

## RISK FACTORS ASSOCIATED WITH DIARRHEA AMONG INTERNATIONAL VISITORS TO CUZCO, PERU

MIGUEL M. CABADA, FERNANDO MALDONADO, WANDA QUISPE, KAREN MOZO, EDSON SERRANO, ELSA GONZÁLEZ, CARLOS SEAS,\* KRISTIEN VERDONCK, JUAN I. ECHEVARRIA, HERBERT L. DUPONT, AND EDUARDO GOTUZZO

*Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru; Universidad Nacional San Antonio Abad del Cuzco, Cuzco, Peru; Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas, Hospital Nacional Cayetano Heredia, Lima, Peru; Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium; University of Texas–Houston School of Public Health; St. Luke’s Episcopal Hospital; and Baylor College of Medicine, Houston, Texas*

**Abstract.** The objective of this study was to determine the risk factors for travelers’ diarrhea (TD) reported by visitors to Cuzco, Peru. In this cross-sectional study, self-administered questionnaires looking at perceived occurrence of health problems and pre-travel health advice were obtained from departing travelers at Cuzco’s International Airport between August and November 2002. A total of 5,988 travelers participated in the study. The mean age was 35 years, and 51% were women. The prevalence of TD was 24%. Factors associated with TD in the multivariable analysis were use of antibiotic prophylaxis (OR: 3.20), vaccination against cholera (OR: 1.44), history of advice for safe food and water consumption (OR: 1.46), being younger than 35 years of age (OR: 1.37), being a resident of the United States (OR: 1.28), not staying in hotels in Cuzco (OR: 1.13), and number of unsafe food or beverages consumed (OR: 1.04). Remaining in Cuzco < 1 week was a protective factor (OR: 0.58). TD is common among travelers to Cuzco. This study suggests that conventional recommendations are not invariably effective at decreasing TD.

### INTRODUCTION

Travelers’ diarrhea (TD) is the most frequent illness affecting travelers from industrialized countries visiting the developing world.<sup>1,2</sup> During the last four decades, extensive research on epidemiology, risk factors, and treatment of this disease has led to a broad spectrum of recommendations aimed at avoiding diarrhea. Despite these efforts, the rates of travelers’ diarrhea have remained high and unchanged.<sup>1,3</sup> Information on general preventive recommendations for travelers, which commonly emphasize food and water precautions, is available from medical and non-medical sources.<sup>4</sup> Compliance with food and water precautions is low,<sup>5,6</sup> and diarrhea remains frequent among travelers.<sup>3,7,8</sup>

There are scarce data on TD among those who visit South America, because the majority of studies conducted in the Americas have focused on persons with destinations to Central and North America.<sup>9</sup> We studied the prevalence of TD and the factors classically associated with this illness among foreign visitors to Cuzco, a popular tourist destination in Peru.

### MATERIALS AND METHODS

Between August and November 2002, we conducted a health survey aimed at documenting the occurrence of symptoms and illnesses and pre-travel health advice among travelers visiting Cuzco. This report includes the data on pre-travel health advice to prevent diarrhea on risk factors for TD and on the occurrence of TD.

International travelers 15–65 years of age were invited to participate in the study while waiting to board departing flights from Cuzco’s international airport. Participants filled out an anonymous questionnaire in English or Spanish, which

contained closed-end questions asking for demographic information, type of accommodation, previous visits to developing countries, occurrence of illnesses or symptoms, general pre-travel advice, use of prophylactic drugs, vaccination status, previous episodes of travelers’ diarrhea, and consumption of unsafe food and beverages during their stay. A case definition of TD was not used. Travelers reported on the presence or absence of TD based on their own interpretation of diarrhea.

Data were stored and analyzed in SPSS program version 9.0 for Windows (SPSS, Chicago, IL). For univariate analyses, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. We compared the demographic and epidemiologic characteristics between those who reported the occurrence of diarrhea during their stay in Cuzco and those who did not. For multivariable analysis, variables with a  $P < 0.1$  were included in a model of logistic regression using a backward elimination approach.

The study protocol was reviewed and approved by the research committee of the Medical School of the University San Antonio Abad del Cuzco.

### RESULTS

A total of 6,798 foreign travelers were approached, and 5,988 (88.0%) agreed to participate by completing the questionnaire. The mean age of the subjects enrolled was  $35 \pm 11$  (SD) years; 51% of the subjects were women. The most frequent countries of origin were the United States (24%), the United Kingdom (20%), and Spain (9%). Tourism was the main reason to visit Cuzco for 90% of respondents; the median length of stay was 5 days. The majority of persons stayed at hotels (58%) and hostels (37%), and most travelers (89%) had visited another Peruvian city for a median of 5 days before arriving to Cuzco. Twenty-three percent of the respondents had traveled to other developing countries in the 6 months before their trip to Cuzco, and 34.0% of them reported a previous episode of TD.

The prevalence of diarrhea during the stay in Cuzco reported by the respondents was 24%. The median time spent

\* Address correspondence to Carlos Seas, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia Av. Honorio Delgado 430, San Martín de Porres, Lima, Peru. E-mail: cseas@upch.edu.pe

TABLE 1  
Demographic and epidemiological characteristics of travelers who had diarrhea compared with those who did not have diarrhea

Characteristic	Diarrhea present*	Diarrhea absent*	OR (95% CI)
Travelers' diarrhea in the previous 6 months	127/311	343/1072	1.48 (1.31 < OR < 1.90)
Age less than 35 years	937/1393	2690/4475	1.36 (1.20 < OR < 1.55)
US traveler	375/1416	1028/4556	1.24 (1.08 < OR < 1.41)
Female sex	737/1409	2271/4538	1.10 (0.97 < OR < 1.23)
Tourism as reason to travel	1289/1419	4112/4565	1.09 (0.89 < OR < 1.34)
Stayed in other Peruvian city for 1 week or less	1014/1401	3298/4496	0.95 (0.83 < OR < 1.09)
Ate mostly at restaurants	1106/1375	3574/4377	0.92 (0.79 < OR < 1.08)
Visited a developing country in the previous 6 months	311/1395	1072/4487	0.91 (0.79 < OR < 1.05)
Stayed in Cuzco hotels	770/1405	2675/4503	0.83 (0.73 < OR < 0.94)
Stayed in Cuzco for 1 week or less	938/1412	3573/4541	0.52 (0.46 < OR < 0.60)

\* Number of travelers with the characteristic/number of travelers without the characteristic.

in Cuzco before becoming ill was 2 days (range: 1–60 days). Diarrhea occurred more frequently among travelers younger than 35 years of age, those who came from the United States, and those who had visited another developing country within 6 months before the current trip (Table 1). Travelers who stayed in hotels and travelers who stayed in Cuzco for 1 week or less had a lower prevalence of diarrhea. Most participants (94%) had sought information about travel-related diseases before leaving their countries of origin; the median number of pre-travel information sources consulted was two, and 60% of the travelers had consulted a physician for advice. The recommendations and or interventions most frequently received were information about safe foods and beverages (86%), cholera vaccination (13%), and prophylactic antibiotics for prevention of TD (14%). TD was highest in those who took prophylactic drugs, sought information about travel-related diseases, received advice regarding safe food and water consumption, and had been given cholera vaccination (Table 2).

Eighty-one percent of the surveyed subjects ate the majority of their meals at restaurants during their stay in Cuzco. While 48% of the participants reported that they had fully complied with food and beverage safety recommendations, 99% admitted the consumption of at least one unsafe food or beverage. The median number of unsafe products consumed was five. Consumption of fruit juice (93%), raw green vegetables (63%), cold sauces (51%), milk (53%), and unpeeled fruits (27%) were the most frequent dietary mistakes. In the univariate analysis, there was no association between having TD and consuming non-recommended food or beverages ( $P = 0.65$ ) or the number of non-recommended products consumed ( $P = 0.07$ ).

In the multivariable model, the number of sources of pre-travel advice received was not associated with TD. Variables

independently associated with diarrhea were age < 35 years, being a US resident, staying in Cuzco for > 1 week, having received safe food and beverage recommendations, having received prophylactic medication, having received vaccination against cholera, and the number of non-recommended products consumed. Type of accommodation and not having received advice from a health care professional were also retained by the model (Table 3).

## DISCUSSION

The subjects included in our study tended to be young tourists mainly from the United States and the United Kingdom visiting Peru for relatively brief periods. These characteristics coincide with the profile of travelers arriving to Peru delineated by the local tourism authorities.<sup>10</sup> It is known that, once in Peru, a high percentage of tourists fly to Cuzco through a single airport. Therefore, we think that the study subjects were representative of the general population of international visitors to Cuzco.

The prevalence of TD among the participants was 24%. Young age was associated with diarrhea in this study. Several reports have addressed this issue and attributed such association to more adventurous travel and lower budget accommodations.<sup>3,11–13</sup> As previously described, length of stay was another risk factor for travelers' diarrhea.<sup>11</sup> US residents reported diarrhea more frequently than persons of other nationalities, which might be because of differences in pre-travel health advice, types of travel, perception of illness, and host genetic susceptibility to diarrhea.

Travelers who consumed so-called "unsafe" food or beverages while visiting Cuzco did not have increased rates of di-

TABLE 2  
Comparison of pre-travel advice, medication, and prophylaxis between those travelers who had diarrhea and those who did not have diarrhea

Characteristic	Diarrhea present*	Diarrhea absent*	OR (95% CI)
Prescribed with travelers' diarrhea prophylaxis	386/1413	456/4534	3.36 (2.89 < OR < 3.91)
Sought information about travel related diseases	1366/1413	4203/4533	2.28 (1.67 < OR < 3.12)
Received safe food and water advice	1278/1408	3814/4528	1.84 (1.51 < OR < 2.24)
Received unspecific cholera vaccine	224/1413	532/4537	1.42 (1.20 < OR < 1.68)
Information given by health care professional	867/1365	2457/4200	1.24 (1.09 < OR < 1.40)
Fully complied with preventive measures	595/1252	1848/3850	0.98 (0.86 < OR < 1.12)
Consulted two or less sources of information	1029/1365	3284/4194	0.85 (0.74 < OR < 0.98)

\* Number of travelers with the characteristic/number of travelers without the characteristic.

TABLE 3

Adjusted ORs for variables associated with travelers' diarrhea in the multivariable analysis

Variable	Adjusted OR (95% CI)
Prescribed travelers' diarrhea antibiotic prophylaxis	3.20 (2.73 < OR < 3.76)
Received safe food and beverage pre-travel advice	1.46 (1.14 < OR < 1.86)
Received unspecific cholera vaccine	1.44 (1.20 < OR < 1.73)
Age less than 35 years old	1.37 (1.18 < OR < 1.58)
United States resident	1.28 (1.09 < OR < 1.50)
Did not stay in a hotel in Cuzco	1.13 (0.98 < OR < 1.30)
Number of unsafe products consumed	1.04 (1.01 < OR < 1.08)
Information not given by a health care professional	0.89 (0.77 < OR < 1.02)
Stayed in Cuzco for 1 week or less	0.58 (0.50 < OR < 0.67)

arrhea compared with those who exercised dietary precautions. Even though we did not expect these findings, they are consistent with other studies from different regions.<sup>5,13-15</sup> As proposed previously, dietary precautions may decrease the amount of bacteria ingested.<sup>16</sup> However, this practice may not be sufficient in settings where food contamination occurs easily, where food handling safety procedures are not routinely displayed, and where travelers have little control over their diet. The slight association between the number of "unsafe" products consumed and diarrhea may reflect the cumulative effect of a repetitive risk behavior.<sup>16</sup>

Although most of the participants reported having received travel health advice and one half complied with food and beverage recommendations, the population studied showed poor practice of dietary restrictions. Nearly all travelers admitted they consumed at least one "prohibited" food or beverage while in Cuzco. This situation shows the disconnection between pre-travel health advice for travelers to developing countries and actual dietary restrictions followed.<sup>17-22</sup> Compliance with strict dietary restrictions is difficult to accomplish wherever public restaurants might serve unsafe foods.<sup>5,15</sup>

In addition to the likelihood that persons with increased susceptibility to diarrhea would more often seek pre-travel advice, they might also more actively report their enteric symptoms. Cavalcanti and others<sup>11</sup> studied 12,499 visitors departing from Fortaleza, Brazil, and similarly found that those previously seeking pre-travel health-advice either took more risks or were more conscious about their health by paying greater attention to their symptoms. McIntosh and others<sup>23</sup> reported that travelers who had sought pre-travel advice were more likely to experience diarrhea while abroad, as well as being more prone to go to high-risk destinations. In this study, almost one quarter of the participants had traveled to other developing countries in the 6 months before coming to Cuzco. We did not find a significant difference in the prevalence of TD between those who had traveled before and those who did not. In contrast, other authors have suggested that some degree of acquired immunity against TD occurs with recent exposure in a high-risk area.<sup>6,13,24</sup> Interestingly, subjects who had experienced TD in a prior trip to a developing country were more likely to have diarrhea in Cuzco. This might reflect maintenance of high-risk behavior, different etiologic agents in various areas, or the role of host genetic factors.<sup>4,25,26</sup>

Fifteen percent of the participants took antibiotics to prevent TD. The lack of effect of chemoprophylaxis in this study

could also be caused by inadequate compliance. Additionally, antibiotics used in prophylaxis could have caused a relative increase in occurrence of non-bacterial enteric infections.<sup>16</sup> Other arguments are less clear in the absence of data on anti-microbial resistance patterns among pathogens commonly causing travelers' diarrhea in Cuzco, especially because we did not clarify if the drugs used for chemoprevention were those likely to reduce rates of TD, such as fluoroquinolones, rifaximin, and azithromycin or to agents showing a high degree of resistance. Diarrhea prophylaxis remains a controversial issue in travel medicine, but it is foreseeable that the availability of non-absorbed (< 0.4%) rifaximin, with a low potential for resistance, may lead to a change in recommendations about chemoprophylaxis.<sup>27</sup> A public health argument in favor of chemoprevention of TD is the common occurrence of post-infectious irritable bowel syndrome among travelers.<sup>28</sup>

Travelers who received cholera vaccination reported diarrhea more frequently. A concern with the use of vaccines and chemoprophylaxis in general is that travelers could have a false sense of security, being therefore less careful with food and water selection.<sup>3,8</sup> It has been shown that B subunit cholera toxin vaccine may give a 50% protection against diarrhea caused by enterotoxigenic *E. coli* (ETEC).<sup>26</sup> In a preliminary study in the same area, we observed a lower prevalence of ETEC than in other Latin American countries (M. Cabada, unpublished data).

In summary, several of the currently recommended methods for reducing the frequency of TD did not show the expected effect in this study. The discrepancy with other reports could be partially explained by differences in study design. The primary aim of the health survey from which our data derive was to describe the perceived well being of travelers to Cuzco. As all preventive interventions were self-imposed, it is possible that people who were more susceptible to diarrhea were also more likely to seek pre-travel recommendations and to use chemoprophylaxis. This could have led to an underestimation of the effect of preventive interventions.

Furthermore, we asked the travelers to report diarrhea without using a specific case definition. This allowed us to focus on illness that the travelers perceived severe enough to report. From the travelers' point of view, severity might relate more to the presence or absence of disabling symptoms than to the number of stools passed, the symptom on which case definitions are usually based. Moreover, self-medication for TD is widely recommended for travelers to developing regions,<sup>29</sup> and some of the available medications have a very rapid effect on the number of stools passed.<sup>30,31</sup> However, and of relevance to this study design, previous studies have shown similarity in epidemiology of mild and moderate diarrhea compared with more severe forms of TD.<sup>6,11,29</sup>

We conclude that diarrhea occurs commonly in international visitors to Cuzco. Young travelers, particularly from the United States staying for longer periods of times in Cuzco, including those who received pre-travel information about likely safe and often unsafe foods and beverages, and those taking chemoprophylaxis against TD were at highest risk. Diarrhea imposes an economic burden on travelers and produces significant morbidity. New and effective strategies are needed to decrease diarrhea rates.<sup>2,6,7,12,32</sup> Undoubtedly, improvements in sanitation and personal and food hygiene in high-risk areas will lead to significant reductions in dis-

ease.<sup>2,33</sup> Further research in this area is needed and creative and effective ways of dealing with pre-travel health advice are urged.

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Authors' addresses: Miguel M. Cabada, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia. Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru, Telephone: 511-9791-5563, Fax: 511-482-3404, E-mail: 03517@upch.edu.pe. Fernando Maldonado, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia. Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: fmaldonado66@yahoo.com. Wanda Quispe, Universidad Nacional San Antonio Abad del Cuzco, Av. La Cultura S/N, Wanchaq, Cuzco, Telephone: 584-261-255, E-mail: thongzhi4@yahoo.com. Karen Mozo, Universidad Nacional San Antonio Abad del Cuzco, Av. La Cultura S/N, Wanchaq, Cuzco, Telephone: 584-237-552, E-mail: karenzit@hotmail.com. Edson Serrano, Universidad Nacional San Antonio Abad del Cuzco, Av. La Cultura S/N, Wanchaq, Cuzco, Telephone: 584-974-3620, E-mail: edsonserrano@yahoo.com. Elsa González, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia. Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: egonzalezlagos@yahoo.com. Carlos Seas, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru and Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas, Hospital Nacional Cayetano Heredia, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: cseas@upch.edu.pe. Kristien Verdonck, Prince Leopold Institute of Tropical Medicine. Nationalestraat 155, Antwerp, Belgium and Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: verweven@amauta.rcp.net.pe. Juan I. Echevarria, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia. Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru and Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas, Hospital Nacional Cayetano Heredia, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: chito@upch.edu.pe. Herbert L. DuPont, University of Texas-Houston School of Public Health, Baylor College of Medicine and St. Luke's Episcopal Hospital, Houston, TX, Telephone: 832-355-4122, Fax: 932-355-4167, E-mail: hdupont@sleh.com. Eduardo Gotuzzo, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia. Av. Honorio Delgado 430, San Martin de Porres, Lima, Peru and Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas, Hospital Nacional Cayetano Heredia, Lima, Peru, Telephone: 511-482-3910, Fax: 511-482-3404, E-mail: egh@upch.edu.pe.

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