American Journal of Infection Control 43 (2015) 739-44

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Multicenter study of health care cost of patients admitted to hospital with *Staphylococcus aureus* bacteremia: Impact of length of stay and intensity of care

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Key Words:
Health care
Cost analysis
Methicillin-resistant *Staphylococcus aureus*
Bacteremia
Hospitalization

Background: Methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S aureus* bacteremia (SAB) have both been associated with high morbidity and mortality and heavy consumption of health care resources. We compared clinical and economic data for hospitalized cases of SAB in the context of a publicly funded health care system.

Methods: A cost analysis was undertaken on an adult cohort of patients from 4 hospitals with SAB diagnosed within 3 days of hospitalization. Primary outcome was direct cost of inpatient care per case, determined at discharge and itemized using a standardized methodology.

Results: A total of 435 patients were admitted with SAB; 58 had methicillin-resistant *S aureus* (MRSA). The median length of stay was similar in patients with MRSA and MSSA. There was no significant difference between the groups for mortality. Median direct medical costs of SAB were $12,078. Patients with MRSA had 1.32 times higher direct costs than MSSA. A similar estimate was derived using a propensity score approach ($P = .148$). Human health care resources comprised >70% of total costs per case, whereas antibiotics comprised 1%-2%.

Conclusion: Understanding the dynamics of resource consumption is critical to improving its efficiency and the quality of patient care. Our findings suggest that hospital length of stay and care intensity should be the major focus of any resource assessment exercise.

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Staphylococcus aureus bacteremia (SAB) is associated with high morbidity, mortality, and consumption of health care resources.[1-3] Rates of methicillin-resistant *S aureus* (MRSA) infection have been declining across the United States over the last decade.[4] However, the relative incidence of SAB caused by MRSA and methicillin-susceptible *S aureus* (MSSA) varies.[5] MRSA may now be adding to the total burden of SAB rather than merely replacing MSSA.[6]

Cost studies have been used to examine health care resource utilization and thereby inform planning and delivery of health services.[7] Numerous cost studies demonstrate that the direct medical costs of bacteremia caused by MRSA exceed those of MSSA, particularly with the emergence of community-associated MRSA.[8-14] Estimates

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Funding/Support: This study was largely unfunded. The Mount Sinai Hospital Antimicrobial Stewardship Program (ASP) is supported by an unrestricted educational grant from Pfizer Canada. Part of the Research Coordinator's (M. Steinberg) and ASP Fellow's (N. Thampi) salaries were supported by this grant at the time of this study. A Mount Sinai Hospital Department of Medicine Summer Studentship Award funded A.D. Bai. A.M. Morris receives partial salary support for his antimicrobial stewardship activities from Mount Sinai Hospital and University Health Network. A Canadian Institutes of Health Research (CIHR)/Canadian Patient Safety Institute (CPSI) Chair in Patient Safety and Continuity of Care supports C.M. Bell.
Conflicts of interest: None to report.

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http://dx.doi.org/10.1016/j.ajic.2015.01.031

of excess costs from these studies range from $3,767-$42,286 (in 2010 US$), approaching 10 times the cost of MSSA. The heterogeneity in patient population, study design, sample size, and cost methodology of the estimates makes it difficult to generalize and formulate potential intervention strategies.

These studies examining the costs of SAB have not incorporated changes in diagnostic and treatment approaches over the last decade.[15] Furthermore, most studies examining resource utilization and costs are single-center studies, limiting their generalizability. Using a standardized costing methodology, we performed a multicenter analysis following established guidelines to determine the costs from the hospital perspective associated with hospitalization for SAB.[7]

PATIENTS AND METHODS

Study setting

The cost analysis examined data gathered from 4 hospitals in Toronto, Canada, as part of a larger cohort study involving the investigation and management of SAB. Research ethics boards at all sites provided approval. During the study period (April 1, 2007-March 31, 2010), demographic, diagnostic, therapeutic, and outcome data for all patients with at least 1 positive blood culture for *S aureus* within 3 days of hospital admission were collected through chart review. We independently conducted source data verification by assessing a random sample of 10% of data entry points for accuracy and performed range edits and value checks to reduce the potential for data entry errors. We referred data gaps and suspected anomalies back to hospital sites for verification. Data were deemed high quality and near complete.

All sites used standard methods conforming to Clinical and Laboratory Standards Institute guidelines for *S aureus* identification and antimicrobial susceptibilities.[16] Echocardiography was performed at the discretion of the primary responsible physician. Infectious disease services consultation was available at all hospital sites. At 3 hospitals, the microbiology laboratory notified the infectious diseases consultants directly when inpatient blood cultures were positive for *S aureus*. Departmental policy at these hospitals included offering a consultation for patients admitted to general internal medicine or the medical-surgical intensive care unit (ICU) and automatically performing a consultation for patients admitted to all other services.

Population

The hospitals are in geographically similar locations with varying subspecialty programs, including oncology, solid organ transplantation, and cardiac disease. Collectively, they comprise >2,300 acute care beds, or 80% of the acute care beds in the Toronto Central area. Patients were entered in the study only once, at the time of the first positive blood culture. We included only adult (age ≥18 years) inpatients with a first SAB episode, and we excluded patients who were deemed palliative, transferred to another facility, or left against medical advice within 48 hours of bacteremia.

Costing

The primary outcome was total cost of inpatient care for each patient using 2010 Canadian dollars. This was determined using the Ontario Case Costing Initiative (OCCI) methodology.[17-20] This methodology is based on the Canadian Institute for Health Information Management Information Systems Guidelines and Ontario's Ministry of Health and Long-Term Care's Healthcare Reporting Standards. Participating hospitals have implemented a standardized approach and participated in a series of milestone reviews and audits conducted by the OCCI to ensure data quality.[21] Aggregate costs of hospitalization are allocated to health care service components, or functional cost centers, based on patient visits and resource use. Direct costs are related to patient care and include laboratory tests, medications, and nursing care on wards and in the ICU. In comparison, indirect costs are related to nonpatient-directed resources, including administration, housekeeping, and information systems. Direct and indirect costs of each functional cost center (eg, allied health, pharmacy, diagnostic imaging, nursing) are integrated and applied to each patient care service according to standardized workload measurement systems.[22] Total hospital costs incurred by each functional center are apportioned to individual patients at the time of discharge based on the mix of services they have received (Supplementary Table 1).[21]

Physician-related costs are not included in the OCCI because they are not remunerated through the hospital. Rather, for each professional service performed, physicians bill a standard amount to the Ontario Health Insurance Plan, which gets its funding from the Ontario Ministry of Health and Long-Term Care. Hospitals that participate in the OCCI undergo annual audits of data submission to ensure their quality and accordance with provincial reporting standards. Echocardiography is not allocated to any department; therefore, the costs of transthoracic or transesophageal echocardiograms for patients in this study were obtained from the Ontario Health Insurance Program's schedule of benefits and added separately.[23] Costs are reported in 2010 Canadian dollars, which approximate 2010 US dollars.

Statistical analysis

Median values with interquartile ranges (IQRs) were derived for nonnormally distributed variables. Hospitalization costs for MRSA compared with MSSA bacteremia were compared using nonparametric means. Demographics, clinical characteristics, and costs were compared according to methicillin susceptibility status using Student *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables, where appropriate. Costs across the 4 hospital sites were compared using Kruskal-Wallis tests.

Logarithmic transformation was applied to direct cost to reduce skewness of the distribution. The log-transformed cost was the dependent variable in linear regression models. Potential predictors considered included hospital sites, age, sex, admitting service, comorbidities, health care–associated infection, sites of infection, and MRSA. Predictors with *P* values <.20 on univariate analyses were included in the multivariable linear regression model along with hospital sites. An exponential transformation was applied to the coefficients of the linear regression models, which were reported as ratios of direct cost. Bootstrap case resampling with 2,000 replications was used to estimate confidence intervals (CIs) for the coefficients in the model. Propensity scores for MRSA or MSSA were estimated using a generalized boosted regression model using all of the potential predictors previously listed. In this context, the propensity score is the probability of a patient in the study having MRSA rather than MSSA. The propensity score is estimated from modeling of the observed covariates using a generalized boosted regression model. Boosting is use of a general, automated, data-adaptive algorithm to fit a nonlinear surface and predict assignment using a large number of covariates.[24] Generalized boosted regression models adds simple functions of regression trees that describe the relationship between a multivariate set of independent variables and treatment assignment to form a smooth function of a large number of covariates predicting the propensity score.[24] A generalized linear regression model was used to compare

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