Concise Communication

Group B Streptococcus in the urine in nonpregnant adults: Disease or distraction?

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Abstract

In this large, retrospective cohort study, we used administrative data to evaluate nonpregnant adults with group B Streptococcus (GBS) bacteriuria. We found greater all-cause mortality in those with urinary tract infections compared to asymptomatic bacteriuria. Differences in patients’ baseline characteristics and the 1-year mortality rate raise the possibility that provider practices contribute to differences observed.

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Invasive infections caused by Group B Streptococcus (GBS), including osteomyelitis, skin and soft-tissue infections, and bacteremia without focus, are increasing in the United States.1,2 The clinical relevance of noninvasive GBS infections is less characterized, in part because of challenges distinguishing infection from colonization. This includes GBS bacteriuria among nonpregnant adults, in whom urinary colonization rates exceed 20%.3,4 We compared people with GBS bacteriuria who were diagnosed and treated for a urinary tract infection (UTI) to those who were not (indicating asymptomatic GBS bacteriuria).

Methods

Case ascertainment and clinical characteristics

We conducted a retrospective cohort study of active users of Veterans’ Affairs (VA) health care from January 1, 2008, through December 31, 2017, by accessing data from the VA Corporate Data Warehouse through the VA Informatics and Computing Infrastructure. The Institutional Review Board (IRB) of the VA Northeast Ohio Healthcare System approved the study protocol. Inclusion criteria were VA healthcare users with at least 1 urine culture and no associated ICD codes for UTI and no antibiotics prescribed for UTI cases. Cases with a UTI ICD code and no antibiotic prescription were unclassifiable and therefore were not included. We analyzed demographics, setting, all-cause mortality at 30 days and 1 year, and the Charlson comorbidity index (CCI) score (determined using ICD codes).5 We also assessed antibiotics prescribed for UTI cases.

Statistical analysis

Clinical and demographic characteristics of patients with UTIs and asymptomatic GBS bacteriuria were compared using t tests for continuous variables and χ² tests for categorical variables. We developed multivariable logistic regression models to report odds ratios (ORs) and 95% confidence intervals (CIs) for all-cause mortality at 30 days and 1 year to assess adjusted mortality differences between patients with UTIs and asymptomatic GBS bacteriuria. These models included age, sex, race, ethnicity, CCI, and setting at the time of the urine culture. All statistical analyses were performed using R version 3.5.1 software (R Project for Statistical Computing, Vienna, Austria). All reported P values are unadjusted.
Results

Patient characteristics

Between 2008 and 2017, we identified 20,906 patients with GBS bacteriuria, of whom 3,223 (15%) were diagnosed and treated for a UTI. Comparing the patients diagnosed and treated for a UTI to those with asymptomatic GBS bacteriuria, the former were older (64.7 ± 15.5 vs 61.2 ± 15.1 years; P < .001), had a higher CCI (2.83 ± 2.7 vs 2.14 ± 2.3; P < .001), and were more likely to be inpatients (17% vs 5%; P < .001). Several chronic conditions, including pulmonary (30% vs 22%; P < .001) and renal diseases (20% vs 13%; P < .001), were more common among patients diagnosed and treated for a UTI than in those with asymptomatic GBS bacteriuria.

Antibiotic use

Fluoroquinolones were the most common antibiotic class prescribed for treatment of UTI cases (Table 2). For outpatient, other commonly prescribed antibiotics included trimethoprim-sulfamethoxazole (20%) and nitrofurantoin (9%). Inpatients received β-lactam/β-lactamase inhibitor combinations (31%), extended-spectrum cephalosporins (26%), and penicillins (17%).

Mortality

All-cause mortality was greater among those with who were diagnosed and treated for a UTI compared to those with asymptomatic GBS bacteriuria at 30 days (1.9% vs 0.3%; P < .001) and at 1 year (10% vs 4%; P < .001). These differences persisted after controlling for age, sex, race, ethnicity, CCI, and inpatient status at time of culture (Supplementary Table 1).

Discussion

This national retrospective cohort study detected greater mortality among people with GBS bacteriuria who were diagnosed and treated for a UTI compared to those with asymptomatic GBS bacteriuria. The difference in all-cause mortality at 1 year was unexpected because this extends long beyond the period when sequelae would be expected for UTIs. Baseline differences in the age and chronic medical conditions between patients diagnosed and treated for UTI compared to those with asymptomatic GBS bacteriuria likely contributed to the observed differences in mortality. Although the data cannot entirely rule out the potential pathogenicity of GBS bacteriuria, the differences between patients diagnosed and treated for a GBS UTI compared to those with asymptomatic GBS bacteriuria likely reflects that clinicians are more likely to recommend antibiotics to patients perceived as being at high risk for poor outcomes. Furthermore, the finding that most of the patients who received an antibiotic were issued a fluoroquinolone (not among the first-line agents for GBS infections) suggests that prescribers were not using culture results to guide their decisions, highlighting an opportunity to improve antimicrobial stewardship. To our knowledge, this is the largest study to assess clinical outcomes among nonpregnant individuals with GBS bacteriuria.

Some clinicians conflate pyuria and/or a positive urine culture with UTI, even in the absence of symptoms specific to the genitourinary tract.6,7 When considered in context with cognitive biases that influence antibiotic prescribing decisions, the finding that patients with GBS bacteriuria who were older, diabetic, or had chronic pulmonary and renal diseases were more likely to have been prescribed an antibiotic is not surprising.8 Increased age, diabetes, cardiovascular disease and renal or urologic pathology are potential risk factors for UTIs due to GBS.9,10 Clinical recognition of these risk factors may have also increased the likelihood of requesting urine cultures.

Our study had several limitations. Our cohort comprised VA healthcare users, who are predominantly male and have a high burden of comorbidities, which may limit generalizability to the US population. Although we excluded patients with other cultures that grew GBS, we did not exclude other types of infections. Patients may have received antibiotics for a different indication and were misclassified as having a UTI. Also, our study relied on administrative data and, therefore, providers’ determinations of UTIs rather than clinical signs and symptoms. Thus, we may

Table 1. Characteristics of VA Healthcare System Users with Monomicrobial Urine Cultures Growing GBS, Stratified by Infection Status

| Variable                  | Urinary Tract Infection (n = 3,223) | Asymptomatic Bacteriuria (n = 17,683) | P Value |
|---------------------------|------------------------------------|--------------------------------------|---------|
| Age, mean y (±SD)         | 64.7 (±15.5)                       | 61.2 (±15.1)                        | <.001   |
| Male sex, no. (%)         | 2,479 (77)                         | 13,143 (74)                         | <.001   |
| Race, no. (%)             |                                    |                                      | <.001   |
| White                     | 2,121 (66)                         | 11,085 (63)                         |         |
| Black                     | 782 (24)                           | 4,420 (25)                          |         |
| Othera                    | 320 (10)                           | 2,178 (11)                          | <.001   |
| Ethnicity, no. (%)        |                                    |                                      | <.001   |
| Not Hispanic              | 2,798 (87)                         | 14,723 (83)                         |         |
| Hispanic                  | 282 (9)                            | 1,927 (11)                          |         |
| Othera                    | 143 (4)                            | 1,033 (6)                           |         |
| Charlson comorbidity index, mean (±SD)a | 2.83 (± 2.7) | 2.14 (± 2.3) | <.001   |
| Comorbidities, no. (%)    |                                    |                                      |         |
| Diabetes mellitus         | 1,456 (45)                         | 7,386 (42)                          | <.001   |
| Chronic pulmonary disease | 951 (30)                           | 3,955 (22)                          | <.001   |
| Chronic renal disease     | 653 (20)                           | 2,299 (13)                          | <.001   |
| Cancer                    | 575 (18)                           | 2,654 (15)                          | <.001   |
| Stroke                    | 537 (17)                           | 1,998 (11)                          | <.001   |
| Chronic heart failure     | 489 (15)                           | 1,645 (9)                           | <.001   |
| Peripheral vascular disease | 456 (14)                      | 1,759 (10)                          | <.001   |
| Liver disease             | 331 (10)                           | 1,533 (9)                           | <.005   |
| HIV                       | 29 (1)                             | 133 (1)                             | 0.358   |
| Status at time of urine culture, no. (%) |                  |                                      | <.001   |
| Inpatient                 | 548 (17)                           | 968 (5)                             |         |
| Outpatient                | 2,675 (83)                         | 16,715 (95)                         |         |
| Mortality, no. (%)        |                                    |                                      |         |
| 30-day all-cause mortality| 60 (1.9)                           | 56 (0.3)                            | <.001   |
| 1-year all-cause mortality| 325 (10)                           | 701 (4)                             | <.001   |

Note. SD, standard deviation; HIV, human immunodeficiency virus.

aAmerican Indian, Alaska Native, Asian, Native Hawaiian or Pacific Islander and unknown; for ethnicity includes unknown.
have overestimated the number of infections because some cases diagnosed and treated by the provider as UTIs may have been asymptomatic GBS bacteriuria. Finally, as discussed above, confirmation bias may have influenced the results; clinicians may have been more likely to obtain urine culture specimens from older, sicker patients and may have been more likely to diagnose and treat such patients for UTI.

In conclusion, our results suggest that GBS bacteriuria is common and that clinicians view only a minority of cases as potential infections. Although patients diagnosed and treated for a GBS UTI had greater all-cause mortality compared to people with asymptomatic GBS bacteriuria, distinctions in patients’ baseline characteristics and 1-year mortality suggest that provider practices contributed to the differences observed.

**Supplementary material.** To view supplementary material for this article, please visit https://doi.org/10.1017/ash.2022.236

**Table 2.** Antibiotic Agents Prescribed for UTI Cases Cultured in the Outpatient and Inpatient Settingsa

| Antibiotic                          | Outpatient Culture (n = 2,675), No. (%) | Inpatient Culture (n = 548), No. (%) |
|-------------------------------------|----------------------------------------|-------------------------------------|
| Fluoroquinolones                    | 1,435 (54)a                            | 315 (57)                            |
| Trimethoprim/Sulfamethoxazole       | 548 (20)                               | 81 (15)                             |
| Nitrofurantoin                      | 230 (9)                                | 16 (3)                              |
| Cephalosporins, extended spectrum   | 186 (7)                                | 144 (26)                            |
| Penicillins                         | 184 (7)                                | 92 (17)                             |
| Cephalosporins, 1st/2nd generation  | 158 (6)                                | 56 (10)                             |
| β-lactam/β-lactamase inhibitors     | 146 (5)                                | 172 (31)                            |
| Vancomycin                          | 53 (2)                                 | 89 (16)                             |
| Macrolides                          | 46 (2)                                 | 16 (3)                              |
| Otherb                              | 122 (5)                                | 77 (14)                             |

The percentage refers to the total number of outpatients or inpatients prescribed an antibiotic from the antibiotic classes listed. Some patients received >1 class of antibiotic in the 3 days following the urine culture, so the cumulative percentage exceeds 100%. Some patients were admitted after outpatient culture or discharged after inpatient culture.

Other includes clindamycin, linezolid, rifaximin, aminoglycosides, and carbapenems.

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