Attributable mortality of hospital-acquired bloodstream infections in Ireland

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SUMMARY

Aim: To estimate the attributable mortality of hospital-acquired bloodstream infections (HA-BSI) in Ireland.

Methods: A retrospective case—cohort study was conducted, based on notifications from Irish microbiology laboratories and administrative patient records from six Irish hospitals from January 2007 to December 2013. Probabilistic linkage was used to link 1252 cases of bloodstream infection from a cohort of 343,189 hospitalized patients. Independent predictors of mortality were determined using a multi-variable logistic regression model, and included: patient age, emergency or re-admission to hospital, length of stay in an intensive care unit, number of procedures, number of diagnoses, major diagnostic category and presence of HA-BSI.

Results: Attributable mortality was calculated from the crude mortality of case subjects after adjusting for other predictors of mortality, and was found to be 15.3% (95% confidence interval 14.8—15.8%). The study was further stratified according to the causative organism, including: *Escherichia coli, Enterococcus faecium, Enterococcus faecalis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus* and *Streptococcus pneumoniae,* and, where available, their antimicrobial resistance patterns. The highest attributable mortality among these organisms was reported for *E. faecium* at 18.1% and the lowest attributable mortality was reported for *E. coli* at 13.6%. A significantly higher attributable mortality was found for antimicrobial resistance patterns of some organisms, most notably for meticillin-resistant *S. aureus* at 19.5%, vs meticillin-susceptible *S. aureus* at 13.3%.

Conclusions: HA-BSI is an important cause of mortality, and attributable mortality differs significantly among causative organisms and antimicrobial resistance patterns.

Introduction

Hospital-acquired bloodstream infection (HA-BSI) is a serious and sometimes fatal complication of hospitalization, particularly among immunocompromised patients.[1] In 2012, a European point prevalence survey, coordinated by the

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European Centre for Disease Prevention and Control (ECDC), reported a prevalence of hospital-acquired infection (HAI) among patients in Irish acute hospitals of 5.2%, with HA-BSI accounting for 13.2% of HAI.[2] For HAI overall, the most common causative pathogens belonged to the family Enterobacteriaceae (35.2%), which comprise normal gastrointestinal tract flora. The second most common causative pathogen was *Staphylococcus aureus* (14.8%), an organism frequently found on the skin and nasal passages of healthy individuals. Enterococci accounted for 10.9% of HAI, often as a complication of prolonged hospitalization in 'at-risk' patients. For HA-BSI, *S. aureus* and *Escherichia coli* were the top two causative organisms (19% and 16%, respectively).[2]

In recent years, antimicrobial resistance has increased in Ireland, particularly for pathogens such as *E. coli, Klebsiella pneumoniae, P. aeruginosa* and *Enterococcus faecium*.[3,4] This is concerning given the frequency at which these organisms cause BSI, and the limited treatment options that are currently available to treat multi-drug-resistant (MDR) infections. A 2009 report estimated that infections caused by five MDR bacteria accounted for 25,000 deaths annually in the European Union, with the United States Centers for Disease Control and Prevention describing antimicrobial resistance as one of the world's most concerning health problems.[5,6]

This study aimed to estimate the attributable mortality of HA-BSI caused by *E. coli, E. faecium, E. faecalis, Pseudomonas aeruginosa, K. pneumoniae, S. aureus* and *Streptococcus pneumoniae,* and the antimicrobial resistance (AMR) patterns of these organisms, in order to provide data to inform future infection prevention strategies in Irish health care. A retrospective study was conducted of patients in Irish hospitals, using patient records from the Hospital In-Patient Enquiry Scheme (HIPE), which is the principal source of national data on discharges from acute hospitals in Ireland, and enhanced data from the European Antimicrobial Resistance Surveillance Network (EARS-Net), a surveillance system designed to collect national data on AMR.

Methods

Study population/variables

A retrospective case—cohort study approach was adopted for this study, in which criteria for inclusion of HA-BSI was defined as a positive blood culture >48 h after admission to the hospital, as reported by Irish microbiology laboratories to Ireland's enhanced EARS-Net system.[7] Data were selected from six Irish hospitals: two large tertiary hospitals, two regional hospitals and two smaller general hospitals. Hospitals were geographically distributed across three of the four Irish Health Service Executive (HSE) regions, with clinical services ranging in complexity. In order to ensure high-quality data, hospitals were chosen based on their consistency of reporting enhanced data to EARS-Net during the study period and on the completeness of the data reported. It was ensured that the enhanced EARS-Net data reported from these six hospitals were consistent during the study period by calculating the proportion of records in the core EARS-Net dataset that had enhanced data.

The HIPE dataset was accessed through the Health Intelligence Ireland secure online healthcare data analytical system managed by HSE Ireland. Enhanced EARS-Net data were obtained from the Health Protection Surveillance Centre, the national centre for surveillance of infectious diseases in Ireland. Quality and consistency checks were integrated within HIPE software. In both schemes, data were collected from paper medical records, which were completed by trained personnel using structured data collection tools.[8]

Data were collected over a seven-year period from 1st January 2007 to 31st December 2013. Variables collected were: age, sex, year, date of admission, type of admission, source of admission, date of discharge, type of discharge, hospital and intensive care unit (ICU) length of stay (transformed as logs after adding 1), specimen date, major diagnosis category (MDC), number of diagnoses, number of procedures, BSI causative organism and AMR results. Number of diagnoses refers to the number of conditions or complaints either co-existing with the principal diagnosis or arising during the episode of admitted patient care. Number of procedures refers to the number of clinical interventions that were surgical in nature, carried a procedural risk and/or carried an anaesthetic risk and/or required specialized training and/or required special facilities or equipment only available in an acute care setting. Patient age was grouped as: ≤4, 5—14, 15—29, 30—49, 50—64, 65—74, 75—84 and ≥85 years. The type of discharge was categorized into four outcome levels. Level 1 included patients discharged home, to prison, to a temporary place of residence, absconded, self-discharged or 'other'. Level 2 included discharge or transfer to a nursing home, convalescent home or long stay accommodation, psychiatric hospital or unit, non-acute hospital or external rehabilitation facility. Level 3 represented transfer to an acute hospital or hospice, and level 4 was death (in-hospital mortality). Date/time of patient death was not collected for all applicable cases and was therefore excluded. MDC codes were obtained from the International Classification of Diseases, 10th Revision, Australian Modification (6th edition). HA-BSI cases included in the study were those that were reported via EARS-Net in Ireland. A case was defined as polymicrobial if more than one organism was isolated from a single episode of BSI. The AMR status of an organism was defined as per clinical breakpoint definitions observed by the European Committee on Antimicrobial Susceptibility Testing.

Sample size estimation

Sample size was calculated using OpenEpi Version 3.03 (http://www.openepi.com/SampleSize/SSCohort.htm), in which Fleiss formulae for unmatched cohort studies with continuity correction were applied to determine the appropriate sample size for a power of 0.8 and significance level of 0.05.[9,10] For a 1:3 ratio, the minimum sample size required was 371.

Study design

Some variables of interest were recorded in the HIPE dataset but not the enhanced EARS-Net dataset. To resolve this, probabilistic record linkage was undertaken, preserving patient confidentiality by linking records based on partially identifiable variables, a method that is advocated frequently.[11—15] Probabilistic linkage was conducted in an Access database (Microsoft Corp., Redmond, WA, USA). The enhanced EARS-Net scheme is voluntary and does not enforce mandatory completion of data collection forms. Therefore, to minimize potential bias arising from incomplete forms, only links that were very highly discriminatory, with a high positive