

# EPIDEMIOLOGICAL PROFILE OF HIV POSITIVE PATIENTS REGISTERED IN THE DISTRICT OF TERESÓPOLIS, STATE OF RIO DE JANEIRO

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## ABSTRACT

**Introduction:** the human immunodeficiency virus (HIV) epidemic began in the 1980's. As there were no therapeutic options at that time, diagnosed patients evolved rapidly to death. With the implementation of anti-retroviral therapy in 1996, HIV infection became a chronic disease, which in many cases can make adherence difficult to the proposed treatment. **Objective:** evaluate the profile of patients monitored at the STD/Aids clinic of the Epidemiological Surveillance Division of Teresópolis-RJ, and relate it to the attendance at consultations rate, CD4 measurements, viral load, and death. **Methods:** this is a retrospective, qualitative and quantitative cross-sectional study. We analysed available medical records of patients diagnosed with aids at the Division of Epidemiological Surveillance of Teresópolis, registered from 2000 to 2010. **Results:** patients with medical follow-up every 3 months had lower viral load and higher CD4 levels compared to those who were not regularly monitored ( $p < 0.01$ ). Patients who died had less regular attendance at consultations, as well as a decreased time in the disease progression ( $p < 0.01$ ). **Conclusion:** there were a few differences between our data and those found in the literature, and the main disagreement is related to the prevalence of HIV/aids cases among female patients and a higher viral load in this group.

**Keywords:** acquired immunodeficiency syndrome, HIV, health profile, STD.

## INTRODUCTION

The world experienced the beginning of the Acquired Immuno-deficiency Syndrome (HIV/aids) epidemic in the 1980 decade. In Brazil, since the identification of the first case, in 1980, until June, 2010, 592,914 cases have been identified, 58% of which in the Southeast region<sup>(1)</sup>. Over the years, several achievements were obtained considering scientific, technological and humanistic terms. However, there was a professional feeling of helplessness, mainly in the early years, when patients were diagnosed and rapidly evolved to death, as there were no therapeutic alternatives<sup>(2)</sup>.

1996 was a milestone, as a treatment with the association of anti-retroviral drugs (ARV) was proposed, transforming aids into a chronic disease. This therapy imposed considerable benefits to its users, such as the extension of survival, the improvement of life quality, the decrease of morbid episodes, and the reduction in the number and frequency of hospitalizations. However, it requires a perfect adherence<sup>(3,4)</sup>.

Adherence is considered a joint activity, in which the individual does not only comply with medical advice, but also follows, understands, and agrees with the prescription established by the attending physician<sup>(3)</sup>. The adherence rate to the treatment of chronic diseases is usually low, with consequences even more significant when it refers to a disease with a limited survival perspective<sup>(2)</sup>. A study has shown an adherence percentage of 64% to the anti-retroviral drugs treatment, which is similar to many specialized services in Brazil<sup>(4)</sup>. However, this value is much lower than the 95% considered necessary for the maximum effectiveness of the chosen therapy<sup>(4)</sup>. Therefore, when HIV/Aids is considered, the poor adherence

generates a deficiency allowing the emergence of resistant viral strains, compromising the patient's prognosis<sup>(5)</sup>.

An indirect way to track adherence to anti-retroviral therapy is the quantification of the viral load<sup>(4)</sup>, as the level to be achieved is a maximum of 50 copies of HIV/mL<sup>(6)</sup>. Aids endangers people of all ages, and their survival has been related to individual, medical-assistance, and social factors. It is also known that it is associated with younger age groups<sup>(3)</sup>. Concerning age, there is a certain consensus in the literature showing that in chronic diseases, the adhesion increases with age, except in the elderly over 75 years, most likely due to the frequency of multiple diseases and to the complexity of the therapeutic schemes. However, there is another extreme: younger people tend to be less adherent, as it is difficult to reconcile treatment with their way of life<sup>(2,7)</sup>.

The preliminary version of the Aids/HIV Epidemiological Bulletin, disclosed in December 2010, revealed that 229,222 deaths from Aids in Brazil were recorded from 1980 to 2009, mostly in the Southeast region, and among them 37,384 occurred in the State of Rio de Janeiro<sup>(1)</sup>. This same publication showed that the number of cases of aids among men is still higher than among women, although this difference has declined over the years. In 2009, the ratio between genders reached 1.6 case in men for each case between women<sup>(1)</sup>. The increase in the incidence of cases among individuals over the age of 60 was another important data showed by the publication. In 1997, the incidence rate for each 100,000 inhabitants of this age group was of 4.0%, and in 2009 it reached 8.4%<sup>(1)</sup>.

## OBJECTIVE

Evaluate the profile of patients attended at the STD/Aids clinic of the Epidemiological Surveillance Division of Teresópolis-RJ, and relate it to the rate of attendance at consultations, CD4 measurements, viral load, and death.

## METHODS

This is a retrospective, qualitative and quantitative cross-sectional study. Medical records of patients diagnosed with aids, availa-

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ble at the Division of Epidemiological Surveillance of Teresópolis, were analysed and registered from 2000 to 2010. Personal information were obtained and related to the treatment and progression of these patients.

This research was conducted after evaluation and approval from the Research Ethics Committee of UNIFESO-CEPq, and it is in accordance with the established in the 196/196 resolution of the Health National Council, under registry 458-10.

## Laboratory Exams

Viral load was evaluated through the b-DNA technique, HIV 30 RNA kit, which minimum and maximum detection corresponded to 50 and 500,000 copies/mL, respectively. Values < 50 copies/mL were considered compatible with an effective treatment. CD4 lymphocytes levels were obtained through the flow cytometry, Facs-calibur/Multitest kit. Levels < 350 cells/mm<sup>3</sup> were considered aids diagnosis, while < 200 cells/mm<sup>3</sup> levels indicated the need for an anti-retroviral treatment.

## Statistical analysis

Data were presented in the average  $\pm$  standard deviation format. Unpaired T-test and Mann-Whitney test were used for the average comparison among the two groups. Fisher exact test was performed for the comparison of category variables. Statistical significance was established as 5%. Analyses were conducted by Epi Info™ version 3.5.1 (Centers for Disease Control and Prevention, USA, 2008) and GraphPad Prism 5 for Windows version 5.04 (GraphPad Software, Inc, USA, 2010) software.

## RESULTS

The study analysed 215 patients, 48.8% of which were male (n = 105) and 51.2% female (n = 110). The average age of patients was of 36.8  $\pm$  12.3 years (males: 38.3  $\pm$  12.2 years; females: 35.4  $\pm$  12.2 years – p = 0.06), and the disease evolution time after diagnosis was of 10.2  $\pm$  22.4 months, 5.4  $\pm$  2.8 months among men, and 14.8  $\pm$  30.5 months among women (p = 0.45).

The percentage of patients at the age over 60 corresponded to 5.6% (n = 12), 58.3% of which were male. The disease evolution time of patients of this age group was not different from the younger ones (14.2  $\pm$  30.5 *versus* 10.0  $\pm$  21.9 months – p = 0.72).

The group of patients who returned to the specialized clinic in a regular basis, that is, every 3 months (72.6% – men = 71.8% *versus* women = 73.3% – p = 0.47), were compared with the sub-group of patients who did not attend consultations regularly. The average viral load of these patients corresponded to 95,090.9  $\pm$  189,540.3 copies/mL, contrasting with 31,761.6  $\pm$  113,512.3 copies/mL for the group of patients who regularly attended consultations (p < 0.01). The average values of CD4 in the group of patients attending consultations reached 462.1  $\pm$  326.5 cells/mm<sup>3</sup>, while the group not attending consultations showed levels of 295.9  $\pm$  264.0 cells/mm<sup>3</sup> (p < 0.01).

When the average age of patients attending consultations regularly was compared to those who did not, we found, respectively, 37.4  $\pm$  12.1 *versus* 35.7  $\pm$  13.7 years (p = 0.26). The first group was composed of 45.2% of men, and 54.8% of women, while the second group reached percentages of 47.1% and 52.9% (p = 0.47),

respectively. The percentage of regular attendance of patients over 60 years of age (72.7%) was similar to the younger group (72.4% – p = 0.63). The average time of regular attendance reached 42.4  $\pm$  33.2 months (men: 42.7  $\pm$  34.7 months; women: 42.2  $\pm$  32.0 months – p = 0.94), and no difference was found when patients over *versus* under 60 years of age were compared (p = 0.15). There was no difference in the disease evolution time in patients who regularly attended consultations (12.0  $\pm$  26.6 months) or not (7.1  $\pm$  15.0 months) (p = 0.86). However, the time of regular attendance at consultations of patients who died was shorter (24.9  $\pm$  34.6 *versus* 46.6  $\pm$  31.5 months – p < 0.01).

Patients were considered absentees when did not attend consultations during a period equal to or over 6 months prior to insertion in the study. Based on this criterion, 30.7% of patients evaluated were considered absentees. The comparison between absentees and non-absentees showed no significant difference concerning patient's age (34.9  $\pm$  10.5 *versus* 37.7  $\pm$  12.9 years – p = 0.21). When men and women results were confronted, the evasion rate was of 37.1% *versus* 24.5% (p = 0.03), respectively. Men were predominant in the absentees group (59.1%), and women were predominant in the non-absentees group (55.7% – p = 0.03). The statistical analysis did not indicate a significant difference when the evasion frequency among patients older than 60 years *versus* younger patients was compared (16.7% *versus* 31.7% – p = 0.23). The disease evolution time of absentee patients was superior to non-absentee ones (12.7  $\pm$  25.2 *versus* 9.2  $\pm$  21.0 months, respectively, p < 0.01).

A total of 21.4% of the studied sample (n = 46) evolved to death. In the studied sample, B24 (*i.e.*, unspecified HIV disease) was the most frequent code of the International Classification of Diseases (ICD), meaning 84.1% of registered codes. These patients were older than those who survived during the completion of this study (40.2  $\pm$  13.4 *versus* 35.9  $\pm$  11.8 years – p = 0.05). However, there was no statistically significant difference in the death rate neither when patients older than 60 years or younger were compared (p = 0.09) nor among men and women (23.8% *versus* 19.1% – p = 0.25). Patients who evolved to death presented a disease evolution time inferior to those who survived (6.7  $\pm$  2.8 *versus* 11.2  $\pm$  25.1 months – p < 0.01). Comparing the death rate of patients who attended consultations regularly with the rate of patients who did not, values of 16.3% and 43.1%, respectively, were found (p < 0.01). However, there was no difference among the death rates of the absentees group (19.7%) and the non-absentees (22.1% – p = 0.42).

The average viral load observed in the studied patients was of 49,126.1  $\pm$  140,872.4 copies/mL, and men presented values of 43,269.0  $\pm$  132,338.2 copies/mL, and women, 54,055.4  $\pm$  148,149.7 copies/mL (p = 0.97). No difference among viral load levels of patients older than 60 years *versus* younger ones was detected (16,458.8  $\pm$  35,509.7 *versus* 51,472.9  $\pm$  145,139.4 copies/mL – p = 0.78). The average viral load of the absentees was of 103,668.9  $\pm$  252,562.7 copies/mL, while the non-absentees reached 35,581.9  $\pm$  91,443.3 copies/mL (p < 0.01). The viral load of patients who evolved to death was significantly higher than those who did not (116,849.8  $\pm$  185,587.2 *versus* 28,141.3  $\pm$  116,873.0 copies/mL – p < 0.01).

In the studied sample, the average dosage of CD4 corresponded to 416.3  $\pm$  318.6 cells/mm<sup>3</sup> (men: 359.0  $\pm$  265.0 cells/mm<sup>3</sup>; women:

264.9 ± 352.0 cells/mm<sup>3</sup> – p = 0.04). Levels of CD4 of the absentees reached 385.9 ± 338.0 cells/mm<sup>3</sup>, and the non-absentees, 423.9 ± 314.4 cells/mm<sup>3</sup> (p = 0.31). When CD4 values of patients who died and those who survived were compared, the following numbers were found: 150.7 ± 145.5 *versus* 499.2 ± 312.8 cells/mm<sup>3</sup> (p < 0.01). The elapsed time since the last dosage of CD4 corresponded to 21.3 ± 28.6 months for men, and 18.0 ± 27.1 months for women (p = 0.66). When data of patients older than 60 years *versus* younger ones were compared, no statistically significant difference was observed referring to time elapsed since last dosage (31.2 ± 32.2 *versus* 18.8 ± 27.4 months – p = 0.37). Time elapsed since last CD4 dosage was 27.2 ± 25.3 months for patients who did not regularly attend consultations, and 16.6 ± 28.1 for those who did (p < 0.01). An average of 30.5 ± 31.7 months elapsed since the last dosage in the absentees group, and 16.8 ± 26.1 months in the non-absentees (p = < 0.01). Patients who died remained more time without dosing CD4 (59.0 ± 32.1 *versus* 7.3 ± 7.6 months – p < 0.01).

## DISCUSSION

A discreet predominance of female was observed in patients involved in the present report. The relation between men and women was of 0.95 man to each woman, and the average age was slightly greater in male patients when compared to female patients. National data show there are more cases among men than among women, but the proportion has declined over the years, and an increase of cases in females was observed. The ratio in 1989 between genders was of 6 cases of aids in male patients for one case in female patients (6:1), while in 2009 this ratio reached 1.6 case in males for each case in females<sup>(1)</sup>. There is another national data that draws attention: since 1998, the number of aids in patients from 13 to 19 years of age has been higher among women, with a proportion of 0.8 man for one woman<sup>(1,8)</sup>. The epidemiological data of aids in the State of Rio de Janeiro showed that 68.8% of the total number of cases occurred in men, and 32.2% in women, and also noted the increase of the proportion of women affected, and in 2010 the ratio man/woman was of 1.8, following the national trend<sup>(9)</sup>.

Thus, despite the increase of cases in females, it seems to be consensual in the various studies that males still dominate individuals affected by HIV/aids. A prospective study in a reference clinic in the city of Belo Horizonte, State of Minas Gerais, also showed the prevalence of HIV/aids in male patients, corresponding to 68%<sup>(10)</sup>. A retrospective study conducted at a tropical diseases reference hospital in the Northeast region, showed that male individuals correspond to 71.3% *versus* 28.7% of female patients<sup>(11)</sup>. A descriptive observational sectional study on aids and aging also showed a predominance of males, 75% of cases, and that this prevalence was among both the younger and the older age groups<sup>(12)</sup>. Another recent report performed in two HIV/aids treatment reference services in the city of Belo Horizonte, related that 66% of patients were male, and more than half of them were under 35 years of age<sup>(13)</sup>.

The average viral load of male patients was lower than the one detected in female patients, which is contrary to data found by other scientific reports. A cohort study of HIV-1 natural history among injecting drug users, measured the viral load of 527 infected individuals, and authors have concluded that the major finding of

the study was that viral load was substantially lower in women when compared to men<sup>(14)</sup>. Another study involving 366 participants found an average geometric value of viral load > 50% lower in women than in men (8,319 *versus* 18,621 copies/mL in results obtained through PCR method by reverse transcriptase)<sup>(15)</sup>. A report on 40 HIV infected individuals also showed a lower viral load in women, with an average value of 50%, when compared to the viral load in men, and this difference occurred not only before, but also after the anti-retroviral therapy<sup>(16)</sup>.

A cross-sectional observational study accomplished in a service of infectious diseases of a hospital in Florianópolis, State of Santa Catarina, found a general average viral load (men and women) of 377,730 copies/mL<sup>(17)</sup>. Studies carried out in two reference hospitals in the city of Belo Horizonte verified an average viral load of 83,000 copies/mL<sup>(13)</sup>, and another study from Rio Grande do Norte State showed an average viral load of 109,114 copies/mL<sup>(18)</sup>. In all these studies the average value of viral load proved well above the 46,126.1 copies/mL found in the present report.

In our study, we observed 12 patients at the age over 60. The HIV/Aids incidence in this group of individuals is increasing, mainly due to the marketing of drugs that improve the sexual performance, with the consequent increase of sexual intercourses among people of this age group without the use of condom<sup>(19,20)</sup>. Another contributing factor for the HIV increased dissemination in this group is their growing role in social life, as they are more participative of senior events<sup>(21)</sup>.

According to the Ministry of Health, older people tend to postpone the anti-HIV test, and the resulting HIV/aids diagnosis, as they consider themselves a group which risk of contracting the disease is lower. The unawareness of people about the growth of aids incidence in older individuals contributes to the epidemic increase, and becomes a threat to public health<sup>(22)</sup>. However, our data showed that the progression period of the disease of patients older and younger than 60 years was not different in the studied population in Teresópolis, Rio de Janeiro.

The epidemiological bulletin from the Ministry of Health about Aids/STD in 2010 reported that there was a significant increase of aids in both genders between 1999 and 2009 among individuals at the age over 60 or more: from 394 to 938 cases among male patients, and from 191 to 685 cases among female patients. The detection rate (per 100,000 inhabitants) of aids cases according to age and gender in Brazil, in 2009, was 6.4 for females and 10.8 for males<sup>(1)</sup>. In our study, the percentage of male patients over 60 years reached 58.3%, and 41.7% in female patients. Due to prejudice and embarrassment, many times some health professionals neglect the sexuality of people in this age group, who have difficulties to address such a subject, therefore disregarding the significant risk of contamination of the elderly by aids, and consequently fail to request HIV diagnostic tests for these patients, contributing to a late diagnosis<sup>(21,23)</sup>.

Normative Instruction 1626, dated July 10, 2007, regulates the procedures and the conduct to the approach agreed upon, in order to protect the secrecy and confidentiality of the diagnosis. It is considered abandonment those cases in which the patient does not collect the prescribed medication for a period equal to or over 90 days after the coverage period concerning the last medication delivery. For a complete evaluation of each case, it is necessary to associa-

te this situation with other monitoring factors, such as, skipping medical consultations scheduled, as well as patient's return within 6 months, besides the above mentioned factors<sup>(24)</sup>. In the present study, patients not attending consultations during a period equal or over 6 months before data survey were also considered absentees.

A 30.7% evasion rate was observed in the present study. There are researches showing that 30% to 50% of people in use of highly active anti-retroviral therapy (HAART) interrupt the treatment by their own, once or several times, throughout the history of treatment during different periods of time<sup>(4,25)</sup>.

Among the main causes of treatment evasion of HIV-positive patients, we can mention the following: adverse events or toxicities (fear and/or manifestation of symptoms and signs); depression and other psychiatric disorders; alcohol and/or recreational drugs abuse; social and economic difficulties; no expectation of treatment conclusion; absence of symptoms justifying therapy, taking into account the culture of a curative medicine and not a preventive medicine; unawareness of the natural progression of the infection, and goals of therapy as well; religious beliefs and overvalue of excludent alternative therapies in relation to ARV<sup>(24)</sup>.

According to Bastos Schilkowsky *et al.* (2011)<sup>(26)</sup>, among younger individuals, the participation in promiscuous relationships, low schooling, unemployment situation or unstable job link, a long period until diagnosis and first consultation, and the psychiatric history acknowledge are increasingly factors of abandonment risk. No significant differences were observed among groups of patients who did abandon and those who did not abandon the follow-up regarding gender, color/race, or home address. On the other hand, older individuals and the previous use of four or more ARV schemes as well, showed a negative association with abandonment, which is, these factors could work as a protector of this outcome<sup>(26)</sup>. However, comparing absentees with non-absentees patients, we did not observe a significant difference in patients' age (even when older and younger than 60 years were compared). In addition, when men and women results were compared, men were predominant in the absentees group (59.1%).

The HIV related morbidity and mortality profile was changed after the introduction of HAART. The deaths were no longer caused by opportunistic diseases, and were replaced by "pre-aids" morbid chronic diseases<sup>(27)</sup>. Data from the present study confirmed those of Santos and Pinheiro (2000), which did not detect any difference between mortality when compared patients according to gender<sup>(28)</sup>.

In our sample, patients who evolved to death had a shorter disease period compared to those who survived. Such results may be explained by the non-adherence to the proposed treatment by patients who died, reflecting in death by natural evolution of this infection. This information agrees with Santos and Pinheiro (2000) results, who observed that the average age of death, being aids the basic cause, was statistically lower than the average age of death in which HIV was the associate disease<sup>(28)</sup>.

The irregularity of HIV/aids patients to attend follow-up consultations is an important predictive factor of non-adherence to treatment<sup>(29)</sup>. CD4 counting lower than 200 cells/mm<sup>3</sup> is also an important factor in determining the death occurrence caused by HIV/aids<sup>(30)</sup>. A 2003 study in Belo Horizonte related that patients who regularly attended consultations showed an average follow-up

period of 37.2 months over two years, while our data observed an average period of 42.4 months during the studied period<sup>(10)</sup>. Considering the average viral load of patients who attended consultations regularly, our data showed that it was lower than the average of patients who did not attend consultations, while CD4 dosage was higher. This indicates that those who regularly attended consultations presented better laboratory evolution, probably due to a better adherence to the therapy.

We have not observed any difference among patients older or younger 60 years when attendance at consultations is concerned. No specific data were found in literature about this subject. However, a study comparing patients younger than 40 years with those older than this age, showed that in the first group the chance of non-adherence to Aids treatment is three times higher, attributing it to a greater commitment of the older patients to the treatment<sup>(31)</sup>.

In HIV-positive patients, CD4 serum level dosage indicates the beginning of the anti-retroviral therapy in asymptomatic patients, and evaluates, together with the viral load quantification and the clinical events in patients as well, the therapeutic answer. Thus, it is an important parameter of adherence to treatment, since it represents the main prognostic marker of HIV infection<sup>(32)</sup>. In 2009, a study carried out in the district of São Paulo showed that the average CD4 in the calculated deaths was of 189 cells/mm<sup>3</sup>, while our study computed 150 cells/mm<sup>3</sup><sup>(30)</sup>.

According to a preliminary version of the 2011 Aids/STD Epidemiological Bulletin, male mortality was significantly reduced, while female mortality showed a lower reduction<sup>(33)</sup>. In the 2003 "Women with HIV/Aids" dossier, this statistic was justified by the women self-care difficulties, and the least access to health services and medication<sup>(8)</sup>. Our report confirms the above mentioned data regarding the importance of CD4 dosage as a parameter of adherence to treatment and death risk, as the average CD4 dosage in the studied women was lower than in men (265 cells/mm<sup>3</sup> and 359 cells/mm<sup>3</sup>, respectively), which could indicate less treatment adherence by women, and consequently allow a greater risk of death. Concerning the CD4 dosage period among patients examined in our study, no other studies were found for comparison in the literature.

## CONCLUSION

We observed a female predominance among HIV/aids patients, in the municipality of Teresópolis, as well as a higher viral load in this group, unlike observed in most of other studies available in the literature. The average dosage of CD4 in women studied in the present report was lower than in men. The average viral load of patients who regularly attended consultations was lower than those who did not, while the value of CD4 was higher.

When groups of absentees and non-absentees were compared, no significant difference was found concerning patients' age, but there was a predominance of absentees among male patients. No difference among patients older or younger than 60 years concerning the regular attendance at consultations was observed. We also noted that patients evolving to death had a shorter disease period than those who survived.

## Conflict of interest

There is no conflict of interest.

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