Barnes et al. J Infect Dis Epidemiol 2016, 2:019
Volume 2 | Issue 3
ISSN: 2474-3658

Journal of
Infectious Diseases and Epidemiology

Original Research Article: Open Access

Antiretroviral Therapy Utilization in the Intensive Care Unit

Mia N Barnes[1], Monika N Daftary[2], Mary K Maneno[2,3] and Faria F Farhat[4]*

[1]PGY-1 Pharmacy Practice Resident, Howard University Hospital, USA
[2]Department of Clinical and Administrative Sciences, Howard University College of Pharmacy, USA
[3]Center for Minority Health Services Research, Howard University, USA
[4]Division of Infectious Diseases, Howard University College of Medicine, Howard University Hospital, USA

***Corresponding author:** *Mia N Barnes, PharmD, PGY-1 Pharmacy Practice Resident, Howard University Hospital, 2300 4th street NW, Washington, DC 20059, USA, Tel: 571-239-3949, Fax: 202-865-4478, E-mail: mianrowe@gmail.com*

Abstract

Background: Although clinical advances have been demonstrated through the use of antiretroviral therapy (ART), the management of an HIV infected patient within the intensive care unit (ICU) has been a topic of controversy due to the lack of evidence-based clinical guidelines to assist in the management of HIV patients admitted to the intensive care unit. The objective of this study was to examine ART utilization in the medical ICU and to assess relationships between therapy, clinical characteristics and mortality.

Setting: The medical ICU of a tertiary-care urban teaching hospital.

Methods: To assess the relationship between ART a retrospective study of HIV infected patients aged 18 and older admitted to the ICU was conducted between the dates of January 1, 2007 to August 31, 2012. Antiretroviral therapy was examined by ART therapy use prior to ICU admission and ART use during ICU admission which included discontinuation of ART during ICU admit, initiation of ART during ICU admit, continuation of ART during admit, and no ART use during ICU admit.

Results: There were 238 patients included within this study. Overall there were 121 (53.8%) patients who were not on ART prior to admission. Findings related to ART utilization during the ICU stay showed that 45 (18.9%) of patients had ART discontinued, 54 (22.7%) had ART continued, 10 (4.2%) had ART initiated and 129 (54.2%) had no documented ART utilization. A higher percentage of patients who were not on ART prior to admission survived compared to those who received ART prior to admission (54.6% vs. 45.4%); however, this relationship was not statistically significant ($p = 0.596$).

Conclusions: The management of HIV infected patient within the ICU needs to be based on an individualized approach; however more studies, particularly prospective studies, are needed to assist in the development of clinical guidelines.

Keywords

HIV infection, AIDS, Antiretroviral therapy, ICU

Introduction

The introduction of combination antiretroviral therapy (cART), previously known as highly active antiretroviral therapy (HAART), has not only reduced the incidence of illnesses associated with Acquired Immune Deficiency Syndrome (AIDS) but also increased the life expectancy of many infected with Human Immunodeficiency Virus (HIV) [1]. Furthermore, hospitalization of HIV infected patients due to various HIV related conditions have also certainly decreased over the years due to the initiation of antiretroviral therapy. However, admission to the intensive care unit (ICU) has remained relatively constant [2,3]. As individuals living with HIV continue to live longer, clinicians are now also faced with non-infection related complications and other co-morbid conditions that previously were not seen in the HIV or AIDS patients [2].

Although there have been numerous clinical advances that have resulted from the use of ART, the management of an HIV infected patient within the ICU setting has remained a topic of controversy. Currently, there is a lack of evidence-based clinical guidelines to assist in the management of HIV patients admitted to the ICU. As a result utilization of ART within the ICU setting may pose a variety of challenges for clinicians. Determining appropriate doses, dose adjustments, drug interactions, and antiretroviral-associated toxic effects are just a few of the factors that must be taken into consideration when treating these already complex patients in the ICU setting [1,3].

The impact of ART utilization on survival outcomes in the ICU is also a topic requiring further research. Several markers have been identified as prognostic factors of ICU mortality for HIV infected patients; such as high Acute Physiology and Chronic Health Evaluation (APACHE) II score, respiratory failure, mechanical ventilation, low serum albumin, and *Pneumocystis jiroveci* pneumonia (PJP); however, no definitive relationship has been demonstrated between ART and ICU mortality [4,5]. The varying conclusions of these studies and many others has made it difficult to truly define whether ART utilization impacts mortality outcomes of HIV patients within the ICU [2,3,6].

Based upon a review of the literature, there are few studies that have documented differences in ART utilization in the ICU based upon discontinuation, continuation and initiation of therapy. Therefore, due to the limited amount of data available clinicians are left with inadequate guidance to formulate treatment decisions of these often extremely complex patients. The objective of this study was to examine ART utilization in the ICU from a sample of US patients and to assess relationships between therapy, clinical characteristics and mortality.

ClinMed International Library

Citation: Barnes MN, Daftary MN, Maneno MK, Farhat FF (2016) Antiretroviral Therapy Utilization in the Intensive Care Unit. J Infect Dis Epidemiol 2:019

Received: June 24, 2016: **Accepted:** November 10, 2016: **Published:** November 14, 2016

Table 1: Characteristics of HIV patients admitted to ICU.

	Total N = 238
Age-mean years ± SD)	48.61 ± 12.6
APACHE II score, mean score ± SD	16.75 ± 8.9
Length of stay in ICU, median (IR)	3 (5)
CD4, Median (IR)	127 (290)
Gender, N (%)	
Male	127 (53.4)
Female	111 (46.6)
Race, N (%)	
AA	222 (93.3)
Caucasian	7 (2.9)
Hispanic	5 (2.1)
African	4 (1.7)
HIV RNA, N (%)	
< 400 copies/mL	21 (42.0)
401 -100,000	10 (20.0)
> 100,000	19 (38.0)
No value reported	188 (79.0)
ART prior to admit, N (%)	
Yes	104 (46.2)
No	121 (53.8)
ART status during admit, N (%)	
ART discontinued	45 (18.9)
ART initiated	10 (4.2)
ART continued	54 (22.7)
No ART Use	129 (54.2)
ICU admission diagnosis, N (%)	
Altered mental status	23 (9.7)
Respiratory related	77 (32.4)
Gastrointestinal	18 (7.6)
Sepsis/Shock	26 (10.9)
Cardiovascular related	24 (10.1)
Other	43 (18.1)
Pneumonia	6 (2.5)
Metabolic disturbance	13 (5.5)
Liver failure	4 (1.7)
Renal failure	4 (1.7)
AIDS defining illness, N (%)	
Yes	52 (26.4)
No	145 (73.6)
Co-morbidities, N (% yes)	
Psychiatric disorders	37 (15.5)
Cardiovascular disorder	101 (42.6)
Hepatic disorder	71 (30.0)
Renal disorder	65 (27.4)
Respiratory disorder	43 (18.1)
Neurological disorder	21 (8.9)
Endocrine disorder	44 (18.6)
Substance abuse	78 (32.9)
Mechanical ventilation, N (%)	
Yes	87 (32.9)
No	150 (67.1)

Methods

Study design and study population

A cross-sectional study conducted via retrospective chart review of paper medical records was completed for all HIV infected patients admitted to the medical ICU (MICU) of a level 1 tertiary care teaching hospital. Inclusion criteria for the study was any HIV infected patient aged 18 and over who was admitted to the MICU from January 1, 2007 to August 31, 2012. Patients were excluded if they were under 18-years-old. If a patient had multiple MICU admissions, only the first admission was included within the study population. To identify hospitalized HIV infected patients a computerized search of admissions using International Classification of Diseases (ICD), diagnostic code 042 for HIV, was conducted. From this initial search, a subset of HIV infected patients admitted to the MICU was captured. This study was approved by the Institutional Review Board of Howard University.

Epidemiological data of study population

The World Health Organization defines generalized epidemics as areas in which HIV is over one percent in the general population. According to the Annual Epidemiology and Surveillance Report for the District of Columbia, in the year 2011, 15, 056 residents or 2.4% of the population was living with HIV [7]. Blacks, Hispanics, and whites with HIV exceed 1% of their respective populations, with blacks disproportionately impacted at 3.7% [7]. However, the number of deaths among persons with HIV decreased by 41% from 425 in 2007 to 251 in 2011 [7].

Data collection

General data collection included patient's demographic and clinical characteristics. The clinical characteristics of interest collected were CD4 count, HIV viral load, ART utilization (prior ART use, discontinuation of ART during ICU admit, initiation of ART during ICU admit, continuation of ART during admit, and no ART use during ICU stay), ICU admission diagnosis, co-morbid conditions, APACHE II score, mechanical ventilation, AIDS defining illness and length of ICU stay. The type of ART regimen used was also recorded. A uniform data collection form was utilized to collect patient information from medical records. Howard University Hospital's laboratory database was also utilized to retrieve any additional information that may have been missing from the patient's chart. Additionally, survival was recorded at the time of hospital discharge.

Statistical analysis

Descriptive statistics including means and frequency distributions were estimated for continuous and categorical variables respectively. Chi square tests were utilized for categorical variables and Independent T-tests, Mann Whitney U, and Kruskal Wallis tests were conducted for continuous variables. To determine predictive factors associated with mortality in the ICU, unadjusted and adjusted logistic regression analyses were conducted. All analyses were conducted using SPSS version 19 at an alpha value of 0.05.

Results

Demographic and clinical characteristics

There were a total of 2838 hospital admissions of HIV infected patients from January 1, 2007 to August 31, 2012. Of these admissions, 238 HIV infected patients were admitted to the medical ICU and met the study inclusion criteria. The socio-demographic and clinical characteristics of the patients are described in table 1. As shown, 53.4% of the study population were men, 93.3% of them were African American, with a mean age of 48.6 (SD = 12.6). Within the total population, 52 (26.4%) patients presented or diagnosed with an AIDS defining illness within the ICU; 44.2% (n = 23) of those diagnoses were attributed to PJP. The median CD4 count was 127 (IQR = 29), the mean APACHE II score was 16.7 (SD = 8.9) and the median length of stay was 3.0 (IQR = 5.0) days. Mechanical ventilation was required for 87 (36.7%) individuals during ICU admission. The most common reason for ICU admission was respiratory related causes (32.4%). Common co-morbid conditions at admission were cardiovascular (42.6%), hepatic (30.0%), and renal disorders (27.4%) (Table 1).

ART utilization prior to admission

Overall there were 121 (53.8%) patients who were not on any ART prior to admission and 104 (46.2%) who were receiving ART prior to ICU admission. The most common regimen utilized prior to ICU admission was two nucleoside/nucleotide reverse transcriptase inhibitors and one protease inhibitor (Table 2).

As shown in table 3, those who were not receiving ART prior to admission were more likely to present with an AIDS defining illness

(70.0% vs. 30.0%; p = 0.02) and were also less likely to be on ART prior to admission (OR = 0.341 (0.171-0.680)). Differences in CD4 count were also found based on prior ART utilization; specifically, those with prior ART and those without had median CD4 count of 179 and 43, respectively (p = 0.02).

ART utilization during the ICU stay

Results related to ART utilization during the ICU stay showed that 18.9% (45/238) had ART discontinued, 4.2% (10/238) had ART initiated, 22.7% (54/238) had ART continued, and 54.2% (129/238) had no ART use throughout the ICU admission. Differences in ART utilization in the ICU were found based on AIDS defining diagnoses (p = 0.006). Further exploration indicated that patients with AIDS defining illnesses were less likely to have ART discontinued compared to those without AIDS defining illness (OR = 0.35 (95% CI 0.13-0.94); p = 0.032). However, no relationship was found between AIDS defining illness and continuation or discontinuation of ART in the ICU. Those with AIDS defining illnesses were more likely to have no ART (OR = 2.53 (1.30-4.90)). Differences in ART utilization in the ICU were found based on median CD4 counts (ART discontinued = 181; ART initiated = 10; ART continued = 201; No ART = 45; p = 0.000).

Table 2: ART regimens utilized by HIV infected patients admitted to MICU.

ARV regimen N (%)	Total number of patients (N = 67)
2 NRTI + NNRTI	19 (28.4)
2 NRTI + PI	30 (44.8)
2 NRTI + Integrase Inhibitor	4 (6.0)
3 NRTIs	2 (3.0)
4 or more ARV agents (not including RTV)	10 (14.9)
Other*	2 (3.0)

NRTI: Nucleoside Reverse Transcriptase Inhibitor; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; PI: Protease Inhibitor, RTV: Ritonavir.

**Regimens considered inadequate or did not fall in any other standard category.*

ART utilization and mortality in the ICU

Overall there were 50 HIV patients (21.3%) who died in the ICU and 185 HIV patients who survived (78.7%). Three persons were excluded due to missing survival information from discharge records and possibly were discharged Against Medical Advice (AMA), these individuals were not included in the analysis. Study findings show that a higher proportion of patients who were not on ART prior to admission survived compared to those who received ART prior to admission (54.6% vs. 45.4%); however, this relationship was not statistically significant (p = 0.596). In the ICU, the proportion of patients who survived and had ART discontinued, initiated, continued or had no ART use were 17.8%, 4.3%, 24.9% and 53.0%. Among those patients who died 58% had no ART use during their ICU stay. There was no association between survival and ART utilization during their ICU stay (p = 0.386). This study did not collect cause of death information in this study; however, we did collect data on any AIDS defining diagnosis at admission. We did explore the possibility of the relationship between ART use and survival being confounded by whether a patient having any AIDS-defining diagnosis at admission by looking at the percentage difference between the crude and adjusted OR as a measure of effect and confounding was observed; however the effect of ART still did not reach statistical significance (Figure 1).

Discussion

Presently, current guidelines recommend initiation of ART in HIV-infected patients regardless of CD4 count [8]. This recommendation to initiate ART is centered on mounting evidence that HIV infection left untreated and/or uncontrolled viremia is associated with development of non-AIDS-defining diseases, including cardiovascular disease, kidney disease, liver disease, neurologic complications, and malignancies [8]. Although this is an update to preceding practice guidelines, the previous recommendations included initiation of therapy for any patient whose CD4 is less than 350 cell/L [8]. Despite low CD4 counts (median = 43 cells/L) and

Table 3: ART use by clinical characteristics.

	ART use prior to ICU admission			ART use during ICU stay				
	Yes N = 104	No N = 121	p-value	ARV discontinued N = 45	ARV initiated N = 10	ART continued N = 54	No ART Use[a] N = 129	p-value
CD4 (Median (IR[b]))	179.0 (348)	43 (254)	0.000	181 (844)	10 (417)	201 (538)	45 (763)	< 0.05
Length of stay (Median (IR)	3.0 (6.0)	3.0 (65.0)	0.140	3.0 (6.0)	3.50 (35.0)	3.0 (6.0)	3.0 (5.0)	0.561
APACHE II score (Mean ± SD)	16.9 ± 9	15.3 ± 11	0.210	19 ± 9.3	14.4 ± 4.8	15.0 ± 6.9	16.6 ± 9.4	0.206
AIDS defining diagnosis (%)								
Yes	30.0	70.0	0.02	9.6	7.7	15.4	67.3	0.006
No	55.7	47.3		23.4	2.8	29.0	44.8	
Co-morbidities (%Yes)								
Psychiatric disorders	40.0	60.0	0.439	10.8	0.0	24.3	64.9	0.222
Cardiovascular disorder	51.5	48.5	0.139	21.8	3.0	27.7	47.5	0.201
Hepatic disorders	48.5	51.5	0.627	22.5	4.2	23.9	49.3	0.765
Renal disorders	52.5	57.5	0.235	18.5	7.7	30.8	43.1	0.070
Respiratory disorders	46.3	56.7	0.959	18.6	2.3	25.6	53.5	0.889
Neurological disorders	52.6	47.4	0.543	28.6	4.8	19.0	47.6	0.695
Endocrine disorders	41.9	58.1	0.546	25.0	0.0	18.2	56.8	0.274
Substance abuse	43.7	56.3	0.635	19.2	5.1	17.9	57.7	0.633
ICU admission diagnosis (%)								
AMS	36.4	63.6	0.329	21.7	4.3	17.4	56.5	0.930
Respiratory/Pneumonia	44.9	55.1	0.767	16.9	3.6	20.5	59.0	0.751
Gastrointestinal	27.8	72.2	0.102	16.7	5.6	11.1	66.7	0.605
Sepsis/Shock	50.0	50.0	0.695	11.5	7.7	23.1	57.7	0.625
Cardiovascular related	56.5	43.5	0.296	12.5	4.2	41.7	41.7	0.133
Metabolic disturbances	53.8	46.2	0.570	38.5	7.7	23.1	30.8	0.206
Liver failure	75.0	25.5	0.338	50.0	0.0	25.0	25.0	0.407
Renal failure	25.0	75.0	0.626	0.0	0.0	25.0	75.0	0.735
Mortality in the ICU (%)								
Survived	45.4	54.6	0.596	17.8	4.3	24.9	53.0	0.386
Died	51.3	48.7		24.0	4.0	14.0	58.0	

[a]These were defined as patients who came in without ART and did not receive any ART while in the ICU; [b]IR = Interquartile range.

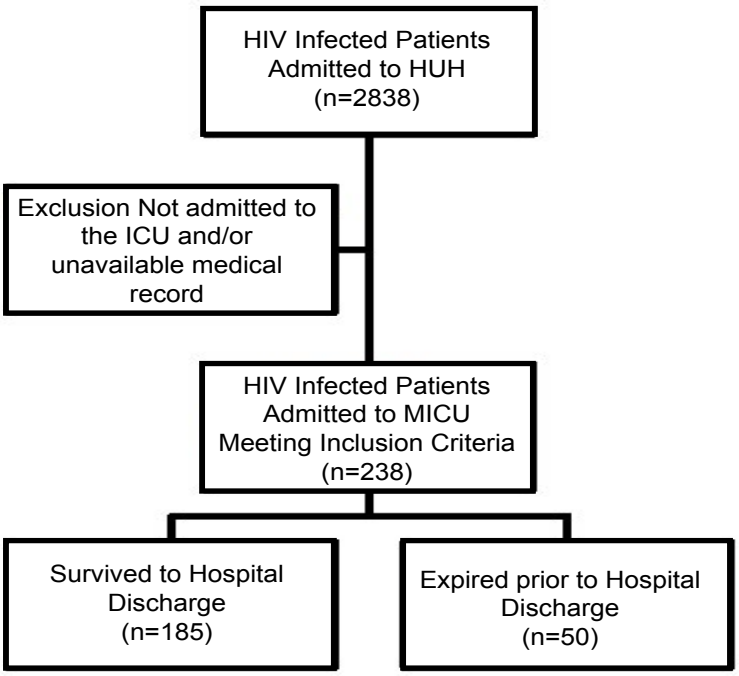

Figure 1: Flow diagram of HIV infected patients enrolled in research study.

potentially meeting the criteria for therapy initiation, the majority (53.2%) of our study population was not receiving any antiretroviral therapy upon ICU admission. These findings were substantiated by other published studies [4,5,9]. Khouli, et. al. documented 52% of patients had no ART use prior to ICU admission, with a median CD4 count of 85 cell/L (range = 0-1261) [5]. A comparative study of HIV infected patients admitted to an ICU over a six-month period found that 25 patients (47%) admitted during the post-HAART era were not on ART prior to admission, with 15 patients of these patients (60%) meeting the criteria for receiving antiretroviral therapy by either presence of CD4 lymphocyte count < 200 cells/L or presenting with a AIDS-defining illness [4]. A French retrospective study conducted in 98 HIV infected patients admitted to the ICU also reported that 55.1% had no ART use at ICU admission with a mean CD4 count of the total population to be 173.5 cells/L (SD = 192) [9]. These findings suggest that more opportunities for treatment initiation exist.

Few studies have examined ART utilization during ICU stay by continuation, discontinuation, or initiation. Within our study population, 22.6% (54/238) of patients were continued on ART in the ICU. These patients comprised at least half (54/104 = 51.9%) of the patients who received ART prior to ICU admission. Antiretroviral therapy was discontinued for 18% (45/238) or patients, with only 10 patients having therapy initiated within the ICU setting. These results proved consistent when comparing to other studies conducted in the ICU setting. A French cohort study consisting of 85 patients admitted to the ICU found that 50% of the patients continued therapy, 44% had therapy and only 3 patients had therapy initiated of the 52 patients who were on antiretroviral therapy at the time of admission [10]. Morquin and colleagues also noted only a 20% continuation rate of antiretroviral therapy and 25% of therapies being discontinued [9]. Another study conducted in 278 HIV-infected patients admitted to a tertiary teaching hospital in Sao Paulo, Brazil examined therapy status within the ICU. Similar to our findings the study noted that 51% of studies participants were already receiving antiretroviral therapy and continued to receive throughout ICU stay [11]. As seen within our study and others, no trends to explain ART discontinuation were found [9-11]. We hypothesize that these findings are related to the limited recommendations regarding ART management within the ICU setting. Antiretroviral use during acute illness may improve immune function and increase cell counts [1,12]. However, the initiation of ART within the ICU setting may pose a variety of challenges, such as risk of immune reconstitution syndromes and increased risk of drug toxicities, which may lead to clinicians to hesitate to continue antiretroviral therapy throughout ICU admission [1-3,12-14].

Further exploration by ART utilization found that patients with AIDS defining illness were less likely to be discontinued during the ICU stay compared to those without AIDS defining illness (OR = 0.35 (95% CI = 0.13-0.94); p = 0.032) and those with AIDS defining illness were more likely to have no ART use throughout ICU admission (OR = 2.53 (95% CI = 1.30-4.90). Croda, et. al. examined factors associated with ART during the ICU stay, and found contrasting findings. This study concluded that even in the presence of a high frequency of AIDS defining diagnoses (80.6%) there was no difference associated with changes in patient's antiretroviral status during ICU admission. Specifically for patients who presented with PJP, 20.3% were continued on ART, 27.9% were initiated on ART, and 25% had no ART use during ICU stay (p = 0.48). Additionally, low median CD4 counts (39, IR = 16-92) did not correlate with patients utilization of ART within the ICU (p = 0.13).

Antiretroviral therapy has somewhat transformed the spectrum of critical illness in HIV-infected patients [2,13,14]. However, even with the recognized benefits of antiretroviral therapy, there is still no definitive answer on the relationship between utilization of ART within the ICU setting and patient survival. Our study further supports the conclusion that prior ART use has association with mortality in the ICU, which is similar to those found in previously published studies. In a study by Khouli, et al. Prior ART was not associated with any significant difference in ICU mortality (p = 0.89) or hospital mortality (p = 0.31) [5]. Nasrasimhan, et al. whose study had a small number of patients who received ART prior to the ICU admission, concluded there to be no difference in the mortality of patients by ART status [4]. Similarly, Meybeck, et al. concluded that starting antiretroviral therapy during an intensive care unit stay in France did not independently improve survival (p = 0.78) [10]. In addition, Croda and colleagues, which had a greater than 50% therapy continuation within the ICU setting concluded there was no difference in mortality among patient with continuous ART use compared to patients who discontinued or modified ART during hospital stay (p = 0.14) [11].

In contrast to the aforementioned studies, other studies have shown improved survival based on ART utilization. Morris et al. found that prior ART use was a predictor of improved survival and

concluded that patients who were using ART at the time of ICU admission were 1.8 times more likely to survive than patients not receiving ART (95% CI = 1.02-3.2, p = 0.04); although, these finding were limited to the univariate analysis [15]. Similarly, Croda, et al. reported an improved survival of patients who initiated ART during ICU stay compared to patients without ART during ICU stay [11]. In addition, a retrospective study of 58 patients admitted to the ICU with *Pneumocystis jiroveci* found decreased mortality in patients who were receiving ART during ICU stay compared to those who did not (25% vs. 63%, p = 0.03) [16]. Overall, this study of 238 patients admitted to the ICU adds to the body of evidence from other studies which show that ART utilization is not associated with survival. Of note was that a 77% survival rate at discharge was observed despite an incoming AIDS-defining median CD4 count (127 cells/μl) and a 26.4% of AIDS-defining illness at admission in our study population. Based upon these findings we hypothesize that additional factors other than ART utilization, are responsible for improving survival. Nevertheless, modest conclusions are urged given that the data was gathered retrospectively. Ultimately, the true nature of this association or lack thereof remains to be further established using prospective cohort studies or randomized controlled trials.

Limitations

There are several limitations associated with our study. First, the retrospective nature of the study makes it impossible to make causal inferences with regards to the impact of ART utilization on survival. Secondly, several unmeasured variables such as adherence, drug interactions, and absorption issues were not able to be assessed. Unlike other studies, survival was only assessed within the ICU compared to inclusion of data six months following discharge. As a result direct comparison of our findings with regards to survival may be limited. Similarly, our study was also unable to capture long-term follow up data such as initiation of ART following hospital discharge and so interpretation of our studies findings are limited to therapy during the ICU stay. Thirdly, this study examined mortality in the ICU and not 30-day mortality as an outcome. The use of 30-day mortality may have included other deaths related to care in the ICU that this study may not have been able to capture.

Conclusion

In conclusion, our study revealed several significant findings that serve to contribute to the overall body of literature related to the use of ART in the ICU. This study in particular makes a significant contribution given that it is among the first to document ART utilization in the ICU in a US population who are predominantly African American. In this regard, our study will add to our understanding of ART utilization and its relationship to clinical characteristics in the ICU in this already at risk population. Ultimately the management of HIV infected patients within the ICU needs to be based on an individualized approach; however additional research is needed to assist in the development of clinical guidelines to assist clinicians in making clinical treatment decisions related to HIV/AIDS management within the ICU setting.

Conflict of Interest

The authors certify that there is no conflict of interest with any organization regarding the material discussed in this manuscript.

References

1. Huang L, Quartin A, Jones D, Havlir D (2006) Intensive care of patients with HIV infection. N Engl J Med 355: 173-181.
2. Akgun K, Huang L, Morris A, Justice A, Pisani M, et al. (2011) Critical illness in HIV-infected patients in the era of combination antiretroviral therapy. Proc Am Thorac Soc 8: 301-307.
3. Lanoix JP, Andrejak C, Schmit JL (2011) Antiretroviral therapy in intesive Care. Med Mal Infect 41: 353-358.
4. Narasimhan M, Posner AJ, DePalo VA, Mayo PH, Rosen MJ (2004) Intensive Care in patients with HIV infection in the Era of Highly active antiretroviral therapy. Chest 125: 1800-1804.
5. Khouli H, Afrasiabi A, Shibli M, Hajal R, Barrett C, et al. (2005) Outcome of critical ill human immunodeficiency virus-infected Patients in the era of highly active antiretroviral therapy. J Intensive Care Med 20: 327-333.
6. Coquet I, Pavie J, Palmer P, Barbier F, Legriel S, et al. (2010) Survival trends in critically ill HIV-infected patients in the highly active antiretroviral therapy era. Crit Care 14: R107.
7. Morris A, Wachter RM, Luce J, Turner J, Huang L (2003) Improved survival with highly active antiretroviral therapy in HIV-infected patients with severe Pneumocystis carinii pneumonia. AIDS 17: 73-80.
8. (2003) Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents, Department of Health and Human Services.
9. Morquin D, Le Moing V, Mura T, Makinson A, Klouche K, et al. (2012) Short- and long-term outcomes of HIV-infected patients admitted to the intensive care unit: impact of antiretroviral therapy and immunovirological status. Ann Intensive Care 2: 25.
10. A Meybeck , L Lecomte, M Valette, N Van Grunderbeeck, N Boussekey, et al. (2012) Should highly active antiretroviral therapy be prescribed in critically ill HIV-infected patients during the ICU stay? A retrospective cohort study. AIDS Res Ther 9: 27.
11. Croda J, Croda MG, Neves A, De Sousa dos Santos S (2009) Benefit of antiretroviral therapy on survival of human immunodeficiency virus-infected patients admitted to an intensive care unit. Crit Care Med 37: 1605-1611.
12. Corona A, Raimondi F (2007) Critical care of HIV infected patients in the highly active antiretroviral therapy era. Minerva Anestesiol 73: 635-645.
13. Morris A, Masur H, Huang L (2006) Current Issues in Critical Care of the Human Immunodeficiency Virus-Infected Patient. Crit Care Med 34: 42-49.
14. Masur H (2006) Management of Patients with HIV in the Intensive Care Unit. Proc Am Thorac Soc 3: 96-102.
15. Morris A, Creasman J, Turner J, Luce JM, Wachter RM, et al. (2002) Intensive Care of Human Immunodeficiency Virus-Infected Patients during the Era of Highly Active Antiretroviral Therapy. Am J Respir Crit Care Med 166: 262-267.
16. District of Columbia Department of Health HIV/AIDS, Hepatitis, STD, and TB Administration (HAHSTA) (2011) Annual Epidemiology & Surveillance Report.