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Risk Factors and Temporal Trends of Hospital-Acquired Infections (HAIs) Among HIV Positive Patients in Urban New York City Hospitals: 2006 to 2014

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Abstract

Background—HIV-infected patients may be at a greater risk of Hospital-Acquired Infections (HAIs) but risks factors for HAIs have not been well described in this population.

Objective—The aim of this study was to examine the incidence, temporal trends and risk factors of HAIs among adult HIV positive patients.

Methods—This was a retrospective cohort study carried out in an academic health system in New York City which included four hospitals over a 9-year period from 2006 to 2014. Simple and multiple logistic regression models were built to determine risk factors associated with sitespecific HAIs such as Urinary Tract Infections (UTIs), Pneumonia (PNUs) and Bloodstream Infections (BSIs).

Findings—There were 10,575 HIV positive discharges and 1,328 had HAIs: 697 UTIs, 555 BSIs and 192 PNUs. The incidence rate of HAIs decreased from 19.8 to 15.1 new infections per 1000 person-days between 2006 and 2014 (p value<0.001). In addition to the expected risk factors of urinary catheter use for UTI and central venous line use for BSI, symptomatic HIV and renal failure were significant risk factors for both UTIs (95% CI OR: (1.24, 2.27) and (1.46, 2.11) respectively) and BSIs (95% CIs OR: (2.28, 4.18) and (1.81, 2.71) respectively).

Conclusion—HIV-infected patients had similar risk factors for HAIs as HIV-uninfected patients. Further research is required to address how patients' CD4 counts and viral loads affect their susceptibility to HAIs.

Keywords

HIV; hospital-acquired infections; incidence rate; risk factors

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

PATIENT CONSENT Declared none.

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INTRODUCTION

Hospital-acquired infections (HAIs), also referred to as nosocomial infections, constitute a serious public health and health care problem in the United States. According to the Centers for Disease Control and Prevention (CDC), 1.7 million of hospitalized patients acquire HAIs annually while being treated for other conditions and approximately 99 000 HAI-related deaths occur annually in the US [1]. While HAIs and prevention strategies have been well described for some patient populations, little is known about risk factors for HAI among people living with the Human Immunodeficiency Virus (HIV) who are admitted to the hospital [2–5].

It is possible that HIV-infected patients may be at a greater risk of HAIs than HIV-negative patients [6]. First, the immunosuppression observed in HIV-infected patients makes them more susceptible to infections [7]. In addition, because of their deficient immune system, HIV-infected patients may be hospitalized more and for longer periods of time when compared to other individuals [7, 8]. Given that there were about 1.2 million of people living with HIV in the US in 2014, the potential burden of HAI in this population may be considerable [9] since inpatient mortality among HIV-positive persons who develop an HAI is greater than that among HIV-patients who do not [8–10]. Hence, assessing risk factors of HAIs in HIV-infected patients may contribute to the identification of potential prevention strategies in this vulnerable population.

Recent studies suggest that acute renal failure and CD4 are associated with HAIs in HIVinfected patients [10, 11]. In addition, Mitha *et al.* previously reported that steroid use was associated with Urinary Tract Infections (UTIs), Blood Stream Infection (BSI) and Pneumonia (PNU) among HIV positive patients. However, that study included only a short period of time and a small sample size [10]. Furthermore, more information is needed about the epidemiology of types of HAIs among HIV-infected patients as well as the causative organisms associated with those infections. Therefore, the aim of this study was to examine the incidence, temporal trends and risk factors of HAIs among adult HIV positive patients from 2006 to 2014 in four urban New York City hospitals.

METHODS

Sample and Settings

Data for this study were collected from an NIH-funded database (Health Information Technology to Reduce Healthcare-Associated Infection, HIT-HAI, R01NR010822) compiled from multiple electronic sources from four hospitals in a large academic medical system in New York City– -a pediatric hospital, a community hospital and two tertiary/quaternary hospitals providing care to a diverse population. The data were collected between 2006 and 2014 and 965,642 discharges were reported during this period. For this study, only HIV positive patients who were aged 18 years old or older were included in the statistical analysis. After excluding all HIV-negative patients, there were 10,525 hospital discharges with positive HIV infection.

Data Collection

The study was approved by the Columbia University Medical Center Institutional Review Board. The data extracted from the database included demographics; laboratory reports including microbiological laboratory results from urine, blood and respiratory specimens; procedures received by the patients including urinary and central catheterization as well as mechanical ventilation; patient medical history; drug use; total length of stay as inpatient; admission to intensive care unit and death.

Study Definitions

HAIs included in the analysis were UTIs, BSIs, and PNUs which developed at least 48 hours after hospital admission. UTIs, BSIs, and PNUs were defined according to a set of algorithms adapted by a group of expert clinicians and researchers from the surveillance definitions from the Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN, http://www.cdc.gov/nhsn/about.html) for HAIs [12].

The six organisms which represented the most common causes of HAI in the study institutions were examined in this study: Acinetobacter baumanii, Enterococcus faecalis/ faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus and Streptococcus pneumoniae.

Statistical Analysis

The incidence rate of HAIs among HIV positive patients was calculated by dividing the total number of HAIs per year by the total number of person-days for each year. A Cochrane-Armitage trend test was performed to assess temporal trends in HAI incidence and the change in length of stay over the 9-year study period [13]. When performing a Cochrane-Armitage test, the Somers' D(R|C) coefficient assessing the association between row variable (incidence rate) and column variable (year) was calculated [14].

Descriptive statistics were summarized and then chi-squared tests were performed to assess the association between HAIs and other categorical variables such as sex, hospital, prior hospitalization and antibiotic use. Independent-sample t-test was performed to assess whether there was any difference in age, Charlson co-morbidity Index [15] score, or length of stay between patients who developed HAIs and those who did not. Separate simple logistic regression analyses for UTI, BSI and PNU were carried out using logistic regression models for each independent predictor. Variables significant in simple logistic regression analyses were included in a multivariable logistic regression model. Odds ratios, p-values as well as 95% Confidence Intervals (CI) were determined to assess if these predictors were significant.

Variables assessed as separate predictors were: symptomatic HIV (defined by the ICD-9-CM code V08 among patients who did not have any HIV-related condition and had not yet been diagnosed with any HIV-related illness), age, sex, length of stay, ICU stay prior to infections, stay in skilled nursing facility, renal failure, presence of malignancy, diabetes mellitus, Charlson Co-morbidity Index, prior hospitalizations. In addition, immunosuppressive and chemotherapeutic agents association with HAIs was also assessed

in simple logistic regression models. In addition, device-related variables known to increase rise of HAI, including Central Venous (CV) lines for BSI, urinary catheterization for UTI, and mechanical ventilation for PNU were also assessed in multiple logistic regression analyses and included in the respective multivariable logistic regression analyses *a priori*.

Finally, we assessed changes in average of length of stay among HIV-positive patients over time. The analyses were conducted using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, North Carolina) and a p value <0.05 was considered significant.

RESULTS

There were 10,575 discharges with HIV positive infection (or as HIV infected patients) and 1,328 had HAIs (12.6%) from 2006 to 2014, about three-fourths of which occurred in men. The mean age among patients with HAIs was 48.5 years vs. 47.6 years for patients who did not develop any HAIs. Patients who developed an HAI stayed on average of twice as long in the hospital compared to those who did not develop any infection (10 days vs. 5 days respectively). Table 1 below summarizes the main characteristics among HIV-positive patients with and without HAIs.

In total, there were 697 UTIs, 555 BSIs and 192 PNUs. There were 75 patients with both a UTI and a BSI, 35 patients who developed both a BSI and a PNU, and 40 patients who had both a UTI and PNU. *Acinetobacter baumannii, Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus* accounted for about 40% of UTIs. These same organisms in addition to *Streptococcus pneumoniae* accounted for about 39% of BSIs and about 79% of PNUs.

Temporal Trends of HAIs from 2006 to 2014

The incidence rate for HAIs was 19.8 new infections per 1000 person-days in 2006 vs. 15.1 new infections per 1000 person-days in 2014 (p<0.001). The Somers' D(R|C) coefficient was -0.014 (95% CI: -0.204, -0.0081). These results indicate that over time there was a slow decrease in incidence rate as shown in Fig. (1). In order to assess whether these findings were due to the fact that the length of stay of inpatients decreased each year, we compared the average of length of stay among HIV-patients who developed an HAI for each year; there was no significant difference in average length of stay of patients between years (p-value =0.06, results not shown).

Risk Factors for HAIs Among HIV-Infected Patients

Tables 2–4 summarize risk factors for UTIs, BSIs and PNUs when assessed in simple and multiple logistic analyses. Symptomatic HIV, male sex, renal failure, and ICU stay were predictors associated with UTIs and BSIs in univariate analysis. In addition, urinary catheter use and the presence of a central venous line were associated with an increased risk in UTI and BSI, respectively, among HIV-positive patients.

After adjusting for all the significant individual predictors in a multivariable logistic regression model, urinary catheter use, symptomatic HIV, female sex, renal failure, ICU stay and previous stay in skilled nursing facility were all associated with an increased risk of UTI

(Table 2). Similarly, adjusting for all the significant individual predictors in a multivariable logistic regression model to assess risk factors for BSIs, central venous line, symptomatic HIV infection, renal failure, ICU stay, high risk medications and presence of a malignancy remained positive predictors for BSIs.

There was no interaction between malignancy and administration of these immunosuppressive and chemotherapeutic agents and therefore both variables were included in the multivariable logistic regression models if there was a significant association in our simple logistic regression models.

Symptomatic HIV (adjusted OR=1.68 and 95% CI (1.24, 2.27) for UTI, adjusted OR=3.09 and 95% CI (2.28, 4.18) for BSI), renal failure (adjusted OR=1.76 and 95% CI (1.46, 2.11) for UTI, adjusted OR=2.21 and 95% CI (1.81, 2.71) for BSI) were both predictors of UTIs and BSIs.

Symptomatic HIV, mechanical ventilation, renal failure, stay in skilled nursing facility, ICU stay and high risk medications were individual predictors associated with PNUs in univariate logistic regression analyses.

Finally, mechanical ventilation, symptomatic HIV, ICU stay and high risk medications were significantly associated with an increased risk of PNUs after adjusting for all significant predictors in a multivariable logistic regression model assessing risk factors for PNUs (Table 3).

DISCUSSION

To our knowledge, this is the first large study to identify risk factors for HAIs and to provide insights for infection control as well as case management in HIV-positive patients. In this study, the incidence rates of HAIs decreased from 19 to about 15 infections per 1000 patients-days between 2006 and 2014. These estimates are higher than what is reported in HIV-uninfected patients [16–18].

In our current study, UTIs were the most prevalent type of infections among HIV-infected patients followed by BSIs and PNUs. Similarly, in two previous studies carried out in the US, UTIs were the most common infections identified in HIV-infected patients whereas in a prospective study carried out in Italy, BSIs were the most common [8, 10, 19].

Our findings are consistent with previous studies carried out in HIV-uninfected patients. It has been established that patients with renal failure are susceptible to HAIs [20, 21].

In a retrospective study assessing the infection burden in 433 HIV-uninfected patients with renal disease from 1992 to 2000, 20 and 10% of those patients had PNUs and UTIs respectively. In another cohort study assessing BSI incidence in HIV-uninfected patients with renal failure in the ICU in a Belgian hospital, the incidence of nosocomial BSIs was 9% higher in patients with renal failure when compared to patients without renal failure [22]. In the same study, HIV-uninfected patients with renal failure had a 10% incidence in UTIs. However, in that particular study the increased incidence did not lead to an increase in

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mortality and length of stay among those patients [22]. In two other multicenter prospective cohort studies carried out in HIV-uninfected patients, renal failure was also shown to be associated with higher incidence of PNUs and UTIs [23, 24]. These studies suggest that association between renal failure and HAIs also observed in our current study is not unique to HIV-infected patients. One explanation that has been suggested is that patients with renal failure have an impaired microflora due to their long-term use of antibiotics [21] which subsequently renders them more susceptible to infections.

Further, stay in skilled nursing facility and ICU stay as well as the presence of malignancy has also been previously described in the general population as risk factors for HAI [25–28]. In a three -year prevalence study carried out in nursing homes of a specific region in the Netherlands from 2007 to 2009, the prevalence of HAIs increased from 6.7% in 2007 to 7.6% in 2009 [29]. Although no information was provided on the HIV status of the patients in that study, HIV prevalence in that region is very low [29]. Similar to our findings, UTIs were also the most common infections diagnosed in those nursing home residents [29]. In another study assessing the prevalence of HAIs in 133 Veteran Affairs nursing home care units in the United States, the prevalence of HAIs was estimated at 5.2% and UTIs were also the most common types of HAIs [30]. As confirmed in a recent study of longitudinal trends of HAIs in 14 000 nursing homes in the United States from 2006 to 2011, HAIs infection rates are rising [31].

The old age of nursing home residents and the shortage of staff are potential factors that could explain the high burden of HAIs in those facilities [25]. In addition, in an earlier study analyzing the prevalence of HAIs in US hospital using the National Nosocomial Infections surveillance system (NNIS) database, more than 30% of HAIs in the US occurs in ICU patients [32].

Also consistent with the literature on HAIs, we found urinary catheter use and central venous line to be associated with an increased risk in UTIs and BSIs respectively [33–35]. Hence reducing inappropriate use of urinary catheters and their rapid removal are key strategies to reduce the risk for UTI in patients [35, 36]. In addition, it has been shown that adequate training of staff as well as the use of antiseptic-impregnated central venous catheter in select high risk patients can reduce the risk of BSIs [36, 37].

Similar to national trends regarding overall rates of HAI, we also observed a decrease in HAIs incidence overtime from 2006 to 2014 [32]. In the national and state HAI progress report published in 2014, there was a 50% decrease in BSIs, a 17% decrease in SSIs from 2008 to 2014 [38], and in non-ICU settings there was also a decrease in UTIs during the same period [38]. This suggests that with time there may be better implementation of infection control strategies by health care personnel [38], but among HIV-positive patients, this could also be due to improved access to antiretroviral therapy and linkage to care among newly diagnosed HIV-infected individuals in New York City. According to New York City Department of Health and Mental Hygiene (NY-CDOHMH), the number of newly diagnosed HIV patients linked to care in NYC increased from 63% in 2010 to 72% in 2014 [39]. During the same period there was also a 13% increase in the number of HIV patients who achieved viral suppression [39]. In our dataset, we also observed a decrease in the

percentage of admissions of patients with symptomatic HIV from 60% in 2006 to 53% in 2014.

There are some limitations associated with this study. Because it was retrospective and used only electronically available data, it is possible that some infections may have been missed. Further, 60% of infections observed in this study were caused by organisms other than the six specific species we analyzed. Because patients included in this study were from an urban academic health system, our findings may not be generalizable to other health care settings. In addition, we did not have measures of viral load and CD4 counts which are important prognostic markers for HIV [40]. In the current study, we used symptomatic HIV as a proxy to assess how well the patients were doing.

CONCLUSION

To our knowledge, this study is the first large study to demonstrate that although rates of HAI among HIV-infected patients are likely to be higher than among HIV-uninfected patients, the risk factors are similar. Therefore, when designing strategies to prevent nosocomial infections among HIV-patients, the same control measures used in HIV-uninfected patients should also apply to HIV-infected patients [2–4]. Further research is needed to assess how CD4+ counts and viral loads affect incidence of HAIs among HIV-infected patients.

Acknowledgments

Declared none.

Biography



Christophe T. Tchakoute

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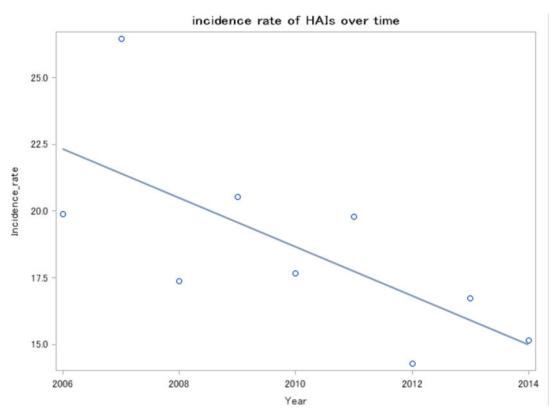


Fig. (1). Incidence rate (new infections per 100 discharges) of HAIs over time.

Characteristics of hospitalized HIV positive-patients with and without a HAI.

	Patients with HAIs	Patients without HAIs	p-value*
N	1328	9247	
Female (%)	529 (39.8)	3055 (33)	< 0.0001
Mean age (years, sd)	48.5 (11.88)	47.6 (11.87)	0.01
Hospital (%) Tertiary hospital 1 Pediatric hospital Community hospital Tertiary Hospital 2	10 756 (56.9) 9 (0.67) 114 (8.58) 449 (33.85)	12 4336 (46.9) 260 (2.81) 814 (8.80) 3837 (41.49)	0<0.0001
Admitted from a skilled nursing facility (N, %)	40 (3.0)	124 (1.3)	< 0.0001
Renal failure (%)	524 (39.5)	1862 (20.1)	< 0.0001
Presence of malignancy (%)	158 (11.9)	957 (10.4)	0.09
Diabetes mellitus (%)	210 (15.8)	1337 (14.5)	0.19
Antibiotic use *(%)	1070 (80.6)	4469 (48.3)	< 0.0001
Median length of stay (IQR, days)	10 (14)	5 (5)	< 0.0001
Median Charlson_score	8	6	< 0.0001
Prior hospitalization (%)	519 (39.1)	3568 (38.6)	0.73
Symptomatic HIV (%)	971 (73.1)	5026 (54.4)	< 0.0001

For patients with an HAI, antibiotic use prior to infection; for those not developing an HAI, antibiotic use throughout hospitalization.

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Risk factors associated with UTIs among HIV positive patients. Unadjusted odds ratio and adjusted odds ratio*

Variables	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio [*] (95% CI)
Urinary catheter use before UTI	2.86 (2.44, 3.35)	2.27 (1.90, 2.70)
Symptomatic HIV	1.63 (1.38, 1.92)	1.68 (1.24, 2.27)
Sex (female)	2.27 (1.95, 2.65)	2. 38 (2.03, 2.80)
Diabetes mellitus	1.36 (1.11, 1.65)	1.21 (0.97, 1.51)
Prior hospitalization in past 30 days	1.18 (1.01, 1.38)	1.02 (0.87, 1.20)
Renal failure	2.18 (1.86, 2.57)	1.76 (1.46, 2.11)
ICU stay	1.55 (1.3, 1.84)	1.53 (1.23, 1.89)
Stay in skilled nursing facility	2.61 (1.69, 4.02)	2.06 (1.31, 3.25)
Charlson Co-morbidity Score	1.08 (1.06, 1.1)	0.99 (0.95, 1.03)
Age	1.01 (1, 1.02)	1.06 (1, 1.02)

Results from the multivariable logistic regression model with all significant risk factors in simple logistic regression analysis.

Risk factors associated with BSIs among HIV positive patients. Unadjusted odds ratio and adjusted odds ratio^{*}.

Variables	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio [*] (95% CI)
Central Venous line use before BSI	4.93 (4.03, 6.09)	2.65 (2.07, 3.4)
Symptomatic HIV	2.97 (2.41, 3.65)	3.09 (2.28, 4.18)
Sex (female)	0.74 (0.61, 0.89)	0.80 (0.66, 0.98)
Prior hospitalization	0.83 (0.70, 1)	0.72 (0.60, 0.87)
Renal failure	3.05 (2.56, 3.63)	2.21 (1.81, 2.71)
ICU stay	3.64 (2.99, 4.42)	1.74(1.36, 2.22)
Stay in skilled nursing facility	1.84 (1.08, 3.15)	1.48 (0.85, 2.6)
Charlson Co-morbidity Score	1.13 (1.11, 1.16)	0.97 (0.93, 1.01)
Malignancy	1.63 (1.28, 2.06)	1.41 (1.04, 1.64)
Immunosuppressive and chemotherapeutic agents	1.98 (1.64, 2.36)	1.22 (1, 1.50)

* Results from the multivariable logistic regression model with all significant risk factors in simple logistic regression analysis.

Risk factors associated with PNUs among HIV positive patients. Unadjusted odds ratio and adjusted odds ratio^{*}.

Variables	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio [*] (95% CI)
Mechanical ventilator use before PNU	19.25 (14.02,26.43)	6.07 (3.76, 9.78)
Symptomatic HIV	5.74 (3.7, 8.89)	6.18 (3.47, 10.98)
Renal failure	2.73 (2.05, 3.65)	1.36 (0.96,1.92)
ICU stay	7.65 (5.72, 10.22)	2.12 (1.35, 3.33)
Stay in skilled nursing facility	2.84 (1.38, 5.89)	2.16 (0.98 4.72)
Charlson Co-morbidity Score	1.143 (1.10, 1.19)	0.93 (0.87, 1)
Immunosuppressive and chemotherapeutic agents	5.42 (4.05, 7.25)	2.08(2.03, 3.86)

* Results from the multivariable logistic regression model with all significant risk factors in simple logistic regression analysis.