Editorial Response: Changing Epidemiology of Nosocomial Infections in Human Immunodeficiency Virus–Infected Patients

Nosocomial infections (NIs) are a major cause of morbidity and mortality in the United States [1]. Immunosuppression, whether secondary to underlying disease, therapeutic agents, or invasive devices or procedures, increases the risk of NIs. However, studies focusing on one rapidly growing immunosuppressed population, HIV-infected patients, have had differing conclusions as to whether this population is at increased risk for acquisition of NI.

Although many studies have addressed the incidence and etiology of bacteremia in HIV-infected patients, in studies that have included hospitalized HIV-infected patients, NIs often are grouped together, and analyses are conducted without stratification by level of immunosuppression or device exposure and without comparison with similar non-HIV-infected controls [2]. Few studies have been conducted to specifically assess the risk of and risk factors for NI in hospitalized HIV-infected patients. A study of all HIV-infected patients admitted to one hospital over 2 years found that the rate of NI was significantly higher among these patients than among all other hospitalized patients (15% [32 of 210] vs. 7% [1,560 of 22,615], respectively; \( P = .043 \)) [3]; however, surprisingly, there was no difference in the rate of NI in patients with AIDS and those with HIV infection but without AIDS. In another prospective cohort study in which patients were stratified by stage of HIV disease (e.g., pre-AIDS/HIV-positive, AIDS, and HIV-negative) [4], rates of NI were not significantly different between pre-AIDS/HIV-positive and HIV-negative patients, but the incidence of NI among both groups was significantly lower than that among patients with AIDS (1.18 and 1.84 cases per 1,000 hospital-days vs. 6.67 cases per 1,000 hospital-days, respectively). The investigators concluded that although HIV infection does not alter the risk of development of NI, patients who have progressed to AIDS are at significantly increased risk of developing NI.

In this issue of Clinical Infectious Diseases, Frank et al. [5] report the incidence of NIs in HIV-infected patients admitted to one San Francisco hospital over a 6-month period and also examine risk factors for NI in this population. The investigators present the overall rate of NI in their cohort and conclude that their results “suggest very strongly” that HIV-infected patients are at increased risk for NIs. However, the ability to generalize and compare these results is limited. The population studied, which predominantly consisted of male patients with AIDS and a mean CD4 cell count of <200/μL, is not representative of most HIV-infected patients in the United States. Without inclusion of a more representative group of HIV-infected patients, both demographically and in disease severity, it is difficult to generalize results from this study to all HIV-infected patients.

Similarly, it is difficult to compare rates of NI in this HIV-infected population with those of NI in all non-HIV-infected hospitalized patients without including a non-HIV-infected control group with a similar severity of illness. Nosocomial infections can be caused either by endogenous organisms that become invasive with increasing immunosuppression or by bacteria introduced by exogenous sources, such as during certain procedures and exposures to medical devices. In the patient population, intensive care unit (adult, pediatric, or neonatal), burn unit, or surgical patients are at greatest risk of NI because of their severity of illness, which is related to the level of immunosuppression and the increased use of medical devices in these settings [6]. Although treatment of NI in HIV-infected patients is more often complicated by atypical presentation, coexisting infections, or multiple-antimicrobial resistance, HIV-infected patients appear to be prone to many of the same risk factors for NI as HIV-negative patients [7]. However, care must be taken when reading and comparing studies of NIs in HIV-infected patients with those of NIs in other populations to ensure that the distribution of such patients by disease stage, types of therapy, and exposure to devices is provided so that comparisons of rates of NI are valid. The degree of immunosuppression and the use of certain medical devices in a cohort of hospitalized patients can influence the rate of NI, and these factors should be carefully considered for inclusion in analyses to avoid confounding in the calculation of such rates.

Studies of bacteremia in HIV-infected patients repeatedly have identified iv catheter use as a risk factor, thus emphasizing the importance of this risk factor in both the hospital and outpatient setting for HIV-infected patients and other patient groups [8–10]. Frank et al. [5] support this association by their finding that insertion of a central venous catheter put patients at increased risk for development of NI. It is interesting that when these investigators presented data on site-specific rates they also found that the skin (rather than the urinary tract, the most common site of NI in the general population [11]) was the most common site for NIs in this cohort. Although data on iv catheterization in this population were presented, the incidence of urinary catheterization or mechanical ventilation (the two most significant risk factors for acquisition of nosocomial urinary tract infection and pneumonia, respectively) was not reported, which may explain reasons for these differences.
Frank et al. [5] also note the presence of certain conditions that were significantly associated with NIs by univariate analysis, including history of reactivation of herpes simplex virus infection, B cell non-Hodgkin’s lymphoma, cytomegalovirus infection, and HIV wasting syndrome. After multivariate analysis, the investigators found that only HIV wasting syndrome was associated with NI. In addition to being at risk for NI from the same factors that other patients are, HIV-infected patients may be at risk for NI from other processes (caused by either endogenous or exogenous organisms) unique to their underlying disease entity or therapeutic exposures that Frank et al. may have uncovered. However, it may be difficult to ascribe increased risk of NI to conditions such as HIV wasting syndrome without knowing the association with other known risk factors for NI, such as level of immunosuppression, surgical procedures, or device exposures (often measured by central venous catheter–days, urinary catheter–days, or mechanical ventilation–days). As Frank et al. carefully point out, there are a number of potential confounders that may be independent risk factors for NI associated with these disease entities, including interventions needed for therapy and side effects of therapy (such as iv catheterization and neutropenia associated with ganciclovir therapy [a first-line treatment of cytomegalovirus infection], respectively).

In the study by Frank et al. [5], Staphylococcus species were the pathogens most commonly reported to cause skin and/or soft-tissue infection, while gram-negative organisms (including Pseudomonas aeruginosa) were the most common causes of pneumonia. Gram-negative rods (Enterobacter cloacae and P. aeruginosa) and enterococci were the most common causes of urinary tract infection. Staphylococcus aureus was the most common cause of bacteremia and was the etiologic agent most frequently isolated overall. Studies have demonstrated that the distribution of pathogens causing bloodstream infections in HIV-infected patients, as in non-HIV-infected patients, depends on the source of infection and the site-specific risk factors present [3, 4]. The site-specific rates, site-specific risk factors, and pathogens reported by Frank et al. are similar to those reported for all hospitalized patients at institutions reporting to the National Nosocomial Infections Surveillance System [11, 12]. However, since the number of patients enrolled in the study was relatively small and represented a select group of HIV-infected patients, it is difficult to draw conclusions about site-specific rates, risk factors, and pathogens. Other investigators have described similar pathogens and sources of nosocomial infection in HIV-infected hospitalized populations [14].

Frank et al. [5] found that increased length of hospitalization, sometimes a marker for severity of illness, was not associated with NI and that “physiological deficits . . . were not predictive for the occurrence of NIs but were predictive for death.” Could these findings be because the cohort of HIV-infected patients were at the end stage of disease and clinicians were less aggressive with therapy for these patients (thereby reducing the risk of NIs and the length of hospitalization) in this subset?

In their comparison of HIV-infected patients with NIs with those without NIs, Frank et al. found that the CD4 cell counts in these two groups were not significantly different; however, one wonders if the sample size of the group with NIs was too small to allow detection of a significant difference between CD4 cell counts.

The study of NI in HIV-infected patients is challenging because of dynamic changes in immune status, exposures, treatment and prophylactic strategies, and interaction between new drugs used for both treatment of HIV infection and treatment of opportunistic infections. Improvement in the health of HIV-infected patients that is associated with the use of protease inhibitors and other new therapies is resulting in a decrease in the hospitalization of these patients and an increase in the use of outpatient and home iv therapy; consequently, a new cohort of patients has been created who are increasingly difficult to study in the era of increasing health care reorganization and obstacles, there remains a growing need for prospective studies examining rates of NI in both inpatient and outpatient HIV-infected patients with end-stage disease [13]. Despite these obstacles, there remains a growing need for prospective studies examining rates of NI in both inpatient and outpatient HIV-infected populations and comparing these patients with subsets of the HIV-infected population and the non-HIV-infected population. Only through such studies, like that of Frank et al. [5], will we better understand the epidemiology of NI in HIV-infected patients so that preventive interventions can be designed and implemented to reduce the risk of such infection.

Matthew J. Kuehnert and William R. Jarvis
Hospital Infections Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

References


