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Appendix A. Twitter Search Query Used to Compile the Data Set

SEARCH_TERM = '(antibiotics OR antibiotic OR levaquin OR levofloxacin OR avelox OR moxifloxacin OR cipro OR ciprofloxacin OR z-pak OR azithromycin OR amoxicillin OR augmentin OR keflex OR cefuroxime OR ceftin OR cefaclor OR cefpodoxime OR vantin OR cefdinir OR omnicef OR bactrim OR clindamycin) (fever OR cough OR bronchitis OR flu OR virus OR asthma OR throat) -RT -sinus -vet -cat -dog -abscess -strep lang:en'

Appendix B. Examples of Tweets Labeled as Possible Misuse and Not Misuse

Tweets labelled as possible misuse:

1. "Anybody have any home remedies or super good meds they know of for cold/flu? I've been sick for 3 weeks. Went to the Dr and got antibiotics today but need to feel better ASAP"
2. "I've had bronchitis since Thursday. It appears to be viral because the antibiotic did nothing."
3. "I had the flu 102 had some leftover antibiotics, started taking them last night, this morning fever broke, feeling a lot better."
4. "The doctor NEVER wants to give me antibiotics. That's the ONLY THING THAT WORKS. Ugh. I got some from my neighbor. Took a pill this morning and feel better already."
5. "Viral bronchitis is my diagnosis this afternoon. Cough suppressant and inhaler in hand as well as a prescription for antibiotics."

Tweets labelled as not misuse:

1. "If you have a cold, antibiotics won't help you feel better. Instead, try sipping warm liquids such as bone broth, hot tea, or soup."
2. "On antibiotics. For my horrible throat infection."
3. "An update: the doctors are pretty sure it's pneumonia, so they've started heavy antibiotics and are keeping her at the hospital for observation."
4. "#Antibiotics Tied to Longer Hospital Stays for #Asthma #pophealth #medicalevidence"
5. "This ear infection is going on 2 weeks with me dealing with about 80% hearing loss in left ear. After 1 week on Amoxicillin (with no results), doc changed me to Amox-Clav which I've been [taking] since Monday."

Risk factors for extended-spectrum beta-lactamase–producing Enterobacteriaceae enteric carriage among abdominal surgery patients

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Recent studies suggest an association between enteric colonization with extended-spectrum β-lactamase–producing Enterobacteriaceae (ESBL-pE) and the occurrence of deep surgical-site infections (SSIs) among abdominal surgery patients, particularly colorectal surgery patients.[1,2] Screening for ESBL-pE and personalized ertapenem use was associated with reduction in the incidence of SSIs caused by ESBL-pE.[3] Despite the potential benefit, screening all patients for ESBL-pE carriage may be considered an excess cost in resource-limited settings. Selective screening for high-risk groups with ESBL-pE carriage may be an alternative approach to surveillance screening and antimicrobial stewardship. This cohort study was conducted to evaluate the risk factors for ESBL-pE carriage in abdominal surgery patients at a tertiary-care center in Thailand.

A cohort study was performed at Thammasat University Hospital (TUH), a 750-bed, tertiary-care hospital in Pratum Thani, Thailand, over a 26-month period from February 1, 2017, to April 1, 2019. At this hospital, ~200 patients undergo abdominal surgery annually, and during the study period, SSIs occurred in 14%. Of these SSIs, 80% were superficial SSIs and 20% were deep or organ-space SSIs.[2] Notably, ESBL-pE SSIs were detected in ~15.6% of these patients.[2] All patients who underwent clean-contaminated, contaminated, or dirty abdominal surgical procedures were enrolled and screened for ESBL-pE colonization by rectal swab culture within 1 day prior to surgery. Data collection included baseline demographic and clinical characteristics, underlying comorbidities, presence of multiple comorbidities (defined as ≥3 comorbidities), previous hospitalization(s), type of surgical procedure, history and type of antibiotic exposure within 3 months prior to surgery, prior history of ESBL colonization ≥3 months prior to surgery, as well as American Society of Anesthesiology (ASA) risk class. Patients were excluded if they had documented infection(s) at the time of surgery. The institutional review board at TUH approved this study.

Enteric surveillance swabs (Becton Dickinson Diagnostics, Sparks, MD) were obtained from each patient within 1 day prior to surgery. Each rectal swab was processed in real time, inoculated into tryptic soy

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broth containing a 30-μg ceftriaxone disk (bioMérieux, Marcy-l'Étoile, France), and incubated at 37°C. Within 48 hours of inoculation, 100-μL broth samples with visible turbidity were plated on sheep blood agar and MacConkey agar with a 30-μg ceftriaxone disk and incubated at 37°C overnight. All recovered isolates within the zone of inhibition underwent routine identification using the Vitek 2 automated system (bioMérieux). Antimicrobial susceptibility testing was performed using the Clinical and Laboratory Standards Institute Interpretive Guidelines (disk diffusion test, bioMérieux), and confirmed by ESBL double-disk synergy testing for Enterobacteriaceae.[4]

All analyses were performed using SPSS version 19 software (IBM, Armonk, NY). The χ^2 or the Fisher exact test was used to compare categorical variables. Mann-Whitney U tests were used for continuous data. All P values were 2-tailed, and a P value $< .05$ was considered statistically significant. To determine factors associated with ESBL-pEnterobacteriaceae carriage, variables that had a significant level of $P < .20$ or variable with a priori significance in univariate analysis were entered into multivariate logistic regression models. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were calculated.

Among 360 patients who underwent abdominal surgery, 234 (65%) patients underwent clean-contaminated surgical procedures, 90 (25%) underwent contaminated surgical procedures, and 36 (10%) underwent dirty surgical procedures. At baseline, 129 patients (35.8%) had preoperative enteric colonization with ESBL-pE; baseline demographic characteristics were similar between the patients with and without ESBL-pE (Table 1). By multivariate analysis, preoperative enteric colonization with ESBL-pE was associated with antibiotic exposure within 3 months of surgery (adjusted odd ratios [aOR], 5.4; 95% CI, 1.4–24.5), multiple comorbidities (aOR, 4.6; 95% CI, 1.24–44.2), and dirty surgical wound classification (aOR, 3.69; 95% CI, 1.19–54.9).

In this study cohort, 35.8% of abdominal surgery patients had ESBL-pE carriage. This high prevalence may reflect reported ESBL-pE carriage in community and healthcare-associated settings among Thai populations as well as the report of injudicious use of antibiotics in community settings in this region.[5-9] The prior exposure to antibiotics, within 3 months prior to surgery, as a risk factor for ESBL-pE carriage is consistent with earlier studies reporting the risk of ESBL-pE in community and healthcare settings.[5,6] Together, multiple comorbidities, recent antibiotic use, and dirty wound classification are key factors that surgeons should consider as risks for deep SSIs by ESBL-pE. The presence of these key factors may identify patients for enteric screening for ESBL-pE carriage or for carbapenem empiric antibiotic prophylaxis prior to abdominal surgical procedures to reduce risk the of deep SSI.

This study has several limitations. It was performed at a single center with endemic ESBL-pE. It is plausible that the study findings are not generalizable to other regions where ESBL-pE is nonendemic. Second, given the small sample size, we were not able to identify other potential risk factors or specific antibiotic relationships. Lastly, the enteric colonization of ESBL-pE was performed using rectal swab culture, which has a <80% sensitivity.[10] Hence, misclassification bias may have occurred with underestimation of the prevalence ESBL-producing Enterobacteriaceae carriage. Despite these limitations, we identified key factors associated with rectal carriage of ESBL-pE that can help inform selective screening for ESBL-pE. Additional studies to evaluate selective screening for ESBL-pE carriage, together with personalized antibiotic prophylaxis among at risk abdominal surgeries, and studies to evaluate the cost effectiveness of these interventions in ESBL-pE prevalence regions are warranted.

Table 1. Demographic, Clinical Characteristics Among 360 Patients Screened for Preoperative Enteric Colonization With Extended-Spectrum β-Lactamase (ESBL)-Producing Enterobacteriaceae

Variable	Enteric Colonization (N=129), No. (%)	No Colonization (N=231), No. (%)	*P* Value
Age, median y (range)	44 (16–64)	41 (15–62)	.46
Sex, male	67 (52)	137 (59)	.19
Comorbidity			
Diabetes	26 (20)	51 (22)	.66
Cardiovascular diseases	49 (38)	94 (41)	.62
Gastrointestinal diseases	30 (23)	50 (22)	.54
Kidney failure (GFR<30)	6 (5)	10 (4)	.56
Immunocompromised[a]	6 (5)	12 (5)	.82
Multiple comorbidities[b]	22 (17)	12 (5)	<.001
ASA risk class			
Class I	25 (19)	46 (20)	.54
Class II	45 (35)	84 (36)	
Class III	49 (38)	74 (32)	
Class IV	10 (8)	27 (12)	
Surgical wound classification			
Clean contaminated	75 (58)	159 (68)	.06
Contaminated	30 (23)	60 (26)	.56
Dirty	24 (19)	12 (5)	<.001
Previous antibiotic exposure in 3 mo	26 (20)	13 (6)	<.001
Type of antibiotic			.36
First- and second-generation cephalosporin	3 (2)	1 (0.4)	
Third generation cephalosporin	10 (8)	5 (2)	
Beta-lactams	2 (2)	1 (0.4)	
Fluoroquinolone	10 (8)	5 (2)	
Other[c]	1 (0.7)	1 (0.4)	

Note. GFR, glomerular filtration rate; ASA, American Society of Anesthesiology.
[a]History on steroid or immunosuppressive agents more than 2 weeks before surgery, underlying human immunodeficiency virus.
[b]≥3 comorbidities; clean-contaminated included abdominal procedures that include hepatobiliary tract with contamination; contaminated surgery included abdominal procedures that include colorectal and hepatobiliary tract surgery with evidence of contamination; and dirty surgery included any abdominal surgery with evidence of massive contamination (eg, perforated colonic obstruction).

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Clostridioides difficile infections complicating combat-injured patients from Iraq and Afghanistan

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Clostridioides difficile-associated diarrhea (CDAD) is the most frequently reported healthcare-associated illness in the United States, with an annual economic burden >$1 billion and up to 9% mortality, and critically ill trauma patients may be uniquely at risk.[1–4] Military trauma patients have multiple CDAD risk factors, including frequent broad-spectrum antimicrobial exposure, transient immunosuppression, and challenges related to infection control in the deployed environment and along the evacuation chain. We describe the epidemiology of wounded military personnel diagnosed with CDAD.

Methods

Wounded military personnel (June 2009 through February 2014) from the Trauma Infectious Disease Outcomes Study[5] with a diagnosis of confirmed (laboratory supported) or presumptive (diarrhea with treatment for CDAD without lab confirmation) CDAD were examined. Inclusion criteria were active-duty or Department of Defense beneficiaries, aged ≥18 years, injured during deployment, requiring medical evacuation to Germany followed by transfer to participating US military hospitals. Infections were defined as previously described.[5] CDAD diagnosis was based on a combination of clinical and laboratory findings suggesting CDAD and/or directed antimicrobial therapy against CDAD for ≥5 days.[5] CDAD severity was defined according to the 2017 guidelines using highest creatinine and white blood cell values on day of diagnosis.[6] The study was approved by the Institutional Review Board of the Uniformed Services University.

Results

Among 2,660 wounded military personnel, 23 patients with CDAD were identified (4 presumptive and 19 confirmed), with an incidence of 2.76 per 10,000 occupied bed days (OBD). Overall, 7 cases were confirmed by toxin enzyme immunoassay, 11 by polymerase chain reaction, and 1 by both methods. Patients were primarily young (median age, 24 years) men (96%) who sustained blast injuries (70%), resulting in critical injuries (median injury severity score [ISS], 38) (Table 1). Prior to CDAD diagnosis, patients were hospitalized a median of 12 days, and 17 (74%) had ≥1 infection, most commonly pneumonia (47%) and skin and soft-tissue infections (SSTIs, 47%). Severe CDAD was diagnosed in 8 (35%) and fulminant CDAD was diagnosed in 6 (26%) patients. Furthermore,

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