



A Closer Look to the Most Frequent Travelers' Disease: A Systematic Update on Travelers' Diarrhea

Morteza Izadi¹, Afshin Sadepur^{1*}

1. Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

*Corresponding Author: Afshin Sadepur, MD, Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
Email: afshin_sa86@yahoo.com

Abstract

The present study, wants to highlight and review the most prevalent disease amongst travelers. In the current review, an updated review regarding epidemiology, involved pathogens, and a brief review of current evidence-based guidelines for prevention and treatment of this disease are provided. A distinguishing feature of the current review is the discussion of the impacts of irritable bowel syndrome, as one of the most prevalent gastrointestinal diseases, on travelers' diarrhea pattern. Moreover, evidence-based data was the primary source for all parts of the current study. A recent review of GeoSentinel Surveillance Network database, with a very large sample size was the basis for epidemiologic appraisals.

Keywords: Traveler's Diarrhea, Review, Epidemiology, Evidence-Based, Management

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Introduction

Tourist health has turned into one of the highest outline issues, which are now connected with the individual tourists' concerns with travel. Thus far, a number of diseases were reported to be specifically studied in the field of travel medicine while certain attention should be paid to the most prevalent disease entities in this progressive body of medicine. It has been stated that gastrointestinal infections are one of the leading causes of illnesses in travelers. This entitlement has been supported by the fact that over 60% of individuals visiting tropical and subtropical regions will develop diarrhea [1-7].

This study, wants to highlight and review current body of evidence in the most prevalent disease amongst travelers. We do believe that a holistic review of all aspects of this disease, namely, the travelers' diarrhea, is mandatory because of the importance of the disease and the need for combining all the features of the disease. In the current review, a closer look to epidemiology, reasons for sex differences in this disease, involved pathogens, and a brief review of current evidence-based guidelines for prevention and treatment of this disease are provided. A distinguishing feature of the current review is the discussion of the impacts of irritable bowel syndrome, as one of the most prevalent gastrointestinal diseases, on the travelers' diarrhea pattern.

Epidemiology

There are numerous studies that [3,8,9] described epidemiological aspects associated with travelers' diarrhea but most of these studies failed to provide a large scale view of the disease due to their small sample size [6,7, 10-12]. It seems that the only large-scale study dates back to a quarter of a century [5]. In all the studies, the results consistently have established

some destination-specific distinctions in risks of developing diarrhea. South Asia is stereotypically among the "most risky" destinations [13-15].

In terms of a comprehensive look at epidemiology of travelers' diarrhea, it has been stated that specific subpopulations are at greater risk of contracting diarrhea during travel. When reporting epidemiologic data in this disease, three certain aspects, should be taken into account. Firstly, age and sex distribution in patients with diarrhea are significantly dissimilar from those of the general traveler population. Indeed, young men reveal the highest incidence among all age and sex groups. Secondly, travelers' diarrhea has a definite seasonal pattern with spring and summer surges, although this seasonality may largely depend on age. Thirdly, traveling some parts of Asia and Africa is significantly associated with contracting diarrhea [16].

A) Age and sex distribution

Travelers age and sex distribution are associated with the travel outlines employed by each age group. Male and females show a different pattern of travelling. Young women tend to travel more than males in the same age group because of their travel preferences [17, 18] whereas middle-aged men travel more than women in the same age group for their business events [17, 18]. Those aged 20 to 29 years showed a higher incidence of travelers' diarrhea than other age groups, a finding which is found in many [19-22]. This may root in the relatively more adventurous and careless behavior [20, 22] or larger appetite in this age group. Differences in disease incidence between sexes might be attributed to sanitation behavior, destination, and the purpose of travel. For instance, young men are more adventurous and thus show higher incidence of travelers' diarrhea than young women in general.

This is while; there exist studies that could not show any significant differences in travelers' diarrhea by gender [20, 22, 23].

B) Chronological trends

Another important aspect of travelers' diarrhea is its chronological trends. It has been found that the disease incidence exhibits a constant yearly pattern even during epochs of marked negative impacts on international tourism [16].

Summer is introduced as the riskiest season for contracting diarrhea in the northern hemisphere [21], because it is usually challenging to maintain food hygiene in warmer weather [24].

C) Destination

As stated earlier, travelling to south-central Asia, Southeast Asia, and North Africa is positively associated with contracting diarrhea. High incidence of travelers' diarrhea [20], with salmonellosis [25], shigellosis [24], and enteric fever are reported in these areas [22]. Hence, information regarding the increased possibility of contracting the disease in these countries should be given to all travelers to these regions of the world.

IBS and travelers' diarrhea

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal (GI) disorders in outpatient practice and hence it would be very important to study impacts of travel on this disease, as well as possible changes of classic travelers' diarrhea in presence of this common functional illness [23]. It should be noted that as much as 7–31% of IBS cases appear just after an onset of infectious diarrhea and are referred to as post-infectious IBS (PI-IBS) cases [24, 25]. Symptoms of PI-IBS and IBS are similar, although slight differences in pathogenesis have been noticed. Of these differences, increased numbers of enteroendocrine cells, chronicity of pain, and more diarrheal episodes in patients with PI-IBS than in those with IBS are more important [26]. The principal cause for these differences remain unknown. However, adjustments in inflammatory processes after initial GI infection have been accused [27].

It is shown that acute gastrointestinal infections causing PI-IBS occur after contact to pathogens, usually bacterial, and often develop during a period of travel, especially to non-industrialized areas such as Latin America, Africa, and southern Asia [28]. Before the description of PI-IBS, the main concern in treating travel-related infectious diarrhea was decreasing symptoms to prevent incapacitation during travel. This approach is now changing to prevention of diarrhea and PI-IBS [29]. Prospective studies have found that PI-IBS will occur in about 7–14% of travelers who experience diarrhea during a trip to a developing country [30].

To the best of current literature, it is not known how travel plays a role in triggering or at least worsening post-infectious forms of IBS, but understanding the pathogenesis of PI-IBS may allow identification of risk factors that enable development of strategies for the anticipation or decreasing the incidence of the disease.

Post-infectious IBS is largely assumed to be a subset of idiopathic IBS because of the resemblance of their general symptoms, but it has been proposed that patients with PI-IBS may have a better prognosis than patients with idiopathic forms of the disease. This is despite the fact that there is little evidence to support this concept [27]. Longitudinal studies have shown that most people with PI-IBS will still have the disorder after five [31] to six years [28]. The frequency of intestinal complaints, including stools of abnormal form, fecal urgency, common experience of incomplete bowel movements, bloating, and functional impairments, is similar for the two entities and this raises question on a more benign course for post-infectious forms of IBS.

Anyhow, travelers' diarrhea has been recognized as an important risk factor for the development of initial-onset IBS [28]. An interesting study on U.S. students who studied in Mexico for summer has shown that as much as 10% of these students who experienced an onset of travelers' diarrhea progressed to having IBS within six months of travel. In a different study conducted in Asia, a similar ratio of new-onset traveler's diarrhea-associated IBS cases was acknowledged [32].

What pathogens do we expect?

There are plenty of databases that gather and report travel-associated diseases and pathogens but GeoSentinel Surveillance Network database is one of the most comprehensive and advanced databases in this regard. This database is a source for many recent papers, as well as for the Center for Disease Control (CDC). In a survey of 17,228 patients in a recent review of GeoSentinel Surveillance Network database, the bacterial agents most frequently reported were *Campylobacter*, *Salmonella* spp., *Shigella* and *Clostridium difficile*. It should be noted that there were no diagnostic codes specifically for enterotoxigenic *Escherichia coli*, which is the most frequent cause of travelers' diarrhea [31, 33, 34] or other commonly described agents such as *Enterococcus* *coli*, *Aeromonas* and *Plesiomonas* in that study. Moreover, *Vibrio cholerae* was very rare and this shows the fact that this pathogen is an uncommon cause of travelers' diarrhea [35, 36]. Moreover, the study showed that *S. typhi* and *S. paratyphi* made up to 5% of pathogens isolated in the registered patients. This supports the significance of travel practitioners recommending the use of typhoid vaccination before to travel to endemic regions [37, 38].

Compared to bacterial pathogens, the abovementioned study showed that parasites have been the etiology of diarrhea in 0 to 12% of cases. The proportion in some regions such as Eastern Europe and Russia has been higher [37–40]. On the other hand, the rates of giardiasis and amoebiasis were highest in travelers' returning from South Asia, the Middle East and South America.

In the GeoSentinel study, only 3.0% of pathogens were of viral origin. This is while, previous studies have reported viral etiology rates of up to 12% for travelers' diarrhea. [33, 34, 41]

It should be clarified that, most centers do not routinely perform testing for viral pathogens such as Rotavirus and Norovirus. Moreover, these viral pathogens are more likely to cause a short illness that resolves before the traveler seeks for medical attention. In that large-scale study, Hepatitis virus A, was noted in as much as 2.3% of all isolates. Indeed, the pathogen continues to be reported in travelers despite the accessibility of a safe and effective vaccine that is recommended for all travel to endemic countries.

Approach to patients in an evidence-based format

Like other areas of current medicine, travel medicine benchmarks are gradually based on evidence and are moving away from reliance on the classic opinion of experts. Here we review an evidence-based approach to patients with travelers' diarrhea (see table 1 for grading of evidence). Where possible, recommendations in this section have been provided using the Infectious Diseases Society of America—United States Public Health Service grading system (see below) [42]. This is one of the intriguing differences of our review. Most of the previous literature in the field of treatments in travel medicine are not prepared in modern evidence-based format. However, even in our review, expert opinion and experience still overshadow many of the topic areas, underscoring the need for continued investigation in the field with evidence-based therapeutic guidelines (figure 1, From <http://www.aafp.org/afp/2005/0601/p2095.html> as accessed in July 21, 14, see references 43, 44 for more details).

As discussed repeatedly, traveler's diarrhea is the most common disease among travelers. Hence, specific management, apart from general measures, should be provided to patients. Providing adequate education about prevention, food and liquid hygiene (A-III), and provision for prompt self-treatment in the event of illness (A-I) (table 2). The key components of self-treatment include hydration; treatment with loperamide for control of symptoms, if necessary (when there is no fever or blood in the stool); and a short course (single dose to 3 days of therapy) of a fluoroquinolone (A-I). Antibiotic resistance of enteric pathogens, chiefly *Campylobacter* species, in the travel destination needs to be considered. For those travelling to these destinations, as well as for other travelers, azithromycin may be indicated (B- II). Use of both loperamide and an antibiotic may be considered for travelers with moderately severe diarrhea (B-III). It should be noted that antibiotic prophylaxis is not suggested for most travelers (A-III) [45-47].

Conclusion

In the current review, we tried to provide a systemic approach with special attention to medically relevant aspects to the travelers' diarrhea. Although numerous studies exist regarding travelers' diarrhea, as the most prevalent disease in the field of travel medicine, but frequent and updated

reviews might be necessary. Moreover, pooling published data in an evidence-based format, especially in diagnosis and treatment, might help practicing physicians to find clinically relevant data more accessible.

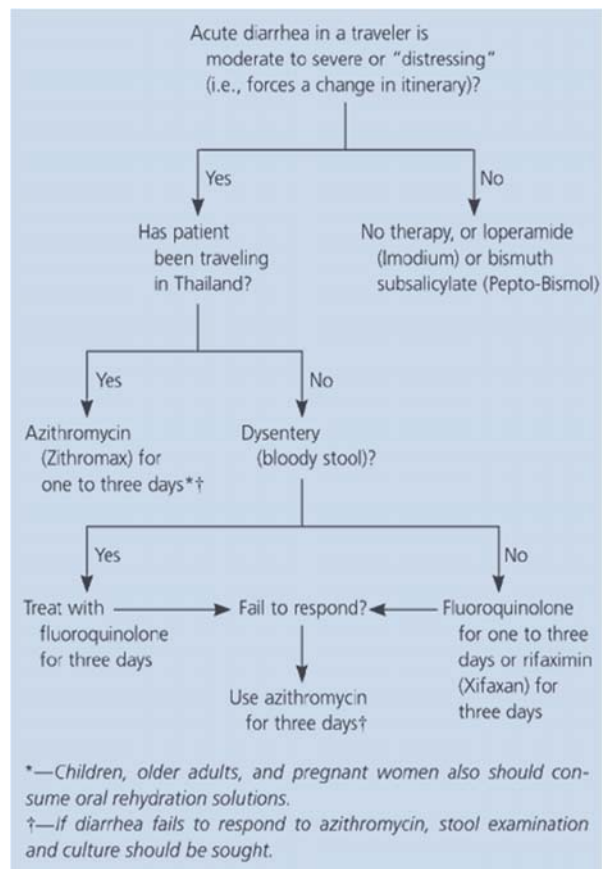


Figure 1. Algorithmic approach to the treatment of traveler's diarrhea

Table 1. Adapted from reference No. 43.

Category, grade	Definition
Strength of recommendation	
A	Good evidence support a recommendation for use
B	Moderate evidence support a recommendation for use
C	Poor evidence support a recommendation
D	Moderate evidence support a recommendation against use
E	Good evidence support a recommendation against use
Quality of evidence	
I	Evidence from ≥1 properly randomized controlled trial
II	Evidence from ≥1 well-designed clinical trial without randomization; from cohort or case-controlled analytic studies (preferably >1 center); from multiple time series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities; based on clinical experience, descriptive studies, or reports of expert committees

Table 2. Antibiotics Used for the Treatment of Traveler's Diarrhea

Antibiotic	Dosage	Comments
Ciprofloxacin (Cipro)	500 mg twice daily for one to three days	Other quinolones (e.g., ofloxacin [Floxin], norfloxacin [Noroxin], and levofloxacin [Levaquin]) are presumed to be effective as well.
Rifaximin (Xifaxan)	200 mg three times daily for three days	Not effective in persons with dysentery
Azithromycin (Zithromax)	In adults: 500 mg daily for one to three days or 1,000 mg in a single dose [46] In children: 10 mg per kg daily for three days [48]	Antibiotic of choice in children and pregnant women, and for quinolone-resistant <i>Campylobacter</i> [47]

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Authors' Contribution

All authors were involved in the study design and result interpretation. All authors confirmed the final draft before submission.

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