Mortality & clinical characteristics of hospitalized adult patients with HIV in Pune, India

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Received May 26, 2006

Background & objectives: In India, data regarding mortality and clinical characteristics of hospitalized HIV-infected patients are sparse, which may limit the effectiveness of new hospital-based HIV programmes providing antiretroviral therapy (ART). The objective of our study was to determine mortality and clinical characteristics of hospitalized HIV-infected individuals in a high HIV prevalence region of India.

Methods: A retrospective chart review was done of known HIV-infected adults admitted to the Medical Service of a large, public hospital in Pune, India, from January 2002 to November 2003.

Results: A total of 655 HIV-infected patients were identified; 489 (74.7%) were male and 4 (0.6%) were on ART. The most common illnesses reported were tuberculosis (55.8%), diarrhoea (4.2%), and alcoholic liver disease (3.7%). The inpatient mortality was 172 (26.3%). The most common causes of death of the 172 people were tuberculosis (52.9%) and cryptococcal meningitis (7.6%). In multivariate analysis, factors associated with increased mortality were male sex (adjusted odds ratio (AOR) 1.92, 95% CI: 1.08-3.41), haemoglobin level < 7 g/dl (AOR 2.75, 95% CI:1.23-6.14), length of stay < 2 days (OR 5.78, 95%, CI: 1.82-18.4), and cryptococcal meningitis (OR 4.44, 95% CI:1.19-16.6).

Interpretation & conclusion: In the era prior to widespread ART, a high inpatient mortality of 26 per cent was found among hospitalized HIV-infected individuals. Thus, while hospitalization is an important access and referral point for HIV care and treatment, earlier identification of HIV-infected persons must occur to ensure they will optimally benefit from the government’s ART programme.

Key words HIV/AIDS - inpatient mortality - India - length of hospital stay - mortality - tuberculosis - retrospective study
Previous studies looking at the clinical profile of hospitalized HIV-infected patients in India have shown tuberculosis (both pulmonary and extrapulmonary) and candidiasis to be common opportunistic infections, with smaller numbers of cryptococcal meningitis, *Pneumocystis jiroveci* pneumonia and cerebral toxoplasmosis. There are limited data, however, that describe inpatient mortality, length of stay and causes of death among HIV-infected persons that are hospitalized. Given that hospitals participating in the national antiretroviral therapy (ART) programme will become an important entry point for accessing HIV care and treatment, such data are necessary to better understand the patient population it is intended to benefit.

Quantitative data on the relative impact of HIV among hospitalized patients will be useful in identifying those patients who will benefit most from ART and can alert practitioners and public health planners to co-morbid conditions other than tuberculosis that may impact future HIV treatment. Such information also has important implications for altering current hospital practices and policies, such as improving the diagnostic capacity and drug availability necessary to manage the common opportunistic infections. This is particularly crucial in a resource-limited setting to guide where funds should be allocated to best meet the needs of HIV-infected persons. The purpose of this study was to conduct a retrospective review to assess mortality and the spectrum of HIV-related illnesses among hospitalized HIV-infected adult patients in one of the large, public hospitals that is now participating in the government’s ART roll-out plan.

**Material & Methods**

**Study population:** The study population was HIV-infected persons >18 yr old who were admitted to the medical wards of Sassoon General Hospital (SGH), Pune between January 1, 2002 through November 22, 2003.

**Data collection and analysis:** A retrospective review of patient medical records was conducted using a standard data extraction form. Records were reviewed and the following variables were extracted, when available: age, gender, income, religion, discharge diagnoses, dates of admission and discharge, discharge disposition, haemoglobin (Hb), white blood cell counts (WBC) and total lymphocyte count CD4+ T-lymphocyte counts, HIV-1 viral loads, and usage of ART. Hospital census data were also reviewed in order to determine the percentage of HIV-related admissions during each month of the study period. Institutional Review Board approval was obtained from Johns Hopkins University School of Medicine, USA and the B.J. Medical College, Pune, Ethical Committee.

**Diagnoses:** The majority of diagnoses reported in the charts were defined by the patient’s clinician based upon clinical findings alone, with a few exceptions. The diagnosis of pulmonary tuberculosis (TB) required a compatible clinical syndrome of fever, productive cough and/or hemoptysis, night sweats, and weight loss with suggestive chest X-ray (CXR) findings. Sputum acid-fast bacilli (AFB) smears were routinely sent on all suspected TB patients, yet diagnosis did not require AFB smear positivity. Sputum AFB cultures were not routinely performed due to laboratory constraints and cost. The diagnosis of TB meningitis required a compatible clinical syndrome (i.e., fever, and one or more of the following signs or symptoms of meningitis: headache, altered mental status, stiff neck and/or photophobia, seizures and/or focal deficits), cerebrospinal fluid analysis demonstrating pleocytosis with mononuclear predominance, elevated cerebral spinal fluid (CSF) protein and low CSF glucose, exclusion of bacterial meningitis and a negative India ink. The diagnosis of TB lymphadenitis required either a lymph node biopsy or fine needle aspiration demonstrating caseating granulomas on histopathology and/or a positive AFB smear. The diagnosis of cryptococcal meningitis required a compatible clinical syndrome (i.e., fever, and one or more of the following signs or symptoms of meningitis: headache, altered mental status, stiff neck and/or photophobia, seizures and/or focal deficits), cerebrospinal fluid analysis to rule out other aetiologies, and a positive India ink. The diagnosis of *Pneumocystis jiroveci* pneumonia (PCP) required the compatible clinical syndrome of fever, dyspnoea and nonproductive cough, interstitial infiltrates on CXR, and clinical response to treatment. For the diagnosis of central nervous system toxoplasmosis, a compatible clinical syndrome consisting of headache, seizure, neurologic deficits and/or fever, and positive IgG serology was required. Neuroimaging was not routinely done in all patients with altered mental status, headache or seizure. For most causes of acute diarrhoea, investigation for an aetiologic organism was inconclusive or not available.

Statistical analyses were performed using STATA 8.0 (College Station, TX) to calculate frequencies of demographic information, clinical spectrum of disease, and mortality. Mean length of stay was calculated for
HIV-infected patients who left the hospital alive and for those who died. Logistic regression was used to identify demographic and clinical factors associated with in-hospital mortality. Separate univariate regression analyses were performed to identify variables significantly associated with mortality ($P<0.05$). Possible interactions between pairs of significant variables were tested by combining variables in the logistic regression. Variables reaching statistical significance at the $P<0.20$ level in univariate analyses were included in the final multivariate regressions using stepwise procedures. All reported $P$ values are two-tailed.

**Results**

**Sociodemographic and clinical characteristics:** A total of 655 HIV-infected patients were admitted to the medical wards during the study period, representing 2.6 per cent of the 25,553 total admissions in the hospital or medicine wards. There were 352 known HIV-infected patients admitted in 2002 and 303 patients admitted between January 1 and November 22, 2003 (Table I). Of the 655 patients, 489 (74.7%) were males and 514 (78.5%) were Hindu. The mean age was 35.2 ± 9.0 yr and the mean income was 439 rupees/month (approximately US $10).

Of the 432 (65.9%) patients for whom a WBC was reported on admission, the mean WBC was 8.61 cells/mm$^3$ and the mean total lymphocyte count was 2316 cells/mm$^3$. Of the 346 (52.8%) patients for whom Hb values were available, the mean Hb was 9.72 ± 2.14 g/dl. CD4+ T-lymphocyte counts were available for 27 (4.1%) patients; the median was 66 cells/mm$^3$ (range 4-446 cells/mm$^3$). Two (0.3%) patients had documented HIV-1 viral loads and 4 (0.6%) reported being on ART.

**Reason for hospitalization, length of stay, and discharge status:** There were a total of 172 inpatient deaths (26.3%) among known HIV-infected individuals (Table II). There were no statistically significant differences in the mortality rates by year (24.7% in 2002 vs. 28.1% in 2003). Overall, 379 (57.9%) were discharged to home, 78 (11.9%) left against medical advice, and 26 (4%) were transferred to the local tuberculosis hospital. The mean length of stay for HIV-infected patients was lower for those patients who died versus those HIV-infected patients who left the hospital alive but the difference was not statistically significant.

TB was the most common diagnosis (55.8%); 204 (31.2%) cases were extra-pulmonary and 161 (24.6%) were pulmonary (Table III). Of those with extra-pulmonary TB, the manifestations reported were

### Table I. Characteristics of HIV-infected adults admitted to medicine ward at Sassoon General Hospital (from January 2002-November 2003)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV-infected adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, yr ±SD</td>
<td>35.2 ± 9.0</td>
</tr>
<tr>
<td>Range, yr</td>
<td>18-80</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>489 (74.7)</td>
</tr>
<tr>
<td>Mean income, Rupees/month ± SD (N=390)</td>
<td>439 ± 149.0</td>
</tr>
<tr>
<td>Religion, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hindu</td>
<td>514 (78.5)</td>
</tr>
<tr>
<td>Muslim</td>
<td>21 (3.2)</td>
</tr>
<tr>
<td>Christian</td>
<td>5 (0.76)</td>
</tr>
<tr>
<td>Unknown</td>
<td>115 (17.6)</td>
</tr>
<tr>
<td>Median haemoglobin, g/dl (± SD) (N=346)</td>
<td>9.72 (2.9-15.5)</td>
</tr>
<tr>
<td>Mean total lymphocyte count, cells/mm$^3$ ± SD (N=432)</td>
<td>2316 ± 756.6</td>
</tr>
<tr>
<td>Median CD4 count, cells/mm$^3$ (range) (N=27)</td>
<td>66 (4-446)</td>
</tr>
<tr>
<td>Reported ART, n (%)</td>
<td>4 (0.6)</td>
</tr>
</tbody>
</table>

**Table II. Discharge disposition and length of stay HIV-infected hospitalized patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N=655)</th>
<th>2002 (N=352)</th>
<th>2003 (N=303)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge disposition, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>379 (57.9)</td>
<td>224 (63.6)</td>
<td>155 (51.2)</td>
<td>0.014</td>
</tr>
<tr>
<td>Death</td>
<td>172 (26.3)</td>
<td>87 (24.7)</td>
<td>85 (28.1)</td>
<td>0.324</td>
</tr>
<tr>
<td>AMA</td>
<td>78 (11.9)</td>
<td>32 (9.1)</td>
<td>46 (15.2)</td>
<td>0.016</td>
</tr>
<tr>
<td>Transferred</td>
<td>26 (4.0)</td>
<td>9 (2.6)</td>
<td>17 (5.6)</td>
<td>0.050</td>
</tr>
<tr>
<td>Length of stay, (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV patients alive at discharge</td>
<td>6.59 ± 6.84</td>
<td>7.13 ± 8.22</td>
<td>5.94 ± 4.56</td>
<td>0.025</td>
</tr>
<tr>
<td>HIV patients who died</td>
<td>5.23 ± 7.75</td>
<td>4.62 ± 8.38</td>
<td>5.85 ± 7.04</td>
<td>0.044</td>
</tr>
</tbody>
</table>

**AMA, against medical advice**
meningitis 78 (38.2%), disseminated 44 (21.6%), abdominal 33 (16.2%), lymphadenitis 31 (15.2%), tuberculoma 11 (5.4%), and pericardial disease (3.4%). Other common reasons for admission were diarrhoeal diseases (4.2%), alcoholic liver disease (3.7%), cryptococcal meningitis (3.1%), cerebrovascular accident (3.1%), cardiac disease (2.3%), and bacterial pneumonia (2.3%).

TB accounted for 91 (52.9%) of inpatient deaths (33.7% were extra-pulmonary and 19.2% were pulmonary) (Table III). Other common causes of death were cryptococcal meningitis (7.6%), aspiration pneumonia (7.0%), and non-alcoholic liver disease (3.5%). Alcoholic liver disease, renal disease and cardiovascular disorders each accounted for 2.9 per cent of deaths.

Factors associated with inpatient mortality: In univariate analysis, factors associated with increased inpatient mortality were Hb level < 7 g/dl (odds ratio (OR) 3.13, 95% CI: 1.45-6.75, \( P = 0.004 \)), length of stay < 2 days (OR 5.99, 95% CI: 3.76-9.55, \( P < 0.0001 \)), and cryptococcal meningitis (OR 5.56, 95% CI: 2.18-14.2, \( P < 0.0001 \)) (Table IV). In multivariate regression, these factors all remained significant. In addition, male sex was associated with increased risk of inpatient mortality (adjusted OR 1.92, 95% CI: 1.08-3.41).

During the study period, there was an average of 1162 admissions/month to the medical wards, with the proportion of known HIV-related admissions ranging from 1.49 to 3.81 per cent. No clear monthly, seasonal or yearly trend in HIV-related admissions was observed. Hospital census reports from 2002 were available for review and showed 44,329 total admissions, 3436 (7.8%) deaths, and a mean length of stay of 7.4 days. Septicaemia, meningitis and pneumonia carried the highest inpatient mortality rates for patients admitted to the Medicine Service, with death rates of 94.3, 50.3, and 34.9 per cent, respectively. HIV/AIDS was the 13th most common reason for admission and, with a mortality of 24.7 per cent, was the 6th most common cause of death for patients admitted to the Medicine Service in 2002.

Discussion

This study demonstrates important clinical and epidemiologic findings regarding hospitalized HIV infected individuals at a large, urban government hospital in western India. The overall percentage of hospital admissions to the medicine wards due to known cases of HIV was low. Nevertheless, among known HIV-infected individuals who were hospitalized, the inpatient...
mortality was significantly higher than rates observed in the United States pre-HAART era (6-12%)\(^3,4\), but comparable to inpatient mortality rates observed in other resource-limited countries (15-44%)\(^5,9\). HIV-related admissions represented the 13\(^{th}\) most common diagnosis on the medicine wards and the 6\(^{th}\) most common cause of death in 2002. The mean length of stay for HIV-infected patients who died, was slightly lower than for those patients who were alive at discharge. This suggests that patients who died during hospitalization were more likely to present with poor functional status and more advanced and severe disease, leading to death early in their hospital course.

Like prior studies in India, this study demonstrated that the majority of hospitalized patients were male, with a 3:1 male-to-female ratio\(^10,11\). Most of these patients were young, with a mean age of 35.2 yr and came from a low socio-economic background. The male predominance may represent the natural history of HIV in India given that the first cases of HIV were reported in a limited number of commercial sex workers who likely infected a larger pool of men\(^12\). Therefore, men would be expected to reflect the first wave of individuals to show signs of advanced disease and require hospitalization. Male gender was also independently associated with increased mortality. This finding may be due to the fact that men have been infected longer than women, are presenting with lower CD4+ T-lymphocyte counts at admission, and thus at increased risk for a poor outcome. Gender-specific differences in hospital admissions could represent disparities in access to and use of health care facilities between males and females. Women with HIV are a vulnerable group that may have less access to health care and thus less access to ART\(^13,14\).

Despite the limited diagnostic capabilities, important co-morbid conditions observed can impact future HIV treatment success. Tuberculosis was the most common inpatient diagnosis and the most common cause of death, with extra-pulmonary cases outnumbering pulmonary. Previous studies in India have shown an HIV seroprevalence between 3-20 per cent in patients with known tuberculosis\(^9,16-18,23,24\) and TB accounts for more than 50 per cent of deaths among HIV-infected persons in India\(^9\). Given the high rates of TB-HIV co-infection and the significant morbidity and mortality associated with it, effective HIV treatment measures will need to improve early TB detection and management. A lower burden of other opportunistic infections, such as cryptococcal meningitis and PCP were seen; although cryptococcal meningitis did represent the second leading cause of death. Diarrhoeal disease was the second most common discharge diagnosis made, however, the exact aetiologic agent was often unknown.

Interestingly, alcoholic liver disease was a common discharge diagnosis for HIV-infected individuals. The prevalence of alcohol abuse in rural communities in India ranges from 36.1 per cent for males and 13.4 per cent for females\(^20,21\). A prospective study of HIV-infected patients in Mumbai showed 45 per cent to be chronic alcoholics on the basis of a history of consumption of at least 80g of alcohol daily for at least 5 yr\(^22\). The existence of alcohol abuse in the setting of HIV deserves special attention given its potential to decrease HIV treatment adherence, weaken the nutritional status of the individual, and increase the risk of adverse events from antituberculosis therapy and ART\(^23,24\). This is particularly important for India given that hepatotoxic drugs, such as nevirapine, are considered as part of first-line ART regimens.

Not surprisingly, the majority of patients were not on ART, nor did they have documented HIV RNA or CD4+ T-lymphocyte counts. There are many potential explanations for this observation including lack of patient awareness of treatment options, difficulties in accessing care, and cost. A hospital-based intervention that increased patient education and awareness prior to discharge could considerably improve future health-seeking behaviours.

In conclusion, our findings showed that the majority of HIV-infected individuals who were hospitalized presented with advanced disease, co-infection with TB, and had a high in-hospital mortality rate. Factors associated with increased mortality, such as tuberculosis, anaemia and cryptococcal meningitis, represent treatable co-morbid conditions, provided that they are detected early and managed promptly. Other factors, such as concomitant alcohol abuse, may negatively impact HIV treatment efforts and thereby, warrant further investigation to clarify the magnitude of the problem.

Acknowledgment

This project was supported by the Fogarty AIDS International Training and Research Program (AITRP) of the National Institutes of Health (NIH) grant 2 D43 TW00010 and the National Institute of Health (NIH) grant 1R01- AI 45462 to Robert C. Bollinger.
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