Outcomes and factors influencing outcomes of critically ill HIV-positive patients in a tertiary care center in South India

I. Ramya[1], Shubankar Mitra[2], Shilpa D'Sa[3], Sowmya Sathyendra[1], Anand Zachariah[1], C. Vignesh Kumar[1], Ronald Albert Benton Carey[2], George M. Verghese[4]

Departments of [1]Medicine, [2]Accident and Emergency Medicine, [3]Infectious Diseases, and [4]Critical Care, Christian Medical College, Vellore, Tamil Nadu, India

Abstract

The incidence of (Human immune deficiency) HIV in India has fallen by 58% since the onset of the HIV epidemic. As of 2016 there are 2.1 million people living in India with HIV and only 49% of the adults with HIV are on ART (1). The HIV infected individuals may require intensive care due to various reasons. This study attempts to look at the outcomes of these patients admitted in the intensive care unit and the predictors of these outcomes. **Aims:** 1. To assess the outcomes of critically ill HIV infected patients admitted in the medical intensive care unit. 2. Assessment of the factors that are likely to influence the outcome. **Materials and Methods:** it is a retrospective medical review of all the patient records available on our electronic database. The study period was January 2008 – October 2013. **Results:** in our study cohort the commonest reason for admission into the intensive care unit was sepsis associated with multi organ dysfunction (64%).A low CD 4 count, renal failure acute respiratory distress syndrome, and hypotension and multi organ dysfunction were predictive of a poor outcome in our study. **Conclusion:** The most common cause of admission of PLHIV in ours study cohort was Infections, ART associated side effects and low CD4 counts, presence of multi organ dysfunction, acute respiratory distress syndrome (ARDS), hypotension were associated with adverse outcomes.

Keywords: HIV-positive patients, intensive care, mortality outcomes

Introduction

India is one of the countries that have been severely affected by the human immunodeficiency virus (HIV) epidemic. Despite having a HIV prevalence of only 0.3%, due to its large population India has the third highest number of people living with human immunodeficiency virus (PLHIV) in the world. As per the million deaths study, an estimated 1.4–1.6 million people are living with HIV/AIDS in India.[1,2]

Under the aegis of the National AIDS control organization, highly active anti-retroviral therapy (HAART) is available free in anti-retroviral (ART) clinics throughout India. Due to relentless efforts, AIDS-related deaths were reduced by 54% between 2007 and 2015. But uptake in ART clinics is still low and ART coverage in the country is 49%.

Before the advent of HAART, the outlook for patients infected with HIV was poor; studies from the United Kingdom during the 1980s showed a mortality of 72% in immunodeficiency patients admitted to intensive care units (ICUs).[3] Recent studies have

Address for correspondence: Dr. I. Ramya,
Department of Medicine, Christian Medical College,
Vellore - 632 004, Tamil Nadu, India.
E-mail: iramya@cmcvellore.ac.in

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shown that mortality has fallen to 33% in seropositive patients admitted to ICU in the United Kingdom.[4] This is similar to outcomes in non-HIV-infected patients.

Recent studies have shown that mortality due to HIV has continued to decrease and the case mix of patients admitted to the ICU with HIV/AIDS has also changed. Recent studies have shown that sepsis is the most common cause of admission into ICU. In this observational study, we aimed at assessing the outcome of critically ill HIV-infected patients.

Materials and Methods

Christian Medical College, Vellore, is a 2999-bedded tertiary care referral teaching center of south India. It has 24 medical intensive care unit (MICU) and medical high dependency unit (MHDU) beds for medical cases. We conducted this retrospective observational study at MICU and MHDU of Christian Medical College, Vellore. Under the department of general medicine, we provide both inpatient and outpatient care for PLHIV. In this study, we enrolled all PLHIV admitted in MICU and MHDU between January 2008 and October 2013 (71 months). After obtaining consent from the admitting units, data on demographic details, Acute Physiology and Chronic Health Evaluation (APACHE)-II score at admission, clinical features, medication history, and laboratory results were accessed from the computerized hospital information processing electronic database. The patients were followed up until death or discharge to collect data on duration of hospital stay and organ systems supported.

Data analysis

Statistical analysis was performed using SPSS software (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. SPSS Inc., Chicago). Continuous data are given as mean [standard deviation (SD)] or as median (range). Chi-square test or Fisher's exact test was used to compare dichotomous variables and *t*-test or Mann–Whitney test was used for continuous variables as appropriate. The differences between the two groups were analyzed by univariate analysis, and their 95% confidence intervals were calculated. For all tests, a two-sided *P* - value of 0.05 or less was considered statistically significant. Institutional Review Board/Ethics committee approval was obtained before the study.

Results

Between January 2008 and October 2013 (71 months), a total of 50 critically ill patients with HIV infection were admitted in MICU and MHDU. The commonest indication for admission into critical care unit was infectious complications (32, 64%) followed by drug-related adverse side effects (6, 12%) as shown in Table 1. The mean age of the enrolled cases was 40.1 years (SD 10.3 years) and 39 (78%) were male. CD_4 T-cell count was estimated among 30 cases, and the median was 44.5 cells/μL (interquartile range = 32.3–175.3).

Table 1: Diagnoses of patients admitted to intensive care units

Illnesses	Number (%)
Infections	33/50 (66)
Drug-related side effects	6/50 (12)
DSH	4/50 (8)
Malignancy (non-Hodgkin's lymphoma)	3/50 (6)
Vascular complications	1/50 (2)
Others	3/50 (6)

DSH: Deliberate self-harm

Of 50 PLHIV admitted, 35 patients expired and 15 were alive. We attempted to compare various clinical and laboratory features of the two groups to identify the correlation between these features and the outcome.

A total of 27 (77.1%) were male among the expired group and 12 (80%) among the alive group (*P* = 0.82). The mean age of the patients in the expired group was 41.1 ± 1.8 years while that of the alive group was 37.6 ± 2.5 years [95% confidence interval (CI) −2.9 to 9.9]. In all, 22 (62.9%) patients among the expired group and 9 (60%) among alive group were on HAART (*P* < 0.85). The mean CD_4 T-cell count among the expired group was 58.6 ± 64.8 cells/μL while that among the alive group was 198.8 ± 157.3 cells/μL (95% CI −224.8 to −55.6).

The mean APACHE-II score at the time of admission between the expired group was 11.7 ± 10.1 and 10.9 ± 10.0 among those alive (95% CI: −5.5 to −7). Totally 24 (68.6%) of the expired patients had adult respiratory distress syndrome (ARDS) while only 3 (20%) of the alive patients had ARDS (*P* < 0.02).

The mean serum albumin among the expired group was 3.0 ± 0.9 mg/dL while it was 3.0 ± 1.2 among the alive group (95% CI: −0.6 to 0.61). Nineteen (54.3%) patients among the expired group had serum creatinine more than 1.5 mg/dL at admission and two (13.3%) among alive group was elevated creatinine level (*P* < 0.007). Nineteen (54.3%) among the expired group had multiorgan dysfunction syndrome (MODS) when compared with three (20%) among the alive group of PLHIV (*P* < 0.02). The observed rate of hypotension requiring vasoactive support was 9 (25.7%) among the expired group which was lower when compared with 13 (86.7%) among those were alive (*P* < 0.001) [Table 2].

Predictors of outcomes

In univariate analysis, the factors predicting poor outcome were presence of acute respiratory syndrome, hypotension, ARDS, and renal failure.

Discussion

Introduction of ART therapy has led to increased life expectancy in PLHIV. This is due to the reduction in the rates of opportunistic infections. But despite this, patients with HIV

are at high risk of mortality compared with non-HIV patients with similar comorbidities.[5,6]

Prior to free availability of ART, among physicians there was a perception that intensive care for patients with HIV is generally futile.[7] The mortality rate among patients with HIV treated in ICU prior to HAART was 70%.[8,9]

Recent studies have shown sepsis is the reason for admission into ICU in 12%–31% of patients with HIV, and these patients with sepsis have a worse outcome compared with non-HIV patients with sepsis.[10]

The reason for admission into ICU in our cohort was due to HIV-related illnesses directly such as sepsis, AIDS-related malignancies, and vascular complications (90%) of the patients, or indirectly drug complications and deliberate self-harm (DSH) due to depression (10%). Hence, all admission for PLHIV in our study cohort was due to HIV-related illnesses despite 62% of patients being on HAART.

In our cohort, admission to ICU due to sepsis was seen in 10 (20%) patients [methicillin-resistant *Staphylococcus aureus* in 2 (4%), Gram-negative sepsis in 3 (6%), and 1 patient each had disseminated cytomegalovirus infection, scrub typhus, atypical mycobacteremia, methicillin-sensitive *Staphylococcus aureus*, and septic abortion].

In nonimmunocompromised patients, predictors of poor outcomes in patients with sepsis include hypotension, altered mentation, elevated blood urea nitrogen, and need for supplemental oxygen.[11] This is similar to our cohort of PLHIV with sepsis.

The study by Amâncio *et al.* has shown that presence of shock in patients with HIV with sepsis is a predictor of poor outcome; other predictor of poor outcome in their study was mechanical ventilation. In our study, the predictor of poor outcome in sepsis was septic shock presence of renal failure.[12,13]

Severe sepsis has been shown to be the single most important factor in determining the outcome of PLHIV admitted to ICU; this was seen in our cohort also where patients with severe sepsis with hypotension, renal failure, ARDS, and or MODS were associated with higher odds of mortality – 16, 7.9, 10, and 5.3, respectively[13] [Table 3]. PLHIV with sepsis have a poorer prognosis due to delay in diagnosis and prompt treatment, and altered pattern of immune response due to immune dysregulation associated with chronic HIV infection.[12,14]

Studies from various parts of the world have shown that the use of HAART among PLHIV is between 24% and 50% prior to admission into ICU, and in our cohort it was 62%. Similar to previous studies, there was no significant reduction in mortality among patients on HAART admitted to ICU when compared with patients not on HAART [Table 3].[7]

Subsequent studies have shown that usage of HAART does not impact the outcome in these patients.[7,15-18] This is similar to the results in our cohort too.

The introduction of ART has changed the spectrum of patients admitted to ICU. In countries with high coverage of ART, patients admitted with non-AIDS diagnosis[16] unlike our cohort.

Studies have shown that prevalence of depression among PLHIV ranges from 20% to 69%. Depression is associated with poorer quality of life among PLHIV, poor adherence to ART, low CD4 counts, increased viral load, and mortality.[19] Chronic HIV infection has been shown as an independent risk factor for depression and DSH.[20] In our cohort, there were four patients who were admitted to ICU with DSH which was most probably due to severe depression; all the patients' survived

Table 2: Predictors of poor outcomes

Descriptive statistics					
	n	Range	Minimum	Maximum	Mean±SD
CD4	30	471	5	476	114.63±129.352
Age	50	40	22	62	40.08±10.351
Gender (male:female)	50	39:11	NA	NA	NA
Albumin	50	6.20	0.00	6.20	3.0460±1.02643
Length of stay	50	24	1	25	9.82±6.766

NA: Not available; SD: Standard deviation

Table 3: Baseline characteristics and their association with outcomes

Baseline characteristics	Expired (SD)	Alive (SD)	*P* (CI)	Likelihood ratio
Age (years) (mean±SD)	41.14±10.5	37.6±9.6	0.27 (−2.9 to+9.9)	Not significant
CD4 (mean)	58.56 (±64)	198.75 (±167)	0.06 (−0.61 to−0.67)	40
On HAART (total=31)	22	9	0.84	Not significant
MODS (total number)	19	3	0.02	5.3
ARDS (total number)	24	3	0.002	10
Renal failure (total number)	19	2	0.005	7.9
Serum albumin	3.03 (±0.9)	3.06 (±1.2)	0.09	Not significant
Duration of hospital stay	7±7.4	13±5.9	0.52	Not significant
APACHE (mean)	11.66 (±10.1)	10.88 (±10)	0.81 (−5.5 to−7)	Not significant
Septic shock	13	9	0.0001	16

SD: Standard deviation; CI: Confidence interval; HAART: Highly active anti-retroviral therapy; MODS: Multiorgan dysfunction syndrome; ARDS: Acute respiratory distress syndrome; APACHE: Acute Physiology and Chronic Health Evaluation

hospitalization, but ICU admissions are associated with high costs and may lead to severe economic burden in these group of patients.

Fifteen patients (30%) survived ICU admission; these patients had higher CD4 count and single-organ involvement with fewer incidences of hypotension renal or pulmonary involvement. Improving HAART coverage and careful selection of patients for ICU care may lead to better ICU outcomes.

HAART-related complications observed in our group were stavudine-induced lactic acidosis in four (8%) patients and zidovudine-induced anemia with cardiac failure and stavudine-induced pancreatitis (1 patient each). These drugs continue to be first-line agents for government-sponsored ART in our country.[21] Studies have shown that zidovudine- and stavudine-based HAART are associated with severe side effects and discontinuation of medications when compared with tenofovir-based regimen.[22]

How can primary care physicians improve the outcome of people living with human immunodeficiency virus admitted to the intensive care units?

Disseminated tuberculosis (9, 18%) and pnuemocyctis jiroveci pneumonia (6, 12%) were the most common infectious causes for admission of PLHIV to ICU. Hence, early detection of tuberculosis using the RNTCP guidelines may lead to better outcomes. In addition, initiation of cotrimoxazole double-strength tablet by primary care physicians once a day in all patients who have a CD4 $<250/mm^3$ will lead to reduction in PCP infections and hence ICU admission.

Sepsis was the main reason for admission into ICU among our patients. Early recognition and intervention has shown to reduce mortality.[23] Early recognition of sepsis in patients with HIV and timely referral may improve prognosis in patients with HIV with sepsis.

Depression resulting in DSH was the reason for admission in three (6%) of the patients. Empathy, emotional support, and counseling about availability of effective drugs and ensuring compliance to medications in primary care may prevent DSH and reduce admissions due to it.[24]

Conclusion

The most common cause of admission of PLHIV in our study cohort was infections; low CD4 counts, presence of multiorgan dysfunction, ARDS, and hypotension were associated with adverse outcomes. Absence of these risk factors may predict better outcomes in PLHIV admitted to ICU.

Limitations

Since this was a retrospective cohort, complete details of duration of HAART, compliance of patients with HAART, and type of medications the patients were taking were not available.

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