*Original Article*

# Clinical characteristics and predictors of mortality in hospitalized HIV-infected Nigerians

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**Abstract**

Introduction: Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) is a chief cause of death in sub-Saharan Africa. In this study, the clinical characteristics and predictors of mortality among hospitalized HIV infected adult Nigerians are reported.

Methodology: The records of 354 patients were reviewed for demographic and clinical characteristics. Predictors of mortality using logistic regression in a retrospective study were also reviewed.

Results: A total of 109 (30.8%) males and 245 (69.2%) females participated in the study. The mean age of all participants was 35 ± 8 years. Median baseline CD4 cell counts and viral load were 91 cells/mm³ and 63,438 copies/ml respectively. There was a total of 123 (34.8%) deaths while 231 (65.2%) patients were discharged home. Tuberculosis (TB) was the most common diagnosis on admission as well as the leading cause of death. Among all subjects, only male gender (adjusted odds ratio [AOR] 4.67, 95% confidence interval [CI]: 2.63-8.29); CD4 cell count ≤ 200 cells/mm$^3$ (AOR 5.28, 95% CI: 2.99-9.31); length of hospital stay < 3 days (AOR 4.77, 95% CI: 1.35-16.86); and age ≥ 35 years (AOR 2.43, 95% CI: 1.41-4.19) were predictive of death.

Conclusion: These findings illustrate the need for early diagnosis of HIV infection, appropriate treatment and prevention of opportunistic infections, and improved access to highly active antiretroviral therapy (HAART).

**Key words:** characteristics, mortality, hospitalized, HIV infected, Nigerians

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## Introduction

With a national prevalence of 4.4% [1], Nigeria ranks third on the list of countries with the highest number of people living with the human immunodeficiency virus (HIV) infection, after South Africa and India. Since the first case of acquired immune deficiency syndrome (AIDS) was publicized in 1986, the burden of the pandemic has grown rapidly, with current numbers of people living with the virus estimated at 3.5 to 5 million [1,2]. In resource-poor settings, between 20% and 52% of hospital beds in medical wards are occupied by HIV-infected patients at any given time, with opportunistic infections (OIs) accounting for the majority of these admissions [3,4].

AIDS is currently the leading cause of illness and death in sub-Saharan Africa [2]. Infection with HIV leads to progressive cell-mediated immunodeficiency, resulting in an increased risk of opportunistic infections and death. As the CD4 cell count declines and the viral load increases, an HIV-infected person becomes increasingly susceptible to OIs that may result in hospital admissions [5]. Hospitalization and death are the principal events resulting from opportunistic infections and form important indicators for interventions carried out in this group of patients.

Reports from high-income countries show that admissions for AIDS-related illnesses decreased following the introduction of highly active antiretroviral therapy (HAART), as these drugs improved quality of life by decreasing HIV-related morbidity and mortality [6]. There is limited data from Nigeria that characterize hospitalized HIV-infected patients in terms of mortality, length of hospital stay, and reason for hospitalization in the era

of HAART. The purpose of this study was to assess the profile of hospitalized HIV-infected patients enrolled for care and treatment, to define the spectrum of illness, and to determine predictors of mortality among HIV-infected adults at the Jos University Teaching Hospital in Nigeria.

## Methodology

The Jos University Teaching Hospital is a tertiary centre that offers comprehensive care to HIV-infected patients both on an inpatient and an outpatient basis. We conducted a retrospective chart review of patients enrolled in the hospital's treatment program between January and December 2007 using a standard data extraction form. These were patients with documented HIV-1 infection enrolled for HIV care and treatment and who required hospitalization. Records of patients aged 18 years and above were reviewed and the following variables were extracted: age, gender, level of education, length of hospital stay (LOS), use of HAART, duration of use of HAART, and discharge disposition (discharged home or died in hospital). The HAART regimen consisted of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI) in line with national guidelines. We also extracted the patients' baseline CD4 count (cells/mm$^3$) and viral load (copies/ml) results. The majority of diagnoses reported in the charts were defined by the patient's clinician based upon clinical findings and accompanying investigations whenever possible.

*Diagnoses*

A diagnosis of pulmonary tuberculosis (PTB) required the clinical syndromes of fever, productive chronic cough (± haemoptysis), night sweats, and weight loss with suggestive chest radiograph (CXR) findings. Sputum acid fast bacilli (AFBs) were routinely ordered for all patients with a productive cough. Cultures for AFB were not routinely performed due to constraints in the availability of culture services. The diagnosis of extra-pulmonary tuberculosis required, in addition to site-specific symptoms, cerebrospinal fluid (CSF) analysis for tuberculous meningitis (TBM), and lymph node biopsies for TB adenitis. The diagnosis of cryptococcal meningitis required a compatible clinical syndrome, CSF analysis with India ink, and culture for *Cryptococcus neoformans*. Malignancies were confirmed by biopsy. For most cases of diarrhea, investigation for a definitive organism was inconclusive. Most other diagnoses were made using clinical presentation and available investigations.

The main outcome measure was patient status at the time of exiting the inpatient service. We were interested in comparing inpatients who died on admission with those patients who were discharged home. The Human Research Ethics Committee of the Jos University Teaching Hospital approved the study.

Statistical analyses were performed using Epi Info version 3.5.1 (CDC, Atlanta, Georgia).

Statistical comparisons were conducted using both parametric and non-parametric tests. Fisher's exact test was used for contingency tables in which 25% or more of the expected cell frequencies were less than five. Odds ratios (OR) and 95% confidence intervals (CI) were obtained. Variables were dichotomized and entered in a logistic regression model in a stepwise fashion to identify independent predictors of mortality. All reported $p$ values were two-tailed and levels less than 0.05 were considered significant.

## Results

We examined records of 354 HIV-infected adults admitted to the medical wards of the hospital during the study period. These were patients whose HIV status had been diagnosed prior to hospitalization. They represented 12.9% of the total admissions (2,725) to the medical wards of the hospital during the period under review. Of the 354 patients, 245 (69.2%) were females and 109 (30.8%) were males. The mean age for the entire cohort was 35 ± 9 years with a range of 18 to 62 years. The mean age for males was 39 ± 9 years and 33 ± 8 years for females ($p$, 0.001). The median CD4 count at baseline was 91 cells/mm³ with a range of 2-782 cells/mm$^3$. Viral load values ranged from 200 to 2,361,858 copies/ml for the entire cohort, and 124 (35%) of the patients had a baseline viral load above 100,000 copies/ml. A total of 141 (39.8%) of the patients had documented use of HAART with a median duration of eight months of use; the range was between 2 weeks to 71 months. The median length of stay (LOS) in the hospital was 18 days; the range was between 1 and 124 days. There were a total of 123 (34.7%) deaths, while 231 (65.3%) of the patients were discharged home alive. None of the patients was documented to have left hospital against medical advice (Table 1).

Tuberculosis was the most common diagnosis, accounting for 119 (33.6%) of the indications for hospitalization. Pulmonary disease accounted for 53% and extra-pulmonary TB at various sites

**Table 1.** Characteristics of 354 HIV-infected adults admitted to medical wards at the Jos University Teaching Hospital

| Characteristic | Frequency (%) |
|---|---|
| Gender: | |
| Female | 245 (69.2) |
| Male | 109 (30.8) |
| Level of education: | |
| No formal education | 91 (25.7) |
| Primary | 44 (12.4) |
| Secondary | 111 (31.4) |
| Tertiary | 108 (30.5) |
| CD4 categorization: | |
| ≤ 200 | 288 (81.4) |
| 201- 499 | 61 (17.2) |
| ≥ 500 | 5 (1.4) |
| Proportion on HAART | 141 (39.8) |
| Discharge disposition: | |
| Home | 231 (65.3) |
| Died | 123 (34.7) |

**Table 2.** Spectrum of illnesses and mortality in hospitalized HIV-infected adults in Jos University Teaching Hospital, Nigeria

| Diagnoses | *n* (%) | In- hospital deaths, *n* (%) |
|---|---|---|
| Opportunistic Infections: | | |
| *Pulmonary TB* | 63 (17.8) | 13 (10.6) |
| *Extrapulmonary TB* | 56 (15.8) | 24 (19.5) |
| *Cryptococcal meningitis* | 31 (8.8) | 16 (13.0) |
| Septicaemia | 58 (16.4) | 21 (17.1) |
| ARV toxicities | 41 (11.6) | 4 (3.3) |
| Chronic diarrhea | 23 (6.5) | 10 (8.1) |
| Opportunistic malignancies* | 17 (4.8) | 12 (9.8) |
| Other infections | 15 (4.2) | 8 (6.5) |
| AIDS dementia complex | 4 (1.1) | 3 (2.4) |
| Non HIV related illnesses | 32 (9.0) | 7 (5.7) |
| N/A** | 14 (4.0) | 5 (4.0) |
| **Total** | **354 (100.0)** | **123 (100.0)** |

*Kaposi Sarcoma (15), Lymphoma (2), **Diagnosis not specified/indicated

accounted for 47% of the TB cases. Other common reasons for admission are shown in Table 2. Compared to patients who were discharged, patients who died during hospitalization were more likely to be male, have a lower median baseline CD4 count, higher median baseline HIV RNA levels, and to have been on HAART for a shorter duration (Table 3).

A logistic regression model that adjusted for age, gender, LOS, CD4 count, viral load and HAART use was used to determine factors predictive of mortality. A total of 143 (58.3%) females and 34 (31.2%) males were below the age of 35. Six (5.5%) males and five (2.0%) females spent fewer than three days on admission. The factors that were predictive of mortality on analysis were male sex, low CD4 count, age greater than 35 years, and short LOS (Table 4).

## Discussion

This study identified important clinical characteristics and determinants of mortality in hospitalized HIV-infected adults in Nigeria in the era of HAART. Opportunistic infections are a major cause of morbidity and mortality in patients with HIV infection. In resource-limited settings, knowledge regarding the prevalence of the various IOs might aid

decision making regarding empirical treatment and would help to prioritize limited resources.

The overall mortality of 34.8% in this group of patients was quite high but comparable to rates of between 16% and 44% in inpatient mortality observed in resource-limited settings [2,7-9]. This mortality rate is much higher than that reported in the United States in the pre-HAART era [10,11]. The high mortality is probably reflective of the advanced nature of the disease at presentation. For example, the majority (81.5%) of the patients had CD4 counts ≤ 200 cells/mm$^3$ and most (92%) of the deaths were inpatients with CD4 counts below this level. In addition, stigma, delay in seeking health care, lack of HIV counseling and testing services, as well as delays in referral and ART initiation are all potential reasons for late presentation. Even though immunologic and virologic responses to therapy in the first year have been reported to be similar among patients from low-income and high-income settings, patients in low-income settings usually start treatment with more advanced immunodeficiency and experience higher early mortality than those from high-income countries [12-16]. This high mortality underscores the need for increased access to early testing and other care and support services to reduce the high burden of HIV disease at enrolment into treatment programs.

The mean age for our cohort was 35 ± 9 years and 69.2% of the patients were females. This age is comparable to that reported from other low-income countries. People within the age bracket of 15 to 44 years are more sexually active as well as more likely to engage in high-risk behavior and are therefore at higher risk of HIV acquisition than other subsets of the population [1]. Even though there are more HIV-positive women than men in sub-Saharan Africa and more women were hospitalized in our cohort, proportionately more men died while admitted to the hospital than women. In our setting, men typically present with lower CD4 counts and more severe OIs and are therefore more likely to have unfavorable outcomes during their hospital stay than women.

The spectrum of opportunistic infections in our patients is similar to those reported from South Africa [17], India [18], Cambodia [8] and Iran [19]. Tuberculosis was the most common inpatient diagnosis. Given the high rates of TB and HIV co-infection and the attendant morbidity and mortality, effective HIV treatment measures will have to integrate the early detection and effective treatment of TB as one of its core components.

Septicemia and cryptococcal meningitis were also frequently diagnosed as was diarrheal disease. ARV toxicities accounted for 11.6% of admissions in our cohort. Proper counseling about the adverse effects of antiretroviral drugs and aggressive monitoring of patients before and within the first few weeks of commencement of HAART will help to reduce morbidity from the use of antiretroviral drugs.

In addition to being the most common indication for hospitalization in our cohort, tuberculosis was also the most common cause of death, with extra-pulmonary cases outnumbering pulmonary cases among those who died while admitted. Septicemia and cryptococcal meningitis were also significant causes of mortality in our patients. Although there are no regional incidence estimates, absolute rates of cryptococcosis were under one case per 100 person-years and it was responsible for a much lower proportion of hospital admissions and deaths in the Abidjan co-trimoxazole trial cohort [20] and in rural Uganda [21]. The majority of our patients had low CD4 counts. This, coupled with the challenges of diagnosis and unavailability of the drug of choice for the treatment of cryptococcal meningitis, may have contributed the mortality from cryptococcal meningitis.

Other non HIV-related medical conditions also contributed to morbidity and mortality in our patients. With increased survival rates from the use of HAART in HIV infected patients, other medical conditions will become important causes of morbidity and mortality for this group of patients [22].

The factors associated with mortality in our patients were short duration of hospital stay, male gender, baseline viral load >100,000 copies/ml, age above 35 years, short duration of HAART use, and CD4 count ≤ 200 cells/mm$^3$. These factors suggest that patients who died during hospitalization were more likely to present with poor performance status and more advanced and severe disease, leading to death early in their hospital stay. Even though CD4 counts ≤ 200cells/mm$^3$ were predictive of death in our cohort, some studies have reported contrary findings [23, 24].

A major limitation we encountered in this retrospective observational study was missing data, especially in the area of definitive diagnosis.

In conclusion, a wide spectrum of opportunistic infections was seen in our patients and the majority of them presented with advanced disease and high rates of TB co-morbidity. Overall, hospitalization of

**Table 3.** Comparison of HIV-infected adults in Jos University Teaching Hospital by disposition at discharge

| Characteristics | Discharged home (*n* = 231) | Died in hospital (*n* = 123) | *p-value* |
|---|---|---|---|
| Median age (yrs) | 34 | 36 | 0.04 |
| Gender (*n*): | | | |
| Female | 168 | 77 | |
| Male | 63 | 46 | 0.01 |
| LOS[†](days) | 17 | 18 | 0.20 |
| Baseline CD4[*] | 69 | 40 | 0.04 |
| Baseline HIV RNA[*] | 75,794 | 137,788 | 0.04 |
| Duration on HAART (months)[*] | 8 | 6 | 0.002 |

**Table 4.** Factors associated with mortality among hospitalized HIV-infected adults at the Jos University Teaching Hospital, Nigeria

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| **Variable** | **OR[*] (95% CI)** | ***p-value*** | **AOR[**] (95% CI)** | ***p-value*** |
| Sex[***] | 2.80 (1.69-4.94) | < 0.001 | 4.67 (2.63-8.29) | < 0.001 |
| CD4 ≤ 200 cells/mm$^3$ | 1.87 (1.08-3.23) | 0.01 | 5.28 (2.99-9.31) | < 0.001 |
| Age > 35 yrs | 2.19 (1.35-3.55) | 0.001 | 2.43 (1.41-4.19) | 0.001 |
| LOS[†] < 3 days | 3.36 (1.18-9.54) | 0.02 | 4.77 (1.35-16.86) | 0.01 |
| HIV RNA > 100,000 c/ml | 1.21 (0.74-1.97) | 0.22 | 1.72 (0.97-3.04) | 0.05 |
| HAART use < 3 months | 3.79 (2.03-7.06) | < 0.001 | 1.17 (0.55-2.48) | 0.68 |

[*]Values are median, [†]Length of stay

HIV-infected persons still carries a significant risk of mortality. Widespread use of prophylactic agents to forestall the occurrence of preventable OIs and increased access to voluntary HIV counseling and testing will improve the outcome in this group of patients.

## References


1. UNAIDS 2007update.data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en. pdf: Accessed 3 April 2008.
2. Sani MU, Mohammed AZ, Adamu B, Yusuf SM, Samaila AA, Borodo MM (2006) AIDS mortality in a tertiary health institution: A four-year review. J Natl Med Assoc 98: 862-866.
3. Kengne AP, Kaze FF, Dzudie A, Awah PK, Ngu KB (2007) HIV/AIDS occurrence in the main University Teaching Hospital in Cameroon. J Int Assoc Physicians AIDS Care 6: 61-65.
4. Buve A (1997) AIDS and hospital bed occupancy: an overview. Trop Med Int Health 2: 136-139.
5. Weber AE, Yip B, O'Shaughnessy MV, Montaner JSG, Hogg RS (2000) Determinants of hospital admission among HIV-positive people in British Columbia. Can Med Assoc J 162: 783-786.
6. Krentz HB, Dean S, Gill MJ (2006) Longitudinal assessment (1995-2003) of hospitalizations of HIV-infected patients within a geographical population in Canada. HIV Med 7: 457-466.
7. Anekthananon T, Ratanasuwan W, Techasathit W, Rongrungrugang Y, Suwanagool S (2004) HIV infection/acquired immunodeficiency syndrome at Siriraj Hospital, 2002: time for secondary prevention. J Med Assoc Thai 87: 173-179.
8. Senya C, Mehta A, Harwell JI, Pugatch D, Flanigan T, Mayer KH (2003) Spectrum of opportunistic infections in hospitalized HIV-infected patients in Phnom Penh, Cambodia. Int J STD AIDS 14: 411-416.
9. Colvin M, Dawood S, Kleinschmidt I, Mullick S, Lallo U (2001) Prevalence of HIV and HIV-related diseases in the adult medical wards of a tertiary hospital in Durban, South Africa. Int J STD AIDS 12: 386-389.
10. Sobhani R, Basavaraj A, Gupta A, Bhave AS, Kadam DB, Sangle SA, Prasad HB, Choi J, Josephs J, Gebo KA, Morde SN, Bollinger RC Jr, Kakrani AL (2007) Mortality and clinical characteristics of hospitalized adult patients with HIV in Pune, India. Indian J Med Res 126: 116-121.

11. Cunningham WE, Tisnado DM, Lui HH, Nakazono TT, Carlisle DM (1999) The effect of hospital experience on mortality among patients hospitalized with acquired immunodeficiency syndrome in California. Am J Med 107: 137-143.
12. The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration and ART Cohort Collaboration (ART-CC) groups (2006) Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. Lancet 367: 817–824.
13. Zachariah R, Fitzgerald M, Massaquoi M, Pasulani O, Arnould L, Makombe S, Harris AD (2006) Risk factors for high early mortality in patients on antiretroviral treatment in a rural district of Malawi. AIDS 20: 2355-2360.
14. Lawn SD, Myer L, Orrell C, Bekker LG, Wood R (2005) Early mortality among adults accessing antiretroviral service in South Africa: implications for programme design. AIDS 40: 336-343.
15. Johannessen A, Naman E, Ngowi BJ, Sandvik L, Matee MI, Aglen HE, Gundersen SG, Bruun JN (2008) Predictors of mortality in HIV-infected patients starting antiretroviral therapy in a rural hospital in Tanzania. BMC Infect Dis 8: 52. doi: 10. 1186/1471-2334-8-52.
16. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R (2008) Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS 22: 1897-1908.
17. Corbett EL, Churchyard GJ, Charalambos S, Samb B, Moloi V, Clayton TC, Grant AD, Murray J, Hayes RJ, De Cock KM (2002) Morbidity and mortality in South African gold miners: impact of untreated disease due to human immunodeficiency virus. Clin Inf Dis 34: 1251-1258.
18. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I, Saha PK (2004) Spectrum of clinical disease in a series of 135 hospitalized HIV-infected patients from north India. BMC Infect Dis 4:52 doi: 10.1186/1471-2334-4-52.
19. Sharifi-Mood B, Alavi-Naini R, Salehi M, Hashemi M, Rakhshani F (2006) Spectrum of clinical disease in a series of hospitalized HIV-infected patients from southeast Iran. Saudi Med J 27: 1362-1366.
20. Anglaret X, Chene G, Attia A, Toure S, Lafont S, Combe P, Manlan K, N'Dri-Yoman T, Salamon R (1999) Early chemoprophylaxis with trimetoprim-sulphametoxazole for HIV-1 infected adults in Abidjan, Cote'd Ivoire: a randomised trial. Cotrimo-CI Study Group. Lancet 353: 1463-1468.
21. Okongo M, Morgan D, Mayanja B, Ross A, Whitworth J (1998) Causes of death in a rural, population-based human immunodeficiency virus type-1 (HIV-1) natural history cohort in Uganda. Int J Epidemiol 27: 698-702.
22. Sherer R, Pulvirenti J, Stieglitz K, Narra J, Jasek J, Green L, Moore B, Shott S, Cohen M (2002) Hospitalizations in HIV in Chicago. J Int Assoc Physicians AIDS Care 1: 26-33.
23. Casalino E, Mendozza-Sass G, Wolff M, Bédos JP, Gaudebout C, Regnier B, Vachon F (1998) Predictors of short- and long-term survival in HIV-infected patients admitted to the ICU. Chest 113: 421-429.
24. Nickas G and Wachter RM (2000) Outcomes of intensive care for patients with human immunodeficiency virus infection. Arch Intern Med 160: 541-547.

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