Emergency department utilization by HIV-positive adults in the HAART era

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Abstract
Background No published study has analyzed emergency department (ED) utilization by human immunodeficiency virus (HIV)-positive adults in the highly active antiretroviral therapy (HAART) era.
Aims The purpose of this study is to describe the demographic and HIV-specific variables associated with ED utilization by HIV-positive adults and their diagnoses when discharged from the ED or subsequently from the hospital.
Methods We conducted a retrospective cohort study of all HIV-positive adults cared for at a tertiary center HIV clinic and ED (1 January–31 December 2006). Demographic, HIV clinical, and HIV lab variables were abstracted from the clinic database. ED/hospital diagnoses coded by the ICD-9 Diseases/Injuries Tabular Index were abstracted from identified discharge records. We used multivariate logistic regression to compute odds ratios (OR) of ED utilization based on the abstracted variables. We described the cohort and diagnoses using descriptive statistics.
Results A total of 356 patients met inclusion criteria. Their mean age was 42.7 years, and 77.2% of included patients were male; 52.5% were Caucasian and 47.5% non-Caucasian; 72 patients (20.2%) presented to the ED during the study period [153 visits; 37 (10.4%) required hospitalization (61/153 visits)]. Income level and mean 2006 viral load had a significant association (p<0.05) with ED utilization. Of 155 ICD-9 ED discharge diagnoses, ill-defined symptoms/signs (25.2%), injury (18.7%), and musculoskeletal disorders (11.6%) were most prevalent. Of 450 ICD-9 hospital discharge diagnoses, endocrine/metabolic (13.3%), psychiatric (12.2%), infectious/parasitic (12%), and circulatory disorders (11.8%) were most prevalent.
Conclusion In this study of HIV-positive adults, income level and mean 2006 viral load had a significant association with ED utilization. Noninfectious diagnoses were alone most prevalent in ED discharged, but not hospitalized, patients.
Keywords Emergency department · HIV · Highly active antiretroviral therapy · Utilization

Introduction
Background
The World Health Organization estimates that as of December 2007, 33.2 million individuals are infected with human immunodeficiency virus (HIV), with 2.5 million
individuals becoming newly infected in the previous 12 months [1]. With the advent of highly active antiretroviral therapy (HAART), HIV-infected adults have experienced an increase in life expectancy. One study has quantified the mean increase in life expectancy for a 20-year-old HIV-infected adult as rising from 9.1 years (+2.3 years) in 1993–1995 to 23.6 years (+4.4 years) in 2002–2004 [2]. This increase in life expectancy, largely attributable to HAART [3], has also resulted in a changing spectrum of illness for HIV-positive adults. Recent studies from the HAART era where patients have access to such medications have found that hospitalizations due to opportunistic infections, especially late-stage conditions such as Cryptosporidium and Mycobacterium avium, have decreased while those related to cardiovascular disease, medication side effects, and malignancies have increased [4, 5]. This pattern stands in contrast to the pre-HAART era when opportunistic infections comprised over 23% of hospital discharge diagnoses, with an additional 10.1% due to respiratory ailments, predominantly pneumonia of an uncharacterized nature [6].

To our knowledge, no published study has analyzed what factors are specifically associated with emergency department (ED) utilization by HIV-infected adults in the HAART era. Similarly, while previous studies have focused on the pattern of inpatient discharge diagnoses among HIV-positive adults [5, 7], the nature of ED and hospital discharge diagnoses in HIV-infected adults who present to the ED has not specifically been examined. Previous articles in the emergency medicine literature have emphasized the treatment of opportunistic infections in the HIV-infected population [8–10]. While one previous study based on ED presentation found that HIV-infected patients often were diagnosed with conditions unrelated to their HIV status, their patient population was examined in the pre-HAART era, though published in 1997 [11]. The changing spectrum of illness in HIV patients requires emergency physicians to have a better understanding of the conditions that can bring HIV patients to the ED and require hospitalization [12]. Previous studies have shown that attempts to develop triage instruments for HIV-positive patients have poor sensitivity and specificity for emergent versus nonemergent conditions, supporting the need for a better understanding of why and how HIV-positive patients present for emergency care [13]. It would also be useful to both emergency physicians and infectious disease specialists to determine if preventable factors are associated with ED utilization that can be addressed in the outpatient setting.

**Study purpose and hypotheses**

The purpose of this study is to describe the demographic and HIV-specific variables currently associated with ED utilization by HIV-positive adults and to describe their diagnoses when discharged from the ED or subsequently from the hospital. We hypothesized that for HIV-positive adults in the HAART era, demographic (age, sex, race, and income level relative to the federal poverty line (FPL)), not HIV-specific clinical (years since diagnosis/on antiretroviral therapy, 2006 use/interruption of HAART) or laboratory (recorded peak and mean 2006 viral load/nadir and mean 2006 CD4 count) factors are significantly associated with ED utilization within this population. We also hypothesized that, with the availability of the improved means to control HIV through HAART, noninfectious ED/hospital discharge diagnoses are most prevalent among HIV-positive adults who present to the ED.

**Methods**

**Study design**

This was a retrospective, observational cohort study of all HIV-positive adults followed in a federally supported HIV clinic located in an urban, level 1 trauma tertiary care center from 1 January 1 to 31 December 2006. The study was approved by the Institutional Review Board for this center.

**Setting**

The study center is a level 1 trauma tertiary care referral center with an ED that sees approximately 50,000 patients per year. The center is located in a county with an estimated prevalence of acquired immunodeficiency syndrome (AIDS) patients between 50–165/100,000 residents [14]. The dedicated HIV clinic in this center is governmentally supported and is a referral center for the region for HIV-infected adults, with treatment provided to local patients as well as those from adjacent states.

**Study population and inclusion/exclusion criteria**

All HIV-positive adults followed in this center’s HIV clinic between 1 January and 31 December 2006 were included in this study. These individuals were identified from a preexisting database maintained by the clinic for outpatient management. Demographic, clinical history, and laboratory information on these patients is entered into this database by treating physicians and nurses and maintained by a program coordinator for the clinic.

**Definition of clinical variables**

Age was calculated as that on 1 January 2006. Some included patients did not have viral load or CD4 count
testing during the study period, either due to presenting late in 2005 and not having follow-up until early 2007, having been diagnosed in 2006 and not having HIV-related lab testing until early 2007, or only having one clinic visit during the study period and not undergoing serum testing as prescribed. For these study subjects, these variables were treated as unknown. Viral loads (copies/ml) were classified as either <400, 401–1,000, 1,001–100,000, or >100,000. Previous studies have found that increases in viral load from undetectable to higher levels are associated with adverse outcome and that categorization of viral load similar to these cutoffs was associated with increased risk of progression to AIDS in HIV-infected adults [15, 16]. CD4 counts (cells/ml) were classified as <200, 201–350, and >350 based on existing guidelines for initiation of HAART to decrease the risk of developing AIDS and AIDS-defining illnesses [17].

All ED and hospital discharge diagnoses were included for analysis as to the prevalence of particular ICD-9 Diseases/Injuries Tabular Index categories during the study period in ED and hospital discharged HIV-infected adults. The only diagnoses excluded from analysis were those coded under the ICD-9 classification as V or E. These codes are used in the ICD-9 classification to provide context to the more specific diagnosis given. Diagnoses coded V50-V59, indicating encountering of health personnel for specific procedures and aftercare, were included for analysis. Previous studies examining HIV-related hospitalizations have only included the first four coded hospital discharge diagnoses [6]. However, as the abstracting investigators for this part of the study were not the treating physicians for these patient visits, it was felt that selection bias was best avoided by including all coded diagnoses for each ED visit.

Data collection and processing

The investigators created a standardized case report form that was used to abstract the specific demographic and HIV-specific variables described above in included study subjects. The study subjects were identified from the preexisting clinic database described above. The case report form also was used to record whether a subject was seen in the ED, was subsequently admitted to the hospital, and ICD-9 coded ED and hospital discharge diagnoses for each patient who presented to the ED. Two investigators concurrently abstracted this information to the case report form and classified these diagnoses using the ICD-9 Diseases/Injuries Tabular Index, which has been used in previous studies to analyze the characteristics of hospital discharge diagnoses in HIV-infected patients [6, 18]. Data from the case report forms were then entered by the investigators into a Microsoft Excel (Microsoft Office for Windows XP, Redmond, WA, USA) spreadsheet, and range and consistency checks were performed to verify accuracy of data entry.

Outcome measures

The primary outcome measure in this study was whether an HIV-infected adult followed at this center’s HIV clinic during the study period utilized the ED. The analytic strategy was designed to identify whether demographic, HIV clinical, or HIV laboratory variables distinguished those who presented to the ED from those who did not. A secondary dependent variable was a descriptive classification of ED and hospital discharge diagnoses in those HIV-infected patients who presented to the ED, as classified by the ICD-9 Diseases/Injuries Tabular Index.

Statistical analysis

Descriptive statistics (percents, means, and standard deviations) were used to characterize the demographic and HIV-specific characteristics of the included subjects. We used SPSS for Windows v. 15.0 (Chicago, IL, USA) to create a multivariable logistic regression model and compute odds ratios (OR) with 95% confidence intervals (95% CI) for the association of the specific demographic, HIV clinical, and HIV laboratory variables abstracted and the likelihood of ED utilization within the cohort from those who did not present to the ED. Given the presence of missing data, we used a χ² analysis (SPSS for Windows v. 15.0, Chicago, IL, USA) to determine if those patients with missing data were differentially more or less likely to present to the ED.
To analyze the prevalence of ED and hospital discharge diagnostic categories within the ICD-9 Diseases/Injuries Tabular Index for those cohort patients who presented to the ED, we calculated the percentage of each ICD-9 diagnostic category using Microsoft Excel (Microsoft Office for Windows XP, Redmond, WA, USA).

Results

Characteristics of study subjects

Table 1 provides a summary of the characteristics of subjects that met inclusion criteria during the study period and the distribution of variables analyzed in this project. A total of 356 HIV-positive adults were followed at the center’s clinic during the study period of 1 January–31 December 2006. Overall, the study cohort was 77.2% male with a mean age of 42.7 (standard deviation: ±8.5 years); 52.5% of the cohort were Caucasian, 46.1% were black, and 1.4% were of a different minority race (Asian, Hispanic, or Native American). For analytic purposes ethnicity was dichotomized (Caucasian vs non-Caucasian) due to the low frequency of individuals of a racial minority other than black. Seventy-two patients (20.2%) presented to this center’s ED during the study period a total of 153 times. Thirty-seven patients (10.4%) in the cohort were admitted to the hospital from the ED. Of the 153 total visits, 61 (39.9%) resulted in hospital admission.

Main results

Table 2 shows the results of the multivariable logistic regression model that analyzed the association of demo-
graphic, HIV-specific clinical, and HIV-specific laboratory variables with ED utilization. Sixty-three patients had missing data, and analysis of this group compared to those with complete data (293 patients) did not reveal differentially greater or lesser likelihood of ED presentation \[\chi^2 (df=1)=1.27, p=0.26\]. The full model for the 293 patients with complete data was significantly reliable \[\chi^2 (df=20)=35.23, p=0.02\] and accounted for between 11.3 and 18.2% of the variance in ED presentation status. Income level greater than 3× the FPL was the only demographic variable with a significant association with ED utilization, showing a decreased likelihood of presenting to the ED \[OR: 0.07 (95\% CI: 0.01–0.52)\]. Those subjects with an income 2–3× the FPL also showed a trend towards lesser likelihood of ED utilization, though not reaching statistical significance \[OR: 0.36 (95\% CI: 0.12–1.09)\]. No other demographic variable (age, sex, or race) showed a significant association with ED utilization in the study cohort.

Among the HIV-specific clinical and laboratory variables, higher mean viral load during the study period was associated with increased odds of ED utilization within the study cohort, contrary to our hypothesis that only demographic variables would show a significant association with ED use. Those with a mean viral load of 1,001–100,000 copies/ml during 2006 were 5.43 times more likely to present to the ED when compared to those with low viral loads \([p=0.02, 95\% CI: 1.26–9.73]\). Similarly, those with very high mean viral loads (>100,000 copies/ml) during 2006 were 5.43 times more likely to present to the ED when compared to those with low viral loads \([p=0.02, 95\% CI: 1.39–21.21]\). No other HIV-specific variables were related to ED utilization.

Figure 1 provides a graphical representation of the distribution of ED discharge diagnoses in the 92 ED visits that did not result in hospital admission. Of the 155 ICD-9 coded ED discharge diagnoses, the most prevalent categories were ill-defined symptoms/signs (25.2% of all ED discharge diagnoses), injury specifically within the category of injury/poisonings (18.7% injury/1.3% poisonings), and musculoskeletal disorders (11.6%). Infectious/parasitic diagnoses represented 4.5% of all ED discharge diagnoses, primarily related to herpes simplex, viral syndromes (two diagnoses each), thrush, and warts (one diagnosis each). Within the category of ill-defined symptoms/signs, diagnoses of abdominal pain not otherwise specified (NOS) (seven diagnoses), diarrhea (five diagnoses), vomiting, chest pain NOS, and convulsion (possible seizure) (four diagnoses each) were most prevalent.

Figure 2 provides a graphical representation of the distribution of hospital discharge diagnoses in the 61 ED visits that resulted in hospital admission. Of the 450 ICD-9 coded hospital discharge diagnoses, the most prevalent
categories were endocrine/metabolic (13.3% of all hospital discharge diagnoses), psychiatric (12.2%), infectious/parasitic (12%), and circulatory disorders (11.8%). Within the category of infectious/parasitic disorders, diagnoses related to thrush (12 diagnoses) and hepatitis C (7 diagnoses) were most prevalent. The most common endocrine/metabolic diagnoses were related to an electrolyte abnormality (14 diagnoses) and diabetes mellitus (14 diagnoses). Among psychiatric diagnoses, substance abuse (22 diagnoses) and depression (20 diagnoses) were most prevalent. In the circulatory disorders category, the most common diagnosis related to cardiomyopathy/congestive heart failure (11 diagnoses).

**Discussion**

This study’s results show that ED utilization among HIV-positive adults in the HAART era was associated with a lower income level and greater mean viral load during the study period and that infectious/parasitic diagnoses continue to be among the most prevalent among hospitalized, though not ED discharged, HIV-infected adults. However, there are a number of limitations that affect the generalizability of these findings. This center resides in a region with a low prevalence of HIV in comparison to other major urban centers, both within the country and worldwide [14]. For centers in higher prevalence areas, the diagnoses distribution and variables associated with ED utilization may be different due to other epidemiological factors, such as lack of knowledge of underlying HIV status and lack of access to clinical resources to manage HIV. Such factors should be addressed in future studies that are larger scale and have the ability to differentiate and follow patients found to be HIV-positive after ED visits suspected to be related to HIV.

In addition, larger epidemiological studies with greater sample sizes may indicate that other demographic and HIV clinical/laboratory variables are associated with ED utilization by this patient population. This study, as such, is preliminary and should be used to guide further evaluation of ED utilization by HIV-positive adults on a multicenter basis.

The retrospective methodology used does not allow the investigators to control for other comorbid conditions that might affect the prevalence of diagnoses in this cohort or as
a confounding variable of ED utilization. Similarly, the retrospective methodology does not allow for the ability to determine the accuracy of all ascribed ED and hospital discharge diagnoses in this cohort. Any attempt to do so by the study investigators would introduce significant selection bias into these findings, and, as discussed above, previous studies on this topic have not controlled for these two factors [6].

Finally, the analysis of ED utilization in this cohort (Table 2) is limited to those patients with complete data to allow multivariable logistic regression. Sixty-three patients had missing data, primarily related to CD4 count and viral load during the study period. This often was related to patients who were followed in the center’s HIV clinic during the study period, but did not require lab testing per the treating physicians, having been seen late in 2005 and not requiring follow-up until 2007, having been diagnosed with HIV in 2006 and not having lab testing related to that diagnosis until early 2007, or due to patient nonadherence with prescribed lab testing during the study period. This limitation would likely apply to any retrospective study on the subject. However, our analysis of these 63 patients, in comparison to the 293 patients with complete data, did not reveal that they were differentially more or less likely to present to the ED. A prospective study may limit this factor, but would introduce the bias of investigator knowledge of the purpose of the study and potentially result in overly careful monitoring of patients in the outpatient setting and decreased use of the ED beyond what is found in this type of observational study.

This study presents the first attempt to determine what variables are specifically associated with ED utilization by HIV-positive adults during the HAART era as well as an analysis of ED and hospital discharge diagnoses of those who presented to the ED for care. The findings that income level and mean viral load during the study period had a significant association with ED utilization supports previous studies that have found that a combination of demographic considerations and health status are in general associated with frequent ED users [19, 20]. Specifically related to HIV, previous studies evaluating outpatient and inpatient utilization in the HIV-positive adult population have found that demographic and HIV-specific factors are associated with increased requirements of inpatient resour-
ces. Fleishman et al. found that black patients, female patients, and those with worsening immunosuppression, as determined by either CD4 count or viral load, were more likely to require inpatient care in the HAART era [21]. Floris-Moore et al. found that female sex and not being on HAART increased the risk of hospitalization among HIV-positive adults [22].

Our study, in contrast, did not find that race or gender had a significant association with ED utilization. That income level was the only demographic variable found to be associated with ED utilization in this study raises the likelihood that either those with higher incomes, due to having better access to outpatient and primary care, had less need for emergency services or that they sought emergency care in other centers unless feeling they would require hospitalization. There is evidence from the pre-HAART era that racial disparities associated with ED utilization by HIV-positive adults in that period were partially explained by the lack of access to outpatient resources such as substance abuse rehabilitation and home health care [23].

The finding that mean viral load during the study period alone was associated with ED utilization among HIV-specific factors suggests that this factor should be further evaluated by infectious disease and emergency physicians as a target for preventing the need for emergency care. Previous studies have come to differing conclusions about the relative importance of viral load versus CD4 count in prognosis of HIV-infected patients. MacArthur et al. found that CD4 count more than viral load had a significant association with progression to AIDS or death [24]. In contrast, Mellors et al. found that increasing viral load was associated with risk of dying of AIDS though the combination of viral load and CD4 count were most predictive of this adverse outcome [16]. The result in our study that increasing mean viral load, and not decreasing CD4 count, was associated with ED utilization may indicate that viral load is a better surrogate marker for acute illness requiring emergency care while CD4 count is a better marker for long-term outcome, such as death or developing AIDS-defining illness. Larger epidemiological studies of known HIV-positive patients should further evaluate this finding.

This investigation did not consider insurance status as a potential variable associated with ED utilization. As this study center is supported by governmental funding, patients treated at the clinic, if not fully covered by private or public insurance, had access to treatment medications through this program. Income level, taken from patient report to the clinic, is an easy financial marker tracked by the clinic database that can be used to determine how socioeconomic status affects the likelihood of ED use. This variable is also more readily considered in practice settings where insurance status is not an issue due to single-payer health systems.

The investigators also did not consider methods of HIV transmission as a variable affecting ED utilization. We had no logical construct as to how transmission status—whether sexual, intravenous drug use, or blood transfusion/professional exposure—would relate to presentation in the ED setting. Fleishman et al. found that adults infected with HIV through intravenous drug use were more likely to require inpatient, though not outpatient, resource use, but could not distinguish whether this was due to ongoing substance abuse [21]. The result in our investigation that psychiatric diagnoses, specifically those related to substance abuse, are the second most prevalent hospital discharge diagnoses suggests that ongoing drug use, as opposed to means of transmission, is more important as a risk factor for ED presentation and inpatient care.

This investigation represents the first study, to our knowledge, that has specifically analyzed the character of ED diagnoses in HIV-infected adults during the HAART era who are discharged after care in the ED. The finding that ill-defined signs and symptoms (Fig. 1) are most prevalent may represent a bias among treating emergency physicians to rule out life-threatening diagnoses and characterize discharged patients in the broadest sense (chest pain or abdominal pain NOS, for example). At the same time, given the association of increased viral load with ED utilization, it is also likely that these ill-defined symptoms/signs represent patient complaints that are potentially related to poor control of their underlying systemic infection or side effects from complex medication regimens. Other studies have found that hospitalizations specifically related to medication side effects have increased in the HAART era [4, 5]. The use of ICD-9 coding and classification would not easily allow examination of whether particular diagnoses were related to HAART regimens or not. The finding that injury and musculoskeletal ailments were also most prevalent suggests that minor trauma is common in the HAART era among HIV-positive patients as it was in the pre-HAART era [11].

This study found that endocrine/metabolic, psychiatric, infectious/parasitic, and circulatory disorders are most prevalent among hospital discharge diagnoses in this cohort of HIV-infected adults. The finding that psychiatric and circulatory disorders in the inpatient setting have become more prevalent in the HAART era supports previous research that has addressed the nature of inpatient diagnoses in the HIV-infected population [5, 7]. However, the finding of high prevalence of infectious/parasitic disorders in the inpatient setting does differ from some of the most recent studies on the subject. Pulivirenti et al. found that admissions for late-stage AIDS-defining illnesses such as Cryptosporidium and Mycobacterium...
avium have declined in their single-center analysis [5]. Our investigation, by using the ICD-9 Diseases/Injuries Tabular Index, more comprehensively analyzed the nature of all hospital discharge diagnoses. While treatment of thrush, for example, may not have been the primary reason for inpatient care, the fact that such treatment was required during the inpatient stay suggests that conditions relating to poor immune function remain an important diagnostic consideration for emergency physicians. The spectrum of illness in the HIV-infected patient population that requires emergency care and hospitalization has grown from just classic AIDS-defining illnesses to other major systemic diseases, such as cardiovascular, neurologic, and orthopedic ailments [12]. Our study confirms that emergency physicians seeing HIV-infected patients must consider both noninfectious and infectious diagnoses in their assessment, even if noninfectious illnesses have become more common.

Future studies on the subject of ED utilization by HIV-infected adults should be conducted in a multicenter fashion to allow capture of patients both in high and low prevalence settings. A larger sample size would also allow analysis of what specific variables are associated with hospitalization, as opposed to ED utilization, which this study was not powered to do. In addition, a prospective methodology will allow a more focused analysis on what are the specific primary ED and hospital discharge diagnoses that require the most health care resources in the HAART era and what factors are associated with their occurrence. However, such a study would require separation of investigators from treating physicians to prevent a Hawthorne effect by increased scrutiny and follow-up care in the outpatient setting than what might normally occur.

Conclusion

In this study of HIV-positive adults in the HAART era, income level and mean viral load during the study period had a significant association with ED utilization. Noninfectious diagnoses were alone most prevalent in ED discharged, but not hospitalized, patients.

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Conflict of interest The authors declare that they have no conflict of interest or disclosures.

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