

Original Article

Travel-associated multidrug-resistant organism acquisition and risk factors among US military personnel

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Submitted 28 October 2020; Revised 29 January 2021; Accepted 8 February 2021

Abstract

Background: International travel is a risk factor for incident colonization with extended spectrum beta-lactamase (ESBL)-producing organisms. These and other multidrug-resistant (MDR) bacteria are major pathogens in combat casualties. We evaluated risk factors for colonization with MDR bacteria in US military personnel travelling internationally for official duty.

Methods: TravMil is a prospective observational study enrolling subjects presenting to military travel clinics. We analysed surveys, antimicrobial use data, and pre- and post-travel perirectal swabs in military travellers to regions outside the continental USA, Canada, Western or Northern Europe, or New Zealand, presenting to one clinic from 12/2015 to 12/2017. Recovered Gram-negative isolates underwent identification and susceptibility testing (BD Phoenix). Characteristics of trip and traveller were analysed to determine risk factors for MDR organism colonization.

Results: 110 trips were planned by 99 travellers (74% male, median age 38 years [IQR 31, 47.25]); 72 trips with returned pre- and post-travel swabs were completed by 64 travellers. Median duration was 21 days (IQR 12.75, 79.5). 17% travelled to Mexico/Caribbean/Central America, 15% to Asia, 57% to Africa and 10% to South America; 56% stayed in hotels and 50% in dormitories/barracks. Travellers used doxycycline (15%) for malaria prophylaxis, 11% took an antibiotic for travellers' diarrhoea (TD) treatment (fluoroquinolone 7%, azithromycin 4%). Incident MDR organism colonization occurred in 8 travellers (incidence density 3.5/1000 travel days; cumulative incidence 11% of trips [95% CI: 4–19%]), all ESBL-producing *Escherichia coli*. A higher incidence of ESBL-producing *E. coli* acquisition was associated with travel to Asia (36% vs 7%, $P=0.02$) but not with travel to other regions, TD or use of antimicrobials. No relationship was seen between fluoroquinolone or doxycycline exposure and resistance to those antimicrobials.

Conclusions: Incident colonization with MDR organisms occurs at a lower rate in this military population compared with civilian travellers, with no identified modifiable risk factors, with highest incidence of ESBL acquisition observed after South Asia travel.

Key words: ESBL-producing Enterobacteriaceae, *Escherichia coli*, Perirectal swab, Colonization, Whole genome sequencing, CTX-M, Antimicrobials

Background

Multidrug-resistant (MDR) bacteria are a concern globally for international travellers in both civilian and military literature.¹ MDR infections in combat casualties were noted in Iraq and Afghanistan during Operations Iraqi and Enduring Freedom (OIF/OEF) with *Acinetobacter baumannii-calcoaceticus* (ABC) more prevalent in casualties coming from Iraq and extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae in casualties out of Afghanistan.^{2–4} In the few studies that looked at incident colonization of MDR bacteria including ESBL-producing Enterobacteriaceae in US military personnel and beneficiaries travelling internationally, rates ranged from 9 to 14%.^{5–7} In civilian literature, international travel has shown post-travel rates of ESBL-producing Enterobacteriaceae incident colonization ranging from 24 to 41%, with rates greater than 50% in travellers returning from South Asia.^{8–14} The majority of literature has described travel associated ESBL-producing Enterobacteriaceae acquisition with primarily CTX-M-producing Enterobacteriaceae. KPC-, VIM-, OXA-48- and NDM-producing Enterobacteriaceae infections have also been described following hospitalization in endemic areas.¹⁵

Prior to entering conflicts in Iraq and Afghanistan, there were few studies to predict MDR ABC colonization and infection in combat casualties. MDR bacteria have been shown to be community-associated pathogens in local, host nation personnel treated in Iraq and Afghanistan combat support hospitals; however, US military personnel have different potential exposures and typically live in a controlled environment with food and water provided from sources approved by preventive medicine.^{16,17} Extensive studies were conducted which demonstrated that the predominant source of ABC infection was nosocomial as little to no colonization was demonstrated in US troops prior to or at the time of injury.^{18–20} The source of ESBL-producing Enterobacteriaceae colonization and subsequent infection is less well established. A prospective study of US military personnel and beneficiaries travelling internationally did identify acquisition of ESBL-producing *Escherichia coli*, but was unable to identify clearly associated risk factors.⁵ No previous study has prospectively evaluated risk factors or incidence of acquisition for ESBL-producing Enterobacteriaceae colonization in travellers on military orders with a variety of destinations and missions.

Methods

Study design and definitions

The Military Travel MDR Surveillance Study is a subset of the larger TravMil study: Deployment and Travel Related Infectious Disease Risk Assessment, Outcomes, and Prevention Strategies Among Department of Defense (DoD) Beneficiaries, which is approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences (Bethesda, MD). TravMil is a prospective, observational cohort study of DoD beneficiaries travelling outside of the USA for ≤ 6.5 months. Participants enrolling into TravMil at single site (Brooke Army Medical Center, TX [BAMC]) were approached about optional participation in the Military Travel MDR Surveillance Study. There were 110 travellers enrolled who were

travelling for official military duties and deployments from December 2015 to December 2017. Exclusion criteria included planned travel limited to Western or Northern Europe, Canada or New Zealand; completed travel time > 6.5 months; and inability to follow-up between 3 days and 8 weeks after travel to collect a post-travel perirectal swab. Participants completed a pre-travel survey, a travel diary, a post-travel survey and an extended follow-up survey at 3 and 6 months. All demographic, itinerary, malaria prophylaxis use, contact with freshwater, detailed food and drink exposures, illnesses during and post-travel, antibiotics used during travel, and contact with medical care during travel collected as part of TravMil were analysed for risk factors for ESBL-producing Enterobacteriaceae acquisition. Antibiotic exposure was defined as taking at least one dose of an antibiotic.

Bacterial susceptibility

At the time of enrollment and again 10 days after return from travel ± 7 days, patients were provided with BD CultureSwab™ MaxV(+) (Becton, Dickinson and Company, Franklin Lakes, NJ) for self-collection of perirectal specimens. Participants were educated on self-collection of a perirectal swab, which has been used as a valid collection method compared with stool samples.²¹ As the second TravMil study visit was not required until 8 weeks after return, participants were given the options to either return the swabs by paid postal package or present to BAMC clinic to drop off a self-collected swab.²² Swabs collected were plated onto sheep blood agar and MacConkey agar. Colonies demonstrating morphology consistent with Gram-negative bacterial colonies were sub-cultured onto sheep blood agar in order to assure culture purity. All isolates were frozen at -80°C in Trypticase Soy Broth with 15% glycerol. Isolates underwent automated testing (BD Phoenix™ Automated Microbiology System-Becton Dickinson, Franklin Lakes, NJ) for identification, anti-microbial susceptibility testing, and identification of ESBL-producing Enterobacteriaceae.

Molecular testing

In participants with ESBL-producing Enterobacteriaceae isolated either pre- or post-travel, all pre- and post-travel isolates of *E. coli* from those participants were forwarded to the multidrug-resistant organism repository and surveillance network (MRSN) for whole genome sequencing (WGS). WGS of all 25 isolates was performed on an Illumina MiSeq® (Illumina, San Diego, CA) and the overall relationship between the isolates determined using a pan-genome sequence analysis program (Panseq).

Statistical analysis

Risk factor analysis was evaluated by univariate analysis with Pearson's χ^2 and Fisher's exact test for categorical variables and Mann-Whitney *U* for continuous variables. Two-tailed *P* values of < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS software (IBM® SPSS® Statistics Version 22, Chicago, Illinois). Agreement between phenotypic and genotypic antibiotic resistance profiles was measured using Cohen's kappa coefficient.

Table 1. Baseline characteristics of participants

Characteristics	Participant number (%)
Participants enrolled	N = 110
Planned trips	N = 99
Participants who returned swabs	N = 64
Trips with returned swabs	N = 72
Gender, Male	81 (74%)
Median age (years)	38 (IQR 31,47.25)
Median duration of travel (days)	21 (IQR 12.75, 79.5)
Region of travel	N = 72
Mexico, Caribbean and Central America	12 (17%)
Asia	11 (15%)
Africa	41 (57%)
South America	7 (10%)
Living conditions	
Hotel with air conditioning	32 (56%)
Hotel without air conditioning	8 (11%)
Military accommodations	4 (6%)
Dormitories/Barracks	36 (50%)
Field water exposure*	5 (7%)
Local water ingestion	
Untreated water	1 (1%)
Ice in beverage	31 (43%)
Antimicrobial exposure since enrollment	58 (81%)
Malaria prophylaxis	57 (79%)
Chloroquine	2 (3%)
Mefloquine	0 (0%)
Atovaquone-proguanil	45 (63%)
Doxycycline	11 (15%)
Primaquine	9 (13%)
Antibiotics for TD	8 (11%)
Ciprofloxacin	4 (6%)
Azithromycin	3 (4%)
Levofloxacin	1 (1%)
Systemic antibiotics for other reasons	3 (4%)
Amoxicillin/clavulanate	1 (1%)
Levofloxacin	1 (1%)
Trimethoprim/sulfamethoxazole	1 (1%)
Illness since enrollment	19 (27%)
Fever	0 (0%)
Influenza like illness	9 (13%)
TD	10 (14%)

*Defined as contact with fresh water from lakes, streams or rivers (wading/bathing/swimming/etc.).

Results

Demographics

Of 72 trips by 64 participants with returned pre- and post-travel swabs, 74% were male and median age was 38 (IQR 31, 47.25) (Table 1). The primary regions of travel were Mexico, the Caribbean, and Central America, Asia, Africa, and South America with a median duration of travel of 21 days (IQR 12.75, 79.5).

ESBL-producing Enterobacteriaceae pre- and post-travel

Eleven bacterial isolates from pre- and post-travel perirectal swab isolates during 72 trips by participants were ESBL-producing Enterobacteriaceae. All ESBL-producing Enterobacteriaceae were *E. coli*. Multiple other Gram-negative isolates were recovered but were not MDR or ESBL-producing to include genus *Acinetobacter*, *Aeromonas*, *Citrobacter*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Kluyvera*, *Morganella*, *Pantoea*, *Proteus*, *Pseudomonas* and *Stenotrophomonas*.

Eight of eleven ESBL-producing *E. coli* represented new acquisition (Table 2). One participant had ESBL-producing *E. coli* pre-travel, but was no longer colonized post-travel. Another participant had ESBL-producing *E. coli* both pre- and post-travel. There was a higher rate of new acquisition of ESBL-producing *E. coli* with travel to South Asia (India and Afghanistan) ($P = 0.02$). For this incident colonization, incidence density was 3.5/1000 travel days and cumulative incidence was 11% of trips (95% CI: 4–19%). No other risk factors such as living conditions, field water exposure, local water ingestion, antimicrobial exposure since enrollment or illness since enrollment was significantly associated with new acquisition of ESBL-producing *E. coli* for military work trips.

A total of 25 *E. coli* isolates were sent for WGS (Figure 1). These included 11 ESBL-producing *E. coli* with an additional 14 non-ESBL-producing *E. coli* isolates from 10 participants with ESBL-producing *E. coli*. All ESBL-producing *E. coli* isolates were unrelated based on the large separation in number of SNPs. Two patients had serial isolation of non-ESBL-producing *E. coli* isolates from pre- and post-travel cultures which were separated by 4–9 SNPs. Three groups of isolates formed close clusters on high-resolution SNP-based analysis. Group 1 isolates were separated by 241 SNPs. Group 2 isolates included two colonizing isolates as well as an isolate separated from the colonizing isolates by 1163 and 1165 SNPs. Group 3 isolates represented two colonizing isolates. On multi-locus sequence typing (MLST), two novel sequence types were identified in post-travel ESBL *E. coli* isolates.

Antimicrobial resistance in Gram-negative organisms after travel

ESBL-producing *E. coli* resistance profiles demonstrated universal resistance to cefazolin. Sixty-three percent were resistant to trimethoprim-sulfamethoxazole (TMP/SMX), tetracycline and ciprofloxacin. Fifty-five percent were resistant to levofloxacin. Twenty-seven percent were resistant to tobramycin and gentamicin. Ten percent were resistant to nitrofurantoin. Isolates were universally susceptible to amikacin, ertapenem, imipenem, meropenem and piperacillin-tazobactam. On WGS, 45 different antibiotic resistance genes in 25 *E. coli* isolates were found. Of the 11 phenotypic ESBL-producing *E. coli*, 10 demonstrated genotypic resistance with presence of *bla*_{CTX-M} genes (CTX-M-3 [two isolates], CTX-M-14 [six isolates], CTX-M-15 [one isolate] and CTX-M-55 [one isolate]), 9 demonstrated *bla*_{TEM} genes (TEM-1 [eight isolates] and TEM-209 [one isolate]) and 8 demonstrated both *bla*_{CTX-M} genes and *bla*_{TEM} genes with all phenotypic ESBL-producing *E. coli* containing one or more ESBL genes (Table 3).

Table 2. Characteristics associated with acquisition of ESBL-producing Enterobacteriaceae

Characteristic	ESBL (n = 8)	No ESBL (n = 64)	P-value
Gender			
Male	6 (75 [34.9–96.8%])	51 (80 [67.2–88.7%])	0.67
Female	2 (25 [3.2–65.1%])	13 (20 [11.3–32.8%])	0.67
Median age (years)	39.5 (IQR 32.25, 46.0)	41.5 (IQR 34.0, 49.0)	0.53
Median duration of travel (days)	17.0 (IQR 7.5, 154.0)	17.0 (IQR 8.0, 24.0)	0.75
Region of travel			
Mexico, Caribbean and Central America	0 (0 [0–36.9%])	12 (18.8 [11.1–30.5%])	0.34
Asia*	4 (50 [15.7–84.3%])	7 (10.9 [4.9–21.2%])	0.02
Africa	3 (37.5 [8.5–75.5%])	38 (59.4 [46.4–71.5%])	0.28
South America	1 (12.5 [0.3–52.7%])	6 (9.4 [3.5–19.3%])	0.58
Living conditions			
Hotel with air conditioning	4 (50 [15.7–84.3%])	28 (43.8 [31.4–56.7%])	1.00
Hotel without air conditioning	1 (12.5 [0.3–52.7%])	7 (10.9 [4.5–21.2%])	1.00
Military accommodations	0 (0 [0–36.9%])	4 (6.3 [1.7–15.2%])	1.00
Dormitories/Barracks	3 (37.5 [8.5–75.5%])	33 (51.6 [38.7–64.2%])	0.71
Food exposures			
Food from street vendors	2 (25 [3.2–65.1%])	13 (20 [11.3–32.8%])	0.67
Meals prepared at local homes	1 (12.5 [0.3–52.7%])	15 (23.4 [13.8–35.7%])	0.67
Unpasteurized dairy products	0 (0 [0–36.9%])	2 (3.1 [0.4–10.8%])	1.00
Poorly cooked or raw meat/seafood	1 (12.5 [0.3–52.7%])	6 (9.4 [3.5–19.3%])	0.58
Poorly cooked or raw vegetables/salad	2 (25 [3.2–65.1%])	7 (10.9 [4.9–21.2%])	0.26
Field water exposure	0 (0 [0–36.9%])	5 (7 [2.6–17.3%])	1.00
Local water ingestion			
Untreated water	0 (0 [0–36.9%])	1 (1.6 [0–8.4%])	1.00
Ice in beverage	3 (37.5 [8.5–75.5%])	28 (43.8 [31.4–56.7%])	1.00
None of the above food or water exposures	1 (12.5 [0.3–52.7%])	19 (29.7 [18.9–42.4%])	0.43
Unable to wash hands regularly before eating	1 (12.5 [0.3–52.7%])	11 (17.2 [8.9–28.7%])	1.00
Antimicrobial exposure since enrollment	6 (75 [34.9–96.8%])	52 (81.2 [69.5–89.9%])	0.65
Malaria prophylaxis	6 (75 [34.9–96.8%])	51 (80 [67.2–88.7%])	0.67
Chloroquine	0 (0 [0–36.9%])	2 (3.1 [0.4–10.8%])	1.00
Mefloquine	0 (0 [0–36.9%])	0 (0 [0–5.6%])	n/a
Atovaquone–proguanil	4 (50 [15.7–84.3%])	41 (64.1 [51.5–75.7%])	0.46
Doxycycline	2 (25 [3.2–65.1%])	9 (14.1 [6.6–25.0%])	0.60
Primaquine	3 (37.5 [8.5–75.5%])	6 (9.4 [3.5–19.3%])	0.06
Antibiotics for TD	2 (25 [3.2–65.1%])	6 (9.4 [3.5–19.3%])	0.22
Ciprofloxacin	1 (12.5 [0.3–52.7%])	3 (4.7 [1–13.1%])	0.33
Azithromycin	1 (12.5 [0.3–52.7%])	2 (3.1 [0.4–10.8%])	0.20
Levofloxacin	0 (0 [0–36.9%])	1 (1.6 [0–8.4%])	n/a
Systemic antibiotics for other reason	0 (0 [0–36.9%])	3 (4.7 [1.0–13.1%])	1.00
Amoxicillin/clavulanate	0 (0 [0–36.9%])	1 (1.6 [0–8.4%])	n/a
Levofloxacin	0 (0 [0–36.9%])	1 (1.6 [0–8.4%])	n/a
Sulfamethoxazole/trimethoprim	0 (0 [0–36.9%])	1 (1.6 [0–8.4%])	n/a
Illness since enrollment	3 (37.5 [8.5–75.5%])	16 (25 [15.0–37.4%])	0.43
Fever	0 (0 [0–36.9%])	0 (0–5.6%)	n/a
Influenza-like illness	1 (12.5 [0.3–52.7%])	8 (12.5 [0.3–52.7%])	1.00
TD	2 (25 [3.2–65.1%])	8 (12.5 [5.6–23.2%])	0.31

*Isolates were from India and Afghanistan.

ESBL, extended spectrum beta-lactamase; all ESBL-producing Enterobacteriaceae were *E. coli*.

Analysis of fluoroquinolone and tetracycline resistance in all isolates from 72 trips demonstrated 6 subjects exposed to a fluoroquinolone, 11 exposed to a tetracycline and 55 exposed to neither (Table 4). Exposure to a fluoroquinolone and acquisition of both fluoroquinolone and tetracycline resistance was demonstrated ($P=0.05$). Otherwise, there was no significant relationship between exposure to a fluoroquinolone or tetracycline and development of resistance. Two of six participants in

our study developed fluoroquinolone resistance with exposure to levofloxacin or ciprofloxacin ($P=0.16$), and 2 of 11 developed tetracycline resistance with exposure to doxycycline ($P=0.19$). No participants were exposed to both a fluoroquinolone and tetracycline. Analysis of antibiotic resistance genes in 25 *E. coli* demonstrated eight *E. coli* isolates phenotypically resistant to fluoroquinolones, but only four with genotypic resistance (genes *qnrB19* [three isolates] and *qnrS1* [one isolate]) (Table 3). All 11

Table 3. Genotypic and phenotypic resistance among 25 *E. coli* isolates

Antibiotic resistance profile	Phenotypic resistance (%)	Genotypic resistance (%)	Concordant phenotypic and genotypic resistance (%)	Discordant phenotypic or genotypic resistance (%)	Cohen's kappa coefficient
ESBL	11 (44%)	13 (52%)	11 (44%)	2 (8%)	0.73
Fluoroquinolone	8 (32%)	4 (16%)	2 (8%)	6 (24%)	0.15
Tetracycline	11 (44%)	11 (44%)	11 (44%)	0 (0%)	1

ESBL, extended spectrum beta-lactamase.

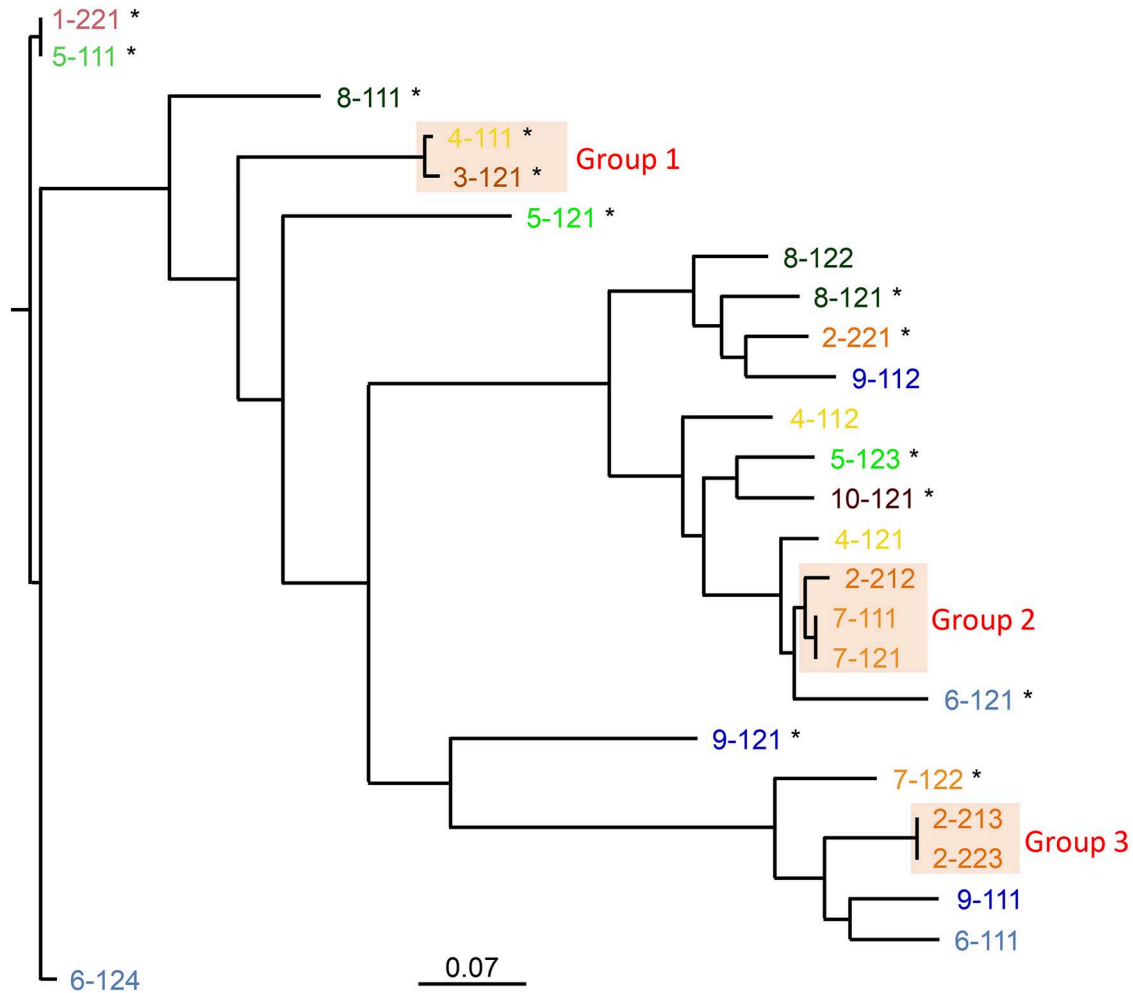


Figure 1. Whole genome phylogeny of the 25 *E. coli*. Branch lengths are indicative of relatedness and the scale bar represent approximate number of SNPs per 1000 bases. Phenotypic ESBL-producing *E. coli* are marked with an asterisk.

E. coli isolates with tetracycline resistance were phenotypically and genotypically concordant (genes tet(A) [four isolates], tet(B) [six isolates] and tet(C) [one isolate]).

Discussion

In order to discover the origin of pre-injury colonization with ESBL-producing Enterobacteriaceae in a population of international travellers with official military duties or deployments, we set out to find associated risk factors through study of the prevalence of ESBL-producing Enterobacteriaceae before and after travel. This prospective study determined that there was

an increased rate of incident colonization with ESBL-producing *E. coli* following travel to Asia especially with travellers returning from India and Afghanistan. ESBL-producing Enterobacteriaceae colonization was not pre-existing in the majority of travellers who returned with colonization of ESBL-producing *E. coli*. In this small study, no other individual risk factors were identified for acquisition of ESBL-producing *E. coli*.

Civilian studies have also associated ESBL-producing *E. coli* incident colonization with international travel, but the majority of studies have been done outside of US cohorts.^{8,9,11,23,24} The one prior prospective civilian study conducted in an American cohort from New York City looking at pre- and post-travel

Table 4. Relationship between fluoroquinolone or doxycycline exposure and acquired resistance

Characteristic	Acquired FQ resistance (<i>n</i> = 9)	Acquired Tet resistance (<i>n</i> = 27)	Acquired both FQ and Tet resistance (<i>n</i> = 5)	No acquired resistance (<i>n</i> = 41)
FQ exposed (<i>n</i> = 6)	2 (<i>P</i> = 0.16)	4 (<i>P</i> = 0.19)	2 (<i>P</i> = 0.05)	2 (<i>P</i> = 0.39)
Doxycycline exposed (<i>n</i> = 11)	2 (<i>P</i> = 0.62)	2 (<i>P</i> = 0.19)	0 (<i>P</i> = 1.00)	7 (<i>P</i> = 0.75)
Exposed to neither (<i>n</i> = 55)	5 (<i>P</i> = 0.20)	21 (<i>P</i> = 1.00)	3 (<i>P</i> = 0.59)	32 (<i>P</i> = 0.78)

FQ, fluoroquinolone; Tet, tetracycline; *No participants were exposed to both a fluoroquinolone and doxycycline.

colonization with ESBL-producing Enterobacteriaceae showed solely the isolation of *E. coli* as did this study. The pre-travel colonization rate of ESBL-producing *E. coli* was 1.7% while post-travel was 25% in the New York City cohort.¹⁰ These rates are similar to other studies outside the USA.^{8,9,23} Consistent with another study that included US military personnel and beneficiaries travelling internationally, this study showed similarly low rates of colonization with 2% pre- and 11% post-travel of ESBL-producing *E. coli*.⁵ This study had a longer duration of international travel (median of 21 days compared to 12 days with the previous US military personnel and beneficiaries cohort), which was more similar to the New York City cohort (median of 21 days).^{5,10}

This was the first study to prospectively evaluate risk factors or incidence of acquisition for ESBL-producing Enterobacteriaceae colonization in travellers on military orders with a variety of destinations and missions. Travel in the military is unique in that travellers were not visiting friends and relatives or having casual contact with locals, food and water supply is regulated, and pre-travel counselling is required. The trips included deployments and short-term travel to include support missions, so these results may not be fully generalizable to the larger population of military personnel at highest risk for combat casualties. While the sample size is relatively low, military members staying in either hotels or military accommodations had similarly low incidence of acquisition. The effect of antibiotic exposure and malaria prophylaxis was not found to have statistical significance for acquiring ESBL-producing Enterobacteriaceae. One of five participants who took a fluoroquinolone for travellers' diarrhoea (TD) acquired ESBL-producing *E. coli*, which is lower than seen in Swedish cohort (three of three) and a US traveller cohort (one of two).^{5,8} Two of eleven participants exposed to doxycycline for malaria prophylaxis acquired ESBL-producing *E. coli*.

Within this cohort, *E. coli* isolates from participants with ESBL-producing Enterobacteriaceae isolated either pre- or post-travel were sent for WGS. Overall, the majority of isolates were separated by a greater relatedness threshold than 10 SNPs indicating that post-travel ESBL-producing Enterobacteriaceae were strains acquired while travelling rather than through horizontal acquisition of an ESBL in a colonizing *E. coli*.²⁵ Consistent with other studies, the most common ESBL were variants of *bla*_{CTX-M} and *bla*_{TEM} genes.^{8-13,15} In addition to beta-lactam resistance, acquisition of fluoroquinolone and tetracycline resistance was observed compared with pre-travel isolates.¹³ Exposure to ciprofloxacin for TD and acquisition of both fluoroquinolone and tetracycline resistance was the only significant relationship demonstrated (*P* = 0.05).

The study had several limitations. Although the targeted enrollment over the proposed study period was similar to studies

with acquisition rates of 24–41%, our relatively low rate of ESBL-producing Enterobacteriaceae colonization resulted in a small cohort size and made the determination of risk factors for acquisition more difficult to determine as the study was not powered to assess individual risk factors. The population is closer in age (median 38 years) to an active duty population of combat related injury and infection (median 24–25) compared with previous studies of travel-related colonization in DoD beneficiaries (median 64).^{3,5} There is the possibility of decreased yield of organism in screening for ESBL-producing Enterobacteriaceae colonization through the use of perirectal swabs rather than stool culture. Numerous studies have however shown adequate sensitivity of perirectal swabs (90%) compared with stool culture in isolation of resistant Gram-negative bacilli, and other studies have successfully implemented perirectal swabs for screening purposes.^{5,9,21} Finally, no clinical significance can be drawn relating these episodes of incident colonization with potential future infectious complications.

Findings of this study support previously observed findings in travel-related colonization studies showing acquisition of antimicrobial resistance in US military personnel travellers. Significant findings included travel to South Asia was found to have higher incident colonization with ESBL-producing Enterobacteriaceae. Compared with civilian literature, acquisition rates of resistant organisms remain comparatively low in our population of study; although, a relationship to individual risk factors for acquisition of ESBL-producing Enterobacteriaceae could not be determined. This study suggests that US military personnel travelling on official duty, particularly in South Asia, are at risk for incident colonization of ESBL-producing Enterobacteriaceae. For the purposes of pre-travel counselling and military planning to reduce post-injury infection, further prospective studies are required to better determine individual risk factors for acquisition of ESBL-producing Enterobacteriaceae.

Author Contributions

Gregory Buchek, MD: Associate investigator, preparation and review of manuscript.

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Funding

This work (IDCRP-037) was conducted by the Infectious Disease Clinical Research Program (IDCRP), a DoD program executed by the Uniformed Services University of the Health Sciences (USU) through a cooperative agreement with The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF). This project has been supported with federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), under Inter-Agency Agreement Y1-AI-5072 and the Department of Defense Emerging Infections Surveillance.

Conflict of interest

Author statements each declare that there is no conflict of interest.

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Author Statements

Gregory Buchek, MD: The authors have declared no conflicts of interest.

Katrin Mende, PhD: The authors have declared no conflicts of interest.

Kalyani Telu, MS: The authors have declared no conflicts of interest.

Susan Kaiser, BS: The authors have declared no conflicts of interest.

Jamie Fraser, MPH: The authors have declared no conflicts of interest.

Indrani Mitra, MS: The authors have declared no conflicts of interest.

Jason Stam, BS: The authors have declared no conflicts of interest.

Tahaniyat Lalani, MBBS, MHS: The authors have declared no conflicts of interest.

David Tribble, MD, DrPH: The authors have declared no conflicts of interest.

Heather C. Yun, MD: The authors have declared no conflicts of interest.

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