AIDS in Intensive Care Unit Patients: Epidemiology and Outcomes

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Abstract

Background: Admission rates to intensive care unit (ICU) remains high in AIDS patients, although data in low-income countries are scarce. The aim of this study was to evaluate the epidemiology, morbidity and mortality risk factors of HIV/AIDS patients admitted to the ICU of a university hospital in southern Brazil.

Methods: Retrospective cohort study with all patients aged >18 years in the ICU from 2004 to 2014 with a diagnosis of HIV/AIDS (previous or newly diagnosed).

Results: 1.7% of ICU patients had HIV/AIDS; of these, 67.1% were male, with an average of 40 years. 91.8% of hospitalizations were due to medical causes, and most patients (83.6%) had no comorbidities. Mean APACHE 25.1, 95.1% required invasive mechanical ventilation (MV), ICU stay 13.9 days, mortality 51.4%. Among AIDS patients, incidence of complications was high: 41.7% acute respiratory distress syndrome (ARDS), 45.8% acute renal failure (ARF), 37.5% pneumonia. Approximately 1/3 had diagnosis during hospitalization and 27.5% were on antiretroviral therapy. Mortality has progressively reduced over the years.

Conclusion: The prevalence of HIV/AIDS was 1.7%. This group had a high incidence of complications, which were related to higher mortality. The mortality of this group has decreased in recent years in this population.

Keywords: Intensive care unit; AIDS; Mortality; Epidemiology

Abbreviations: AIDS: Acquired Immunodeficiency Syndrome; HAART: Highly Active Antiretroviral Syndrome Therapy; APACHE: Acute Physiology and Chronic Health Evaluation score; HIV: Human Immunodeficiency Virus; ARDS: Acute Respiratory Distress Syndrome; ICU: Intensive Care Unit; ARF: Acute Renal Failure; MV: Mechanical Ventilation; ART: Anti-RETROVIRAL THERAPY; PaO₂: Pressure of Arterial Oxygen; CD₄: Cluster of Differentiation 4 Lymphocytes; PEEP: Positive End-Expiratory Pressure; CHF: Congestive Heart Failure; PO: Post-Operative; COPD: Chronic Obstructive Pulmonary Disease; Rtx: Radiotherapy; CRF: Chronic Renal Failure; SAPS: Simplified Acute Physiology Score;Ctx: Chemotherapy; SD: Standard Deviation; DM: Diabetes Mellitus; SH: Systemic Hypertension; FiO₂: Fraction of Inspired Oxygen; SOFA: Score of Failure Organ

Introduction

According to the United Nations, in 2015 about 36.7 million people were living with the human immunodeficiency virus (HIV) in the world, with only about 43% having access to treatment. In Brazil, a prevalence of 0.4 to 0.8% of the population is estimated, with about 830,000 people living with acquired immunodeficiency syndrome (AIDS) [1]. Although the number of new cases in the world remains stable (around 2 million a year), the complexity of the epidemiological, social and clinical conditions involved makes the epidemic central to the concerns of international health authorities [2]. The costs related to the disease are astronomical: in the United States, it is estimated that treatment of infected persons could cost about 450 billion in health care per year [3,4]. Obviously, these costs do not measure the impressive social impact of the disease, which in low-income countries has reached a level of national tragedy [1].

Due to significant advances in the treatment of patients with AIDS (the 'HAART' [Highly active antiretroviral therapy] era); the hospitalization of patients infected with HIV has reduced significantly in recent years, although not hospitalizations in intensive care unit (ICU) [5]. Among the factors that justify this paradox are the increase in hospitalization for causes not related directly to AIDS (as post-operative), 'general' diseases but that increase in frequency late in the HIV patient (e.g. coronary atherosclerosis), and a change in the assistance paradigm and prognostic definition of this group of patients (increasing the chance of being transferred to the ICU) [5,6].

In Brazil, the incidence of new AIDS cases is stable at about 39,000 new cases a year, with mortality of 5.6/100,000 inhabitants/year (although it reaches 8.5 in the current study). In public hospitals approximately 33,000 patients are hospitalized per year, with expenditures of at least $43 million a year [7,8].

The objective of the present study was to evaluate the prevalence, epidemiological/demographic aspects and morbidity and mortality risk factors in HIV/AIDS patients admitted to a general ICU of a public teaching hospital in southern Brazil.

Methods

In this cohort study, data were obtained retrospectively from the medical records of all patients hospitalized in the adult ICU of the Hospital Universitário do Oeste do Paraná (a public hospital with 173 beds), in Cascavel (southern Brazil) between 2004 and 2014, with a diagnosis of AIDS or HIV positive (previous or diagnosed in this

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hospital stay) and compared with non-AIDS patients. A more detailed spreadsheet was generated over a period of 2 years (2013-2014), only for patients with AIDS. The reason for not including HIV-AIDS patients from previous years (2004-2012) was the impossibility of obtaining their full data. Thus, the sample size was chosen by convenience.

The exclusion criterion was patients admitted to the ICU who were under 18 years of age. The data were compared with a general database of the adult ICU (with patients tabulated since 2004).

As a definition of mortality, it was considered ICU or hospital mortality.

Criteria

- Acute Renal Failure (ARF): Any serum creatinine ≥ 1.50 mg/dl, excluding patients with known prior renal disease;
- Thrombocytopenia: Any platelet count <100,000 cells/mm³;
- Use of vasoactive drugs: Any dose of noradrenaline, dopamine or vasopressin;
- Comorbidities (e.g. Chronic Obstructive Pulmonary Disease [COPD], Chronic Heart Failure [CHF], Chronic Renal Disease [CRD]): clinically defined by the care team;
- Acute Respiratory Distress Syndrome (ARDS): According to the criteria of the European-American Consensus [9], in force at the time of patient management;
- Hepatitis: Total transaminase elevation (alanine+aspartate) above 5 times the reference value.

The data were tabulated in the Excel program. Descriptive statistical analysis was performed and percentages expressed as frequency, mean and standard deviation.

The quantitative variables were evaluated by Mann-Whitney-U test. For the qualitative variables, the Chi-square test for independence was performed, and in cases of not reaching the minimum expected frequency assumption equal to 1, the Chi-square test for Independence was applied with the Monte Carlo permutation method. For the univariate statistical analysis, a significance level of 0.05 was used.

Binary logistic regression was performed to find factors related to mortality in HIV/AIDS patients. It was made selection of the predictor variables of the model using the odds ratio criterion that P<0.10 was statistically equivalent to 1. A model was obtained with a reduced number of variables, selected from the application of the criterion that P<0.05 of the adjusted odds ratio was statistically equivalent to 1. A final model was then achieved after testing for all possible multiple iterations, by using the maximization of the Wald function. Hosmer and Lemeshow statistic was used to verify the fit of the models. Once the final logistic regression model was decided, for each of the mentioned objectives, the probabilities were calculated from the formula Pr=1/[1+e-(α+Σ (βi xi))], where α is the constant of the model.

The study was conducted in accordance with the recommendations in Resolution 466/2012 of the Brazilian National Council of Health. This study was approved by the Research Ethics Committee of the Universidade Estadual do Oeste do Paraná-UNIOESTE.

Results

During the study period (July 2004 to December 2014), 4188 patients were admitted to the ICU. Of these 73 (1.74%) had HIV/AIDS and were included in the study. Among the patients with AIDS, 67.12% were male and 40 years old. Almost all (91.78%) hospitalizations of patients with AIDS were due to medical causes. Most of the patients (83.6%) had no previous diseases. They were very serious patients: the mean Acute Physiology and Chronic Health Evaluation (APACHE) of admission was 25.1; 95.08% required invasive mechanical ventilation (MV), the mean ICU stay was 13.9 days and ICU mortality was 51.35%.

Table 1 shows the clinical-demographic characteristics of patients with AIDS and non-AIDS in this period.

Figure 1 shows the evolution of the prevalence and mortality of patients with AIDS in the ICU in 2004-2014, with a progressive reduction in mortality, particularly in the last period.

When only patients with AIDS were evaluated (years 2013-2014), the incidence of complications was high: 41.7% presented ARDS, 45.8% ARF (although only 4.2% required dialysis), 43.8% thrombocytopenia, 37.5% nosocomial pneumonia and 20.8% hepatitis. Approximately 1/3 of the patients were diagnosed with AIDS during the current hospitalization and 37.5% were using antiretrovirals. However, perhaps due to reduced ‘n’, only the presence of ARDS and/or ARF was associated with higher ICU mortality (Table 2).

Among HIV/AIDS patients (n=24), the variables considered significant (risk of death) by the logistic regression method were: cause of hospitalization (neurological and emergency surgery), admission APACHE II and MV length of time (Table 3).

Discussion

Despite the reduction in hospital admissions of patients with AIDS due to improved treatment, admissions in ICU of AIDS patients remain high [10]. In 2 years period, up to 33% of AIDS patients require hospitalization; of these, 17.8% need admission to the ICU [6]. In national studies, the incidence of AIDS patients in the general ICU population varies between 0.16% (Holland) [11] and 2.6% (France) [12]. In the current study, the prevalence of HIV/AIDS patients in the total ICU population was 1.7%.

In our population, most (67%) were male and the mean age was 40.6 years. Despite the increased incidence of women with AIDS in recent years [1], there is in general a clear predominance of male gender among AIDS patients admitted to the ICU, and this trend has not changed over the years [13-15]. There has been a clear change in the profile of patients, with increasing age [12,15] and, consequently, the frequency of comorbidities among these patients admitted to the ICU.

The population of our study was severely ill: APACHE II admission was significantly higher in AIDS patients compared with the non-AIDS group. Despite a higher score in patients who died, we did not find statistically significant differences of APACHE II as a predictor of mortality. The authors believe that this was due only to the insufficient number of patients to detect this difference. However, the literature is controversial about severity scores (APACHE, SOFA and SAPS) in AIDS patients compared with non-AIDS patients in ICUs [6,13,16-20].

In the current study, AIDS patients had a lower frequency of comorbidities than non-AIDS patients. The incidence of smoking, alcohol consumption and use of illicit drugs was slightly higher, although without statistical difference.

Since the introduction of antiretroviral therapy, the mortality attributed to opportunistic infections associated with AIDS has decreased significantly with a proportional increase in HIV-infected patients who are living with viral replication control and preserved immune function. Increased survival translates into an ageing
population with increased chronic diseases such as hepatitis C and hepatic cirrhosis, cardiovascular diseases (e.g. atherosclerotic diseases), renal insufficiency, lung diseases (COPD) and neoplasms [6]. On the other hand, admissions due to elective surgeries have increased by up to 100% in recent years in this population [12], evidence of a change in the approach and prognosis paradigm of the disease.

Despite evidence of greater alcohol use [23], smoking [24] and illicit drug use [25] in patients with AIDS and the potentiation of these factors in the morbidity and mortality of the disease, few studies have evaluated the extent of these habits in hospitalized patients in ICU. In elderly male AIDS patients, the incidence of smoking and alcohol consumption was higher among patients requiring hospitalization, although among inpatients there were no differences with those requiring ICU admission [6].

In the population of our study, the most common cause of admission was due to clinical diseases. Despite the improvement in the treatment of patients with AIDS and a consequent increase in quality of life and life span, most hospitalizations of AIDS patients continue to be due to clinical conditions [12-14,17-19], although increasingly by conditions not necessarily related to AIDS (such as coronary disease, cirrhosis, COPD and neoplasms) [6]. On the other hand, admissions due to elective surgeries have increased by up to 100% in recent years in this population [12], evidence of a change in the approach and prognosis paradigm of the disease.

The incidence of complications among AIDS patients was high in the current study: 41.7% had ARDS, 45.8% ARF (although only 4.2% needed dialysis), 43.8% had thrombocytopenia, 37.5% nosocomial pneumonia and 20.8% hepatitis. In patients with AIDS, the incidence of complications was obviously higher in patients who died. Respiratory (ARDS) and renal (ARF) were the most complications associated with the risk of death.
Figure 1: Prevalence and mortality of patients with AIDS in ICU, in period 2004-2014.

| Male gender, n (%) | Total AIDS n=24 | Alive n=15 | Death ICU n=9 | p |
|--------------------|-----------------|------------|---------------|---|
| Age, years         | 43 (34-46.25)   | 45(35-46.5) | 39 (30-45)    | 0.982 |
| Comorbidities, n (%)|                 |            |               |    |
| No (none)          | 14 (58.3)       | 7 (46.7)   | 7 (77.8)      | -   |
| SH                 | 5 (20.83)       | 4 (26.66)  | 1 (11.11)     |    |
| DM                 | 2 (8.33)        | 2 (13.3)   | 0             |    |
| Obesity            | 0               | 0          | 0             |    |
| COPD               | 2 (8.33)        | 2 (13.33)  | 0             | 0.479 |
| Liver disease/cirrhosis | 2 (8.33) | 2 (13.33) | 0 | |
| Others             | 4 (16.66)       | 2 (13.33)  | 2 (22.22)     |    |
| Habits, n (%)      |                 |            |               |    |
| Smoking            | 12 (50)         | 8 (53.33)  | 4 (44.44)     | 1.000 |
| Alcoholism         | 10 (41.66)      | 7 (46.66)  | 3 (33.33)     | 0.631 |
| Illicit drugs      | 4 (16.66)       | 3 (20%)    | 1 (11.11)     | 1.000 |
| Cause of ICU admission, n (%) |            |            |               | 0.561 |
| Trauma             | 1 (4.17)        | 1 (6.67)   | 0             |    |
| PO elective surgery| 0              | 0          | 0             |    |
| PO non-trauma emergence surgery | 2 (8.33) | 2 (13.33) | 0 | |
| Medical (includes obstetrics) | 21 (87.5) | 12 (80%) | 9 (100%) | |
| APACHE II          | 24.5 (19.5-28)  | 24 (18.5-27.5) | 27 (22-28) | 0.348 |
| Was the diagnosis of AIDS made before hospitalization? Yes, n (%) | 16 (66.7) | 10 (66.7) | 6 (66.7) | 0.655 |
| Time of AIDS diagnosis before hospitalization (months), n (%) |            |            |               | 0.672 |
| 0 (Diagnosis in this admission) | 8 (33.3) | 5 (33.3) | 3 (33.3) | |
| 1-2                | 5 (8.33)        | 2 (13.3)   | 3 (33.3)      |    |
| 3-6                | 1 (4.16)        | 1 (6.7)    | 0             |    |
| 7-12               | 1 (4.16)        | 1 (6.7)    | 0             |    |
| >12                | 9 (37.5)        | 6 (40.0)   | 3 (33.3)      |    |
| Previous ART n (%) | 9 (37.5)        | 6 (40.0%)  | 3 (33.3)      | 0.915 |
| Last CD4 before hospitalization, cells/mm³, mean ± SD | 333.0 ± 316.43 | 328.0 ± 334.7 | 339.6 ± 363.0 | 0.937 |
| Invasive VM, days  | 7 (4-12.5)      | 5 (3.5-11) | 8 (6-13)      | 0.067 |
| Invasive VM, days, n (%) |            |            |               |    |
| 0                  | 1 (4.17)        | 1 (6.67)   | 0             |    |
| 1-2                | 2 (8.33)        | 1 (6.67)   | 1 (11.11)     | 0.274 |
| 3-5                | 8 (33.33)       | 7 (46.66)  | 1 (11.11)     |    |
| 6-10               | 6 (25%)         | 2 (13.33)  | 4 (44.45%)    |    |
| >10                | 7 (29.17)       | 4 (26.67)  | 3 (33.33%)    |    |
AIDS patients admitted to ICU: one study described an incidence of 5.4% [26], although possibly underestimating its true incidence. On the other hand, the impact of ARDS on patients with AIDS, although with high mortality, does not seem to differ from the non-AIDS patients [17,27]. The high incidence of ARDS in our AIDS population could reflect factors related to the greater severity of the patients (due to the scarcity of ICU beds and the need to select only more critical patients) or factors related to suboptimal management of precipitating conditions of ARDS, such as sepsis and trauma.

We sought to evaluate the timing of the diagnosis of HIV/AIDS, and the number of patients diagnosed during hospital stay. In our sample, approximately one-third of the patients had AIDS diagnosed during the current hospitalization; 55% of those who already knew of the diagnosis were using antiretroviral therapy (ART) before admission. Despite improvements in care and management of AIDS patients, literature shows a disproportion about previous diagnosis among patients admitted to ICU with AIDS: whereas in high-income countries only 19-28% of patients had no previous diagnosis [10,16,20], in poor or low-income countries this number reaches 47% [14], making the discussion about whether or not to start ART in this newly diagnosed group in critical situation more frequent in these places [28].

ICU and hospital length of stay and mortality (ICU and hospital) were significantly higher in patients with AIDS. The main risk factor for mortality in HIV+ patients was, as already described, the severity of the acute disease (e.g. higher APACHE), neurological causes and the presence of clinical complications and MV length of time (Table 3). AIDS-related factors (such as presence of Kaposi’s sarcoma, CD4 level and viral count, for example) are described in the literature as associated with higher hospital mortality [6,14,22]. However, as found in our population, most of the deaths are related to the severity of the current clinical condition and its complications, such as sepsis, respiratory failure/ARDS, ARF and organ dysfunction, similar to non-AIDS patients [14,17,19,20,22,29].

Table 2: Baseline characteristics and outcomes of patients in ICU with AIDS, 2013-2014.

| Variable                                      | Coefficient | Pr>Qui² | OR low (95%) | OR upper (95%) |
|-----------------------------------------------|-------------|---------|--------------|----------------|
| Intercept                                     | -0.067      | 0.916   |              |                |
| Admission cause: Emergency Surgery            | -3.109      | 0.175   | 0.045        | 0.000          | 4.011          |
| Admission cause: Neurological                 | -1.144      | 0.300   | 0.318        | 0.037          | 2.778          |
| APACHE                                        | 0.037       | 0.495   | 1.038        | 0.932          | 1.156          |
| MV length of time (days)                      | 0.095       | 0.164   | 1.100        | 0.962          | 1.257          |

ICU: Intensive Care Unit; SD: Standard Deviation; SH: Systemic Hypertension; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; PO: Post-Operative; APACHE: Acute Physiology and Chronic Health Evaluation; MV: Mechanical Ventilation; ARDS: Acute Respiratory Distress Syndrome; PEEP: Positive End-Expiratory Pressure; ARF: Acute Renal Failure; ART: Antiretroviral Therapy

The data of quantitative variables are expressed as median (1st quartile-3rd quartile).

Table 3: Parameters obtained for the model created through the application of logistic regression in HIV/AIDS patients in order to find the factors associated with mortality (n=24).
Despite the small number of patients in this study, we found that there is a progressive reduction in the mortality of AIDS patients in recent years in our ICU, even with high severity (perceived by the APACHE of little admission altered) (Figure 1). It is possible that this improvement is due to better training of the team in general; our database shows that overall ICU mortality has been falling in this period, even with the general patient severity; (APACHE score) relatively unchanged. However, factors related to the specific management of patients with AIDS may have contributed to this result. One is the change in philosophy of approaching the patient living with HIV from an initial nihilistic attitude towards a current aggressive strategy (considering now to deal with a chronic disease such as Diabetes Mellitus, COPD or CHF). In addition, the very cause of this change (the use of HAART) guaranteed by the Brazilian health system has allowed an undeniable change in the prognosis of this disease in the country. Finally, the indispensable intensivist infectious diseases specialist collaboration allows individualizing the management of these patients and their serious infectious complications, specific or not.

This study has some limitations, some of them intrinsic to its nature. Because it is a retrospective cohort, data reliability may be impaired by non-standardized data collection. Because it is a single centre, the number of patients and the local characteristics may not allow generalizations of the data the researchers found. For example, it is a public teaching hospital with a low-income population and a referral hospital with limited beds availability (therefore, the population assigned to the ICU will be more severe patients). The population of non-AIDS patients follows the specific characteristics of the hospital: few cancer patients and many patients with trauma (therefore with a lower average age). In addition, not all laboratory data relevant to AIDS are available at inpatient care (e.g. CD4 or viral load). In addition, patient management was based on the team’s clinical decision, which impedes further evaluation of the impact of certain strategies (e.g. ventilatory or antibiotic management) on patient outcomes. However, the objective of this study was a ‘real life’ evaluation of a Brazilian public hospital, evaluating the epidemiological and clinical characteristics of these patients, and therefore this study was used to this end.

Conclusion
In this sample of patients in a general ICU in a university hospital in southern Brazil, the prevalence of HIV/AIDS was 1.7%. This group had a high incidence of complications, which was related to higher mortality. Nevertheless, the mortality of this population has decreased in recent years.

Ethical Approval and Consent to Participate
This study was conducted in accordance with the recommendations of Resolution 466/2012 of the Brazilian National Health Council. The project was approved by the Research Ethics Committee of the Universidade Estadual do Oeste do Paraná-UNIOESTE. Accordingly, post-informed consent was waived, since this current study only describes the results of a population already previously treated.

Statement of Patient Data Confidentiality
The authors declare that they guarantee the confidentiality of patient data regarding the publication of this study.

Author’s Contributions
PADD designed the study, analyze the data, wrote the manuscript; KHO, ACJ, CSO analyzed the data, wrote and reviewed the manuscript. All the authors read and approved the final manuscript.

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