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Temporal trends and risk factors for healthcare-associated vancomycin-resistant enterococci in adults

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SUMMARY

Background: Published data regarding temporal trends in vancomycin-resistant enterococci (VRE) prevalence within specific regions or healthcare systems are scarce.
Aim: To characterize temporal trends and risk factors for healthcare-associated infections caused by VRE.
Methods: The study included all adult discharges occurring from 2006 to 2014 with an enterococcal infection from three hospitals in a large academic healthcare system. Bivariate analyses were used to identify statistically significant factors associated with vancomycin-susceptible or -resistant infection. Statistically significant variables were included in a final logistic regression model. Trends assessed whether the proportion of enterococcal infections resistant to vancomycin changed over time.
Findings: The sample included 10,186 adults with first-time healthcare-associated enterococcal infection. Significant risk factors ($P \leq 0.05$) for VRE in the final logistic regression model included: tertiary 1 hospital, intensive care unit length of stay, higher Charlson Comorbidity Index, previous immunosuppressive or chemotherapeutic medications, previous hospitalization, renal failure, malignancy, longer length of stay prior to infection, taking an antibiotic prior to infection, being female, and having an infection in winter or spring. Between 2006 and 2014, the rate of resistance varied from 37.1 to 42.9% but there were no significant differences in the proportion resistant to vancomycin over time ($P = 0.36$).
Conclusion: Research targeted at risk factors is important to decrease the amount of VRE infections.

Introduction

Healthcare-associated infections (HCAIs) are frequent (4% of hospitalized patients), often preventable, and associated with medical devices: central line-associated bloodstream infection (BSI), surgical site infection (SSI), catheter-associated urinary tract infection (UTI), and ventilator-associated pneumonia.[1,2] Enterococci are one causative agent of HCAIs; these bacteria are a component of the faecal flora and may be contracted by direct or indirect by faecal–oral transmission; invasive devices are another important portal of entry.[3] *Enterococcus faecium* accounts for the majority of vancomycin-resistant infections and *Enterococcus faecalis* constitutes 2–20% of vancomycin-resistant enterococci (VRE) isolates.[3,4]

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Similar to other infectious agents, populations largely affected by VRE include the elderly, those with compromised immune systems, and critically ill patients in the intensive care unit (ICU).[5] Other risk factors include prolonged length of hospital stay, previous exposure to vancomycin, anti-cancer chemotherapeutic agents, immunosuppressants and anti-inflammatory drugs, renal insufficiency, malignancies, comorbidities, and surgical procedures.[4–6]

According to the Centers for Disease Control and Prevention's National Nosocomial Infections Surveillance (NNIS) system, the proportion of HCAIs caused by VRE rose from 0.3% to 7.9% between 1992 and 2004.[7] In addition, infections caused by VRE have been associated with higher treatment costs, prolonged morbidity, and greater mortality rates.[8] However, information regarding temporal trends in VRE prevalence within specific regions or healthcare systems is scarce. Therefore, the aim of this study was to characterize temporal trends and risk factors for HCAIs caused by VRE during a nine-year period (2006–2014) in a large academic healthcare system in New York City.

Methods

Study population

The study was conducted as part of a federally funded project, 'Health Information Technology to Reduce Healthcare-Associated Infection' (National Institute of Nursing Research, National Institutes of Health; R01NR010822). In this project a clinical research database was created of patients hospitalized within three adult acute tertiary care hospitals of the largest healthcare system in New York City. This analysis included all adult (≥18 years) patient discharges from the three hospitals between 2006 and 2014. The hospitals comprised two-tertiary/quaternary care hospitals, designated as hospital 1 and hospital 2 (about 650 and 910 beds), and an approximately 220-bed community hospital designated as hospital 3.

Data collection

The study database was constructed using electronic data from clinical and administrative systems shared between the study institutions.[9] The database drew information from numerous sources, including patients' electronic health record, laboratory and medication administration records, and included admission and discharge data, International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM) codes, age, sex, comorbidities, and surgical procedures. A subset of this larger dataset was used, with the primary outcome of interest being the first healthcare-associated (i.e. occurring >2 days after hospital admission) BSI, UTI, or SSI caused by *E. faecalis* or *E. faecium*. Infections were identified using a combination of time-stamped microbiology laboratory records and ICD-9-CM procedure and diagnosis codes, based on modified criteria from the CDC National Healthcare Safety Network (NHSN).[10]

Bloodstream infection was defined as positive *E. faecalis* or *E. faecium* blood culture with no positive culture with the same organism at another body site within the previous 14 days. In a previous study we verified that the definition of BSI was 100% congruent with a review of 122 medical records.[11] UTI was defined as a positive *E. faecalis* or *E. faecium* urine culture with $\geq 10^5$ colony-forming units (cfu) per mL and no more than one other species of micro-organism, or 10^3–10^5 cfu/mL plus pyuria. SSI was defined as positive *E. faecalis* or *E. faecium* wound culture within 30 days of an ICD-9-CM-documented National Healthcare Safety Network (NHSN) operative procedure.[12] Additionally, individual patient records were linked using their medical record number, and each patient's first positive VRE infection was used to remove patients with multiple cases of VRE infections. The year and season of each infection (winter, December–February; spring, March–May; summer, June–August; autumn, September–November) were also recorded. Vancomycin susceptibility patterns were obtained from the clinical microbiology reports.

Patients' demographic characteristics and medical conditions were collected from electronic sources. The institution's time-stamped electronic medication administration record was used to determine whether patients received antibiotics or other medications that might increase patient risk of infection (chemotherapeutic agents, immunosuppressants, and anti-inflammatory drugs), which we term 'high-risk medications' at least 24 h before infection. Comorbidities (diabetes, renal failure, and malignancies) and the Charlson Comorbidity Index were collected.[13] Other data collected included patients' age, sex, length of hospitalization, hospital location, length of stay prior to infection (calculated as the difference between first date of infection and date of admission), ICU stay prior to admission, prior within-network hospitalization, and admission from a nursing facility.

Identification of organisms was done in the study institution's clinical microbiology laboratory using Clinical and Laboratory Standards Institute standards; additionally, Vitek2 (bioMérieux, Inc., Durham, NC, USA) and/or E-test were used for antibiotic susceptibility testing.[14,15]

Statistical analysis

The frequency of BSI, UTI, and SSI caused by vancomycin-susceptible and -resistant *E. faecalis* and *E. faecium* were recorded by year. Initially, bivariate analyses using χ^2-tests for categorical variables or simple logistic regression for continuous variables were used to identify statistically significant ($P \leq 0.05$) factors associated with a susceptible or resistant enterococcal infection, including age, sex, hospital, ICU stay prior to infection, Charlson Comorbidity Index, diabetes, renal failure, malignancy, length of hospital stay prior to infection, antibiotic and high-risk medication use prior to infection, season and year (2006–2014), prior stay in a nursing facility, prior in-network hospitalization, infection site (BSI, UTI, or SSI), and medical invasive device. Those variables that were statistically significant in the bivariate analyses were included in a multivariate logistic regression model in a stepwise forward fashion. All analyses were performed using SAS version 9.4. The Cochran–Armitage test for trends was used to assess whether the proportion of *E. faecalis* and *E. faecium* infections resistant to vancomycin changed over time.

Results

A total of 10,186 adults with first-time healthcare-associated enterococcal infections were identified from 2006 through 2014: 4094 patients (40.2%) with VRE and 6092 (59.8%) with susceptible strains. Differences between patients with antimicrobial-resistant versus -susceptible enterococcus