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OUTCOMES FOR CRITICALLY ILL PATIENTS WITH HIV AND SEVERE SEPSIS IN THE ERA OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

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Abstract

RATIONALE—With the advent of Highly Active Antiretroviral Therapy (HAART), sepsis has become a more frequent ICU diagnosis for patients with HIV infections. Yet, little is known about the etiologies of acute infections in critically ill patients with HIV and the factors that affect in-hospital mortality.

METHODS—Cases of patients with HIV requiring intensive care specifically for severe sepsis were identified over 27 months. Demographic information, variables related to acute illness severity, variables related to HIV infection, and all acute infections contributing to ICU stay were recorded.

RESULTS—Of 990 patients admitted to the ICU with severe sepsis, 136 (13.7%) were HIV-infected. There were 194 acute infections among the 125 patients with full data available; 112 of the infections were nosocomial/healthcare-associated, 55 were AIDS-related, and 27 were community-acquired. Patients with nosocomial/healthcare-associated and AIDS-related infections had lower CD4 counts and were less likely to be on HAART ($p < 0.05$). The inpatient mortality was 42%. In a multivariable logistic regression model, only the APACHE II score (odds ratio, OR 1.12, 95% CI 1.02–1.23) was significantly associated with hospital mortality, although any HAART use (OR 0.53, 95% CI 0.22–1.33, $p = 0.18$) approached statistical significance.

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Dr. Martin: contributed to the conception and design of the study; statistical analysis; drafting, critical revision, reading, and approval of the manuscript.

CONCLUSIONS—In this large cohort study, nosocomial/healthcare-associated infections were common in ICU patients with HIV and severe sepsis. Hospital mortality was associated with acute illness severity, but not clearly associated with variables related to HIV infection. Interventions that aim to prevent or more effectively treat nosocomial infections in critically ill patients with HIV may favorably impact clinical outcomes.

INTRODUCTION

In critically ill patients with HIV infections, mortality has been more closely associated with acute illness severity than with degree of immunosuppression or use of highly active antiretroviral therapy (HAART).^{1–9} Hospital admission patterns for patients with HIV have changed in the modern antiretroviral therapy era.^{2,10,11} Patients are less likely to be hospitalized for AIDS-related opportunistic infections. Meanwhile, sepsis has become a more frequent reason for admission to an Intensive Care Unit (ICU)^{2,10} and is a risk factor for both short and long-term mortality.^{1,12,13}

Although several studies have examined the predictors of outcomes for HIV-infected patients admitted to the ICU for all causes, to date, little is known about factors that affect outcomes for patients with HIV who require ICU care specifically for sepsis. Immune system dysregulation plays a key role in pathogenesis of sepsis; it is unknown whether the severity of immunodeficiency related to HIV infection affects outcomes for a subset of ICU patients with sepsis. In addition, the frequency of community-acquired, nosocomial/healthcare-associated, and AIDS-related infections in ICU patients with HIV has not been well characterized. The purpose of this study was to examine the etiologies of acute infections in critically ill patients with HIV and the factors that affect in-hospital mortality.

MATERIALS AND METHODS

This study was approved by the Emory University Institutional Review Board and the Grady Memorial Hospital Research Oversight Committee. These committees waived the need to obtain informed consent because this was a retrospective study. Patients who were admitted to an ICU at Grady Memorial Hospital in Atlanta, Georgia from October 22, 2006 to January 9, 2009 were prospectively screened for severe sepsis or septic shock based on ACCP/SCCM consensus criteria:¹⁴ patients were registered in the “severe sepsis database” if they met at least two of the four systemic inflammatory response syndrome (SIRS) criteria, were suspected of having an acute infection, and had evidence of organ dysfunction. Criteria for the systemic inflammatory response syndrome are 1) body temperature less than 36°C or greater than 38°C; 2) heart rate greater than 90 beats per minute; 3) respiratory rate greater than 20 breaths per minute; or, an arterial partial pressure of carbon dioxide less than 32 mmHg; or 4) white blood cell count less than 4000 cells/mm³ or greater than 12,000 cells/mm³ or the presence of greater than 10% immature neutrophils.

To identify cases, the “severe sepsis database” was cross-referenced with an HIV database by unique medical record numbers. Beginning in 2001, patients were included in the HIV database if they 1) ever had a positive test for HIV at Grady Hospital that was confirmed by Western blot or HIV viral load or 2) received care for HIV at Grady Hospital or an affiliated clinic. The laboratory notified the creators of the database of any new HIV diagnoses in hospitalized patients.

A patient was excluded if after reviewing the medical records, the patient's CD4 count was unknown, he or she did not require ICU level care for sepsis, or it was likely that the patient did not have an acute infection. For cases involving recurrent ICU admissions within the same hospitalization, all events during ICU care were recorded as a single case. If a patient

was discharged from the hospital and returned to the ICU during a later hospitalization, events during the second hospitalization were recorded as a unique case.

After identification of the common patients in the HIV and severe sepsis registries, their medical records were retrospectively reviewed. Inpatient mortality was the primary outcome measure. Demographic information including age, gender, and race as well as length of hospital stay, mechanical ventilation/vasopressor support requirements, and disposition status were collected. Laboratory values were recorded within 24 hours of the diagnosis of severe sepsis and were used to calculate APACHE II and SOFA scores; this was not necessarily the day of hospital admission. The patient's most recent CD4 count and HIV viral load, if available, were recorded. It was noted whether a patient was using HAART prior to admission or whether it was initiated during the hospitalization. Also recorded were past infections or syndromes more prevalent in patients with HIV (Pneumocystis, Mycobacteria, Cryptococcus, Toxoplasma, Cytomegalovirus, Herpes Simplex virus, AIDS dementia, viral encephalitis, thrush/esophagitis, retinitis, syphilis, or HIV-associated skin lesions). Finally, it was noted whether a patient had a history of hepatitis or malignancy (Kaposi's sarcoma, lymphoma, lung cancer, breast cancer, cervical dysplasia, or rectal/anal cancer).

Organisms responsible for acute infections were determined primarily by positive blood, sputum, urine, stool, abscess, or soft tissue cultures. Less frequently, organisms responsible for acute infections were determined without a positive culture result, only if the treating physicians had such a high clinical suspicion for a particular organism as to render therapy only for that organism. If a specific organism was cultured from both blood and an organ system, this was recorded as a single infection from that particular organ system. For instance, if *E. Coli* was cultured from blood and urine, this was entered only as an *E. Coli* urinary tract infection. Otherwise, all cultured organisms were recorded as unique entries. Organisms were recorded as infections, and not contaminants, only if the treating physicians believed they were contributing to the sepsis syndrome and subsequently initiated appropriate antimicrobial therapy.

Sources of sepsis were categorized as "community-acquired," "nosocomial/healthcare-associated," and "AIDS-related." The classification of a "nosocomial/healthcare-associated" infection was based on the Centers for Disease Control definition,¹⁵ as well as guidelines for the management of healthcare-associated pneumonia.¹⁶ A "healthcare-associated" infection was one that the treating physicians believed could be due to an antibiotic-resistant organism because it occurred in a patient who 1) had been hospitalized for at least two days within the last ninety days 2) had been treated with antibiotics for an acute infection within the past thirty days, or 3) had been residing in nursing home or long-term care facility. An "AIDS-related" infection was one that was more likely to occur in patients with compromised immune systems such as Pneumocystis, Cryptococcus, Toxoplasma, Histoplasma, Mycobacteria including tuberculosis, *Aspergillus*, *Cytomegalovirus*, *Parvovirus*, and other infections involving the central nervous system. A "community-acquired" infection was one that occurred in a patient who was not in a healthcare setting at the time of infection and did not meet the criteria for a "health-care associated" or "AIDS-related" infection.

Sources of infection were also categorized by organ system, which included respiratory tract, bloodstream, central nervous system, gastrointestinal, urinary, and skin/soft tissue. Determination of involvement of a particular organ system was based on a combination of positive culture results and clinical suspicion on the part of the treating physicians.

Descriptive statistics are presented as means $\pm$ standard deviation (SD) for normally distributed continuous variables, as median $\pm$ interquartile range (IQR) for non-normally

distributed continuous variables, and as counts with percentages for categorical variables. Continuous data were analyzed by Student's t-test and categorical variables by chi-square analysis. Independent predictors of mortality were assessed in a multivariable logistic regression model yielding odds ratios and 95% confidence intervals (95% CI). Variables for inclusion in the regression model were selected from variables with statistically significant associations on univariate analysis (**Table 5**) or previously reported predictors (age, CD4, HAART use) associated with the clinical outcome of interest (death) after exclusion of variable collinearity by analysis of correlation/association. P-values less than 0.05 were considered to indicate statistical significance. All statistics were performed using NCSS (Number Cruncher Statistical Software).

RESULTS

There were 990 patients who were included in the severe sepsis database from October 22, 2006 to January 9, 2009 and 136 (13.7%) of these patients had HIV infections. Three patients were subsequently excluded because their CD4 counts were unknown; three patients were excluded because sepsis was not thought to be contributing to the ICU admissions; and five patients were excluded because sources of sepsis could not be determined after reviewing their medical records. The remaining 125 cases represented 120 unique patients.

The study population had a mean age of 44 years old, was 65% male, and 85% African-American. The median CD4 count was 30 cells/mm³. Approximately 50% of patients had CD4 counts drawn during the index hospitalization and over 80% within three months; all but two patients had CD4 counts drawn within one year of presentation. Only 11% of the patients were newly diagnosed with HIV during the hospitalization. Of the 87 patients for whom an HIV viral load was available, 64 (74%) had a detectable viral load; the median viral load for these 64 patients was 179,000 copies/mL.

A total of 22% of the population was on HAART prior to hospitalization and 12% were started on HAART during the hospitalization (**Table 1**). Only three of the 15 patients who were started on HAART were newly diagnosed with HIV during the hospitalization. Of the remaining 12 patients who were known to have HIV prior to hospitalization, seven were started on HAART in part because they were being discharged to skilled nursing facilities and compliance could be more assured. Three patients were started on HAART because their condition was deteriorating in the ICU.

There were 194 sources of acute infection among the 125 cases in this population, the majority of which were nosocomial/healthcare-associated (**Table 2**). There were a total of 112 nosocomial/healthcare-associated infections, and 79 patients had at least one infection of this type. There were a total of 55 AIDS-related infections, and 46 patients had at least one infection of this type. There were 27 community-acquired infections, and 27 patients had this type of infection.

Of the pathogens isolated from patients with community-acquired infections, the most common isolated organism was *S. pneumoniae*. Of organisms cultured from patients with nosocomial/healthcare-associated infections, 36 were gram-positive cocci, 35 were gram-negative rods, 5 were *C. difficile*, and 13 were *Candida* species. A total of 23 infections were categorized as “unknown bacterial” based on clinical suspicion for bacterial infections and/or response to empiric antibiotics. Of the organisms identified in patients with AIDS-related infections, 51% were *Pneumocystis jirovecii* pneumonia (PCP). There were 28 unique cases of PCP infections; 16 were cytologically confirmed and 12 were clinically confirmed. There were an additional eight respiratory tract infections that were empirically

treated as both bacterial pneumonia and PCP, which were categorized as “unknown bacterial infections.”

Patients with community-acquired, nosocomial/healthcare-associated, and AIDS-related infections had similar disease severities and mortalities (**Table 3**). Patients with nosocomial/healthcare-associated or AIDS-related infections had significantly lower CD4 counts and were less likely to be on HAART ($p<0.05$). Patients with both healthcare-associated and AIDS-related infections tended to have lower CD4 counts than patients with only one type of infection.

The most common organ systems involved were respiratory tract, bloodstream, and central nervous system (**Table 4**). There were more respiratory infections, bloodstream infections, and gastrointestinal infections per patient among those with lower CD4 counts and more central nervous system infections and urinary tract infections among those with higher CD4 counts, but this difference was not significant. There was a trend towards a greater number of infections contributing to ICU stay for patients with lower CD4 counts, but this was not significant ($p=0.17$).

The overall in-hospital mortality was 42%. Of the 73 patients who survived, 36 were discharged home, 34 were discharged to another facility (skilled nursing facility, personal care home, long-term acute care setting, or hospice), and 3 had unknown dispositions. Under univariate analysis, in-hospital mortality was associated with higher APACHE II and SOFA score, need for mechanical ventilation or vasopressor support (**Table 5**). There were 15 patients who were started on HAART during the hospitalization, but this intervention did not affect mortality ($p=0.56$). Because APACHE II and SOFA were associated with each other (correlation $R^2=0.61$, $p<0.0001$) as measures of illness severity, we tested each individually in a multivariable regression model with the other parameters and found the APACHE II model to be superior (total model $R^2=0.21$). Therefore, in a multivariable logistic regression model, only the APACHE II score (odds ratio, OR 1.15, 95% CI 1.07–1.25) was significantly associated with hospital mortality, although any HAART use (OR 0.61, 95% CI 0.24–1.54, $p=0.18$) and mechanical ventilation (OR 3.76, 95% CI 0.95–14.89, $p=0.06$) approached statistical significance. When substituted for APACHE II in the regression model, SOFA score was similarly predictive (OR 1.28, 95% CI 1.10–1.48, $p=0.001$) without significant change in other parameter estimates. There was a non-significant trend in improved mortality for patients with any HAART use and HIV RNA viral loads less than 10,000 copies/mL ($p=0.15$).

DISCUSSION

This study contributes the most comprehensive accounting of etiologies of acute infections for HIV infected patients with sepsis, and uniquely represents the epidemiology and outcomes of HIV patients in an urban safety net healthcare system. Similar to authors of previous studies who have examined outcomes for critically ill patients with HIV infections in the HAART era,^{1–9} we found that inpatient mortality was more closely associated with acute illness severity than with markers of immunodeficiency. Our findings extend those of Powell et al., who reported that 40% of their ICU patients had an unknown infectious source, 18% had gram-negative rods, 13% had staphylococcus, and 8% had pneumococcus.⁹

Patients with HIV are thought to be at increased risk for nosocomial infections compared to those without HIV because of immunosuppression, frequent antibiotic administration, and frequent invasive procedures.^{20,21} To our knowledge, we are the first to describe a high burden of nosocomial/healthcare-associated infections in a critically ill patient population in the current HAART era. It is interesting that even though most patients in our study were

severely immunosuppressed and not on HAART, they were more frequently infected with pathogens associated with prolonged care in hospital or healthcare settings than pathogens associated with poor immune function. Our findings suggest that using resources to develop better preventative and treatment options for nosocomial/healthcare-associated infections in this population may be effective both clinically and financially.

Also for the first time, we report outcomes data on critically ill patients with HIV from the Southeastern United States. In 2009, 45% of the new HIV diagnoses and the largest number of people living with HIV were from the southern United States.²³ A key difference between our ICU population and those previously described from urban hospitals in California^{3,9} and New York,^{4,5} is the predominance of African-Americans. African-Americans have a disproportionately high number of current and new HIV infections and most live in the southern United States.²⁴ Compared to other racial groups, African-Americans typically have different perceptions of HIV infection and access to healthcare,²⁴ which affects their admission diagnoses and severity of illnesses at hospitalization. Our data set not only represents people from a new geographic location, but also comprises patients who are demographically similar to a large subpopulation of predominantly urban individuals living with HIV in the United States.

An unanswered question in the field is whether HAART offers a short-term benefit for critically ill patients with HIV. In our study, we found a trend towards increased survival for those using HAART. The benefit may have been non-significant because only 34% of the patients in the study used HAART. Another reason for this non-significant finding may be that HAART is most beneficial for patients with acute AIDS-related infections and most of the patients in our study did not have these types of infections. In two recent studies that showed a short-term survival benefit of HAART, greater than 75% of the patients had AIDS-defining conditions.^{13,17} Finally, many patients categorized as being on HAART may not have been compliant with or may have failed therapy. This may explain the trend toward improved survival for patients on HAART with viral loads less than 10,000 copies/mL, which is the subset of our population that was both compliant with and responding to therapy.

A limitation of this study is that we were not able to definitively link one source of sepsis with outcome for a number of patients. While this limitation was partly due to the retrospective design of the study, it was also related to high illness severity and multiple infectious sources for some patients. As a result, many patients were being treated for multiple sources of sepsis at the time of death. For a particular patient, we chose to record all sources of sepsis that the treating physicians thought were contributing to ICU stay. We believe that this approach provided a more complete description of the infection patterns for this population as a single infection was often not responsible for both ICU admission and mortality for a particular patient. Specifically, deaths were often related to nosocomial infections, which would have been misclassified using only sources of infection on admission. At the same time, our approach may have resulted in an overestimation of the sources of severe sepsis as some of the infections may not have caused our patients to require ICU care on their own. Another limitation was that some types of infections, particularly PCP, were diagnosed clinically rather than using culture techniques, although diagnoses relied upon clinical response to treatment as well. Because this study was performed in a single hospital, the organisms responsible for sepsis may be partly related to the infection patterns at our institution.

There were also limitations related to HIV-associated variables in this study. First, we were not able to determine adherence to HAART. In addition, since only 18% of our sample had completely suppressed viral loads, we were not able to analyze complete suppression as an

independent factor associated with survival. However, it is noteworthy that only this small proportion of our population had complete viral suppression. Because this was a retrospective study, we were unable to ensure measurement of CD4 count and viral load during the index hospital admission, although this was the case for the majority of patients. Finally, there were relatively few patients on HAART, which could limit the external validity of this study to populations with high rates of HAART use. However, these results are similar to the experience of many urban hospitals where resource constraints and case-mix limit utilization of HAART.^{9,22} Moreover, there would likely be an insufficient number of ICU cases to perform a study of this nature in HIV populations with high prevalence of HAART use.

CONCLUSION

Overall, the majority of sources of acute infection in this study were not AIDS-related and the in-hospital mortality was more closely associated with the severity of acute illness than with markers of immunodeficiency. Most infections were nosocomial/healthcare-associated and further research and resources should focus on preventing and treating these types of infections. The appropriate use of HAART in the ICU still needs further clarification and the subpopulation that would most benefit from HAART in the ICU has not been fully clarified. Randomized prospective trials examining initiation of HAART in the ICU are warranted.

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LIST OF ABBREVIATIONS USED

AIDS	Acquired Immunodeficiency Syndrome
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
PCP	<i>Pneumocystis jirovecii</i> pneumonia
VL	Viral Load

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KEY MESSAGES

- There was a high burden of nosocomial/healthcare-associated infections in this population of ICU patients with HIV and severe sepsis.
- Patients with nosocomial/healthcare-associated or AIDS-related infections tended to have lower CD4 counts and were less likely to be on HAART.
- In-hospital mortality was more closely associated with acute illness severity than with markers of immunosuppression.

Table 1

Demographic and physiological characteristics of 125 hospitalized patients with HIV and severe sepsis.

Characteristic	N=125
Age [years, (mean $\pm$ SD)]	44 $\pm$ 9
Gender - no. (% male)	81 (65%)
Race [# (%)]	
African-American	107 (85%)
Caucasian	7 (6%)
Other / Unknown	11 (9%)
Duration of hospital stay [days, (median, 25%–75%)]	24
Duration of ICU stay [days, (median, 25%–75%)]	7
Opportunistic Infection History [# (%)]	66 (53%)
Candida Thrush/Esophagitis [# (%)]	20 (16%)
PCP [# (%)]	15 (12%)
Treated Tuberculosis [# (%)]	13 (10%)
AIDS dementia [# (%)]	12 (10%)
Hepatitis B or C History [# (%)]	22 (18%)
Malignancy History [# (%)]	18 (14%)
CD4 - median (range)	30 (1–1501)
Viral load - median copies/mL	77,000
Patients with Undetectable Viral Load [#(%)]	23 (18%)
HAART use on admission [# (%)]	28 (22%)
HAART started during hospitalization [# (%)]	15 (12%)
Mortality [# (%)]	52 (42%)

Table 2

Organisms responsible for severe sepsis.

Community-Acquired	N=27	Nosocomial/Health Care-Associated		N=112	AIDS-Related
<i>S. pneumoniae</i>	8	Gram Pos Cocci	<i>S. aureus</i>	21	<i>P. jirovecii</i>
<i>S. aureus</i>	2		<i>Enterococcus</i> sp.	8	<i>Aspergillus</i> sp.
<i>E. coli</i>	3		Coag Neg <i>Staphylococcus</i>	5	<i>C. neoformans</i>
<i>N. meningitidis</i>	1		Viridians <i>Strep.</i>	2	<i>H. capsulatum</i>
					<i>M. kansasii</i>
Unknown Bacterial	12	Gram Neg Rods	<i>Acinetobacter</i> sp.	9	<i>M. avium-intracellulare</i> complex
			<i>P. aeruginosa</i>	9	<i>M. tuberculosis</i>
Herpes Simplex Virus	1		<i>E. coli</i>	5	<i>T. gondii</i>
			<i>Klebsiella</i> sp	4	
			<i>Enterobacter</i> sp	3	<i>Cytomegalovirus</i>
			<i>Proteus</i>	2	<i>Parvovirus</i>
			<i>Morganella</i>	1	JC Virus
			<i>Serratia</i>	1	
			<i>Citrobacter</i>	1	Unknown CNS lesions
		Unknown Bacterial		23	
			<i>C. difficile</i>	5	
		<i>Candida</i>	Albicans	4	
			Glabrata	3	
			Parasitosis	1	
			Krucei	1	
			Tropicalis	1	
			Unknown	3	

Table 3

Characteristics of patients with different infection types.

N=125	Community -Acquired Only N=20	Nosocomial/ Healthcare- Associated Only N=53	AIDS-Related Only N=25	Nosocomial/ Healthcare-Associated and AIDS-Related N=20	Other N=7	Significance
CD4 avg	206±251	105±213	53±70	20±24	128±89	p=0.02
% on HAART	21±42	38±49	4±20	5±22	29±49	p=0.001
% with VL <10,000	15±38	30±46	9±30	13±35	0	p=0.26
APACHE II	24.6±9.6	24.4±7.5	20.0±7.0	25.8±6.4	20.7±5.8	p=0.12
Mortality N(%)	8 (40)	21 (40)	12 (48)	10 (50)	1 (14)	p=0.52

Table 4

Frequencies of organ system involvement related to CD4 count.

N = 125	CD4 < 50 N=71	CD4 50–200 N=38	CD4 > 200 N=16	Significance
Resp. Tract [N (avg per pt)]	67 (0.94)	25 (0.66)	10 (0.63)	NS
Bloodstream [N (avg per pt)]	29 (0.41)	14 (0.37)	3 (0.19)	NS
Central Nervous System [N (avg per pt)]	9 (0.13)	6 (0.16)	3 (0.19)	NS
Gastrointestinal [N (avg per pt)]	8 (0.11)	1 (0.03)	0 (0.00)	NS
Skin/Soft Tissue [N (avg per pt)]	2 (0.03)	3 (0.08)	0 (0.00)	NS
Urinary Tract [N (avg per pt)]	4 (0.06)	6 (0.16)	4 (0.25)	NS
Total	119 (1.68)	55 (1.45)	20 (1.25)	p=0.17

Table 5

Relationship between key variables and inpatient mortality

N = 125	Survived N=73	Deceased N=52	Significance
Age (years)	44.6	44.0	P=0.06
APACHE II (mean)	20.8	27.6	p<0.0001
SOFA (mean)	6.2	9.5	p<0.0001
Intubated [# (%)]	51 (70%)	49 (94%)	p=0.0008
Pressors [# (%)]	43 (60%)	42 (84%)	p=0.004
Albumin g/dL (mean)	1.9	1.9	p=0.85
Length of Hospital Stay (mean days)	37.7	27.3	p=0.07
Days until ICU Admission (mean days)	8.5	8.1	p=0.90
CD4 count (mean)	104	91	p=0.71
HAART use on admission [# (%)]	18 (25%)	10 (20%)	p=0.58
HAART started during admission [# (%)]	10 (14%)	5 (10%)	p=0.56
No HAART [# (%)]	45 (62%)	37 (71%)	p=0.27

Patients categorized by HA ART use and respective HIV viral loads.

	NO HAART (N= 47)			HAART STARTED (N=14)			HAART ON ADMISSION (N=26)		
*N=87	VL> 10,000 N=42	VL< 10,000 N=5	Sig	VL> 10,000 N = 12	VL< 10,000 N = 2	Sig	VL> 10,000 N = 10	VL< 10,000 N=16	Sig
Deceased [N(%)]	10 (23%)	3 (60%)	p = 0.12	4 (33%)	0 (0%)	p = 0.56	6 (60%)	3 (19%)	p = 0.05
APACHE II (mean)	22.4±6.9	29.7±12.9	p = 0.10	24±5.7	8±1.1	p = 0.50	26.5±7.7	22.3±6.9	p = 0.15
CD4 (mean)	44±65	81±46	p = 0.84	88±113	10±1.1	p = 0.59	52±56	241±371	p = 0.09

* A total of 38 patients had unknown viral loads and were not included