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Original Article

Comparative epidemiology of hospital-onset bloodstream infections (HOBSIs) and central line-associated bloodstream infections (CLABSIs) across a three-hospital health system

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Abstract

Objective: To evaluate the comparative epidemiology of hospital-onset bloodstream infection (HOBSI) and central line-associated bloodstream infection (CLABSI)

Design and Setting: Retrospective observational study of HOBSI and CLABSI across a three-hospital healthcare system from 01/01/2017 to 12/31/2021

Methods: HOBSIs were identified as any non-commensal positive blood culture event on or after hospital day 3. CLABSIs were identified based on National Healthcare Safety Network (NHSN) criteria. We performed a time-series analysis to assess comparative temporal trends among HOBSI and CLABSI incidence. Using univariable and multivariable regression analyses, we compared demographics, risk factors, and outcomes between non-CLABSI HOBSI and CLABSI, as HOBSI and CLABSI are not exclusive entities.

Results: HOBSI incidence increased over the study period (IRR 1.006 HOBSI/1,000 patient days; 95% CI 1.001–1.012; $P = .03$), while no change in CLABSI incidence was observed (IRR .997 CLABSIs/1,000 central line days, 95% CI .992–1.002, $P = .22$). Differing demographic, microbiologic, and risk factor profiles were observed between CLABSIs and non-CLABSI HOBSIs. Multivariable analysis found lower odds of mortality among patients with CLABSIs when adjusted for covariates that approximate severity of illness (OR .27; 95% CI .11–.64; $P < .01$).

Conclusions: HOBSI incidence increased over the study period without a concurrent increase in CLABSI in our study population. Furthermore, risk factor and outcome profiles varied between CLABSI and non-CLABSI HOBSI, which suggest that these metrics differ in important ways worth considering if HOBSI is adopted as a quality metric.

Introduction

Central line-associated bloodstream infection (CLABSI) incidence has been one of the fundamental measures of infection prevention-related quality of care monitored by the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) in the United States. Though CLABSIs remain a major cause of morbidity and mortality,[1] there are drawbacks in utilizing CLABSIs as a quality metric. First, CLABSI criteria as defined by the NHSN[2] can be complex, subjective, and require significant time investment by infection preventionists for reporting purposes.[3,4] Second, NHSN-defined CLABSI criteria are imperfect measures of true clinical diagnoses of central line-

associated bacteremia, with limited sensitivity and specificity.[5] As such, both under- and over-reporting of CLABSIs may be occurring across the United States, at the cost of accurate surveillance as well as the valuable time and effort of infection preventionists.

Over the past several years, a new quality metric- hospital-onset bloodstream infection (HOBSI)- has been proposed.[5,6,7,8] Given its simpler definition, HOBSI may serve as a more objective and easily automated metric compared to its CLABSI counterpart.[5,7,8] Furthermore, previous studies have suggested that HOBSI surveillance is able to better discriminate between the quality of care provided across units or facilities compared to CLABSI surveillance.[7] Finally, HOBSI may provide a more holistic assessment of overall quality of care compared to CLABSI: while CLABSI diagnoses are limited to those with a central line, HOBSI diagnoses include bacteremia from all potential healthcare-related infections (ex. ventilator-associated pneumonia or urinary

tract infection), each of which have important infection prevention measures whose adherence may be better captured by HOBSI compared to CLABSI.[7,8,9]

Others have found that HOBSI and CLABSI incidence are correlated.[8] We hypothesized that there may be important differentiating characteristics unique to each metric that are worth examining, particularly if HOBSI is adopted as a future healthcare quality metric alongside or in place of current CLABSI definitions. To that end, we sought to evaluate the epidemiology of HOBSI, CLABSI, and—since HOBSI and CLABSI are not exclusive entities- non-CLABSI HOBSI incidence across our healthcare system over a five-year period, including the COVID-19 pandemic era.

Methods

Study population and design

We performed a multi-center retrospective analysis of HOBSI epidemiology at the Duke University Health System (DUHS), which includes one academic hospital and two community hospitals, from 01/01/2017 and 12/31/2021. The academic hospital (Hospital A in Table 1) has approximately 1,048 inpatient beds, while the two community hospitals have 338 beds (Hospital B) and 186 beds (Hospital C), respectively. While each hospital has independently functioning infection prevention programs, all sites use the same system-wide policies for central line and urinary catheter care, which includes infection prevention measures. For example, the central line care policy states that all patients across all sites with central venous access should receive daily chlorhexidine gluconate baths; daily review of indication for central venous access; and cap, dressing, and tubing changes at appropriate intervals, among other measures.

Our analysis consisted of three components: 1) a hospital-level time-series analysis evaluating temporal trends in CLABSI and HOBSI incidence; 2) a comparative patient-level analysis comparing patient demographics and microbiologic differences between CLABSIs and non-CLABSI HOBSIs; and 3) a comparative patient-level analysis of differences in outcomes between CLABSIs and non-CLABSI HOBSIs.

Definitions

We defined HOBSI as any occurrence of growth in one or more blood culture bottles collected on or after hospital day 3 with 1) no prior positive blood culture in prior 14 days and 2) not a commensal per laboratory-generated algorithm based on CDC NHSN Common Commensal Organisms.[2,5] If a potential commensal was identified by the CDC NHSN Common Commensal Organisms list, it was excluded from the HOBSI definition unless >1 blood culture was positive for the same organism on the same or consecutive calendar days.[2] Central line-associated bloodstream infection (CLABSI) was defined in accordance with CDC NHSN definitions as any laboratory-confirmed bloodstream infection (LCBI) where an eligible BSI organism is identified, and an eligible central line is present on the LCBI date of event or the day before.[3]

Data collection

For our time-series analysis, we extracted surveillance data including BSI counts, patient days, central line days, and demographic data for HOBSIs and CLABSIs in each hospital from 01/01/2017 to 12/31/2021. For our patient-level analysis, patient characteristics, microbiologic data, and device-related data for all patients with a positive blood culture in the DUHS were retrospectively extracted from the electronic medical record from 01/01/2017 to 12/31/2021. Variables of interest included age, sex assigned at birth, race, admission and discharge dates, culture date, pathogens, presence of urinary catheter and/or ventilator at time of infection, and associated comorbidities (extracted from inpatient billing codes based on International Classification of Diseases, Tenth Revision, Clinical Modification codes). All patients diagnosed with an HOBSI or CLABSI as defined above during the study period were included.

Statistical analysis

We applied negative binomial regression models to estimate the monthly change in incidence of HOBSI and CLABSI rates over the study period from 1/1/2017 to 12/31/2021. Models included an offset variable for patient days or central line days. To account for the loss of independence related to repeated measures over time at each hospital, generalized linear mixed models were used. In case the COVID-19 pandemic impacted rates of HOBSI and/or CLABSI,[10] nested regression models comparing exclusively time-dependent models to those that also included time-defined COVID-19 variables were assessed for fit using likelihood ratio tests (Supplementary Table 2).

Because CLABSI and HOBSI are not mutually exclusive entities that would allow for direct statistical comparisons, we evaluated risk factors and outcomes of CLABSI compared to non-CLABSI HOBSI. We felt that notable differences in non-CLABSI HOBSI and CLABSI would still offer indirect insight into how overall HOBSI might differ from CLABSI, particularly as the majority of HOBSIs (approximately 80%) were non-CLABSI HOBSIs rather than CLABSIs (Table 2). While count data were available for both HOBSIs and CLABSIs from 1/1/2017 to 12/31/2021, patient-specific demographic data could only be linked to CLABSIs from 7/1/2017 to 12/31/2021 due to changes in data storage methods for CLABSIs. Fisher's exact test or Chi-squared testing was used to evaluate for statistically significant differences between non-CLABSI HOBSI and CLABSIs.

Finally, to characterize outcomes from non-CLABSI HOBSIs as compared to CLABSIs, we developed univariable and multivariable regression models. The exposure variable was a dichotomous variable that represented CLABSI or non-CLABSI HOBSI. Outcome variables of interest were post-infection length of stay, duration of post-infection antibiotic receipt, and in-hospital mortality. Covariates of interest included in the models were age, pre-infection length of stay, hospital, ICU status, ventilator status, urinary catheter usage, and infection during the pre-pandemic versus COVID-19 pandemic period. Hospitalizations with more than 1 BSI (n = 137 hospitalizations or 241 BSIs) were excluded to avoid mixing of exposure variables. Covariate linearity and interaction with the primary exposure were assessed using visual inspection and likelihood ratio tests. All statistical analysis was performed using R (version 4.3.1) and RStudio (version 2023.06.1+524) software.

Ethical statement

The Duke University Health System Institutional Review Board approved this research.

Table 1. Count, denominator, and device utilization ratio data for hospital-onset bloodstream infections (HOBSIs) and central line-associated bloodstream infections (CLABSIs)

	HOBSI					CLABSI				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Total	480	497	496	515	629	138	112	136	101	135
Hospital A	400	400	395	401	510	132	103	124	89	120
Hospital B	58	67	62	55	73	3	5	4	3	7
Hospital C	21	30	39	59	46	3	4	8	9	8
	Patient Days					Central Line Days				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Total	450376	419095	426215	408121	449181	121932	121627	127480	131578	140857
Hospital A	324736	291007	292395	282008	305118	104174	103354	106794	110479	116505
Hospital B	74191	75926	79021	73289	87111	10654	10059	11094	10570	13675
Hospital C	51449	52162	54799	52824	56952	7104	8214	9592	10529	10677
	Central Line Utilization Ratio									
	2017		2018		2019		2020		2021	
Total	.27		.29		.30		.32		.31	
Hospital A	.32		.36		.37		.39		.38	
Hospital B	.14		.13		.14		.14		.16	
Hospital C	.14		.16		.18		.20		.19	

Results

Identification of HOBSI and CLABSIs

After exclusion of 307 entries that were not associated with hospital admission, 36 duplicate entries, and 33 entries without ultimate culture growth, a total of 15876 positive blood culture collection events without a positive blood culture in the prior 14 days across the hospital system from 1/1/2017 to 12/31/2021 were identified (Supplementary Figure 1). Four-thousand eight hundred forty-eight (4848) culture events were deemed potential commensals based on a single positive blood culture with an organism considered a CDC NHSN common commensal organism. Eight thousand four hundred and ten entries (8410) were excluded due to the date of blood culture occurrence prior to hospital day 3 of admission. A total of 2617 HOBSIs and 622 CLABSIs were included in our time-series analysis (Table 1).

Time-series analysis

Across the three-hospital system, HOBSI per 1000 patient days slightly increased over time within each hospital across the 5-year study period (incidence rate ratio (IRR) 1.006, 95% CI 1.001–1.012, $P = .03$; Fig. 1). No statistically significant changes in CLABSI incidence by 1000 central line days (IRR .997, 95% CI .992–1.002, $P = .22$) or 1,000 patient days (IRR 1.000, 95% CI .996–1.005, $P = .84$) were identified within each hospital (Fig. 2). Estimates were robust across differing modeling strategies (Supplementary Tables 1).

Epidemiology of CLABSI, HOBSI, and non-CLABSI HOBSIs

We then sought to characterize the comparative epidemiology of CLABSI and non-CLABSI HOBSI. Patient-level data were only available from 07/01/2017 to 12/31/2021 due to changes in database storage practices; nine (9) CLABSIs did not have associated patient-level data. A total of 2373 HOBSIs and 550 CLABSIs were available for patient-level analysis. Eighty-five (85) CLABSIs were not captured by the applied HOBSI definition: 57 were excluded due to a prior positive blood culture, while the remaining 28 were excluded due to classification as a potential commensal. This left a total of 1908 non-CLABSI HOBSIs for comparison (Table 2).

Distribution of HOBSIs, CLABSIs, and non-CLABSI HOBSIs across age, sex, and race were similar, though younger individuals, women, and Black individuals tended to comprise a higher proportion of CLABSIs compared to non-CLABSI HOBSIs (Table 2). *Candida*, coagulase-negative *Staphylococcus,* and *Enterococcus* infections were more common among CLABSIs, while gram-negative enteric pathogens including *E. coli* and *Klebsiella* were more common among non-CLABSI HOBSIs. Higher proportions of severe renal disease, hematologic malignancy, and chronic pulmonary disease were observed among CLABSIs compared to non-CLABSI HOBSI (Table 2).

Comparative outcomes between CLABSI and non-CLABSI HOBSI

In univariable regression analyses, CLABSIs were associated with increased post-infection antibiotic duration compared to non-CLABSI HOBSIs; a similar trend was noted with post-infection length of stay, but this did not reach statistical significance (Table 3). No convincing difference in in-hospital mortality was noted between the two BSIs on univariate analysis. These trends reversed upon multivariable analysis, however, and the odds of in-hospital mortality were lower among patients with CLABSIs as compared to non-CLABSI HOBSIs (odds ratio .27, 95% CI .11, .64; Table 3).

Table 2. Epidemiology and demographic characteristics of hospital-onset bloodstream infections (HOBSIs), central line-associated bloodstream infections (CLABSIs), and non-CLABSI HOBSIs. *P*-values test for differences between CLABSIs and non-CLABSI HOBSIs (Chi-square or Fisher exact tests). Note that non-CLABSI HOBSI and CLABSI columns will not sum to equal the HOBSI column, as the proposed HOBSI definition did not capture all CLABSIs as defined by the NHSN (n = 85 not captured)

| | HOBSI | CLABSI* | Non-CLABSI HOBSI | |
	All, n (%)	All, n (%)	All, n (%)	*P*-value
Total	2373	550	1908	–
Age				<.01
<18	250 (10)	84 (15)	182 (9)	
18–39	303 (12)	80 (14)	238 (12)	
40–64	964 (40)	227 (40)	773 (40)	
65–80	737 (31)	143 (25)	610 (31)	
>80	119 (5)	16 (2)	106 (5)	
Sex				.01
Female	957 (40)	248 (44)	746 (39)	
Male	1415 (59)	302 (54)	1162 (60)	
Race				.06
American Indian or Alaskan Native	35 (1)	6 (1)	32 (1)	
Asian	46 (1)	11 (1)	38 (1)	
Black or African American	861 (36)	229 (40)	668 (34)	
White	1220 (51)	261 (46)	1000 (52)	
Other, including Two or More Races	145 (6)	33 (6)	114 (6)	
Not Reported/Declined	66 (2)	10 (1)	57 (2)	
Common Pathogens				<.01
Staphylococcus aureus	348 (14)	68 (12)	288 (15)	
MRSA	123 (5)	30 (5)	99 (5)	
Escherichia coli	254 (10)	28 (5)	232 (12)	
Enterococcus species	232 (9)	78 (13)	168 (8)	
Klebsiella species	261 (10)	36 (6)	227 (11)	
Candida species	188 (7)	76 (13)	126 (6)	
Coagulase-negative *Staphylococcus* species	179 (7)	81 (14)	110 (5)	
Enterobacter species	149 (6)	31 (5)	123 (6)	
Pseudomonas aeruginosa	120 (5)	23 (4)	101 (5)	
Serratia species	83 (3)	13 (2)	70 (3)	
Proteus species	29 (1)	5 (0)	24 (1)	
Streptococcus species	61 (2)	4 (0)	57 (2)	
Other	469 (19)	116 (20)	383 (20)	
Comorbid Conditions				<.01
Diabetes	788 (33)	198 (36)	624 (33)	
Hypertension	1605 (68)	391 (71)	1274 (67)	
Chronic Pulmonary Disease	972 (41)	260 (47)	755 (40)	
Congestive Heart Failure or Valvular Disease	695 (29)	192 (35)	533 (28)	
Renal Disease, Severe	373 (16)	115 (21)	276 (14)	
Liver Disease, Moderate to Severe	185 (8)	45 (8)	146 (8)	
Hematologic Malignancy (Leukemia or Lymphoma)	358 (15)	120 (22)	257 (13)	
Solid Tumor Malignancy	465 (20)	106 (19)	379 (20)	

*As defined by NHSN criteria.

HOBSI Rate, 2017–2021
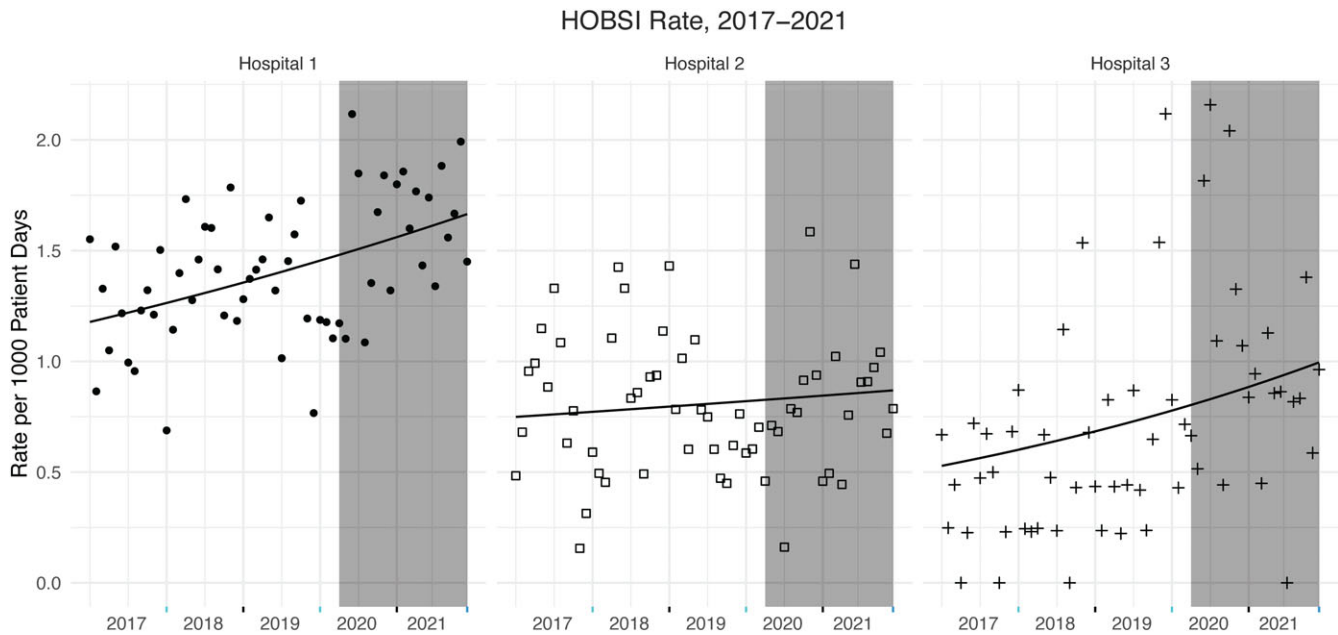
Figure 1. Regression analysis of monthly rates of HOBSIs per 1,000 patient days. Gray areas denote COVID-19 pandemic period (April 2020 to December 2021). A statistically significant increase in HOBSI incidence was noted over time across facilities (IRR 1.006 HOBSIs/1,000 patient days; *P* = .03).
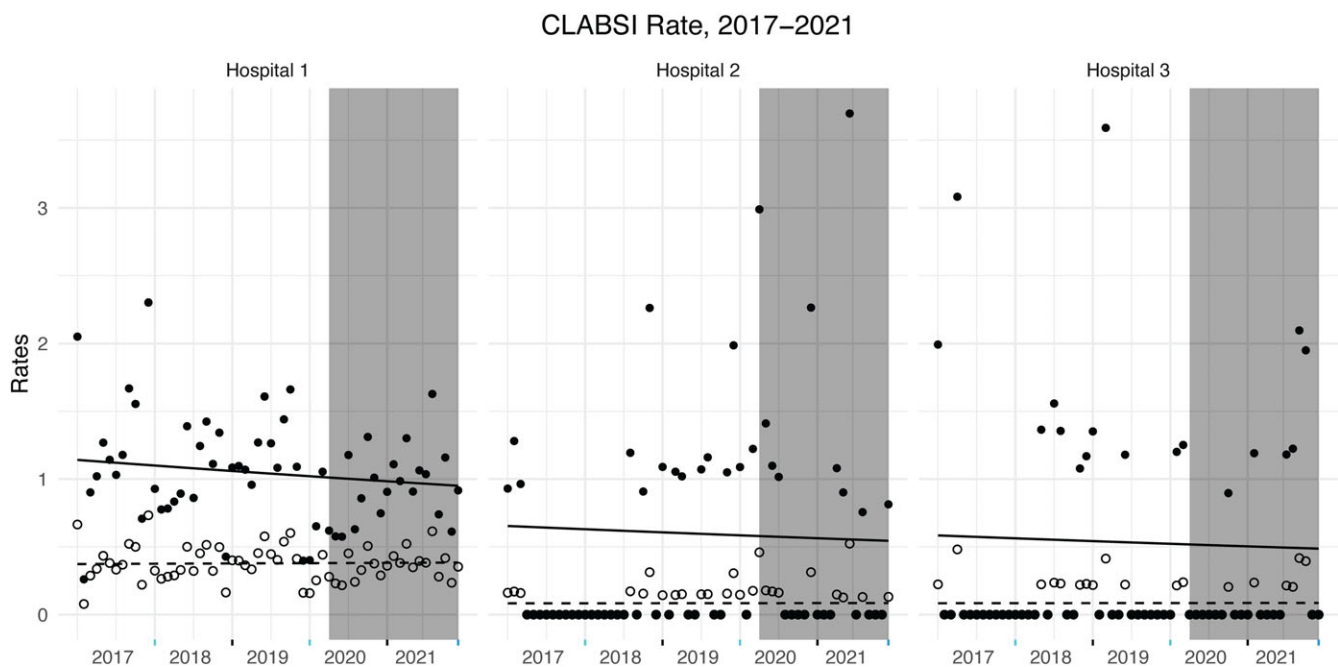
CLABSI Rate, 2017–2021

Figure 2. Regression analysis of monthly rates of CLABSIs per central line days (solid circles, solid line) and patient days (empty circles, dashed line). Gray areas denote COVID-19 pandemic period (April 2020 to December 2021). Models did not indicate a change over time per 1,000 central line days (IRR .997, 95% CI .992–1.002, *P* = .22) or 1,000 patient days (IRR 1.000, 95% CI .996–1.005, *P* = .84).

Discussion

We evaluated the comparative epidemiology of HOBSI and CLABSI from 1 January 2017 to 31 December 2021 across a three-hospital healthcare system. We found that HOBSI incidence increased over time, while no change in CLABSI incidence was observed during this time period within each study hospital. Additionally, we found key differences in risk factor profiles and

outcomes between CLABSI and non-CLABSI HOBSI that suggest that these metrics—and therefore CLABSI and overall HOBSI—may differ in important ways as quality metrics.

While we found the incidence rate of HOBSI increased over time, we did not find a coincident increase in CLABSI incidence in our hospital system from 2017 to 2021, which was an unexpected finding based on prior literature.[7] Given the observed difference in trends between CLABSI and HOBSI incidence in this healthcare

Table 3. Descriptive statistics and effect estimates for post-infection length of stay, post-infection antibiotic duration, and in-hospital mortality comparing central line-associated bloodstream infections (CLABSIs) versus non-CLABSI hospital-onset bloodstream infections (non-CLABSI HOBSIs). Adjusted models included variables for age, BMI, date of onset, ICU status, ventilator status, urinary catheter usage, occurrence during the COVID-19 pandemic, and hospital day of infection onset while excluding outlier outcome observations

	CLABSI	Non-CLABSI HOBSI	P-value
Post-Infection Length of Stay (Days)			
Median (IQR)	14 (8, 28)	13 (7, 25)	
Expected Increase in LOS (Crude)*	1.07 (.97, 1.19)	.98 (.90, 1.06)	.17
Expected Increase in LOS (Adjusted)*			.63
Post-Infection Antibiotic Duration (Days)			
Median (IQR)	15 (8, 29)	11 (5, 23)	
Expected Increase in Duration (Crude)*	1.28 (1.15, 1.44)	1.00 (.91, 1.09)	<.01
Expected Increase in Duration (Adjusted)*			.93
In-Hospital Mortality			
Deaths (Risk)	119 (25)	417 (24)	
Odds Ratio (Crude)*	1.06 (.84, 1.34)	.27 (.11, .64)	.60
Odds Ratio (Adjusted)*			<.01

*CLABSI versus non-CLABSI HOBSI.

system, HOBSI incidence- in certain settings- may measure quality of care in a manner different from CLABSI incidence. Compared to the restrictive criteria required for diagnosis of CLABSI by NHSN criteria, the utilized HOBSI definition captures bacteremia of all potential hospital-acquired sources. Accordingly, HOBSI incidence may reflect how well other infection prevention measures (ex. urinary catheter- or ventilator-related care) are implemented on a consistent basis. This finding is an important consideration for institutions as HOBSI is potentially implemented as a quality metric, as it may guide where infection prevention teams should focus their efforts (i.e. toward CLABSI prevention or otherwise).

We compared microbiologic data, demographic data, and comorbidity profiles across CLABSI and non-CLABSI HOBSI in our cohort. We chose to compare CLABSI and non-CLABSI HOBSI because CLABSI and overall HOBSI are not exclusive entities. Gram-negative pathogens constituted proportionally more non-CLABSI HOBSIs as compared to CLABSIs, while common line-associated pathogens such as *Candida, Enterococcus,* and coagulase-negative *Staphylococcal* species comprised a larger proportion of CLABSIs than non-CLABSI HOBSIs (Table 2). Drawing conclusions regarding demographic differences based on CLABSI versus non-CLABSI HOBSI incidence is difficult without assessment of demographic distribution in the underlying inpatient population, but this topic certainly warrants further exploration in case systematic differences in care delivery might exist between demographic groups. Finally, a higher burden of chronic comorbidities was observed among patients with CLABSIs as compared to non-CLABSI HOBSIs, which may reflect the generally higher severity of illness associated with central line use.

Outcomes varied between CLABSI and non-CLABSI HOBSI as well. Univariable analyses suggested that CLABSIs were associated with increased post-infection antibiotic duration compared to non-CLABSI HOBSIs, and while not statistically significant, post-infection length of stay and mortality trended in a similar direction. These findings were not replicated on multivariate analysis. Furthermore, multivariable analysis suggested a lower mortality

for CLABSIs compared to HOBSIs when adjusted for covariates that predict for severity of illness such as ICU status. One hypothesis to explain this may be that- when all else is equal- CLABSIs at least have a readily removable source compared to non-CLABSI HOBSIs. Further exploration and replication of this finding is needed.

Our study has several limitations. First, several iterations of HOBSI definitions exist in the literature,[5,6,8,9] such that definitive conclusions regarding HOBSI from our study as a broader quality metric may not be possible until a definition is finalized. Second, we relied upon an electronic method for HOBSI identification of blood culture contamination based on CDC NHSN Commensal organisms, which may have resulted in exclusion of true HOBSIs. Third, patient-level data was not available for patients prior to 7/1/2017 due to changes in database storage practices. However, we do not anticipate the missing data to have affected effect estimates since we excluded both HOBSIs and CLABSIs from that period. We also do not expect that patient-level HOBSI or CLABSI epidemiology during that period was substantially different from the epidemiology after 7/1/2017. Finally, definitive causal conclusions regarding differential outcomes across BSI types are difficult to conclude from our observational study, though we hope our findings provide useful descriptive epidemiology for these BSIs that might be hypothesis-generating.

In conclusion, while the incidence rate of HOBSI increased over time, we did not find a coincident increase in CLABSI incidence across hospitals in our healthcare system. We found notable differences in risk factors and outcomes between CLABSI and non-CLABSI HOBSI. These findings suggest that, in certain settings, CLABSI and HOBSI differ in important ways that should be considered closely, particularly if HOBSI is adopted as a future healthcare quality metric alongside or in place of current CLABSI definitions. Specifically, prevention strategies for CLABSI would not be expected to be similarly effective for reducing HOBSI. Future work examining the preventability of HOBSI will be important moving forward.

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