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BRIEF REPORT

Comparison of the Clinical Characteristics of Hospital-Acquired and Non-Hospital-Acquired *Acinetobacter calcoaceticus-baumannii* Complex in a Large Midwest US Health Care System

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We retrospectively compared the clinical characteristics of hospital-acquired (HA) vs non-hospital-acquired (nHA) *Acinetobacter calcoaceticus-baumannii* complex isolates in a large health care system in St. Louis, Missouri, from 2007 to 2017. More than 60% of the total isolates were nHA; they were predominantly from nonrespiratory sources and exhibited ~40% carbapenem resistance rates and stably persisted, though HA occurrence waned.

Keywords. *Acinetobacter baumannii*; hospital-acquired infections; multidrug resistance.

The *Acinetobacter calcoaceticus-baumannii* complex (Abc) is a group of gram-negative bacteria capable of colonizing diverse host and abiotic environments. Abc infections exhibit high rates of antibiotic resistance, and the increasing prevalence of carbapenem-resistant *A. baumannii* is an urgent global health threat [1, 2]. The Abc is widely regarded as a group of opportunistic pathogens that principally cause hospital-acquired (HA) pneumonia and bacteremia in critically ill or immunocompromised patients [3, 4]. Multiple studies, however, support that Abc isolates are routinely identified in outpatient settings [5–8], that is, that they are non-hospital-acquired (nHA). Few investigations have compared contemporaneous HA and nHA Abc, so it remains unclear whether interventions tailored against "classical" HA Abc populations equally impact nHA counterparts. Here we report a retrospective longitudinal analysis of Abc isolates in a large, multihospital system. Notably, effective local interventions against nosocomial infections occurred during this period, allowing us to observe their impacts on different Abc populations.

METHODS

Study Location and Period

We performed a retrospective analysis of clinical isolate data in the BJC HealthCare System (BJC) from January 2007 to September 2017. BJC is a large integrated health care system in and around the Greater Metropolitan Area of St. Louis, Missouri. It includes 9 community hospitals, a pediatric hospital, and a 1250-bed academic adult medical center (hereafter "BJC1"), totaling >3200 inpatient beds and >140 000 admissions annually. For longitudinal analyses, we used full-year data from 2007 to 2016.

Isolate Identification and Definitions

Using the BJC Clinical Data Repository (CDR), we identified all *Acinetobacter* isolates obtained from individuals aged ≥18 years as part of regular medical care. Only isolates from the first isolation event per patient ("index culture") were eligible for inclusion. Subsequent cultures from the same patient were excluded. Isolates were identified using automated biochemical methods or matrix-assisted laser desorption/ionization and time-of-flight spectroscopy. Only index cultures identified as *Acinetobacter baumannii* (n = 990) or *Acinetobacter calcoaceticus-baumannii* complex (n = 1052) were included for analysis. Patient information, isolation source, hospital day of index culture (if applicable), and antibiotic susceptibility data were obtained from the BJC CDR and electronic chart review. Isolates were classified into 5 anatomical categories according to source: "respiratory," "skin and soft tissue/musculoskeletal" (SST/MSK), "urinary," "blood" (including isolates obtained from central lines, endovascular devices, or grafts), or "other." Isolates were defined as HA if the index culture was performed ≥48 hours after hospital admission and before discharge. All other isolates were defined as nHA.

Antibiotic Susceptibility Reporting

Antibiotic susceptibility testing was performed using the Vitek 2 system or Kirby-Bauer disk diffusion on Mueller-Hinton Agar and interpreted per CLSI guidelines [9]. Due to temporal and hospital variation in testing practices, some antibiotic susceptibility profiles were incomplete. Isolates lacking data for an antibiotic were excluded from their respective analyses. Isolates reported as "resistant" or "intermediate" were classified as "nonsusceptible." If an isolate was nonsusceptible to any

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antibiotic in a class, it was labeled "nonsusceptible" for that class (Supplementary Table 1).

Statistical Methods

Univariate analyses were performed with SPSS, version 25 (IBM Corp., Armonk, NY, USA). The chi-square test or independent *t* test was performed for comparing categorical or continuous variables, respectively. *P* values <.05 were considered statistically significant.

RESULTS

Of the 2042 eligible Abc index cultures identified in BJC hospitals from January 2007 to September 2017, 48.3% were from BJC1 and 51.7% were from other BJC hospitals (hereinafter, referred to as "non-BJC1" hospitals). The number of isolates from each anatomical source is listed in Supplementary Table 1. As seen in Figure 1A, annual index cultures at BJC1 increased through 2009 then steadily decreased, whereas annual

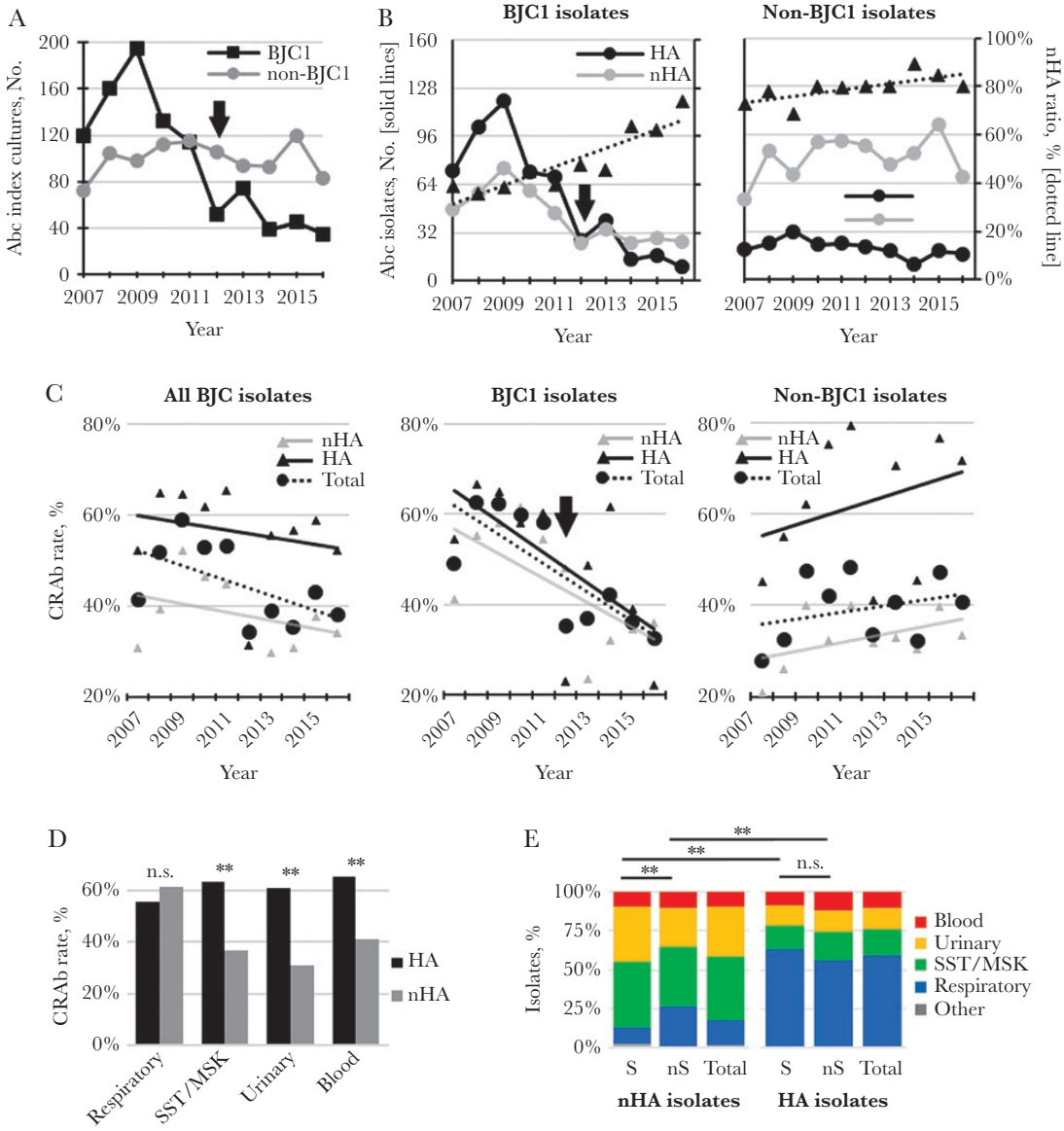

Figure 1. Annual occurrence and carbapenem nonsusceptibility trends among adult Abc isolates, BJC 2007–2016. A, Annual BJC1 ("BJC1," black) and non-BJC1 (gray) Abc index cultures. B, Annual amounts of non-hospital-acquired (nHA; gray) and hospital-acquired (HA; black) isolates among BJC1 and non-BJC1 isolates. Black triangles depict annual percentages of isolates that are nHA ("nHA ratio"), and dotted lines are best-fit trend lines for annual nHA ratios (values on right y-axis). C, Carbapenem nonsusceptibility rate ("CRAb rate") among all BJC, BJC1, and non-BJC1 Abc isolates. Graphs depict annual CRAb rates among total (black circles, dashed lines), HA (black triangles and solid line), and nHA (gray diamonds and solid line) isolates. D, CRAb rates among isolates from each anatomic source, grouped by HA (black) and nHA (gray). CRAb rates was compared between HA and nHA isolates. E, Proportion of carbapenem-susceptible (S), -nonsusceptible (nS), or total Abc isolates from each anatomic source. Isolates were grouped into HA and nHA. The proportion of isolates from each source was compared between compartments. $^{**}P < .005$ by chi-square test. Black arrows in (B) and (C) depict the year during which a BJC1 intensive care unit that was implicated in multiple nosocomial Abc outbreaks was relocated (see text). Abbreviations: n.s., not significant; SST/MSK, skin and soft tissue/musculoskeletal.

non-BJC1 index cultures remained relatively constant. Changes in annual BJC1 isolates were largely driven by ~70% decreases in annual respiratory, urinary, and blood isolates between 2009 and 2016 (Supplementary Figure 1).

Thirty-seven point nine percent and 62.1% of all Abc isolates were HA and nHA, respectively (Supplementary Table 1), but the percentage of isolates that were nHA ("nHA ratio") changed over time. Annual BJC1 HA isolates experienced a >10-fold decrease during 2009–2016 (Figure 1B), resulting in annual nHA ratios increasing from 39.2% to 74.3%. Annual BJC1 nHA isolates also exhibited a ~3-fold decrease from 2009, though they remained relatively stable after 2012. Annual nHA ratios among non-BJC1 isolates averaged 78.7% and remained largely unchanged (Figure 1B). Fifty-six point five percent of total HA isolates were from respiratory sources, followed by SST/MSK (19.1%), urinary (13.0%), blood (10.5%), and "other" (0.9%). In contrast, nHA isolates were primarily SST/MSK (42.9%) and urinary (30.4%).

As seen in Supplementary Figure 2, 2007–2011 annual nHA ratios among BJC1 respiratory and urinary isolates averaged 23.5% and 61.8%, respectively. After a sharp decline in 2012, annual nHA ratios among BJC1 respiratory isolates varied between 15.4% and 66.7%. Contemporaneously, annual BJC1 HA urinary isolates decreased to 0, whereas ~10 nHA urinary isolates were identified annually through 2016. The nHA ratios of both BJC1 and non-BJC1 blood isolates gradually increased over the study period. In contrast, BJC1 SST/MSK isolates and non-BJC1 SST/MSK, urinary, and respiratory isolates displayed relatively stable nHA ratios, averaging 60.4%, 83.3%, 87.5%, and 46.8%, respectively (Supplementary Figure 2).

All groups of Abc isolates exhibited >20% antibiotic nonsusceptibility rates (Supplementary Table 2). Greater nonsusceptibility was observed among older patients, HA (vs nHA) isolates, and respiratory and blood (vs urinary and SST/MSK) sources (Supplementary Table 2). All 867 carbapenem-nonsusceptible Abc isolates were resistant to at least 2 other antibiotic classes. Among all Abc isolates, annual carbapenem nonsusceptibility rates ("CRAb rate") ranged from 34.2% in 2012 to 58.9% in 2009. Annual CRAb rates for nHA and HA isolates averaged 38.1% and 56.3%, respectively (Figure 1C). BJC1 CRAb rates declined beginning in 2012, averaging 58.3% during 2007–2011 and 36.6% during 2012–2016 (Figure 1C). In contrast, non-BJC1 CRAb rates were stable throughout the study period, averaging 39.3% (Figure 1C).

CRAb rates were comparable among HA isolates from different anatomic sources (Figure 1D, black bars) and were indistinguishable between nHA and HA respiratory isolates (61.2% and 55.8%, respectively; $P = .22$). In contrast, CRAb rates were lower in nHA vs HA isolates from SST/MSK (36.7% and 63.4%, respectively), urinary (30.8% and 61.1%), and blood (41.2% and 65.3%) sources ($P < .001$ for all comparisons) (Figure 1D). Respiratory isolates composed 55.0% of HA CRAb isolates but only 25.8% of total nHA CRAb isolates (Figure 1E). Conversely, SST/MSK and urinary isolates composed 40.8% and 31.9%, respectively, of nHA CRAb isolates while composing only 18.5% and 13.7%, respectively, of the HA CRAb reservoir. Thus, although HA CRAb isolates were principally from respiratory sources, nHA CRAb isolates were principally from urinary and SST/MSK sources.

DISCUSSION

In prior cohorts, 25%–65% of Abc clinical isolates were identified within 48–72 hours of hospital admission or in the ambulatory setting [5–8]. Using comparable criteria, we determined that 60%–80% of Abc isolates in our cohort were nHA. The higher nHA ratio in our study may result from the inclusion of multiple regional community hospitals, yielding a more comprehensive survey of local Abc pools. Our retrospective database analysis was limited by not identifying which nHA isolates were likely health care–associated (HCA) [10]. For example, we could not identify whether individuals were recently hospitalized, resided in long-term acute care (LTAC) facilities, or were transferred from non-BJC hospitals. However, important epidemiological distinctions were made between HA and nHA cases. First, we observed that nHA isolates were most often from SST/MSK or urinary sources and that HA isolates were predominately from respiratory sources (Figure 1E). Though the anatomic sources of isolates are probably influenced by the variable culturing practices in each patient population, these associations are consistent with observations from hospitals in Hong Kong and Spain [11, 12]. Second, CRAb rates were lower among nHA (~40%) vs HA (~60%) isolates (Supplementary Table 2). This difference in resistance rates is consistent with observations from other US observational studies [6, 8].

An important observation is that the occurrence of nHA isolates persisted even after the significant decline in BJC1 HA Abc cases. Multiple 2007–2012 HA isolates were obtained in a BJC1 ICU implicated in several nosocomial outbreaks from 2007 to 2011. The physical relocation of this ICU ward in 2012 and robust hospital-wide infection control practices coincided with a 10-fold decrease of annual BJC1 HA isolates. A concomitant 3-fold decrease in nHA isolates was possibly due to an accompanying reduction of related HCA cases. Nevertheless, the decrease in HA respiratory, urinary, and blood isolates to near-0 levels unmasked an endemic occurrence of nHA isolates with epidemiologic features similar to nHA isolates from non-BJC1 hospitals (ie, urinary and SST/MSK isolates with ~40% CRAb rates). Consistent with the existence of nHA reservoirs, genomic analysis of *A. baumannii* isolates in another US Midwest medical center suggested that transmissible isolates at 2 independent hospitals originated from a single, external, nonhospital pool [13]. The location of outpatient Abc pools, their trafficking into

hospital environments, and the impact of nHA strains on local Abc disease require further investigation.

In conclusion, similar to reports from a California medical center [14], our findings reaffirm that control of HA infections is an effective way to reduce drug-resistant Abc incidence in a local population. However, even in the absence of local nosocomial outbreaks, our Abc MDR rates remained stably above 40%. This highlights that the battle against MDR Abc disease must involve outpatient and LTAC settings, where MDR isolates are commonly obtained from SST/MSK and urinary sources.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Author contributions. J.J.C. designed and performed this study and wrote this manuscript. J.P.B. and M.F.F. participated in the design of this study and in developing the manuscript.

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