Travelers' Diarrhea and Other Gastrointestinal Symptoms among Boston-Area International Travelers

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Abstract. This prospective cohort study describes travelers' diarrhea (TD) and non-TD gastrointestinal (GI) symptoms among international travelers from the Boston area, the association of TD with traveler characteristics and dietary practices, use of prescribed antidiarrheal medications, and the impact of TD and non-TD GI symptoms on planned activities during and after travel. We included adults who received a pre-travel consultation at three Boston-area travel clinics and who completed a three-part survey: pre-travel, during travel, and post-travel (2–4 weeks after return). TD was defined as self-reported diarrhea with or without nausea/vomiting, abdominal pain, or fever. Demographic and travel characteristics were evaluated by χ^2 test for categorical and Wilcoxon rank-sum test for continuous variables. Analysis of dietary practices used logistic generalized estimating equation models or logistic regression models. Of 628 travelers, 208 (33%) experienced TD and 45 (7%) experienced non-TD GI symptoms. Of 208 with TD, 128 (64%), 71 (36%), and 123 (62%) were prescribed ciprofloxacin, azithromycin, and/or loperamide before travel, respectively. Thirty-nine (36%) of 108 took ciprofloxacin, 20 (38%) of 55 took azithromycin, and 28 (28%) of 99 took loperamide during travel. Of 172 with TD during travel, 24% stopped planned activities, and 2% were hospitalized. Of 31 with non-TD GI symptoms during travel, six (13%) stopped planned activities. International travelers continue to experience diarrhea and other GI symptoms, resulting in disruption of planned activities and healthcare visits for some. Although these illnesses resulted in interruption of travel plans, a relatively small proportion took prescribed antibiotics.

INTRODUCTION

Travelers' diarrhea (TD) and non-TD gastrointestinal (GI) symptoms are common among international travelers. In a study of short-term travelers from Switzerland to developing countries, the most common symptom experienced was severe diarrhea (8.5%) followed by vomiting or abdominal cramps (4%).¹ GI illnesses were the most frequently reported diagnoses (34%) among ill-returned travelers to GeoSentinel clinics.² Of those returning to U.S. GeoSentinel clinics, acute diarrhea (30%) was the most common diagnosis.³ In one cohort of U.S. travelers, 46% reported diarrhea.⁴ GI illnesses can last from 2 days to weeks or longer,⁵ disrupting plans during travel or after returning home. Eighty percent of those who experienced diarrhea during travel treated themselves with medication and 6% sought medical care.⁴

Pre-travel medical advice typically includes destination-specific food and water precautions (such as eating only food that is cooked and served hot and drinking only bottled water), counseling about management of diarrhea, and prescriptions for medications to self-treat diarrhea. Adhering to food and water precautions can be difficult while traveling and does not eliminate the risk of TD, emphasizing the need for pre-travel medical providers to counsel travelers on self-treatment strategies.⁵

Prevalence of GI symptoms during travel and the impact of TD on travel-related activities have not been well described in recent years; current recommendations are derived from studies from > 20 years ago.^{1,6–9} The objective of this study is to describe the types of GI symptoms occurring during and after travel among more recent U.S. international travelers. Specifically, we described the occurrence of TD and non-TD GI symptoms, analyzed whether travelers took prescribed antidiarrheal medications (including antimotility and antibiotic agents), the impact of TD and non-TD GI symptoms on planned activities, the association of demographic and trip characteristics with TD, and adherence to recommended dietary prevention measures.

METHODS

The Boston Area Travel Medicine Network (BATMN) is a research collaboration of travel clinics in the greater Boston area representing urban-, suburban-, academic-, and university-affiliated facilities. A convenience sample of travelers ≥ 18 years of age attending three BATMN clinics between 2009 and 2011 for pre-travel consultations completed pre-travel surveys, at least one survey weekly during travel, and a post-travel survey 2–4 weeks after return. Travelers were asked to complete a survey at the end of each week of their trip. Institutional review board approvals were obtained at all sites and the Centers for Disease Control and Prevention, and participants provided written informed consent. Information collected included demographic and trip characteristics, vaccines and medications recommended/prescribed before travel,

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medications taken during travel, dietary practices during travel (consumption of tap water, ice in drinks, unpasteurized dairy products, and salads), symptoms experienced, and impact of illness during and after travel. Vaccinations, prescriptions, and travel health advice given during the pre-travel consultation were recorded by a clinician, and the remainder of the surveys were completed by the traveler. Data were entered into a password-protected database (CS Pro, U.S. Census Bureau, Washington, DC).

TD was defined as diarrhea with or without nausea/vomiting, abdominal cramps, or fever.¹⁰ Non-TD GI symptoms described included the following in the absence of diarrhea: nausea/vomiting, abdominal pain, and constipation. Participants who reported non-GI symptoms (e.g., joint pain, skin problems, or motion sickness) were excluded from this analysis. An overview of all health problems experienced by this cohort has been published elsewhere.¹¹ We compared those with TD to those who remained healthy, defined as those who did not report any symptoms during or after travel. Travel destinations were grouped by: 1) 2011 United Nations (UN) human development index (HDI)¹² (if a traveler went to ≥ 1 country, the lowest ranked country was used) and 2) UN geographic regions¹³ (if traveler went to ≥ 1 region, they were categorized as "multiple").

Demographic and trip characteristics were evaluated by χ^2 test for categorical and Wilcoxon rank-sum test for continuous variables. Analysis of weekly dietary practices during travel used logistic generalized estimating equation models, and analysis of dietary practices during or after travel used logistic regression models. Variables that were statistically significant in bivariate analysis were used in multivariable analysis; destination was included in the final models because risks for foodborne and waterborne diseases vary by destination.⁵ Trip duration in days was included in the multivariable models as a continuous variable. All two-tailed P values < 0.05 were considered statistically significant. SAS 9.3 (SAS Institute, Cary, NC) was used for all analyses.

RESULTS

We enrolled 987 travelers; 628 (64%) completed all three parts (pre-, during, and post-travel) and were included in the study. Comparison of the 628 to the 359 who did not complete all three parts (noncompleters) revealed no differences, except that completion rates were higher for white travelers than all other racial/ethnic groups ($P < 0.001$) and for older travelers (median age 47 years versus 32 years in noncompleters, $P < 0.001$).¹¹ Of those 628

travelers, 208 (33%) experienced TD, 45 (7%) experienced non-TD GI symptoms, 147 (23%) experienced non-GI symptoms, and 228 (36%) did not experience any symptoms during or after travel. Of the 208 with TD, 140 (67%) reported diarrhea as their only symptom, whereas 33 (16%) also experienced nausea/vomiting, 23 (11%) abdominal pain, and 27 (13%) fever (Table 1). Of the 45 who reported non-TD GI symptoms, 21 (47%) experienced nausea/vomiting, 19 (42%) experienced constipation, and 10 (22%) experienced abdominal pain during or after travel (Table 2). Almost all travelers (99%) received advice about food and water precautions and diarrhea management during pre-travel consultation.

Trip characteristics in those with TD versus those who remained healthy. Duration of travel was slightly longer for the 208 with TD than for the 228 travelers who remained healthy (median, 13 days versus 11 days, $P < 0.0001$, Table 3). India (total 89 travelers, 48% experienced TD), South Africa (total 41 travelers, 24% experienced TD), and Tanzania (total 35 travelers, 43% experienced TD) were the most common destinations of all travelers. The relationships of geographic region to TD and level of development to TD were not statistically significant ($P = 0.06$ for the UN region and $P = 0.08$ for the HDI groupings; Table 3).

Vaccines and medications prescribed pre-travel and those taken during travel. Of all 628 travelers, 366 (58%) were administered hepatitis A vaccine and 445 (71%) received either oral (164 travelers, 37%) or injectable (281, 63%) typhoid vaccine at the pre-travel consultation. Of those who experienced TD during or after travel, 126 (61%) of 208 travelers received hepatitis A vaccine and 151 (73%) had received typhoid vaccine at the pre-travel consultation. Those who experienced TD during or after travel were no more likely to have been vaccinated for hepatitis A ($P = 0.43$) or typhoid ($P = 0.5$) at the pre-travel consultation than those who remained healthy.

Overall, 434 of 628 (69%) travelers were prescribed ciprofloxacin, 170 (27%) azithromycin, and 377 (60%) loperamide for TD at the pre-travel consultation. Twenty-three travelers were not prescribed any antibiotic for TD, eight of whom reported experiencing diarrhea during or after travel.

Of 208 travelers who developed TD during or after travel, 200 had been prescribed either ciprofloxacin, azithromycin, loperamide, or a combination before travel. Of the 200 prescribed, 128 (64%), 71 (36%), and 123 (62%) were prescribed ciprofloxacin, azithromycin, and loperamide before travel, respectively. One hundred-twenty travelers (58%) were prescribed loperamide and either ciprofloxacin or

TABLE 1
Gastrointestinal symptoms during and/or after travel among travelers who reported diarrhea ($N = 208$)

Symptom*	n (% of 208)			
	During and after travel	During travel only	After travel only	Total during or after travel
Diarrhea	41 (20)	131 (63)	36 (17)	208 (100)
Nausea or vomiting	1 (< 1)	21 (10)	11 (5)	33 (16)
Constipation	4 (2)	19 (9)	7 (3)	30 (14)
Abdominal pain	0 (0)	6 (3)	17 (8)	23 (11)
Fever	0 (0)	21 (10)	6 (3)	27 (13)

* ≥ 1 symptom possible for each traveler.

TABLE 2
Gastrointestinal symptoms during and/or after travel among travelers who did not report diarrhea (*N* = 45)

Symptom*	n (% of 45)			
	During and after travel	During travel only	After travel only	Total during or after travel
Nausea or vomiting	2 (4)	12 (27)	7 (16)	21 (47)
Constipation	2 (4)	13 (29)	4 (9)	19 (42)
Abdominal pain	1 (2)	2 (4)	7 (16)	10 (22)

*≥ 1 symptom possible for each traveler.

azithromycin, two travelers were prescribed azithromycin and ciprofloxacin, and three travelers were prescribed loperamide alone.

Of the 164 travelers who experienced TD during travel and were prescribed a specific antibiotic or antidiarrheal medication at their pre-travel consultation, 75 (46%) of 164 took at least one prescribed medication during travel. Specifically, 39 (36%) of 108 took prescribed ciprofloxacin, 20 (38%) of 55 took prescribed azithromycin, and 28 (28%) of 99 took prescribed loperamide. Twelve reported taking loperamide in addition to either ciprofloxacin or azithromycin.

Changes in planned activities. Of the 172 who experienced TD during travel, 41 (24%) stopped activities, seven

(4%) saw a doctor, and three (2%) were hospitalized (Figure 1). Of the 41 travelers who experienced TD and stopped planned activities during travel, 40 had received a prescription for ciprofloxacin, azithromycin, or loperamide, or a combination of either ciprofloxacin and loperamide, or azithromycin and loperamide. Of those who experienced TD, stopped planned activities during travel, and were prescribed ciprofloxacin, 12 (46%) of 26 self-treated with ciprofloxacin. Of those who experienced TD, stopped planned activities during travel, and were prescribed azithromycin, five (36%) of 14 self-treated with azithromycin. Of the three who self-treated with loperamide during travel, two took it in combination with either ciprofloxacin or azithromycin, one took it alone. Among the 77 who reported TD after

TABLE 3
Reported TD during or after travel by demographics and trip characteristics (*N* = 436)

	Reported TD during and/or after travel (<i>N</i> = 208)		Did not report any symptoms during or after travel (<i>N</i> = 228)		<i>P</i> value
	<i>n</i> (row %)				
Gender					0.4
Female	125	(49)	128	(51)	
Male	83	(45)	100	(55)	
Birth country					0.1
Foreign born	31	(39)	48	(61)	
U.S. born	176	(49)	180	(51)	
Travel reason					0.6
Tourism/vacation	104	(47)	117	(53)	
Business	26	(43)	35	(57)	
Volunteer/missionary/aid work	20	(42)	28	(58)	
Visiting friends and relatives	4	(44)	5	(56)	
Educational/research	4	(67)	2	(33)	
Other†	48	(54)	41	(46)	
Accommodations*					
Hotel	139	(49)	143	(51)	
Home/local residence	41	(49)	42	(51)	
Hostel/budget hotel/guest house	29	(52)	27	(48)	
Dormitory	9	(41)	13	(59)	
Tent	28	(49)	29	(51)	
Ship/yacht/boat	17	(45)	21	(55)	
Other‡	27	(39)	43	(61)	
Destination§					0.06
Low human development	50	(45)	61	(55)	
Medium human development	120	(52)	111	(48)	
High human development	38	(40)	56	(60)	
Destination¶					0.08
Africa	48	(44)	61	(56)	
Asia	74	(56)	58	(44)	
Latin America and Caribbean	67	(42)	92	(58)	
Multiple	19	(53)	17	(47)	
			Median (range)		
Trip duration (days)	13	(4–65)	11	(3–36)	< 0.0001
Age (years)	47	(20–83)	48	(19–81)	0.51

TD = travelers' diarrhea; UN = United Nations.

*Other category includes those traveling for multiple travel reasons.

†Respondents could have ≥ 1 choice.

‡No text specified.

§Based on UN human development ranking, if traveler went to > 1 country, the lowest ranked country was used.

¶Based on UN regions, if traveler went to > 1 region, they were categorized as "multiple."

||Based on dates reported in post-travel survey, *P* < 0.0001, comparing TD versus no symptoms.

FIGURE 1. Impact of travelers' diarrhea during and after travel.

travel, 17 (22%) stopped activities, 11 (14%) saw a doctor, and none were hospitalized.

Of the 31 who experienced non-TD GI symptoms during travel, six (13%) stopped planned activities, three (10%) saw a doctor, and none were hospitalized. Of the 19 who reported non-TD GI symptoms after travel, four (21%) stopped planned activities, three (16%) saw a doctor, and one went to the emergency room.

Dietary practices during travel. Half or more of those with TD during or after travel drank tap water, consumed drinks with ice, ate salads, or consumed unpasteurized dairy products (Table 4). Consuming any unpasteurized dairy products was significantly associated with TD ($P = 0.02$ during or after travel, $P = 0.01$ during travel, Table 4), and those who experienced TD reported a higher mean number of days consuming unpasteurized dairy products compared

TABLE 4

Bivariate and multivariable analysis of dietary practices and other factors for those who reported TD during or after travel compared with those who did not report any symptoms

Practice*	Bivariate		P value†	P value‡
	Reported TD during or after travel	Did not report any symptoms during or after travel		
	(N = 208)	(N = 228)		
	n (row %)			
Drank tap water	32 (50)	32 (50)	0.69	0.84
Had ice in drinks	107 (48)	114 (52)	0.8	0.87
Consumed unpasteurized dairy products	59 (58)	43 (42)	0.02	0.01
Ate salads	119 (50)	120 (50)	0.36	0.58
Variable	Multivariable§			
	During or after travel (logistic)		During travel only (GEE)	
	OR (95% CI)	P value	OR (95% CI)	P value
Consumed unpasteurized dairy products	1.69 (1.06–2.70)	0.03	1.00 (0.99–1.00)	0.08
Trip duration¶	1.06 (1.02–1.09)	< 0.01	1.06 (1.03–1.10)	< 0.01
Destination		0.43		0.32
Asia	Ref		Ref	
Africa	0.65 (0.38–1.11)		0.68 (0.39–1.20)	
Latin America and Caribbean	0.84 (0.50–1.40)		0.81 (0.47–1.40)	
Multiple	1.01 (0.47–2.16)		1.31 (0.61–2.82)	

BATMN = Boston Area Travel Medicine Network; CI = confidence interval; GEE = generalized estimating equation; GI = gastrointestinal; OR = odds ratio; TD = travelers' diarrhea.

*Totals: drank tap water = 64 (15%), had ice in drinks = 221 (51%), consumed unpasteurized dairy products = 102 (24%), and ate salads = 239 (55%).

† If yes during any week during travel, then yes for the total trip (χ^2). Outcome is anybody who reported GI illness during or after travel.

‡ Yes/no response for each week during travel (GEE model with autoregressive correlation matrix). Outcome is anybody who reported GI illness during travel only.

§ All models control for BATMN site.

¶ Continuous variable (in days).

with those who remained healthy (2.3 days [range 0–21] versus 1.2 days [range 0–24], $P = 0.008$). In multivariable analysis, trip duration (days, continuous) remained associated with TD (odds ratio [OR] = 1.06, 95% confidence interval [CI] = 1.02–1.09, for TD during and/or after travel, OR = 1.06, 95% CI = 1.03–1.10 for TD during travel only, Table 4).

DISCUSSION

Travelers experienced both TD and non-TD GI symptoms during and after travel. Together, TD and non-TD GI symptoms affected 40% of travelers resulting in interruption of planned trip activities and healthcare visits for some. Despite receiving advice about food and water precautions before travel, travelers still engaged in risky dietary practices and experienced TD. Of those who experienced TD, 83% reported diarrhea during travel, and one-third experienced diarrhea in addition to other GI symptoms. TD continues to remain the leading illness experienced during and after travel.^{1,14,15}

Trip duration was found to be statistically associated with TD in our study, with those experiencing TD traveling slightly longer than those who did not experience TD. Other studies have shown longer duration of travel to be associated with an increase in certain GI symptoms (e.g., diarrhea) in travelers.^{7,14} Although greater quantitative detail about disruption in activities during and after travel could not be provided through our study, TD may interrupt plans for approximately 20–25% of travelers, including missing work, school, or other planned activities. Clinicians should take special note of those traveling for longer periods of time and emphasize strategies to avoid or treat TD. Although the association of TD with geographic region and level of development were not statistically significant, larger proportions of travelers to multiple regions and travelers to Asia or Africa experienced TD compared with travelers to Latin America and the Caribbean. Similarly, a larger proportion of travelers to medium and low HDI groups experienced TD than those in the high HDI group. Previous studies have generally demonstrated a higher risk for TD in travelers to Africa and Asia^{10,16,17} or among travelers visiting medium and low HDI countries.^{14,18,19}

When travelers experienced TD during their trip, 46% of those prescribed antidiarrheal or antibiotic agents before travel took them to treat their symptoms. The proportion of ill travelers who took some form of self-treatment of TD was lower than reported in other cohort studies of American travelers going to developing countries who were prescribed antidiarrheal and antibiotic agents before travel.^{7,20} Because TD resulted in interruption of activities and healthcare visits in this study, providing antimicrobials for self-treatment of TD remains an acceptable practice, but advising travelers about judicious use of these antimicrobials, such as reserving their use for more severe illness, would be appropriate.

Pre-travel medical advice for the traveler consists of destination-dependent food and water precautions, as well as counseling about, and prescription for, self-treatment if illness occurs.²¹ Steffen and others found that there was no difference between travelers with or without diarrhea and their relative consumption of high-risk foods or drink¹⁶; travelers who followed at least three food/water precautions actually had a higher incidence of TD than those who did not.⁸ Adherence to recommended food and water precautions has not demonstrated clear efficacy in

preventing illness, and it has been suggested that risk of TD is related more to the sanitation level at the destination rather than the traveler's ability to adhere to dietary measures.²² Consequently, pre-travel advice on self-treatment strategies is recommended, as avoiding illness may, in many cases, be beyond the traveler's control.⁵ Although our study did not collect outcome data for those who self-treat their illness during travel, studies have found TD treatment during travel to be effective.^{7,23} Advice about food and water precautions continues to be prudent in a global environment where safe water cannot be assured; however, advice from healthcare providers about self-treatment strategies should be detailed enough to allow the traveler to make better decisions regarding when to use prescribed and recommended medications.

Several limitations exist for our study. Patients seen at the three BATMN clinics may not be representative of international travelers in general. Symptoms were self-reported; we were unable to confirm etiology of symptoms during or after travel. We cannot confirm that the travel diaries were completed during travel and not at a later date since participants were allowed up to 4 weeks after their trip to turn in the travel diaries and post-travel surveys, therefore recall bias may be present. GI symptoms with onset reported after travel may not necessarily be travel-related due to the timing of the post-travel survey. We were unable to collect data to determine whether travelers were recommended for hepatitis A or typhoid vaccine, only if they had received vaccine at the pre-travel visit. Despite receiving a prescription for an antibiotic or loperamide and experiencing diarrhea during travel, we were unable to determine the reasons for not self-treating with prescribed medication. Lastly, ORs overstate the relative risk when the outcome is common; therefore, the adjusted odds ratios may suggest biased results.²⁴

In summary, travelers continue to experience GI symptoms during and after travel which can interrupt their travel activities and plans after returning home. Non-TD GI symptoms occur in travelers, and clinicians may consider strategies in the pre-travel consultation to help patients mitigate the effects of both TD and non-TD GI symptoms during and after travel. Pre-travel counseling about safe food and water consumption practices does not necessarily prevent illness. Healthcare providers should consider providing medications to treat TD for those traveling for longer periods; clearly communicating the utility of, and specific indications for, self-treatment will help to minimize the disruption these illnesses may cause.

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