# Profile analysis of patients with HIV/AIDS hospitalized after the introduction of antiretroviral therapy

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**Abstract** *Since the introduction of highly active antiretroviral therapy (HAART) in 1996, there have been worldwide shifts in the causes of hospitalization for patients with HIV/AIDS. The aim of this study was to describe the characteristics of HIV/AIDS patient hospitalizations between 1997 and 2012. This cross-sectional study used a hospital database that centralizes records of admissions in 31 hospitals, both public and private, across 26 municipalities in the interior of São Paulo. In order to verify associations between the variables, we used the prevalence ratio (PR) and a 95% confidence interval. Among 9,797 adults and children, 10,696 admissions were registered, which was equal to 1.09 admissions per patient. Most (62%) of the patients were male, and the predominant age group was 21 and 50 years (63.5%). Mortality was higher among male patients from all age groups (PR= 1.42 [95% CI: 1.28-1.57]; p < 0.05). The main cause of hospitalization (54.5% of the total) was infectious disease, whether opportunistic or not. This was true, even in the post-HAART era. Furthermore, gender and age differences were noted in patient mortality rates.*

**Key words** *HIV/AIDS, HAART, Hospitalization, Brazil*

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## Introduction

Since it was first identified in 1981, AIDS has been responsible for more than 25 million deaths worldwide, undoubtedly constituting one of the most overwhelming epidemics in history. More than 34 million people worldwide carried HIV in 2012, and in that year approximately 2.5 million new cases were diagnosed that resulted in a total of approximately 1.7 million deaths. This was a relatively better rate compared to that of 2005, when there were 3 million deaths due to the disease[1-3].

In the first 15 years of the HIV/AIDS epidemic, infected and sick individuals had few treatment options. The first drug that was partially successful in combating the syndrome was AZT, but it is not without its limitations. Fortunately, the accumulation of knowledge regarding the etiology and pathogenesis of HIV/AIDS, coupled with the large investments in pharmaceutical research and new diagnostic methods due to technological advances have led to the rapid development and release of several antiviral drugs. These have undoubtedly and definitively changed the natural history of the syndrome. Since the release of AZT in 1987, a true revolution has taken place year after year with the introduction of new antiretroviral drugs of different classes. First, there was an increase in the availability of new nucleoside reverse transcriptase inhibitors starting in 1991, and then there were the protease inhibitors introduced at the end of 1995. Finally, the reverse transcriptase non-nucleoside inhibitors were made available in June of 1996. In a short period of time, patients began to be able to rely on several new options from the three aforementioned classes, in addition to the fusion inhibitors that emerged in 2003. Subsequently, significant studies demonstrated the effectiveness of various combinations of antiretrovirals, otherwise known as highly active antiretroviral therapy (HAART), for the treatment of patients, especially in combination with protease inhibitors. Thus, several countries, including Brazil, began to provide these medications gratuitously, and this initiated profound changes in the epidemiological profile of the disease. HAART had a positive impact on the natural history of HIV/AIDS infection in the first years after its introduction, and there was a significant reduction in the morbidity and mortality of the disease from the outset[3-5].

A marked reduction in the incidence of opportunistic infections, hospitalizations, and mortality among HIV-positive individuals became more evident in 1996, which ushered in the so-called post-HAART era. The results of several studies conducted with children, adolescents, and adults demonstrate these facts. Specifically, it was discovered that the rate of opportunistic infections dropped from 18.32 infections/person-year to 2.63 infections/person-year, in the pre- and post-HAART eras, respectively[4-7]. In other studies on the impact of combination antiretroviral therapy, it has been shown that the mortality of patients with AIDS fell from 75.6 deaths/100 person-years in 1995 to 33.2 deaths/100 person-years in 1998-1999, which was a reduction of more than 50% and showed an increase in survival among patients undergoing treatment of approximately 2.8 additional years of life[8-9].

Therefore, with the advent of combination antiretroviral therapy, the occurrence of opportunistic infections and AIDS-defining illnesses underwent a significant decline that also resulted in a decrease in the numbers and durations of hospitalizations, in addition to a change in the hospitalization causes. Thus, these factors could be seen to create a relative improvement in the quality of life and the survival possibilities of people with HIV and AIDS[10]. Given this, the purpose of this study was to describe and analyze the clinical and epidemiological characteristics of hospitalized patients after the introduction and gratuitous provision of antiretroviral drugs in Brazil.

## Methods

This was a cross-sectional study in which HIV-carrying adult and child inpatients of both genders were selected from the records of the Hospital Data Processing Center (PCHR) of the Department of Social Medicine of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, which handles information from 26 hospitals (both public and private), located in 31 municipalities of the macro-region of Ribeirão Preto/SP-Brazil. We analyzed data from 1997 to 2012, which was after the introduction of HAART.

### Inclusion criteria

The International Classification of Diseases (ICD-10) was used to diagnose cases of HIV/AIDS. The latest revision was used, with codes ranging from B20 to B24, which resulted in 29

selection options. All diagnoses (according to the ICD-10) reported at either admission or discharge for the patients with HIV/AIDS (B20 to B24) were considered in the causes for hospitalization. The variables of interest included gender, age, name of hospital, admission date, length of stay, diagnoses leading to hospitalization, discharge diagnosis, comorbidities, and evolution (such as discharge, healing, complications, and death) for all patients admitted between 1997 and 2012 whose records were complete and reliable.

### Statistical analysis

We employed the chi-squared test to analyze the differences between proportions, and the Student's t or ANOVA tests to verify the distribution and differences between measures of central tendency and associated dispersions when referring to averages. The Kruskal-Wallis test was used when referring to medians. To analyze the possible associations between variables and predictors of hospitalization, the prevalence ratio (PR) and a 95% confidence interval (95% CI) were employed as estimators of association.

### Ethical aspects

This research project was approved by the Ethics Research Committee of the Hospital das Clínicas of the Faculty of Medicine of Ribeirão Preto, University of São Paulo.

## Results

During the study period, 10,696 hospitalizations were registered for 9,797 adults and children; in other words, there were 1.09 admissions per patient, and this resulted in a hospitalization rate of 6.19/10,000 inhabitants. The total population for the middle of the study period was 1,327,989 inhabitants in the 31 regional municipalities. This rate was lower than that which was witnessed before the introduction of HAART (1983-1996), when there was a coefficient of 17.03 hospitalizations per 10,000 inhabitants. However, this time ICD-9 prevailed, and this did not include the specific diagnosis of HIV/AIDS, nor its consequences or related diseases. Therefore, the records of this period were unreliable for the disease in question. However, the rate currently found is close to the rate of hospitalization for other infectious and parasitic diseases considered

in Chapter I of the ICD for the year 2012, which was 8.3/10,000 in Brazil.

In Table 1, the distribution of patients and hospitalizations is organized by age group and gender. Most (62%) of the hospitalized individuals were male (), and the male/female ratio was 1.63/1.0 (p<0.05). There were more females in the younger (0-20 years old) group, while more males were in the >21 years age group. There were significant differences (p<0.05) in the gender distributions for all groups, except for those between the ages of 11 and 20.

In Table 2, by distributing the patients into the age groups of childhood, adolescence, and post-adolescence (>19 years), we noted that the group over 19 years of age (adults) had the highest number of hospitalizations, while children aged under 1 year had the lowest.

**Table 1.** Distribution of HIV/AIDS patient hospitalizations from 1997 to 2012, arranged according to gender and age.

| Age Group (years) | Gender | | Total | P* |
|---|---|---|---|---|
| | Male N(%) | Female N(%) | | |
| 0 to 10 | 399 (47.5) | 441 (52.5) | 840 | < 0.05 |
| 11 to 20 | 147 (47.3) | 164 (52.7) | 311 | > 0.05 |
| 21 to 30 | 1087 (55.4) | 874 (45.6) | 1961 | < 0.05 |
| 31 to 40 | 2762 (67.8) | 1312 (32.2) | 4074 | < 0.05 |
| 41 to 50 | 1246 (68.3) | 578 (31.7) | 1824 | < 0.05 |
| 51 to 60 | 327 (59.0) | 227 (41.0) | 554 | < 0.05 |
| 61 to 70 | 121 (63.0) | 71 (37.0) | 192 | < 0.05 |
| > 70 | 544 (58.2) | 406 (41.8) | 934 | < 0.05 |
| Total | 6633 (62) | 4063 (38) | 10696 | <0.05 |

* Z Test.

**Table 2.** Frequency distribution of children/adolescents (up to 19 years of age) and adults (> 19 years) hospitalized with HIV/AIDS between 1997 and 2012, arranged according to age group.

| Age Group | Gender | | % |
|---|---|---|---|
| | Male | Female | |
| ≤ 1 year | 97 | 171 | (2.7) |
| > 1 and ≤ 5 years | 153 | 139 | (3.0) |
| ≥ 5 and ≤ 13 years | 211 | 177 | (4.0) |
| > 13 and ≤ 19 years | 85 | 118 | (2.1) |
| > 19 years | 5569 | 3077 | (88.3) |
| Total (%) | 6115 (62.4) | 3682 (37.6) | 9797 (100) |

The average length of hospital stay for patients with HIV/AIDS between 1997 and 2012 was 10.7 days (± 14.3), and the median length of stay was 6 days (min: 1 day; max: 195 days). There was a significant (p <0.05) gender difference in length of stay. The average for males was 11.2 days, with a median of 6 days, while the average for females was 9.9 days, with a median of 5 days. Regarding hospitalization outcomes (Table 3), mortality was 42% higher among males (PR = 1.42 [95% CI: 1.28–1.57]; p < 0.05) during the study period.

We observed that slightly more than 9% of the admissions involved patients 13 years old or younger (Table 4). There were no gender differences among children and adolescents aged ≤ 13 years (males: 48.9%; females: 51.1%; p > 0.05). However, in the group of individuals older than 13 years, there was a clear predominance (p < 0.05) of males (63.3%).

Hospitalization frequency was 23% lower among male children and adolescents up to 13 years of age compared to their older male counterparts (PR = 0.77 [95% CI: 0.72–0.82]; p < 0.05). In children and adolescents up to 13 years of age, the average length of hospitalization was

8.7 days (± 15.9), while the average was 10.8 days (± 14.2) among adults and adolescents >13 years of age. These differences were significant (p < 0.05). Infectious diseases, primarily opportunistic infections (AIDS-defining), accounted for 54.5% of all hospitalization causes, in both male adults and children (Table 5).

## Discussion

Antiretroviral drugs were introduced at the end of 1995 to treat patients with AIDS, especially those with CD+ levels ≤350 cells/mm$^3$ and a high viral load. The first published results, some which came after the establishment of the new proposed therapy, stated that the disease would change its natural history over time, passing from a knowingly acute disease to a chronic condition due to the significant increase in individual survival rates, relative improvement in quality of life, and decreased hospitalizations from the opportunistic infections typical of AIDS[11,12]. These gains were quickly noticed, and between 1996 and 1997 the Brazilian Ministry of Health, through the Department of STD, AIDS, and Viral Hepatitis, had already begun to render antiretroviral drugs universally available to patients through the Unified Health System (SUS), making Brazil the first country to implement a program of this magnitude[13].

In the years following the introduction of widely available antiretroviral drugs through SUS, many publications on HIV/AIDS in Brazil showed changes in the behavior of the disease that were in line with those observed in other countries. These changes included reduced

**Table 3.** Hospitalization outcomes of HIV/AIDS patients admitted from 1997–2012, arranged according to gender.

| Gender | Hospitalization Outcome | | | Total |
| | Death | Discharged (Cure/improvement) | | |
|---|---|---|---|---|
| Male | 1050 | 5583 | | 6633 |
| Female | 454 | 3609 | | 4063 |
| Total | 1504 | 9192 | | 10696 |

PR = 1.42 (95% CI: 1.28-1.57); p < 0.05.

**Table 4.** Hospitalization distribution of HIV/AIDS patients in the age group ≤13 years and those over that age who were admitted between 1997 and 2012, arranged according to gender.

| Age | Gender | | Total |
| | Male | Female | N (%) |
|---|---|---|---|
| ≤ 13 years | 473 | 495 | 968 (9,1) |
| Over 13 years of age | 6160 | 3568 | 9728 (90,9) |
| Total | 6633 | 4063 | 10696 (100) |

PR = 0.77 (95% CI: 0.72–0.82); p < 0.05.

**Table 5.** Distribution of the five major causes of hospitalization (according to the ICD-10) among children and adults with HIV/AIDS hospitalized between 1997 and 2012.

| Causes of hospitalization | N | % |
|---|---|---|
| OI* (AIDS-defining) | 3506 | 32.7 |
| CAP** | 1187 | 11.1 |
| Gastrointestinal infections | 700 | 6.5 |
| Urinary tract infections | 237 | 2.2 |
| Tuberculosis (pulmonary and extrapulmonary) | 170 | 2.0 |
| Total | 5800 | 54.5 |

* Opportunistic infections. ** Community-acquired pneumonia.

mortality, incidence rate stabilization, decreased vertical transmission, and a new characterization of the profile of hospitalization causes among patients with HIV and AIDS[14-17]. This study evaluated the profile of hospitalized patients in the post-HAART period and included an evaluation of the sociodemographic, biological, epidemiological, and clinical characteristics related to hospital admission causes. This examination was based on records from various hospitals in a large and populous region of the state of São Paulo, in southeastern Brazil. The results showed a significant number of admissions (more than 10,000) in a population predominantly made up of young adult men from 21 to 40 years of age, which is consistent with the results mentioned in the majority of Brazilian and international publications[18-21].

Another interesting finding of this study was the small proportion (only 5% of the total, 487 people) of hospitalized children (<13 years old) hospitalized, which suggests a decrease in vertical transmission. Data from countries in which vertical transmission is still high, such as in some African nations, suggests that the hospitalization of children tends to highly exceed the rates reported herein. A study carried out in Ghana recorded 102 admissions for HIV/AIDS in children[22] in just one year, while another study conducted in South Africa reported that the majority of pediatric beds in public hospitals are filled by children who carry the disease[23]. Another finding that is not in line with those previously mentioned about the African setting is a lower prevalence of hospitalization among younger patients, notably those ≤13 years of age and male (PR = 0.77 [95% CI: 0.72–0.82]; p < 0.05). This again suggests that the Brazilian epidemic is a significant problem among the adult population.

Mortality rates among those hospitalized were 42% higher for men (PR = 1.42 (95% CI: 1.28–1.57; p < 0.05). This corresponds to the results of a large Brazilian survey[24] and is in direct contrast to studies in African countries[25], where the mortality rate tends to be similar between genders, or even higher among women.

Finally, this study revealed that the leading causes of hospitalization during the study period were infectious diseases, especially opportunistic ones (many of these AIDS-defining conditions) and community-acquired pneumonia. These findings suggest a limited ability of antiretroviral drugs to reduce the incidences of infections and other opportunistic conditions. This may be attributable to not only a lack of effectiveness of HAART but to other factors as well; for example, low patient drug adherence. Many studies have shown that adherence to prescribed care, just like adherence to antiretroviral drugs, is low worldwide[26-28]. The most common variables that influence low adherence to HAART are low education, low socioeconomic status, use of illicit drugs and alcohol, and being male[29,30]. Over 60% of the patients in our study were male, which may partially explain the high incidence of hospitalization due to opportunistic infections because of men's often poor adherence to treatment.

## Conclusions

As shown in this study, there are still a high number of hospitalizations of patients with HIV/AIDS, even in the post-HAART era (after 1996; specifically, 1997–2012), on which this survey focused. Most patients admitted to the hospital were males between the ages of 21 and 50. Mortality was significantly higher among males, and length of hospital stay was considerably longer. Hospitalization was much more frequent among adults compared to children, and length of hospitalization was greater for the female than the male children.

Although many studies have demonstrated a decrease in hospitalization due to the opportunistic infections occurring after the introduction of HAART, the present study found that infectious diseases, especially those that are opportunistic, represent a significant portion of hospitalizations.

## Collaborations

AA Nunes worked on the project design, data analysis and interpretation, as well as the writing, revision, and final approval of this article. LS Caliani collected the data, wrote the article, and participated in the approval of the final revision of the article. MS Nunes collected and organized the data, wrote, reviewed, and approved the final revision of the article. AS Silva and LM Mello wrote the article and participated in the data analysis and the reviewing/approval of the final version of the manuscript.

## Acknowledgements

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