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Major article

Relative frequency of health care-associated pathogens by infection site at a university hospital from 1980 to 2008

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Key Words:
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Background: We describe the relative frequency of health care-associated pathogens by infection site over 29 years using hospital-wide surveillance data from a large academic hospital.

Methods: Comprehensive hospital-wide surveillance was provided by trained infection preventionists using Centers for Disease Control and Prevention definitions. Five 5-year blocks and one 4-year block were created for each site: bloodstream infections (BSI), urinary tract infections (UTI), respiratory tract infections (RTI), and surgical site infections (SSI). The blocks of relative frequency of health care-associated pathogens were compared by χ^2 analysis, and trends for each pathogen were estimated by regression analysis.

Results: At least 1 pathogen was isolated from 28,208 (83.5%) of 33,797 health care-associated infections (HAI). *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), *Enterococcus* species, and *Clostridium difficile* and other anaerobes significantly increased, whereas *Escherichia coli, Pseudomonas aeruginosa*, *Klebsiella* species, *Enterobacter* species, and other streptococci significantly decreased in the relative proportion of pathogens during the study period. By infection site, results showed significant increasing trends of *S aureus* in UTI, RTI, and SSI; CoNS in BSI and SSI; *Candida* in SSI; and *Enterococcus* in BSI and UTI.

Conclusion: Significant changes in relative frequency of health care-associated pathogens by infection site occurred over the 29-year period. These findings have implications for implementation of infection prevention strategies.

Health care-associated infections (HAI) are one of the most common adverse events threatening patient safety. HAI are estimated to be one of the top 10 causes of death in the United States.[1] According to the Centers for Disease Control and Prevention (CDC), approximately 1.7 million HAI and 99,000 HAI-related deaths occur each year in the United States.[2] From 1975 to 1995, the overall incidence of HAI in the United States reported to the National Nosocomial Infections Surveillance System (NNIS) has increased by 36%.[3]

Information about the relative frequency of isolated pathogens from HAI cases by infection site has implications for the implementation of infection control and prevention strategies. The National Healthcare Safety Network (NHSN) data from 2006 to 2007 reported the top 10 commonly isolated pathogens as follows: coagulase-negative staphylococci (CoNS), *Staphylococcus aureus*, *Enterococcus* species, *Candida* species, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter* species, *Acinetobacter baumannii*, and *Klebsiella oxytoca*.[4] The spectrum of health care-associated pathogens may have changed over time following increased use of broad-spectrum antibiotics and invasive procedures and increasing numbers of immunocompromised patients.[5] Although national data on commonly isolated pathogens have been reported by the NHSN, the frequency of these reported pathogens cannot be compared over time because the participating NHSN hospitals are not randomly selected and do not consistently participate over time and therefore do not represent a well-defined

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cohort, which is a designated population traced over time.[6] For this reason, we reviewed the relative frequencies of health care-associated pathogens isolated in our institution during almost 3 decades, from 1980 to 2008.

METHODS

All data for pathogens associated with HAI during 1980 to 2008 were extracted from the University of North Carolina Health Care (UNCHC) electronic epidemiology database. HAI data including pathogen information have been collected since 1978 through comprehensive hospital-wide surveillance by trained full-time infection preventionists at UNCHC, currently an 800-bed teaching facility. HAI were determined based on the CDC's NNIS and NHSN case definitions,[7] with 2 exceptions: diagnosis of lower respiratory tract infection required chest radiography with an infiltration (even prior to the requirement by NHSN); bacteriuria required signs and symptoms of infection (ie, asymptomatic bacteriuria was not considered a UTI).[8] Otherwise, all updates to NNIS/NHSN case definitions were adopted. Separate codes for methicillin-resistant *S aureus* (MRSA) and vancomycin-resistant *Enterococcus* were introduced in 1996 to distinguish from susceptible *S aureus* and susceptible *Enterococcus.*

Based on the previous study from the same facility,[5] pathogens were categorized into 18 groups of related species. For frequency analysis of isolated pathogens by infection site, all cases regardless of device utilization were classified into 5 major categories: bloodstream infections (BSI), urinary tract infections (UTI), respiratory tract infections (RTI), surgical site infections (SSI), and other sites (eg, endocarditis, osteomyelitis, meningitis) as specified by NNIS/NHSN definitions.

To analyze the relative frequencies of pathogens isolated during 29 years, 6 time blocks were created (ie, five 5-year blocks and one 4-year block), and noninformative data such as "no growth" and "mixed flora" were deleted. To compare the relative frequency of isolated hospital-associated pathogens by time blocks, χ^2 tests were conducted using SAS version 8.2 (SAS Institute, Cary, NC). For trend analysis, logistic regression analysis was conducted across the 6 time blocks, and overall relative percentage change was calculated across the entire linear trend (from the first time block to the last time block) using the slope and intercept values. Significance for these multiple comparisons was set at $P < .003$ (Bonferroni correction, 0.05/17). Additional analyses of the yearly proportions and the actual number of isolates were conducted to aid in the interpretation of the relative frequency trend.

RESULTS

Overall, at least 1 pathogen was isolated from 28,208 (83.5%) of the 33,797 HAI during 29 years. In total, 35,510 pathogens were isolated from these 28,208 HAI (mean number of pathogens per HAI, 1.26). For the remaining 5,589 HAI, no pathogens were isolated, and infections were classified based on clinical criteria alone as specified by NNIS/NHSN definitions. The probability of isolating a pathogen differed by site as follows: urinary tract, 98.8%; respiratory tract, 75.5%; surgical site, 81.8%; and other, 68.8%. The probability of isolating a pathogen in the blood differed over time (1980 to January 1999, 99.9% vs February 1999 to 2008, 82.0%) because, after February 1999, all pathogens for secondary bloodstream infections were recorded as "no growth" even if a pathogen was isolated to avoid duplicate reporting of the same pathogen.

The overall relative frequency of pathogens by time blocks is displayed in Table 1. In total, the top 5 pathogens were *S aureus*, *E coli,* CoNS, "*Candida* and other yeasts," and *Enterococcus* species during 29 years, accounting for a total of 54.8% of all pathogens. The trend analyses showed significantly increasing relative frequency trends (Fig 1) with gram-positive cocci (*S aureus*, CoNS, and *Enterococcus* species) and significantly decreasing trends (Fig 2) with gram-negative bacilli (*E coli*, *P aeruginosa*, *Klebsiella* species, and *Enterobacter* species). The most dramatic change in health care-associated pathogens was the marked increase in infections with *S aureus*, and, from 1990 to 2008, *S aureus* was the most predominant pathogen in relative frequency (data not shown). Since a separate code for MRSA was introduced in 1996, the relative proportions of MRSA among *S aureus* HAI cases remained relatively constant from 55.9% to 44.4%.

Clostridium difficile, an emerging health care-associated pathogen, was categorized to "*C difficile* and other anaerobes" which had a 10th relative frequency ranking. We observed that, since 1987, *C difficile* comprised most of the proportion for the "*C difficile* and other anaerobes" category (data not shown). From 1995 to 2008, "*C difficile* and other anaerobes" showed a 4.0% increase from 1.5% to 5.5% in relative frequency.

The overall significant percent change of relative frequency of pathogens is summarized in Table 2. Among BSI, CoNS and *Enterococcus* species were significantly increased, whereas *E coli, Enterobacter* species, *P aeruginosa*, "*C difficile* and other anaerobes," *Klebsiella* species, and "*Candida* and other yeasts" were significantly decreased in relative frequency during 1980 to 2008. The most prominent relative frequency change in isolated pathogens from BSI was CoNS, which increased suddenly as an overwhelming predominant pathogen since 1995 (data not shown). Among UTI, *Enterococcus* species and *S aureus* showed significantly increasing trends, whereas *E coli and P aeruginosa* showed significantly decreasing trends in relative frequency. For the period of 2000-2004, "*Candida* and other yeasts," which did not show a significant change in the trend analysis, surpassed *E coli* as the proportional leading pathogen for UTI (ie, "*Candida* and other yeasts," 22.0% vs *E coli* 19.6%; data not shown). Although a significantly increasing trend for *Enterococcus* species was also observed across the time blocks, vancomycin-resistant *Enterococcus* contributed a relatively low frequency (<2%) to UTI. Among RTI, *S aureus* increased significantly, whereas *Klebsiella* species, *Enterobacter* species, *E coli*, and other streptococci decreased. Among SSI, *S aureus* and "*Candida* and other yeasts" showed significantly increasing trends, whereas *P aeruginosa*, *Klebsiella* species, *Enterobacter* species, and "*C difficile* and other anaerobes" decreased significantly in relative frequency. Over the time period, *S aureus* dramatically doubled (15% to more than 30%) in relative frequency as a predominating pathogen of both RTI and SSI.

DISCUSSION

This study is unique in that we were able to perform analyses on the relative frequency of pathogens isolated from HAI over almost 3 decades at a single hospital. Over the study time period, our hospital conducted comprehensive surveillance using standardized CDC case definitions by trained infection preventionists with low staff turnover. Although NNIS/NHSN did not recommend that participating hospitals perform hospital-wide surveillance after 1986 and most adopted a targeted surveillance method (eg, intensive care unit only, device-related infections),[8] our hospital maintained a comprehensive hospital-wide surveillance program for the entire time period. Comparable studies that provide relative frequency of pathogens hospital-wide and for an extended time period are lacking. Although the NHSN does periodically report data on frequency of health care-associated pathogens, these data are limited in that they cannot be compared over time because the participating NHSN hospitals do not represent a true or well-defined cohort[7] and are not a random selection of hospitals in the United States.