies and percents was performed to describe the changes in interested variables in these time frames. Differences among proportions were assessed using Pearson Chi-square distribution statistics and Fisher's exact test (for cell counts less than 5% of the total sample). The significance level was set in a $p < 0.05$. The Statistical Package for the Social Sciences (SPSS) version 14 was used to analyze the data (17).

RESULTS

Socio-demographic characteristics

From January 1992 to December 2008, 4016 patients have agreed to participate in the RRC and were included in this analysis. The majority of patients were found to belong to the first period (56.0%), 27.0% to the second period, and 17.0% to the third period.

Table I shows an outline of the socio demographic profile of our patients across the three periods of time. In all three time frames most of our participants were male (74.9%, 67.8% and 67.3%), with 70.8%, 77.2% and 75.8% having between 31 and 54 years of age. Educational status of at least a 12 grade education was 63.2%, 74.8% and 69.2% respectively with most patients reported being unemployed with a decreased prevalence during the last period (82.6%, 80.5% and 71.2%), the majority of patients reported not having a current partner (71.2%, 70.1% and 69.3%), the majority lived with family members (67.6%, 65.1% and 64.8%) and reported having children (57.9%, 64.5% and 60.9%).

Significant differences across the years was seen in the following variables: female gender (25.1%, 32.2% and 32.7%, respectively), and patients 55 years old or more (4.1%, 6.2% and 8.7%, respectively). Significant differences were seen also seen in the employment status, education, and the variable of having children.

HIV risk behavior profile

Table II describes our data as it pertains to the risk behavior profile of HIV/AIDS patients since the inception of the RRC. Studies of proportion showed little differences in heterosexual sex as risk factor for HIV infection (84.2%, 84.0% and 85.8%). A significant increase in homosexual relationship as risk factor was seen (13.2%, 13.5% and 23.1%, respectively), increased in psychoactive drug use (29.2%, 27.8%, and 32.3%), increase in the proportion of patients reporting amphetamines use (10.6%, 18.9% and 27.8%), crack use (27.8%, 23.5% and 28.8%), and cannabis use (44.3%, 41.3% and 49.5%) was seen. A decrease in illicit-drug injection (60.9%, 44.1% and 32.8 %), heroin use (57.1%, 47.0% and 35.6%), cocaine use (58.7%, 55.6% and 51.4%), and the mix of heroin and cocaine (speedball 32.9%, 39.3% and 31.5%) was observed between period 1 to period 3. In addition, a decrease in tobacco use (82.1%, 73.4% and 74.0%) and alcohol use (56.9%, 46.4% and 55.5%) was observed among period 1 and 3. Significant differences were seen across the three periods of years in the following variables ($p < 0.05$): tobacco use, alcohol use, intravenous drug use, heroin, cocaine, speedball, amphetamines, crack, cannabis and homosexual practices.

Clinical and Immunological profile

Table III shows the clinical, immunological and treatment profile of RRC HIV/AIDS patients at the three periods of time. At study entry, the proportion of patients with HIV (non-AIDS) infection was 51.5%, 46.5% and 50.7%, with the proportion of patients with CD4 cells count greater than 200 cells count/μL being 50.0%, 53.3% and 59.1%. No history of antiretroviral therapy was seen in 97.7%, 65.0% and 79.1% of patients. The proportion of patients with immunologic AIDS was seen to be gradually increasing between Period 1 to Period 3 (20.6%, 34.5% and 43.3%, respectively). Conversely, a decrease in patients with clinical AIDS diagnosis was evident with 27.9%, 19.0% and 6.0%. The proportion of patients who were enrolled with a CD4 cells count of less than 200 cells count/μL decreased from 50.0% in Period 1 to 40.9% in Period 3. As anticipated an increase in a history of HAART use was ob served between period one and two (2.3% vs. 35.0%, respectively) with a decrease in period three (20.9%).

An increase in several non-AIDS defining conditions among our population of patients was evident. An increase inpatients with diabetes was seen (1.0%, 5.8% and 6.5%), hypertension (1.0%, 10.4% and 11.6%), Hepatitis A (0.2%, 2.2% and 1.8%), Hepatitis B (1.9%, 4.1% and 4.2%) and Hepatitis C (0.8%, 32.9% and 35.3%). An increase in diabetes, hypertension and Hepatitis C was observed through the three periods. HIV constitutional signs and symptoms that were more frequently reported were diarrhea (24.2%, 2.3% and 0.0%), headaches (28.3%, 2.2% and 0.0%), night sweats (29.8%, 3.6%, 0.0%) and weight loss of more than 10 pounds (18.1%, 12.1% and 7.2%). These conditions decreased significantly between the three periods of time studied.

In Table IV we present the changes in the clinical profile of AIDS patients in the three periods of time. The most common AIDS defining conditions among patients were: Pneumocistis Cariini pneumonia (PCP) (34.1%, 16.2% and 2.7%), toxoplasmosis of brain (TP) (18.4%, 13.7% and 8.15), and wasting syndrome (WS) (20.1%, 45.1% and 0.0%). A significant decrease was observed from Period 1 to Period 3 in all three conditions. Other AIDS defining conditions reported among patients with clinical AIDS were: candidiasis of

the lung, herpes simplex, Kaposi Sarcoma, lymphoma of the brain and tuberculosis. It is relevant that none of these conditions were reported in the last period.

DISCUSSION

The HIV epidemic in Puerto Rico is notably different from the epidemic in the continental United States, including Hispanics living in the United States (12). The RRC cohort remains predominantly male, with an increase in the female population observed in the last five years. In the Caribbean and Puerto Rico, an increase in HIV infections among women has been also reported in the last five years (13, 14). The most common HIV transmission mode is still illicit-drug injection, but an increase in heterosexual sex and men having sex with men has been reported more often in the last period. In Puerto Rico, the most common modes of transmission continue to be injection drug use followed by risky heterosexual contact and finally male to male sexual contact (14).

In the United States for the same year, male-to-male sexual contact represented 72% of new infections among males; for females, high-risk heterosexual contact was the predominant transmission category (80%) (12). We have also seen an increase in alcohol consumption, and the use of psychoactive drugs which may be factors which increase the risky practices associated to HIV infection.

Of relevance is the finding that AIDS-defining illnesses and conditions have been substituted by new co-morbid conditions (19). These conditions include cardiovascular disease, renal and hepatic disorders, osteopenia, endocrine and metabolic abnormalities, and non– AIDS-defining neoplasm (20). The increased survival associated to HAART therapy is likely a major reason for the presence of these chronic conditions. Analysis of the clinical and immunological spectrum of the disease in our cohort revealed a significant decrease of several AIDS-defining conditions commonly observed in HIV/AIDS patients during the last decades. The presence of toxoplasmosis of the brain, wasting syndrome and pneumocistis cariini pneumonia has clearly decreased from Period 1 to Period 3 in patients with clinical AIDS. This finding may be explained by the improvement of CD4 cell count at study entry of many of our patients, the frequent use of prophylactic therapy against CE, PCP and TP and the use of HAART and ART among our patients. (21–25) Patterns of HIV morbidity among patients have significantly changed over the last two decades. The introduction of HAART in developed countries has increased the life expectancy of HIV infected persons (24–28). HAART suppress the HIV viral load and improves immunological and clinical well-being. (24–28) Consequently, AIDS-defining conditions have declined substantially (23–31).An improvement of general well-being of HIV infected patient that entered our Center among the three periods of time is evident. In these periods of time, HIV infected patients have a higher CD4 cells count (200 mm/cm3) and a decreased manifestation of AIDS-defining conditions.

The study of the interplay of the multiple chronic conditions which often are seen in the generation of recently HIV infected patients will require further consideration and study in the future. Early diagnosis and effective treatment for these conditions may enhance the quality of life of HIV-infected patients. A recent US, HIV outpatient study has shown that although the death rate from AIDS-related causes fell significantly between 1996 and 2004, the proportion of deaths from non-AIDS-related diseases is increasing (22, 33). This increase was especially prominent in non-AIDS malignancies; hepatic disease and cardiovascular disease. The findings can help to guide future implementation of HIV prevention programs, and services culturally appropriate for this patient population.

Acknowledgments

References

1. Karon JM, Fleming PL, Steketee RW, De Cock KM. HIV in the United States at the turn of the century: an epidemic in transition. Am J Public Health. 2001; 91:1060–1068. [PubMed: 11441732]

2. Pomerantz RJ, Horn DL. Twenty years of therapy for HIV-1 infection. Nat Med. 2003; 9:867–873. [PubMed: 12835707]

3. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Racial/ethnic disparities in diagnoses of HIV/AIDS—33 states, 2001–2004. Morb Mortal Wkly Rep. 2006; 55:121–125.

4. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. HIV/AIDS surveillance report, 2004. Vol. 17. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; Atlanta, GA: Dec. 2005 http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2004report/pdf/2004SurveillanceReport.pdf

5. World Health Organization. Second generation surveillance for HIV/AIDS. World Health Organization; Geneva, Switzerland: 2006. posting datehttp://www.who.int/hiv/topics/surveillance/2ndgen/en/

6. Hariri S, McKenna MT. Epidemiology of human immunodeficiency virus in the United States. Clin Microbiol Rev. 2007; 20(3):478–88. [PubMed: 17630336]

7. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Update: mortality attributable to HIV infection among persons aged 25–44 years—United States, 1994. Morb Mortal Wkly Rep. 1996; 45:121–125.

8. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men—New York City and California. Morb Mortal Wkly Rep. 1981; 30:305–308.

9. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988–94. Series 1: programs and collection procedures. Vital Health Stat. 1994; 1:1–407.

10. Fleming PL, Ward JW, Karon JM, Hanson DL, De Cock KM. Declines in AIDS incidence and deaths in the USA: a signal change in the epidemic. AIDS. 1998; 12(Suppl A):S55–S61. [PubMed: 9632985]

11. Holtgrave DR. Causes of the decline in AIDS deaths, United States, 1995–2002: prevention, treatment or both? Int J Sex Transm Dis Acquir Immune Defic Syndr. 2005; 16:777–781.

12. United States of America, Centers for Disease Control and Prevention; Divisions of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Subpopulation Estimates from the HIV Incidence Surveillance System -United States, 2006. MMWR. Sep 12; 2006 57(36):985–989. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5736a1.htm.

13. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO). AIDS Epidemic Update. 2009. Available from: http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en.pdf

14. Commonwealth of Puerto Rico; Department of Health, Central Program for AIDS and Sexually Transmitted Diseases. AIDS Surveillance Report, April 2009. San Juan (Puerto Rico): Department of Health; 2009.

15. Estado Libre Asociado de Puerto Rico. Negociado del Censo Federal, Oficina del Censo, Junta de Planificación de Puerto Rico. Definiciones: Áreas Metropolitanas. [Web page]. Available from: http://www.gobierno.pr/Censo/GeografiaCensal/Definiciones/areasMetropolitanas.htm

16. Gómez MA, Velázquez M, Hunter-Mellado RF. Outline of the Human Retrovirus Registry: Profile of a Puerto Rican HIV infected population. Bol Asoc Med P Rico. 1997; 89(7–9):111–116. [PubMed: 9419928]

17. Statistical Package for the Social Sciences (SPSS). Vol. 14. Chicago, IL: 2005.

18. Baez-Feliciano DV, Thomas JC, Gomez MA. Changes in the AIDS epidemiological situation in Puerto Rico following health care reform and the introduction of HAART. Pan Am J Public Health. 2005; 17(2):92–101.

19. Llibre JM, Falco V, Tural C, et al. The changing face of HIV/AIDS in treated patients. Curr HIV Res. 2009; 7(4):365–77. [PubMed: 19601771]

20. Buchacz K, Rangel M, Blacher R, Brooks JT. Changes in the Clinical Epidemiology of HIV Infection in the United States: Implications for the Clinician. Current Infectious Disease Reports. 2009; 11:75–83. [PubMed: 19094828]

21. Baez-Feliciano DV, Quintana R, Gomez MA. Trends in the HIV and AIDS epidemic in a Puerto Rican cohort of patients: 1992–2005. Bol Asoc Med P Rico. 2006; 98(3):174–181. [PubMed: 19610556]

22. Jain MK, Skiest DJ, Cloud JW. Changes in mortality related to human immunodeficiency virus infection: comparative analysis of inpatient death in 1995 and in 1999–2000. Clin Infect Dis. 2003; 36:1030–1038. [PubMed: 12684916]

23. Palella FJ, Delaney KM, Moorman AC, et al. Decline morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV outpatients study investigation. N Engl J Med. 1998; 338:523–860.

24. Valdez H, Chowdhry TK, Asaad R. Changing spectrum of mortality due to human immunodeficiency virus: analysis of 260 deaths during 1995–1999. Clin Infect Dis. 2001; 32:1487–1493. [PubMed: 11317251]

25. Mayor AM, Gómez MA, Ríos-Olivares E, et al. Mortality trends of HIV-Infected patients after the introduction of highly active antiretroviral therapy: analysis of a cohort of 3,322 HIV-infected persons. Ethn Dis. 2005; 15:S5-57–62. [PubMed: 16312941]

26. Van Sighem AI, Van de Wiel MA, Ghanic AC, et al. Mortality and progression to AIDS after starting highly antiretroviral therapy. AIDS. 2003; 17:2227–2236. [PubMed: 14523280]

27. Ledermann MM, Valdez H. Immune restoration with antiretroviral therapies: implications for clinical management. JAMA. 2000; 284:223–228. [PubMed: 10889597]

28. Kroon FP, Rimmelzwaan GF, Roos MT, et al. Restored humoral immune response to influenza vaccination in HIV-infected adults treated with highly active antiretroviral therapy. AIDS. 1998; 12:F217–F223. [PubMed: 9863863]

29. Wolff AJ, O'Donnell EA. Pulmonary manifestation of HIV infection in the era of highly active antiretroviral therapy. Chest. 2001; 120:1888–1893. [PubMed: 11742918]

30. Lewden C, Raffi F, Chene G, et al. Mortality in a cohort of HIV-infected adults started on a protease inhibitor-containing therapy. J Acquir Immune Defic Syndr. 2001; 26:480–482. [PubMed: 11391169]

31. Escolano Hortelano CM, Ramos Rincon JM, Gutierez Rodero F. Changes in the spectrum of morbidity and mortality in hospital admission of HIV-infected patients during the HAART era. Med Clin (Barc). 2004; 122:21–23.

32. Bica I, McGovern B, Dhar R, et al. Increasing mortality due to end stage liver disease in patients with human immunodeficiency virus infection. Clin Infect Dis. 2001; 32:492–497. [PubMed: 11170959]

33. Palella FJ Jr, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune Defic Syndr. 2006; 43:27–34. [PubMed: 16878047]

Table I

Sociodemographic characteristics of Puerto Rican HIV/AIDS patients at the RRC by periods of study.

Variable	1992–1997 n	%	1998–2003 n	%	2004–2008 n	%	p (value)
Gender							0.001 *, 0.001 **
Female	570	25.1	348	32.2	219	32.7	
Male	1697	74.9	732	67.8	450	67.3	
Age							0.001 *, 0.001 **
30	568	25.1	179	16.6	104	15.5	
31–54	1606	70.8	834	77.2	507	75.8	
55	93	4.1	67	6.2	58	8.7	
Employment status							0.001 *, 0.001 **
Non-Employee	1625	82.6	849	80.5	479	71.8	
Employee	342	17.4	206	19.5	188	28.2	
Education							0.001 *, 0.001 **
Less than 12th grade	721	36.8	260	25.5	205	30.8	
12th grade or higher	1236	63.2	772	74.8	461	62.9	
Partner status							0.593 *, 0.309 **
No	1466	71.2	741	70.1	461	69.3	
Yes	592	28.8	316	29.9	204	30.7	
Familiy status							0.345 *, 0.183 **
No	364	32.4	371	34.9	235	35.2	
Yes	761	67.6	693	65.1	433	64.8	
Children status							0.002 *, 0.025 **
No	825	42.1	358	35.5	259	39.1	
Yes	1135	57.9	651	64.5	404	60.9	

*
Pearson Chi-square,

**
Pearson Chi-square for linear trends

Table II

HIV risk behavior profile of Puerto Rican HIV/AIDS patients at the RRC by periods of study.

Variable	1992–1997		1998–2003		2004–2008		p (value)
	n	%	n	%	n	%	
Tobacco use							0.001,* 0.001 **
No	183	17.9	278	26.6	174	26.0	
Yes	838	82.1	767	73.4	494	74.0	
Alcohol use							0.001,* 0.254 **
No	413	43.1	557	53.6	297	44.5	
Yes	546	56.9	483	46.4	370	55.5	
Psychoactive drug use							0.134,* 0.221 **
No	496	70.8	728	72.2	450	67.7	
Yes	205	29.2	280	27.8	215	32.3	
IV drug use							0.001,* 0.001 **
No	868	39.1	595	55.9	449	67.2	
Yes	1352	60.9	470	44.1	219	32.8	
Heroin use							0.001,* 0.001 **
No	897	42.9	563	53.0	430	64.4	
Yes	1194	57.1	499	47.0	238	35.6	
Cocaine use							0.003,* 0.001 **
No	860	41.3	471	44.4	324	48.6	
Yes	1222	58.7	589	55.6	343	51.4	
Heroin & cocaine use							0.001,* 0.649 **
No	1262	67.1	626	60.7	457	68.5	
Yes	618	32.9	405	39.3	210	31.5	
Amphetamines use							0.001,* 0.001 **
No	1650	89.4	834	81.1	480	72.2	
Yes	196	10.6	194	18.9	185	27.8	
Crack use							0.025,* 0.797 **
No	614	72.2	789	76.5	474	71.2	

Variable	1992–1997		1998–2003		2004–2008		p (value)
	n	%	n	%	n	%	
Yes	236	27.8	242	23.5	192	28.8	
Cannabis use							0.004 *, 0.072 **
No	474	55.7	609	58.7	336	50.5	
Yes	377	44.3	429	41.3	329	49.5	
Heterosexual relationship							0.564 *, 0.431 **
No	337	15.8	167	16.0	95	14.2	
Yes	1795	84.2	875	84.0	575	85.8	
Homosexual relationship *							0.001 *, 0.001 **
No	1712	86.8	881	86.5	512	76.9	
Yes	261	13.2	137	13.5	154	23.1	

*
Pearson Chi-square,

**
Pearson Chi-square for linear trends

Table III

Immunological, clinical and treatment profile among Puerto Rican HIV/AIDS patients attending the RRC by periods of time.

Variables	1992–1997		1998–2003		2004–2008		p (value)
	n	%	n	%	n	%	
HIV status at study entry							0.001 *, 0.001 **
Clinical AIDS	631	27.9	204	19.0	37	6.0	
Immunologic AIDS	467	20.6	370	34.5	265	43.3	
HIV infection	1167	51.5	498	46.5	310	50.7	
CD4 cells count/μL							0.001 *, 0.001 **
<200	733	50.0	447	46.5	250	40.9	
200	732	50.0	515	53.3	361	59.1	
HAART use							0.001 *, 0.001 **
No	2214	97.7	697	65.0	484	79.1	
Yes	51	2.3	375	35.0	128	20.9	
Hypertension							0.000 *, 0.000 **
No	2243	99.0	961	89.6	541	88.4	
Yes	22	1.0	111	10.4	71	11.6	
Nephrolithiasis							0.000 *, 0.000 **
No	2263	99.9	1055	98.4	604	98.7	
Yes	2	.1	17	1.6	8	1.3	
Pancreatitis							0.000 *, 0.000 **
No	2262	99.9	1059	98.8	606	99.0	
Yes	3	.1	13	1.2	6	1.0	
Diabetes							0.000 *, 0.000 **
No	2242	99.0	1010	94.2	572	93.5	
Yes	23	1.0	62	5.8	40	6.5	
Hepatitis A							0.000 *, 0.000 **
No	2260	99.8	1048	97.8	601	98.2	
Yes	5	.2	24	2.2	11	1.8	
Hepatitis B							0.000 *, 0.000 **

Variables	1992–1997		1998–2003		2004–2008		p (value)
	n	%	n	%	n	%	
No	2222	98.1	1028	95.9	586	95.8	
Yes	43	1.9	44	4.1	26	4.2	
Hepatitis C							0.001 *, 0.001 **
No	2247	99.2	719	67.1	396	64.7	
Yes	18	.8	353	32.9	216	35.3	
Diarrhea							0.000 *, 0.000 **
No	1718	75.8	1047	97.7	612	100.0	
Yes	547	24.2	25	2.3	0	0.0	
Headaches							0.000 *, 0.000 **
No	1624	71.7	1048	97.8	612	100.0	
Yes	641	28.3	24	2.2	0	0.0	
Night sweats							0.000 *, 0.000 **
No	1590	70.2	1033	96.4	612	100.0	
Yes	675	29.8	39	3.6	0	0.0	
Weight loss >10 lbs							0.000 *, 0.000 **
No	1854	81.9	942	87.9	568	92.8	
Yes	411	18.1	130	12.1	44	7.2	

*
Pearson Chi-square,

**
Pearson Chi-square for linear trends

Table IV

Changes among the clinical profile of AIDS diagnosed patients at study entry attending the RRC by periods of time.

AIDS defining conditions	1992–1997N=631		1998–2003N=204		2004–2008N=37		p (value) *
	n	%	n	%	n	%	
Candidiasis lungs							0.581 *, 0.464 **
No	623	98.7	200	98.0	37	100.0	
Yes	8	1.3	4	2.0	0	0.0	
Herpes simplex							0.398 *, 0.524 **
No	603	95.6	194	95.1	37	100.0	
Yes	28	4.4	10	4.9	0	0.0	
Kaposi Sarcoma							0.365 *, 0.215 **
No	601	95.2	196	96.1	37	100.0	
Yes	30	4.8	8	3.9	0	0.0	
Lymphoma primary of brain							0.563 *, 0.314 **
No	628	99.5	204	100.0	37	100.0	
Yes	3	.5	0	0.0	0	0.0	
Tuberculosis							0.265 *, 0.105 **
No	615	97.5	202	99.0	37	100.0	
Yes	16	2.5	2	1.0	0	0.0	
Pneumocistis Cariini							0.000 *, 0.000 **
No	416	65.9	171	83.8	36	97.3	
Yes	215	34.1	33	16.2	1	2.7	
Toxoplasmosis of the brain							0.106 *, 0.034 **
No	515	81.6	176	86.3	34	91.9	
Yes	116	18.4	28	13.7	3	8.1	
Wasting syndrome							0.000 *, 0.000 **
No	504	79.9	112	54.9	37	100.0	
Yes	127	20.1	92	45.1	0	0.0	

*
Pearson Chi-square,

**Pearson Chi-square for linear trends