Acute Diarrhea in North American Students after Relocation to Israel: A Pilot Study

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ABSTRACT:
Background: Travelers' diarrhea (TD) is frequently encountered in people traveling from high-income to low-income countries; however, its epidemiology in those traveling between high-income countries is not known.

Objectives: To evaluate the incidence of diarrhea in North American students relocating to Israel.

Methods: A retrospective cohort study involving medical students from the United States and Canada relocating to Israel was conducted. Students who relocated to Israel during 2010–2016 were contacted by email to participate in an anonymous survey. Data included demographic information as well as occurrence, timing, duration, and outcome of diarrhea after relocation.

Results: Ninety-seven students participated in the survey. Most (93.7%) students relocated from the United States or Canada. The period-prevalence of diarrhea was 69.1%. The incidence of diarrhea declined from 34.8 cases per 100 student-months during the first month after relocation to 1.3 cases per 100 student-months after 1 year. The duration of diarrhea was up to 1 week in 72.7%. Students who reported diarrhea were younger than students who did not (mean age 24.0 ± 2.2 and 28.4 ± 1.8 years, respectively, $P < 0.001$). No other demographic parameter was significantly associated with a higher likelihood of diarrhea.

Conclusions: A high proportion of North American medical students relocating to Israel reported diarrhea with clinical and epidemiological features similar to classic TD. Further studies are needed to elucidate the causative agents of TD in Israel.

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KEY WORDS: diarrhea, Israel, travelers' diarrhea, travel

Travelers' diarrhea (TD) is the most prevalent medical condition reported among travelers. TD is considered to be an infectious disease that can be caused by a variety of bacterial and other pathogens, although a specific pathogen is found in fewer than half of the cases [1]. The incidence of TD is very high among individuals traveling from high-income to low-income countries, and reflects the increased likelihood of fecal-oral transmission of gastrointestinal pathogens in regions with poor food and water hygiene. The likelihood of developing TD correlates with both destination and duration of travel. For example, among Israeli travelers to India, who typically travel for several months, rates of up to 80% have been recorded [2]. Theoretically, travel from one country with a very low incidence of food and water pathogens to a similar country should not result in an increased incidence of diarrhea. However, little data exist on the epidemiology of TD among people traveling from one high-income country to another. We have evaluated the incidence of TD in a unique population of North American medical students after relocation to Israel.

PATIENTS AND METHODS

A retrospective cohort study was conducted to evaluate the incidence of TD in medical students attending the Sackler School of Medicine – New York State/American Program of Tel Aviv University. This long-established medical education program for American and Canadian medical students is based in the Tel Aviv region, where students reside for 4 years.

STUDY POPULATION AND SURVEY DETAILS

The study was approved by the institutional review board at the Sheba Medical Center. Willingness to participate and complete the survey was considered as informed consent.

Students from the classes that started between 2010 and 2016 were contacted by email and asked to participate in an anonymous survey. Email contacts for current students and recent alumni were available through a student-maintained listserve. Non-responders were sent one repeat email. The survey included demographic data, history of past residence in Israel, past medical history, and data on first occurrence of diarrhea after relocation to Israel, including timing, duration, effect on activities, diagnosis, treatment, and recovery [Appendix].

Acute diarrhea was defined as three or more loose/watery stools during 24 hours, with/without additional symptoms such as fever, vomiting, and abdominal pain (this definition was also included in the questionnaire).

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*These authors contributed equally to this study

STATISTICAL ANALYSIS

Fisher's exact test and Student's *t*-test were used to analyze categorical and continuous variables respectively.

RESULTS

Active emails were available for 252 students and alumni, of whom 97 returned a completed survey. The median time from relocation to the survey among responders was 3 years (range 6.9–0.7 years).

The complete demographic data is presented in Table 1. Male/female ratio was 1.74. Age at relocation to Israel was 24.2 ± 2.1 years. Most (93.7%) students were born in the United States or Canada, four (4.2%) were born in Israel, one in Vietnam, and another in Uzbekistan (1.0% each). All were long-term residents of North America prior to relocation. Twenty-one students (21.7%) had a history of a previous residence of > 1 year in Israel prior to relocation; however, none were living in Israel before joining the program. North American regions of residence prior to relocation were the northeast United States (56.4%), western United States (19.1%), mid-western United States (9.6%), southern United States (4.2%), and Canada (10.6%). Most students reported being in good health prior to relocation. Four students (4.3%) disclosed former or current treatments for migraine, asthma, psoriasis, and Hashimoto's disease. An additional 13.4% reported previous chronic gastrointestinal conditions including inflammatory bowel disease (2.1%), irritable bowel syndrome (8.2%), and lactose intolerance (6.2%).
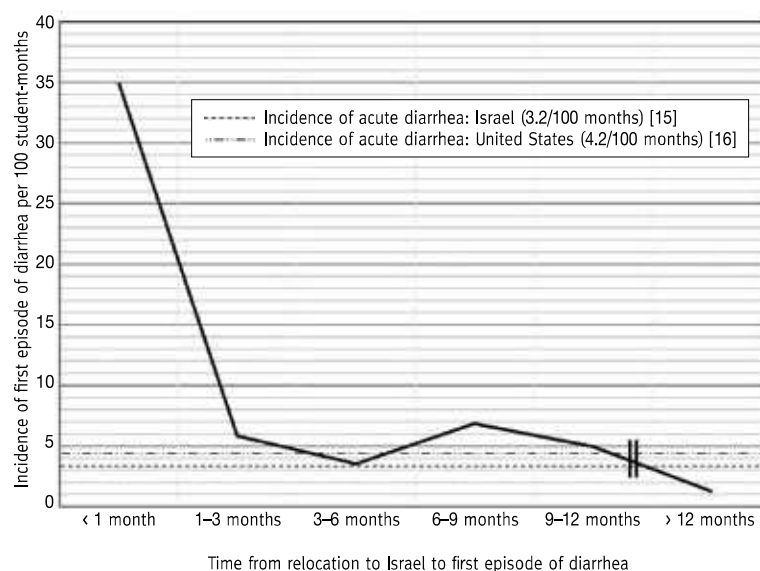
The period-prevalence for the study period of an episode of diarrhea among responders was 69.1%. The prevalence of diarrhea was similar between classes, ranging from 60% in the class of 2010 to 83% in the class of 2015. The likelihood of developing diarrhea showed a decline over time after relocation, with 34.8% of cases reporting diarrhea within one month after relocation and another 30.3% during months 2–12. The incidence of diarrhea declined from 34.8 cases per 100 student-months during the first month to 1.3 cases per 100 student-months during years 2–4 [Figure 1]. The duration of diarrhea was mostly short, with 72.7% having diarrhea for up to one week, another 18.2% for up to one month, and 3.0% having protracted diarrhea for over one year. None of the students who developed protracted diarrhea after relocation reported a past history of gastrointestinal disease. Most students reported recovery with self-treatment with antidiarrheal or antimicrobial agents, 5.9% required outpatient care, and none were hospitalized.

Students who reported diarrhea after relocation were younger than students who did not (mean age 24.0 ± 2.2 and 28.4 ± 1.8, respectively, P < 0.001). None of the other demographic parameter was significantly associated with a higher likelihood of diarrhea [Table 1]. Consumption of street food did not differ significantly between the two groups.

Table 1. Demographic data of North American students and the incidence of diarrhea after relocation to Israel

	All students (N=97)	Students with diarrhea after relocation (n=67)	Students without diarrhea after relocation (n=30)	P value
Male/ female ratio	1.71	1.87	1.42	0.64
Age at relocation, years	24.2 ± 2.1	24.0 ± 2.2	28.4 ± 1.8	‹ 0.001
USA resident	82.5%	83.5%	80.0%	0.77
Past residence (› 1 year) in Israel	21.6%	57.1%	30%	0.19
Consumption of street food	92.8%	92.5%	96.7%	0.66
History of chronic gastrointestinal disease	13.4%	16.4%	6.7%	0.33

Figure 1. Incidence of first episode of diarrhea according to time from relocation

Incidence of first episode of diarrhea per 100 student-months

Incidence of acute diarrhea: Israel (3.2/100 months) [15]
Incidence of acute diarrhea: United States (4.2/100 months) [16]

Time from relocation to Israel to first episode of diarrhea

DISCUSSION

TD remains the most frequent medical condition encountered by travelers. It is associated with morbidity and travel disruption as well as with significant healthcare and other costs [3]. Our survey suggests that nearly 70% of medical students relocating from North America to Israel develop diarrhea after their arrival, a proportion that is well within the range described for classic TD [4].

Most clinical and demographic parameters were not significantly associated with diarrhea [Table 1]. This finding may reflect the limitations of the small sample size; however, our findings in students who developed diarrhea are suggestive of those reported in studies of classic TD. The likelihood of diarrhea was highest soon after relocation and then declined; however, incidence did not disappear completely even after long stays. This result is similar to findings in expatriates relocating to countries such as Nepal [5]. Younger age was associated with

higher likelihood of diarrhea, which again mimics the findings in classic TD [5,6]. In addition, students with a history of past residence in Israel were not less likely to develop TD; which is similar to the data on travelers visiting friends and relatives (VFRs) in low-income countries, who are probably as likely as non-VFR tourists to develop TD, although are less likely to present to a post-travel clinic for acute diarrhea [7,8]. The lack of association between diarrhea after relocation and street food consumption in our survey may reflect the fact that most students indeed consumed street food. It should be noted, however, that among travelers to low-income countries, adherence to dietary precautions is not protective against TD [1,9].

Among travelers with classic TD, female gender is associated with an increased risk of diarrhea [10]. In our study, gender was not associated with diarrhea risk; however, the study may have lacked statistical power to evaluate this issue as women were underrepresented in the study population. The clinical course of diarrhea in our study was also similar to that of classic TD [1]: most students recovered within one week (although 4.5% had diarrhea for more than 3 months) and most had recovered with self-medication.

Thus, clinical and epidemiological parameters suggest that the syndrome of diarrhea after relocation to Israel is similar to classic TD. However, Israel is not perceived as an area of risk for TD, and the U.S. Centers for Disease Control and Prevention does not recommend any specific food or water precautions during travel to that country [11]. In registries of ill-returning travelers such as the GeoSentinel Global Network, Israel did not feature as a source of significant diarrheal disease [12]. Similarly, in a study of travel-related foodborne infection reported to FoodNet USA, the number of cases of diagnosed agents of TD reported from travelers returning from Israel was similar to that reported from western European countries [13]. In fact, cases of TD that resulted from travel between any high-income countries patients are reported only anecdotally in registries of travel-related diseases [14].

Acute infectious diarrhea is, of course, not limited to developing countries. Many viral and bacterial pathogens are globally distributed, and travelers may encounter them anywhere. Theoretically, travel between high-income countries that enjoy similar high levels of food and water safety should not result in an increased incidence of diarrhea among travelers, and the rates of diarrhea among travelers should mimic the low rates in the general population. However, the incidence of diarrhea in our cohort was much higher than reported rates in the general population of either the United States or Israel [15,16] [Figure 1].

Very little data exist on the incidence of diarrhea after travel between high-income countries; however, historical studies have shown that the incidence is not negligible. In 1966, 14% of all foreign students relocating to California developed diarrhea within one month after arrival [17]. A seminal study by Steffen et al. [18] on the global epidemiology of TD in the 1980s, including a survey of 20,000 returning European travelers, reported an incidence of TD of 5% and 15% in travelers returning from North America and southern Europe (Italy, France, Greece), respectively [18]. Similarly, gastrointestinal diseases including TD were the fourth most common medical condition and accounted for 16.3% of tourists seeking medical assistance in Zakynthos, Greece [19]. Unfortunately, most recent studies of TD were limited to travelers returning from low-income countries. An exception is a 2003 study, in which a small cohort of Tasmanian students spent a 6-week period in Europe/North-America, of whom 63% reported TD [20].

Our study has several limitations. The retrospective nature of the study may introduce recall bias that could have led to an underestimation of diarrhea incidence in the earlier student cohorts; however, recall bias is less likely to have affected more recent classes, and the rate of reported diarrhea was similar among classes. In addition, only 38.5% of students who were contacted completed the survey. Selection bias could have led to an overestimation of diarrhea incidence as students without diarrhea may have failed to participate. However, even with the assumption that all non-responders did not report diarrhea, the rate of diarrhea reported early after relocation is still much higher than the rates reported for Israeli or North American populations [Figure 1].

Our study addressed a unique population of medically erudite young adults relocating to Israel for an extended period. Whether our findings may apply to other populations, such as short-term recreational tourists, business travelers, or other age groups is unknown.

The design of the study prevented us from determining the causative agents of diarrhea in our cohort. The incidence of non-typhoidal salmonellosis in Israel exceeds that reported in the United States, although rates continue to decline [21]. Strains of *Escherichia coli* (*E. coli*), including enteropathogenic, enterotoxigenic, and enteroaggregative, are the most frequently diagnosed pathogens in TD [22]. In addition, viral agents of TD [23] are known to circulate in Israel and account for a significant proportion of endemic diarrheal disease. In light of the incidence rates of diarrhea after relocation, a prospective study of future student cohorts is likely to provide data on the etiologies of diarrhea in this population.

CONCLUSIONS

The incidence of diarrhea among medical students from the United States and Canada who relocate to Israel is high. Many features of this diarrhea, including a high incidence immediately after relocation, a short duration, and a generally benign course are similar to those seen in classic TD. The epidemiology of TD after travel between high-income countries is poorly defined. Prospective studies using modern diagnostic methods are needed.

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Appendix. Online questionnaire: details

- Gender
- Country of birth
- Age at relocation
- Birth year
- Place of residence when not in Israel (State or Province)
- Year of entry to Sackler program
- Year of completion or anticipated year of completion of studies
- Past residence in Israel for > 1 year prior to joining the Sackler program
- Number of years of residence in Israel
- Gastrointestinal illnesses prior to attending Sackler
- Any other chronic condition prior to attending Sackler
- Street food consumption
- Have you suffered from acute diarrhea (definition: at least 3 loose stools per day for at least 1 day +/- other symptoms including abdominal pain, nausea, vomiting, fever) at any time during your stay in Israel?
- How long after you moved to Israel did you first experience symptoms of acute diarrhea?
- How long did it take your gastrointestinal symptoms to resolve?
- How long did your symptoms interfere with your activities of daily life, such as school work, studying or volunteering?
- Did you require medical assistance during acute diarrhea?
- Was a specific pathogen diagnosed?