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The epidemiology of travelers' diarrhea in Incirlik, Turkey: a region with a predominance of heat-stabile toxin producing enterotoxigenic *Escherichia coli*

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Abstract

This study evaluated travelers' diarrhea among US military personnel on short-term deployment to Incirlik Air Base, Turkey, from June through September 2002. Upon reporting for care for travelers' diarrhea, subjects were enrolled into the study and completed a series of questionnaires and provided stool specimens for pathogen identification and antimicrobial susceptibility testing. Fifty-three percent of the 202 participating subjects had a pathogen isolated from their stool. Enterotoxigenic *Escherichia coli* (ETEC) was the predominant pathogen (41%), followed by *Campylobacter* spp. (12%). The most common ETEC phenotype recovered was stable toxin (ST) CS6 (47% of all ETEC). Most (91.1%) of the cases presented with water diarrhea regardless of isolated pathogen. However, there were some differences in nongastrointestinal symptoms among subjects with *Campylobacter* spp. All illnesses were well managed with antibiotics with or without loperamide with a median time to the last unformed stool of 9 h (interquartile range, 1–32 h). We found no food or environmental factors associated with a differential risk of infection with a specific pathogen. Travelers' diarrhea among a US military population in and around Incirlik, Turkey, can commonly be attributed to ETEC and *Campylobacter* spp. The high proportion of ST-only–producing CS6 ETEC in this region highlights the pathogen's worldwide diversity. Future studies of travelers' diarrhea in this population should adapt more novel microbiologic techniques such as polymerase chain reaction and enhanced culture methods to increase the likelihood of identifying pathogenic *E. coli*.
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Keywords: Enteric disease; Travelers' diarrhea

1. Introduction

Acute infectious diarrhea is recognized as a common illness of travelers, affecting up to 60% of short-term international travelers, with at least 20% being bedridden for part of their trip and 40% changing their itinerary because of diarrhea (Ryan and Kain, 2000). In addition, infectious diarrhea is a common medical problem for deployed US military personnel, with an average incidence of 29% per month and rates up to 60% in high-risk regions such as in Southwest Asia (Riddle et al., 2006; Sanchez et al., 1998). During Operation Desert Shield/Operation Desert Storm in the early 1990s, up to 57% of deployed troops reported an episode of diarrhea (Connor and Farthing, 1999), and 20% reported a temporary inability to perform their assigned duties

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14. ABSTRACT

This study evaluated travelers' diarrhea among US military personnel on shon-tenn deployment to lnei rlik Air Base. Turkey. from June through September 2002. Upon reporting for care for travelers? diarrhea, subjects were enrolled into the study and completed a series of questionnaires and provided stool specimens for pathogen identi fica tion and antimicrobial susceptibility testing. Fifty-three percent of the 202 panicipating subjects had a pathogen isolated from their stool. Entcrotoxigenic Escherichia c:oli (ETEC) was the predominant pathogen (41 %). followed by Campylobacter spp. (12%). The most common ETEC phenotype recovered was stable toxin (ST) CS6 (47% of all ETEC). Most (91. 1 %) of the cases presented with water di:IIThea regardless of iso lated pathogen. llowever, there were some diffcrcnc.:s in nongastrointestinal symptoms among subjects with Campylobac:ter spp. All illnesses were well managed with antibiotics with or withoutloperamide with a median time to the last unformed stool of9 h (interquanilc range, 1- 32 h). We found no lood or environmental factors associated with a diflercnti al risk of infection with a specific pathogen. Travelers? diarrhea among a US military population in and around lncirlik, Turkey, can commonly be attributed to ETEC and Campvlobacter spp. The high proponion ofST-only producing CS6 ETEC in this region highlights the pathogen 's worldwide diversity. Future studies of travelers? diarrhea in this population should adapt more novel microbiologic techniques such as polymerase chain reaction and enhanced cu lture methods to increase the likelihood of ident ifying pathogeni~.: ?. coli.

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(Hyams et al., 1991). More recently, estimates of diarrheal incidence among US military personnel deployed to Afghanistan and Iraq were as high as 49% per month during combat, with *Shigella* and norovirus being the most common etiology (Thornton et al., 2005). Subsequent studies found diarrheagenic *Escherichia coli* to be the most common pathogen associated with travelers' diarrhea among military personnel (Monteville et al., 2006; Sanders et al., 2004; Thornton et al., 2005; Riddle et al., 2006). The short-term morbidity related to acquired diarrhea increases health care service utilization, loss of man-hours, and a transient shortage among the deployed forces (Monteville et al., 2006; Sanders et al., 2004).

The epidemiology of travelers' diarrhea (TD) is diverse both across and within given populations, and it is important to appreciate the pathogen-specific risks in a given region to ensure appropriate empiric therapy is provided. Turkey is one country for which little travel-related diarrhea data exist. Quickly becoming a favorite tourist destination with just more than 20 million international tourists in 2005, Turkey has seen a rapid increase in the number of tourists over the past decade (http://www.unwto.org). It is anticipated that these numbers will continue to increase over the next several decades, as evidenced by the continual rise in the number of international tourists since 1990. In addition, Turkey is a key strategic site for military operations in and around the Middle East. To provide insight into travelers' diarrhea epidemiology in this region, we assessed the clinical presentation and pathogen etiology of infectious diarrhea among US military personnel seeking health care services for diarrheal disease.

2. Materials and methods

A prospective clinic-based, case series study was conducted at Incirlik Air Base, Incirlik, Turkey (Sanders et al., 2007). During the study period, June through September 2002, approximately 4400 long-term (>18 months) and 1200 short-term (≤90 days) military personnel and dependents resided at the air base in support of Operation Northern Watch.

All on-base US military personnel or their adult dependents reporting for medical care because of diarrhea were eligible to enroll. Eligibility required acute diarrhea (3 or more loose stools in preceding 24 h or 2 or more loose stools combined with fever or other gastrointestinal symptoms). Following informed consent, participants underwent a standard clinical evaluation, completed a pretested questionnaire, and provided blood and stool specimens. The clinical presentation of the illness was categorized as dysentery if there was visible gross blood in the stool; otherwise, the illness was categorized as watery diarrhea. Cases were described to have gastroenteritis if they had an illness characterized as predominant vomiting with noninflammatory diarrhea. Subjects were asked to return to the clinic for additional assessments and to provide stool and blood samples 3, 7, 14, and 28 days after enrollment.

Stool specimens were cultured using standard laboratory procedures for the isolation and identification of typical enteric bacteria (e.g., *Campylobacter* spp., *Shigella* spp., *Salmonella* spp., and *Vibrio* spp.) (Bopp et al., 1999; Farmer, 1999). For *Campylobacter* spp., hippurate hydrolysis was used to differentiate isolates into *Campylobacter jejuni* and non-*C. jejuni* following manufacturer's instructions (Hardy Diagnostics, Santa Maria, CA). For enterotoxigenic *E. coli* (ETEC) identification, 5 individual, lactose-fermenting, *E. coli*-like colonies were picked from the primary isolation MacConkey plate and evaluated using the GM1 enzyme-linked immunosorbent assay (GM1-ELISA) for heat labile toxin (LT) and competitive inhibition ELISA for the detection of heat stable toxin (ST) (Sanchez et al., 1990; Svennerholm and Wiklund, 1983). Toxin-expressing *E. coli* colonies were further characterized for the presence of surface colonization factors (CFA/I, CS1-CS7, CS8 [CFA/III], CS12 [PCFO159], CS14 [PCFO166], and CS17) using an immunodot blot method that employed monoclonal antibodies against the CFAs and their subtypes (Binsztein et al., 1991; Viboud et al., 1993). Antimicrobial susceptibility testing was performed using the disk diffusion methodology in compliance with the Clinical and Laboratory Standards Institute (National Committee for Clinical Laboratory Standards, 2000). Enzyme immunoassays were used to evaluate stool samples for rotavirus (Rotaclone, Meridian Diagnostics, Cincinnati, OH) and norovirus (Jiang et al., 2000). For *Cryptosporidium parvum*, *Giardia lamblia*, and *Entamoeba histolytica*, a colorimetric immunoassay was used—Triage (Biosite, San Diego, CA) (Sharp et al., 2001). Additional ova and parasite screening was performed by light microscopy using both iodine and trichrome staining methods. Each stool specimen was also evaluated for occult blood, lactoferrin, and fecal leukocytes in the laboratory.

All data were entered into Microsoft Access data table, validated through range checks and random review of source data. Continuous variables were analyzed using Student's t test or analysis of variance and categorical variables by the Pearson χ^2 test or the Fisher's exact test, as indicated. Statistical analyses were conducted using SAS version 8.2 for Windows (SAS Institute, Cary, NC). Two-tailed statistical significance was evaluated using an α of .05.

3. Results

3.1. Study population

During the enrollment period, 202 subjects met the inclusion criteria and signed the informed consent document. The demographics of the study participants are listed in Table 1. Most of the participants were male, enlisted personnel on short-term deployment. The median time for all study participants from arrival in Turkey to presenting for care was 28 days; however, this was significantly different between those on long-term (median, 72; interquartile range [IQR], 17–377) and short-term (median, 28; IQR, 13–51) deployment (Wilcoxon, $P = 0.04$). Approximately 25% (50/

Table 1
Demographics of study participants (n = 202)

Variable	n (%)
Age (mean, SD)	34 (9.0)
Gender (n, %)	
Male	179 (89)
Female	23 (11)
Race/ethnicity (n, %)	
Caucasian	153 (76)
African-American	28 (14)
Hispanic	15 (7)
Asian	5 (2)
Other	1 (1)
Deployment type (n, %)	
Short term	145 (89)
Long term	14 (7)
Other	5 (3)
Rank[a] (n, %)	
Enlisted	167 (83)
Officer	32 (16)
No. of days in Turkey before presentation (median, IQR)	28 (14–54)
Hours of illness before presentation (median, IQR)	32 (15–73)
Prior episode of travelers' diarrhea (n, %)	
Before this deployment	63 (31)
During this deployment	50 (25)

[a] Four missing.

202) of participants had a prior episode of TD during this deployment before enrollment in this study.

3.2. Pathogen etiology

A pathogen was identified in 53% (n = 108) of the cases, with ETEC (82/202, 40.6%) and *Campylobacter* spp. (25/202, 12.4%) (*C. jejuni*, n = 15; *Campylobacter coli*, n = 9; other, n = 1) being the most common pathogens recovered (Table 2). Coinfections were observed in 14 (13% of samples with pathogen isolated) baseline samples. Similarly, multiple ETEC phenotypes were identified from 6 (7%) subjects with ETEC infections. The most common toxin type detected was ST produced by 76.1% of the isolated ETEC (Fig. 1). Less commonly identified were LT (12.5%) and LT ST (11.4%). CS6 was the predominant colonization factor (39.8%) followed by CS3 (27.3%) coexpressed with either CS1 or CS2. No CF was detected in 17.0% of ETEC isolates.

Table 2
Pathogens identified from stool specimens at initial presentation

Pathogen	n (%)[a]
ETEC[b]	82 (41)
Campylobacter spp.[b]	25 (12)
Plesiomonas shigelloides[b]	2 (1)
Shigella spp.[b]	2 (1)
Nontyphoidal *Salmonella* spp.	2 (1)
G. lamblia[b]	5 (2)
C. parvum	3 (1)
E. histolytica[b]	2 (1)
Rotavirus[b]	1 (0.5)
Norovirus[b]	1 (0.5)
No pathogen identified[c]	94 (47)

[a] May not sum to 100% because rounding and coinfection.

[b] Includes 14 coinfections (*Campylobacter* and *E. histolytica*: n = 1; *Campylobacter* and *P. shigelloides*: n = 1; ETEC and *Campylobacter*: n = 5; ETEC and *P. shigelloides*: n = 1; ETEC and Rotavirus: n = 1; *Shigella* and *Giardia*: n = 2; ETEC, *Giardia* and norovirus: n = 1; *Campylobacter*, *Cryptosporidium* and *E. histolytica*: n = 1; *Campylobacter*, *Cryptosporidium* and *Giardia*: n = 1).

[c] Includes *Blastocystis hominis*, *Providencia alcalifaciens*, and *Morganella morganii*.

3.3. Clinical description

Most of the cases (91.1%) presented with watery diarrhea, whereas 8.3% had dysentery and 0.5% had gastroenteritis. Associated symptoms were frequently reported with abdominal cramps and nausea being most common (Table 3) with similar frequencies regardless of pathogen isolation. Compared to those with ETEC, subjects with only *Campylobacter* spp. isolated from their stool were more likely to report fever (69% versus 25%, P = 0.001), headaches (75% versus 41%, P = 0.01), myalgias (75% versus 20%, P < 0.001), and arthralgias (31% versus 8%, P = 0.01). Most (61%) of the subjects reported to the clinic within 48 h of symptom onset (median, 32 h; IQR, 15–73 h) with a median of 9 loose stools before presentation. Most subjects reported an adverse impact of the illness on their ability to perform their mission (decreased ability, 46%; inability, 21%), and 23% were confined to quarters (placed on bed rest) after clinical evaluation. Inability to work was more common in subjects with *Campylobacter* sp. only than in subjects with ETEC only (53% versus 18%, P = 0.004). Eight subjects (4%) were provided intravenous fluid rehydration, and no persons required hospitalization.

The most commonly used treatment was a combination of a fluoroquinolone and loperamide. The median time to the last unformed loose stool was 9 h (IQR, 1–32 h); however, subjects with *Campylobacter* spp. (regardless of other pathogens isolated) had significantly prolonged time (median, 36.6 h; IQR, 8.8–51.0 h) to last unformed loose stool compared to all other participants (median, 7.5 h; IQR, 0.5–24.5 h) (hazard ratio, 1.85; 95% confidence interval, 1.15–2.96). Likely attributable to the relatively small number of subjects with only *Campylobacter*, this comparison was not statistically different between subjects with only ETEC and those with only *Campylobacter* spp., but it trended toward a longer duration in the subjects with *Campylobacter* sp. only. There were no clinical failures during the course of the study.

A total of 121 (59.9%) subjects met the definition of moderate to severe diarrhea (defined as ≥6 loose stools as part of a diarrheal episode), most (64.5%) of which had a pathogen identified from their stool specimen. Only 4 subjects with moderate to severe diarrhea had pathogens other than ETEC and *Campylobacter* isolated (1 with *C. parvum*, 2 with nontyphoidal *Salmonella* spp., and 1 with both *Shigella* spp. and *G. lamblia*). Approximately 70% of subjects with only ETEC isolated from their stool met the moderate to severe definition. This was only slightly higher

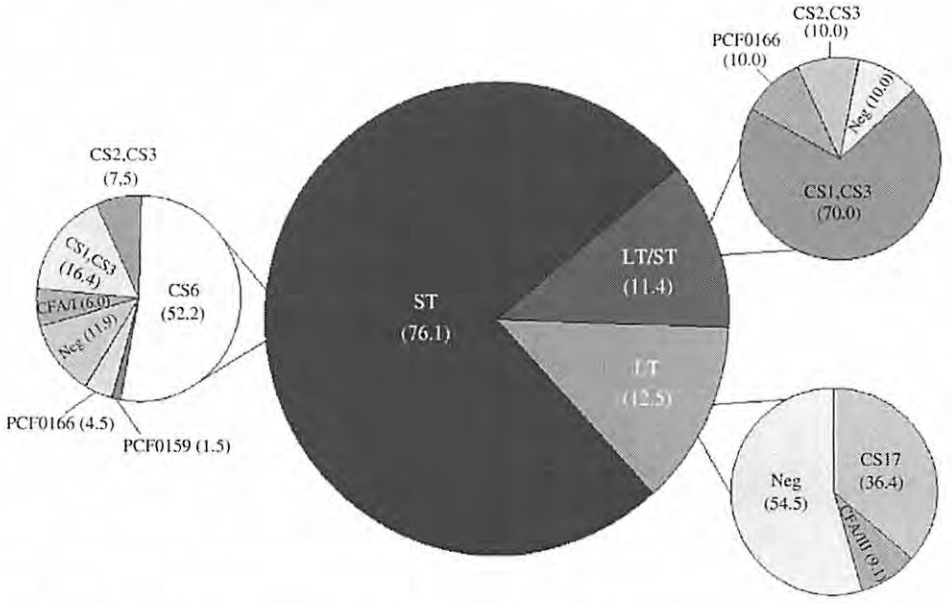

Fig. 1. Phenotype distribution by percentage of all isolated ETEC recovered from diarrheic patients in Incirlik, Turkey, 2002.

Table 3
Frequency (*n* [%]) of clinical signs, symptoms, and medical history upon initial clinic presentation

Symptom	ETEC only	*Campylobacter* only	Any pathogen	No pathogens
Diarrhea	74 (100)	16 (100)	108 (100)	94 (100)
Moderate–severe diarrhea[a]	52 (70.3)	12 (75.0)	78 (72.2)	43 (45.7)
No. of loose stools last 24 h[b]	6 (4, 9)	8 (5, 11)	6 (4, 10)	4 (3, 6)
No. of loose stools since onset[b]	10 (6, 20)	10 (6, 17)	10 (6, 20)	7 (4, 15)
Nausea	41 (55)	11 (69)	59 (55)	44 (47)
Vomiting	6 (8)	3 (19)	10 (9)	10 (11)
No. of episodes[b]	1 (1, 2)	3 (2, 4)	2 (1, 3)	2 (1, 3)
Cramps	65 (88)	12 (75)	93 (86)	77 (82)
Headache	30 (41)	12 (75)	51 (47)	34 (37)
Myalgias	15 (20)	12 (75)	31 (29)	21 (22)
Joint pains	6 (8)	5 (31)	14 (13)	13 (14)
Subjective fever	19 (26)	11 (69)	40 (37)	29 (31)
Documented fever[c]	1 (1)	5 (31)	9 (8)	0 (0)
Median temperature[b]	100.5	101.1 (100.7, 102.0)	101.3 (100.7, 102.0)	
Self-medicating	31 (42)	6 (38)	45 (42)	29 (31)
Imodium	19 (61)	2 (33)	25 (56)	13 (45)
Pepto-Bismol	8 (26)	2 (33)	13 (29)	7 (25)
Antibiotic	0 (0)	0 (0)	0 (0)	0 (0)
Other	9 (29)	4 (67)	15 (33)	14 (50)
Intravenous fluids administered	2 (3)	2 (13)	5 (5)	3 (3)
Treatments provided				
Imodium	70 (95)	12 (75)	93 (86)	83 (88)
Ciprofloxacin	71 (96)	14 (88)	103 (95)	87 (93)
Levofloxacin	1 (1)	1 (6)	2 (2)	2 (2)
Azithromycin	2 (3)	1 (6)	3 (3)	0 (0)
Time to last unformed loose stool (h)[b]	7.3 (0.3, 26.0)	25.0 (8.0, 45.0)	13.4 (2.3, 39.0)	7.0 (0.1, 23.0)
Ability to work				
Normal (A)	25 (34)	3 (19)	31 (29)	29 (31)
Decreased (B)	34 (46)	4 (25)	48 (44)	45 (48)
Not able (C)	13 (18)	8 (50)	25 (23)	18 (19)

[a] Defined as ≥6 loose or liquid stools.
[b] Median (lower quartile, upper quartile).
[c] Oral temperature ≥100.5 °C.

(75%) for persons with only *Campylobacter* isolated. For subjects with ETEC-attributed diarrhea, there was no statistically significant difference (Fisher's exact test, $P = 0.23$) in disease severity by ETEC toxin phenotype (LT only, 50% severe; ST and/or LT ST strains, 73% severe).

A list of common exposures by identified pathogens is shown in Table 4. In general, most exposures were relatively common regardless of pathogen identification. However, there did appear to be a trend toward subjects with ETEC isolated having more common exposure to ice and tap water. However, these differences were not statistically significant. In addition, most exposures occurred off base, and most of the cases (71.3%) reported eating at facilities outside the base.

3.4. Bacterial enteropathogen antimicrobial susceptibility

A total of 5 (6.1%) subjects had ETEC isolates recovered that were resistant to nalidixic acid with another 6 (7.3%) showing only intermediate susceptibility. A similar antibiotic profile was found with ciprofloxacin (resistant, 3.7%; intermediate, 1.2%), whereas approximately 50% of the strains were resistant to trimethoprim–sulfamethoxazole and tetracycline (46.9% and 49.4%, respectively). All *Campylobacter* sp. isolates were highly susceptible to azithromycin, but 14 of 25 (56%) were resistant to ciprofloxacin (MIC ≥ 4 μg/mL) with an MIC_{50} = 32.0 μg/mL. Of the *C. jejuni*, 73.3% were ciprofloxacin resistant compared to 33.3% *C. coli* cases (Fisher's exact test, $P = 0.09$). Among subjects with *Campylobacter* spp., most (92.0%) received ciprofloxacin with only 1 subject each receiving levofloxacin and azithromycin. Time to last unformed stool was not significantly different regardless of treatment or strain susceptibility (data not shown).

Table 4
Frequency (%) of common food and beverage exposures within 5 days preceding clinic presentation

Risk factor	ETEC only (n = 74)		*Campylobacter* only (n = 16)		No pathogens (n = 81)	
	On base	Off base	On base	Off base	On base	Off base
Salad	23.0	43.2	18.8	56.3	22.2	25.9
Beef	29.7	46.0	31.3	56.3	33.3	40.7
Chicken	31.1	64.9	18.8	75.0	34.6	58.0
Seafood	6.8	9.5	0.0	0.0	4.9	14.8
Pork	16.2	16.2	12.5	12.5	19.8	12.4
Lamb	2.7	17.6	0.0	6.3	3.7	9.9
Fish	6.8	12.2	0.0	18.8	8.6	9.9
Fruits	20.3	31.1	18.8	25.0	23.5	14.8
Vegetables	31.1	64.9	31.3	62.5	35.8	54.3
Milk	23.0	9.5	31.3	0.0	14.8	8.6
Tea, juice, etc.	24.3	32.4	31.3	25.0	37.0	22.2
Ice	32.4	27.0	18.8	6.3	30.9	19.8
Tap water	24.3	5.4	12.5	0.0	17.3	3.7
Pool, river, or ocean water	1.4	9.5	6.3	18.8	0.0	11.1

4. Discussion

Recent reports have described the incidence, etiology, and impact of infectious diarrhea among deployed troops to the Middle East and North Africa regions (Hyams et al., 1995; Monteville et al., 2006; Oyofo et al., 1995, 1997; Sanders et al., 2004, 2005a, 2005b). Turkey, another country in this region, falls in the medium category based on the Human Development Index (hdr.undp.org) and is a strategic location for the North Atlantic Treaty Organization (NATO) and is a popular tourist destination (Hürriyet, 2006). High diarrhea rates among troops and the concern of invasive pathogens and antibiotic resistance from recent reports among host-country pediatric populations supports a need to understand the etiology of diarrhea in US troops deployed to Incirlik, Turkey (Ergonul et al., 2004; Ozmert et al., 2005; Uysal et al., 1997).

In this study, ETEC (41%) and *Campylobacter* spp. (12%) were the predominant pathogens recovered from participants reporting to a clinic with symptoms of acute infectious diarrhea. A recent systematic review among US military and similar travel populations to the Middle East and North Africa region found that among 13 studies, the summary prevalence of ETEC was 28.3% and 1.3% for *Campylobacter* spp. (Riddle et al., 2006). The *Campylobacter* sp. rates we observed were higher than those reported in the systematic review possibly because of differences in the populations evaluated, methodological differences, or a true difference in *Campylobacter*-attributable diarrhea rates at Incirlik, Turkey. Although most of the personnel reported a significant impact of disease on their ability to perform their mission at initial presentation, the typical response to antibiotic treatment was very fast, resulting in minimal days missed from work, although the time to clinical cure was longer for subjects with *Campylobacter*-associated illness, confirming previous reports (Evans et al., 2009; Gallardo et al., 1998; Nelson et al., 2004).

The most common ETEC phenotype we observed was ST CS6 accounting for 43.0% of all isolated ETEC. Although the prevalence of ETEC phenotypes differs greatly by time, region, epidemiologic methods, and study populations, the prevalence of CS6 ETEC in our study highlight its importance in disease-causing ETEC infections, a phenomenon increasingly being recognized in other regions (Gupta et al., 2007; Qadri et al., 2005; Rao et al., 2003; Steinsland et al., 2002). Others have highlighted that ETEC expressing ST either alone or in combination with LT causes more severe diarrheal illness than LT-only strains (Qadri et al., 2000). Although we were unable to identify a significant difference in disease severity, it is important to note that that was not the objective of this study, which was likely underpowered for this comparison.

Most of the subjects included in this study (60%) met the definition of moderate–severe diarrhea (≥6 loose/liquid stools). This represents a higher proportion than is commonly reported in similar populations. Utilizing a cross-sectional survey, Putnam et al. (2006) reported that among the troops

reporting an episode of diarrhea while deployed to Iraq or Afghanistan, the proportion of severe diarrhea was 21% and 14%, respectively. The apparent discrepancy may reflect a difference in pathogen etiology or a difference in the methodologies utilized to capture disease severity data.

Forty-seven percent of the subjects reporting for care had no enteric pathogens identified from their stool specimens. This is consistent with other epidemiologic studies of travelers' diarrhea and highlights an ongoing gap in disease epidemiology. In a recent study evaluating polymerase chain reaction methods on fecal specimens for pathogen identification, Meraz et al. (2008) identified a relatively high prevalence of ETEC and diffusely adherent *E. coli* (EAEC) in diarrheal stool specimens previously identified as pathogen negative using traditional culture-based methodologies. Similarly, Galbadage et al. (2009) evaluated a modified methodology for ETEC identification by increasing the number of isolated *E. coli* colonies tested for the presence of heat-stabile or heat-labile encoding genes. In addition, for this study, specimens were not tested for EAEC or other diarrheagenic *E. coli*, pathogens that can account for a measurable proportion of travelers' diarrhea (Riddle et al., 2006; Meraz et al., 2008; Galbadage et al., 2009). Only 1 case of norovirus was identified in our study sample. Recent studies have identified that this pathogen can cause not only epidemic gastroenteritis but also sporadic illness among travelers (Chapin et al., 2005; Ko et al., 2005; Patel et al., 2008). The lack of identification of this organism may have been due to the summer sampling frame where these infections may occur less frequently or due to our case definition, which required at least 2 diarrhea stools to be eligible for enrollment. There may have been vomiting predominant illnesses because of these and other acute viral enteric infections that were not detected. Future studies should be designed to evaluate all potential acute gastrointestinal infections and increased utilization of molecular techniques on enteric specimens, and advances in culture-based methodologies may serve to decrease the number of pathogen-negative specimens in future epidemiologic studies.

Military travelers are unique in that often they are deployed to environments where control of food sources may vary from only approved sources (military dining facilities or military supplied meals) to relying on food sources from the local community, to a mixture of these settings as found at Incirlik Air Base, Turkey. The study design lacking a control population does not allow us to say with confidence what particular exposures are considered high risk; however, it is interesting to note that there was a high frequency of potential known exposures reported, underscoring the challenge of providing safe food and fluids during deployment. Not surprising, when looking at exposures relative to pathogen identified, water exposure (e.g., tap water, ice) was more commonly associated with ETEC infections (Hoge et al., 1996; Tellier and Keystone, 1992).

Military travelers may also differ in respect to the standard of care received when seeking TD-related treatment, which varies between different traveler populations and settings. Within the Department of Defense deployment settings, returning the service member back to full health in a timely manner and avoiding dehydrating illness complications in the rigorous occupational settings are critical; therefore, treatment with antibiotics, usually in combination with an antimotility agent, is commonly employed. A randomized controlled trial performed at the Incirlik Air Base demonstrated, in this ETEC predominant setting, equal efficacy for empiric treatment with a single dose of either levofloxacin or azithromycin combined with loperamide (Sanders et al., 2007). As seen in this investigation, *Campylobacter* accounted for approximately 15% of cases with almost half being fluoroquinolone resistant supporting first-line use of azithromycin among travelers presenting with dysentery or other evidence increasing likelihood of campylobacteriosis such as associated fever.

This study was limited to subjects reporting to health care services with the primary complaint of diarrhea. This likely represents a small subset of diarrheic persons, potentially skewing the pathogen distribution. In addition, the lack of a true control group in our study limits the ability to make strong inferences regarding pathogenicity, risk factor, or other epidemiologic issues. Future studies should further evaluate the epidemiology of travelers' diarrhea and acute gastroenteritis in a population-based setting in Turkey where all-cause illness can be assessed using advanced diagnostic testing strategies and where appropriate controls can be utilized. However, these data continue to underscore the bacterial predominance of these infections, and providers should be aware of the appropriate empiric antibiotic therapy to treat these patients.

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