Epidemiology of Recurrent Bacterial Bloodstream Infections in the US Military Health System

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Abstract

Background: The epidemiology of recurrent bacterial bloodstream infections (rBSI) has not been fully characterized. Evaluating rBSI represents opportunities to inform morbidity risk factors and prevention strategies. We describe the clinical and microbiological features of rBSI in the US Military Health System (MHS) in a prospective cohort study, including retired and active-duty US uniformed service members and their beneficiaries.

Methods: We collected data for rBSI episodes from MHS beneficiaries (Jan 2010 – Dec 2019). A rBSI is defined as growth of the same bacterial pathogen in blood culture >14 days after the index or previous episode. Demographics and comorbidities were collected prior to the index BSI. Microbiological data were obtained from the Navy and Marine Corps Public Health Center. Descriptive statistics are presented.

Results: A total of 12,749 beneficiaries were diagnosed with a BSI attributed to 1 of the 15 most common bacterial pathogens associated with BSI in the MHS, with 646 (5.1%) experiencing a rBSI. *Escherichia coli* had the largest proportion among all patients with rBSI (31% of 646); however, *Enterococcus* spp. accounted for the highest proportion of rBSI within a given pathogen subgroup (7.4% of 1,154 *Enterococcus* BSI; Table). *Pseudomonas aeruginosa* BSI had the shortest average time to recurrence (119 days), and *Acinetobacter* spp. had the highest frequency of BSI recurrences per patient (mean of 3). Male sex (59.9%) and age ≥65 years (52.9%) were most common among the rBSI patients. The updated Charlson Comorbidity index score preceding the index BSI was a median of 5.0, and chronic pulmonary disease (57.3%) and diabetes (56.6%) contributed the largest proportion of common comorbidities. A total of 88 (13%) rBSI patients had their index BSI while hospitalized following trauma where *S. aureus* was the most common (37.5%) bacterial pathogen.

Conclusion: Overall, the proportion of rBSI (5.1%) in our cohort of MHS beneficiaries was generally lower than that previously reported in the literature. Individuals with rBSI had a substantial burden of comorbid disease with 13% having trauma precede the index BSI. Identifying risk factors for recurrence may improve management strategies of primary BSI and may reduce morbidity of subsequent BSI.

Background

- Recurrent bacterial BSI has been associated with increased mortality, especially in military trauma casualties
- *Staphylococcus aureus* and *Escherichia coli* have been established as the most common primary bacterial BSI organisms, but less is known about the epidemiology of recurrent BSI
- The Military Health System (MHS) provides an opportunity for retrospective review of a cohort of patients with recurrent bacterial BSI
- These data will be used to describe epidemiologic and clinical features of recurrent bacterial BSI

Methods

- Study population: ≥18 years, MHS beneficiary with index BSI diagnosis treated at a MHS facility (Jan 2010 – Dec 2019) and attributed to a bacterial pathogen, and had a recurrent BSI
- Recurrent BSI was defined as growth of the same species of bacteria from blood culture >14 days after index or previous BSI episode
- Top 15 common and clinically-relevant bacterial pathogens were included in analysis (**Table 1**). Bacterial pathogens were subcategorized based on clinical similarities using 4 organism categories:
  - Lactose-fermenting Gram-negative bacilli, non-lactose-fermenting Gram-negative bacilli, *Staphylococcus aureus* and *Streptococcus spp.,* and *Enterococcus* spp.
- Demographics were collected prior to index BSI
- Microbiologic data were obtained from Navy and Marine Corps Public Health Center

Results

12,749 MHS beneficiaries with index bacterial BSI

- **646 (5.1%) beneficiaries with a recurrent BSI for a total of 679 recurrent BSI episodes**

Table 1: BSI recurrence, time to BSI recurrence (recurrence of the index pathogen), and mean number of episodes per pathogen

Bacterial Species	Total Patients with BSI Episodes	Patients with Recurrent BSI Episodes, No. (%)	Average Days to Recurrence (SD)	Mean BSI Number (SD)
Escherichia coli[#]	4356	200 (4.6)	546.9 (603.9)	2.2 (0.4)
Staphylococcus aureus	2825	175 (6.2)	356.7 (475.2)	2.2 (0.6)
Klebsiella pneumoniae[#]	1272	81 (6.4)	327.1 (395.5)	2.2 (0.5)
Enterococcus spp.	1154	85 (7.4)	264.6 (448.7)	2.2 (0.5)
Streptococcus β-Hemolytic group	1018	56 (5.5)	554.9 (701.1)	2.2 (0.5)
Streptococcus spp.	1015	20 (2.0)	512.6 (686.4)	2.0 (0.0)
Streptococcus viridans group	989	15 (1.5)	508.7 (679.1)	2.1 (0.4)
Streptococcus pneumoniae	672	14 (2.1)	726.1 (710.7)	2.1 (0.4)
Pseudomonas aeruginosa[$]	556	20 (3.6)	118.8 (128.0)	2.2 (0.5)
Serratia spp.[#]	192	2 (1.0)	234.5 (289.2)	2.0 (0.0)
Acinetobacter spp.[$]	180	3 (1.7)	273.4 (411.2)	3.0 (1.7)
Citrobacter spp.[#]	141	3 (2.1)	259.7 (216.2)	2.0 (0.0)
Enterobacter spp.[#]	87	3 (3.4)	244.7 (119.5)	2.0 (0.0)
Stenotrophomonas spp.[$]	75	2 (2.7)	178.3 (206.8)	2.5 (0.7)
Proteus spp.[#]	19	0	0	0
Total	**12,749***	**646***		

[#] Lactose-fermenting Gram-negative bacilli. *Serratia* spp. included in this group based on clinical characteristics.
[$] non-Lactose-fermenting Gram-negative bacilli
* not mutually exclusive

Results (cont.)

Figure 1: Distribution of bacterial pathogens for the 679 recurrent BSI episodes

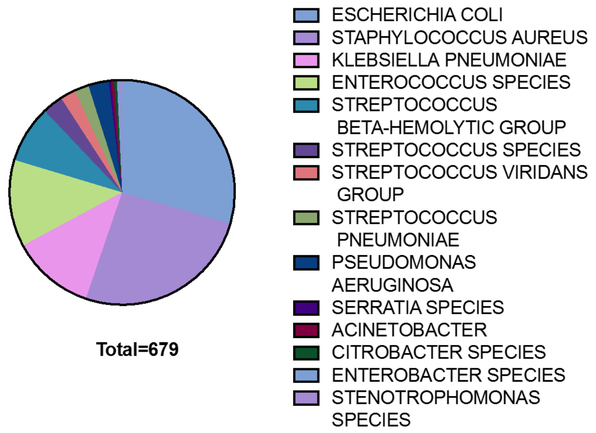

Table 2: Age and sex for subcategorized recurrent BSI episodes

Characteristics	Total Recurrent BSI Episodes, No. (%) (N=679)	BSI Episodes, No. (%) Lactose-Fermenting GNB (N=289)	*Streptococcus / Enterococcus* spp. (N=190)	*Staphylococcus aureus* (N=175)	Non-Lactose-Fermenting GNB (N=25)
Age Group, years					
18-25	30 (4.4)	7 (2.4)	8 (4.2)	8 (4.6)	7 (28.0)
26-35	22 (3.2)	8 (2.8)	7 (3.7)	7 (4.0)	0
36-45	34 (5.0)	10 (3.5)	12 (6.3)	10 (5.7)	2 (8.0)
46-64	234 (34.5)	88 (30.5)	73 (38.4)	66 (37.7)	7 (28.0)
≥65	359 (52.9)	176 (60.9)	90 (47.4)	84 (48.00)	9 (36.0)
Sex					
Female	272 (40.1)	131 (45.3)	66 (34.7)	71 (40.6)	4 (16.0)
Male	407 (59.9)	158 (54.7)	124 (65.3)	104 (59.4)	21 (84.0)

GNB – Gram-negative bacilli

Table 3: Ten most frequent comorbidities associated with recurrent BSI episodes

Comorbidity, No. (%)	Total Recurrent BSI Episodes (N=679)*
Chronic pulmonary disease	389 (57.3)
Diabetes without chronic complication	384 (56.6)
Renal disease	301 (44.3)
Any malignancy (except malignant neoplasms of the skin)	296 (43.6)
Peripheral vascular disease	262 (38.6)
Congestive heart failure	259 (38.1)
Cerebrovascular disease	244 (35.9)
Diabetes with chronic complication	235 (34.6)
Mild liver disease	195 (28.7)
Myocardial infarction	144 (21.2)

* not mutually exclusive

Results (cont.)

Table 4: Frequency of recurrent BSI episodes with a preceding trauma event

Characteristics, No. (%)	Total Recurrent BSI Episodes (N=679)	Recurrent BSI Episodes with Preceding Trauma Event (N=88)
Lactose-Fermenting GNB	289 (42.6)	27 (30.7)
Streptococcus / Enterococcus spp.	190 (28.0)	20 (22.7)
Staphylococcus aureus	175 (25.8)	33 (37.5)
Non-Lactose-Fermenting GNB	25 (3.7)	8 (9.1)

GNB – Gram-negative bacilli

- Trauma was associated with 13% of recurrent BSI episodes with open extremity wounds being the most frequent trauma diagnosis (24%, 21 of 88)
- Burns occurred in 7 (8%) of 88 recurrent BSI with a preceding trauma diagnosis

Conclusions

- The burden of recurrent BSI among MHS beneficiaries is 5.1% of all BSI episodes reported during a ten-year period
- Trauma preceded 13% of recurrent BSI episodes, indicating the burden of this disease process in a military population
- Further evaluation of risk factors surrounding index BSI may elicit management strategies to prevent mortality in subsequent BSI episodes

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