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Major Article

Microbiology of surgical site infections in patients with cancer: A 7-year review

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Background: Health care–associated infections (HAIs) have arisen as major sources of multidrug-resistant bacteria. Surgical site infections (SSIs) are the most frequent HAIs in many countries, with high antimicrobial-resistant prevalence.

Methods: A 7-year retrospective review (2008-2014) of microbiologic data within a prospective surveillance program on patients with SSI at a cancer hospital in Mexico.

Results: There were 23,421 surgeries performed during the study period. The SSI rate was 7.9%. Gram-negative bacilli (GNB) were found in 56.5% of samples. *Escherichia coli* was the most frequent microorganism (27.5%), followed by *Staphylococcus aureus* (16.3%). SSI caused by *S aureus* showed a decreasing trend ($P = .04$). Extended-spectrum β-lactamase (ESBL)–producing *E coli* increased from 39.5% in 2008 to 72.5% in 2014 ($P < .001$). Fluoroquinolone resistance also increased in all members of the *Enterobacteriaceae*. Methicillin-resistant *S aureus* (MRSA) was isolated in 32% of cases with no significant increase (*P* value is not significant).

Conclusions: GNB caused most SSIs, with an increase of ESBL *E coli* strains. In breast and thoracic surgery, *S aureus* remained the most frequent isolate. MRSA remained stable throughout the study period. We observed a decreasing trend in *S aureus*. These findings show the differences in the microbiology of SSIs in a middle-income country and the increasing trend of ESBL enterobacteria and other multidrug-resistant organisms, such as *Enterococcus faecium*.

BACKGROUND

Surgical site infections (SSIs) are one of the most frequent health care–associated infections (HAIs) in low- and middle-income countries,[1,2] where 75% of the world's population resides.[3] The incidence of SSI in Mexico and other Latin American countries is higher than that reported by the U.S Centers for Disease Control's National Health Safety Network and in a recent review from the International Nosocomial Infection Control Consortium.[4,5]

SSIs increase health care costs, increase hospital readmissions, and are associated with higher morbidity and mortality.[2] Patients with SSI have a 60% increased rate of admission to the intensive care unit (ICU), a 15 times higher risk of rehospitalization within 30 days after discharge, and 6.5 extra hospitalization days.[6] In patients with cancer, the number of SSIs tends to be increased, with a negative impact on patients quality of life.[7,8] In addition to these observations, oncologic patient populations might be uniquely and more severely affected by emerging antimicrobial-resistant strains[9] because patients with cancer are frequently exposed to multiple antimicrobial regimens, creating selective pressure on this population. In regions with a high prevalence of antibiotic resistance, nearly one-half of gram-negative bacilli (GNB) isolated from surgical wards were found to be multidrug resistant (MDR).[10]

In the United States, gram-positive cocci are the most frequent bacteria found in SSIs.[2,5] Methicillin-resistant *Staphylococcus aureus* (MRSA) is highly prevalent, representing >40% of isolates in some series. GNB are becoming more important as etiologic agents of SSI.[4] Extended-spectrum β-lactamase (ESBL)–producing *Enterobacteriaceae* have increased in many regions of the world, and in some

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regions, they are the most frequent isolates of HAI.[11] Other MDR gram-negative bacteria, such as *Acinetobacter baumannii*, although less frequent as a causative agent, have also increased in surgical infections, especially among severely ill patients hospitalized in the ICU.

SSIs have comprised the most prevalent HAIs at the Instituto Nacional de Cancerología (INCan) since 1992, when a prospective surveillance program was initiated, with rates between 8% and 14%. *Escherichia coli* has been the most frequent isolate from SSIs during the last 20 years, and a steady increase in ESBL strains has been observed since 2008.

Despite the increased rate of HAI caused by MDR bacteria, there is little recent information on the pathogens causing SSIs. In the present report, we describe the microbiology and susceptibility patterns of SSI at a cancer referral center in Mexico City.

METHODS

Study population and case definition

The INCan is a 130-bed referral and teaching hospital for adult patients with cancer, with >3,500 surgical procedures performed each year. Seventy percent of patients at this institution are women, 30% are between 30 and 50 years old, and 63% are >50 years. Breast and cervical cancer are the 2 most common neoplasms, followed by other colorectal, ovarian, and prostate cancer. More than one-half of patients exhibit advanced disease stages and comorbidities, such as diabetes mellitus (19%), hypertension (32%), and obesity (15%).

Prospective surveillance of all surgical procedures is regularly conducted with a full chart review 30 days after discharge.

For the purpose of this study, we included all surgical specimens (wound, abscess, pus aspirate, or tissue) cultured at the microbiology laboratory between January 1, 2008, and December 31, 2014, regardless of surgery type or cancer diagnosis. Plating in blood, chocolate, and MacConkey agar was regularly conducted for microorganism identification. Identification of isolates was performed with MicroScan (AutoScan4, Dade, Behring, Germany) from 2008-2010. In 2011, the automated equipment was changed to BD Phoenix 100 (BD, Sparks, MD). Since 2014, isolates have been processed using matrix-assisted laser desorption/ionization–time of flight mass spectrometry. Susceptibility to antimicrobial agents was determined according to current Clinical Laboratory Standards Institute criteria. Susceptibility tests were identified by means of an automated microbiology system (BD Phoenix 100; BD, Sparks, MD). Resistant microorganisms were confirmed through a disk diffusion method.

Case definition

SSI was defined if any of the following conditions were met: (1) the surgical procedure registry or the medical chart was consistent with a diagnosis of SSI, or (2) the hospital surveillance system reported an SSI according to the Centers for Disease Control and Prevention's definition criteria. Duplicate cultures of a previously identified SSI were excluded from the analysis.

Identification and susceptibility testing

The following MDR bacteria were evaluated: MRSA, vancomycin-resistant *Enterococcus faecium* (VRE), ESBL-producing *E coli* and *Klebsiella* spp, and *Pseudomonas aeruginosa* and *Acinetobacter* spp resistant to third-generation cephalosporins and carbapenems. Other GNB were considered MDR if they were resistant to fluoroquinolones, third-generation cephalosporins, and carbapenems.[12]

Each sample was cross-referenced with the patient's medical record. Age, sex, surgical procedure, type of surgery (clean, clean-contaminated, contaminated, or infected), and SSI type were recorded. Cases with SSI that occurred within 30 days of surgery were included, or within 1 year if a prosthesis was inserted.

Statistical analysis

A descriptive analysis was conducted. Microbiologic findings were subcategorized by type of surgical procedure; frequency and susceptibility trends were described for each year and for the group of surgical procedures. Changes over time of selected microorganisms were evaluated by means of linear regression, and the annual changes in proportions of resistant isolates over this 7-year period were compared by the χ^2 test for trends. Data were analyzed using SPSS version 19.0 statistical software (SPSS, Chicago, IL).

RESULTS

During the study period, 23,421 surgeries were performed: 12,439 were clean (class I); 8,763 were clean-contaminated (class II); 578 were contaminated (class III); and 1,641 were infected (class IV). We identified 1,863 (7.9%) microbiologic proven SSI in 1,458 patients. Nine hundred eighty-six (67.6%) SSIs occurred in women, and 472 (32.4%) occurred in men. Mean age of patients was 54 ± 14.4 years.

There were 3,149 cultures taken; of these, 2,399 (76.2%) were positive. There were 2,782 isolates identified in 1,863 SSIs (7.9% of the surgical procedures performed). Class III surgeries had the highest infection rate (21%), followed by class II (8.2%), and class I (8.1%). SSIs in which a culture was obtained and that demonstrated a positive isolate were more frequently found from abdomen and pelvis (525 infections of 2,962 surgeries = 14.5%), breast (497 infections of 5,050 surgeries = 10.4%), and soft tissue and sarcoma (189 infections of 2,685 surgeries = 7.04%) surgical procedures.

Sixty percent of infections (1,137) were monomicrobial, and 40% (n = 726) were polymicrobial. GNB were the most prevalent microorganisms, accounting for 56.5% (n = 1,561) of the isolates, regardless of the surgery type. Overall, *E coli* was the most frequent microorganism (n = 759, 27.3%), followed by *S aureus* (n = 451, 16.2%), *Enterococcus faecalis* (n = 258, 9.3%), and *P aeruginosa* (n = 215, 7.7%), as depicted in Figure 1. The proportion of SSI caused by *E coli* increased from 25% in 2008 to 34.7% in 2014 (linear regression $R^2 = 0.313$, $P = .1917$), whereas *S aureus* significantly decreased from 19.5% in 2008 to 7.4% in 2014 (linear regression $R^2 = 0.5736$, $P = .0486$).

The most frequent microorganisms for selected surgical procedures are summarized in Figure 2. For detailed information regarding the most common procedures, and the most frequent microbial isolates for specific group of surgeries, see Supplementary Appendix S1.

Antimicrobial susceptibility

From 2008-2014, fluoroquinolone resistance increased for all members of the *Enterobacteriaceae* family; *E coli* resistance increased from 60.7% to 80.8% (χ^2 for trend = 11.22, $P = .0008$), *Klebsiella pneumoniae* increased from 16.7% to 55.2% (χ^2 for trend = 8.399, $P = .0038$), and ciprofloxacin-resistant *P aeruginosa* increased from 23.1% to 37.8% (χ^2 for trend = 0.7751, $P = .3787$). ESBL-producing *E coli* also increased from 39.5% to 72.5%, (as illustrated in Fig 3) (χ^2 for trend = 45.05, $P < .001$). *K pneumoniae* was rare (n = 83), but ESBL *K pneumoniae* accounted for 22.9% (n = 19) of all these isolates. Most were found during 2012-2013.

Of *P aeruginosa* isolates, 32 out of 215 (14.9%) were resistant to carbapenem over the study period, decreasing from 25.6% in 2008 to 8.3% in 2014 (χ^2 for trend = 4.059, $P = .0439$). MDR *P aeruginosa* isolates were uncommon (n = 25, 11.6% of *P aeruginosa*). MDR isolates