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Zahra Slail Date

Incidence of Traveler's Diarrhea and Associated Risk Factors in Travelers from a US Travel Clinic

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Master of Public Health - Infectious Disease 2020

Hubert Department of Global Health

Bachelor of Medicine – King Abdul-Aziz University 2011

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A thesis submitted to the faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Hubert Department of Global Health
2020

Abstract

Incidence of Traveler's Diarrhea and Associated Risk Factors in Travelers from a US Travel Clinic

By Zahra Slail

Background:

A pre-travel visit to a doctor to receive a consultation before a trip is considered the best way to avoid any travel-related illness. The most common travel related illness is diarrhea with 60% of travelers reporting diarrhea. (Fedor, Bojanowski, & Korzeniewski, 2019).

Methods:

A longitudinal study of adult travelers done between June 2018 to August 2019 at Emory Travel Well Center was conducted. An in-person pre-travel survey was administered to participants at the travel clinic to measure the patient knowledge about travel safety followed by an electronic (by email) post-travel survey sent to every patient by the end of the trip.

The pre-travel questionnaire included questions about demographics and on the destination of their trip, the length of the trip, the reason for their travel, medical history, and other details about their trip.

The post-travel-surveys questions asked about developed any travel related illness during the trip focusing mainly on diarrhea, are what preventive measure was followed, and type of food they consumed. Relative risks were calculated to correlate the occurrence of diarrhea with unsafe behaviors practice by the travelers, the effect of following preventive measure, travelers' activities, destination and reason for travel.

Results:

A total of 422 surveys collected pre-travel and 224 surveys collected post-travel. The age means 44.99 years. We found that the most common visited region is East Africa 28.44%. And thirty-three travelers developed diarrhea (14.67%). The measures of association showed there is a positive relative risk between eating raw produce (RR1.5, 95% CI 0.74, 3.2), and drinking freshly squeezed juices (RR 1.81, 95%CI= 0.60 - 5.46). Also, washing hands or using sanitizer showed a positive relative risk as a preventive measure against diarrhea (RR 2.77, 95%CI 0.40, 19.1). Tourism found to be having a positive risk ratio in relation to traveler's diarrhea (RR 1.188, 95%CI 0.38, 3.64).

Conclusion:

We found a lower then reported proportion of diarrhea in our study, perhaps due to the travel advice received showing that following safe practice and behaviors during the travel is highly recommended to prevent traveler's diarrhea. The results of our analysis also supported the association of some unsafe eating and drinking behaviors with diarrhea, although not statistically significant. Larger studies with improved response rates will help to further study these associations.

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Chapter 1: Introduction:

In this day and age with the abundance of travel advertisements, websites, and applications, traveling has become more common and easier than ever before. Accommodations, transportation, and destinations in 2019 have become highly dependent on social media to advertise their services to travelers, which in turn, bring more revenue and tourism (Manoukian, 2019). Due to the increase in globalization, people tend to travel internationally more often for various reasons, including for business, education, tourism, and to visit family. The annual number of international trips for tourism exceeded 1 billion travelers in 2016. Traveler's diarrhea is considered the most common travel-related illness with up to 70% risk of occurrence in travelers (Vilkman, Pakkanen, Laaveri, Siikamaki, & Kantele, 2016). More focus on travelers' diarrhea should be made especially with the annually increasing number of travelers and the rising rate of antimicrobial resistance of many diarrheal pathogens (Frost, Van Boeckel, Pires, Craig, & Laxminarayan, 2019). In particular, travelers should be educated on high risk destinations for traveler's diarrhea, high risk activities, and how to protect travelers from contracting travelers' diarrhea.

Problem Statement:

As the number of travelers grows each year due to the rapid industrialization and globalization of the world. The number of travel-related illnesses is growing as well. The most common travel-related illness is travelers' diarrhea, affecting 20%-70% of travelers, especially those who are going to middle- and lower-income countries (DynaMed, 2018). With the continuous need to travel for several purposes such as business, education, tourism, adventure, vacation,

research or humanitarian work, and family/ friends visits, the risk of traveling to high-risk countries cannot be avoided. Travelers' diarrhea is still a presenting challenge to travelers and health care providers. Traveler's diarrhea can place a significant burden on the individual health, family wellness, financial status, and public health burden. For example, although commonly traveler's diarrhea is mostly self-resolving, some people who travel to high-risk regions are at risk of developing traveler's diarrhea which in term can harm their health and increase the need for family support or seeking medical help. Public health awareness about the prevention of traveler's diarrhea, such as, following safety instructions for food and drinks, washing hands, and using hand sanitizers is needed to help prevent morbidity from traveler's diarrhea(2019, CDC).

Purpose Statement:

- This study focuses on the occurrence of diarrheal disease due to international travel and its relation to receiving medical advice/ treatment prior to the travel and taking safety measures.
- To know which regions present a higher risk of contracting travelers' diarrhea.
- To identify behaviors during travel that are associated with diarrhea.

Significant Statement:

This study investigates the importance of traveler's medical advice and to highlight effective behaviors that lower the risk of contracting traveler's diarrhea while traveling. This study was conducted at the Emory TravelWell Center, Atlanta, GA on travelers to identify factors

associated with traveler's diarrhea and investigate the impact of medical consulting before traveling on traveler's diarrhea health outcomes.

Definitions:

- Travel Medicine: A branch of medicine that exclusively treat diseases that are acquired during travel (Shiel, 2018).
- Travelers Diarrhea: passage of 3 or more soft/liquid stools per day with 1 or more associated gastrointestinal symptom, such as abdominal colic, occurring in a traveler after arrival, usually in a resource-limited destination (Giddings, Stevens, & Leung, 2016)

Chapter 2: Literature review

- Background of Travelers' Diarrhea

The number of US citizens traveling internationally for business and leisure is increasing in comparison to previous years, which also has led to an increase in the number of travel-related diseases (Association, June 2019). The most recent studies showed that around 93 million Americans traveled abroad in 2018(Statistics, 2018). With the huge number of travelers there have been many studies published reporting the main causes of travelers' diarrhea. These are enterotoxigenic Escherichia coli, followed by enterotoxigenic E. coli (ETEC) and Campylobacter (Z. D. Jiang & H. L. DuPont, 2017; Z.D. Jiang & H.L. DuPont, 2017). With the vast variety of traveling reasons and the country of destination travelers are exposed to a wide range of diseases but travelers' diarrhea is the most common (Chen & Blair, 2015).

It's proven that improving hygiene practice among travelers lowers the risk of conducting travelers diarrhea (DuPont, 2006) and it is highly advised to receive a medical consultation before traveling internationally to receive any needed medication and advice. (Steffen, Hill, & DuPont, 2015) Travelers diarrhea usually occurs when travelers travel from high income countries to lower income, middle income or developing countries (Steffen, Hill, & DuPont, 2015). Among gastrointestinal symptoms, travelers' diarrhea was reported as the most common complaint among participants with 33% (Stoney et al., 2017). The percentage of travelers' diarrhea can get as high 30% to 70% among travelers who travels to tropical areas, or countries with endemic diseases in some series (DCD, 2019). The causative pathogen may also differ based on the seasons. For instance, winter season lowers the chance of travelers'

diarrhea incidence in some countries such as Nepal and Mexico. On the other hand, rainfalls and summer time cause lower rate of travelers' diarrhea (Scarpignato & Rampal, 1995). The location of trip, types of planned activities and the length of the trip will affect the chances of developing traveler's diarrhea accordingly. (Stoney et al., 2017).

Traveler's diarrhea is defined as sudden occurrence of frequent loose stool. The characteristic of stool may vary from mild to severe or acute verses persistence and typically self-limiting, (DynaMed, 2018). The causes of the traveler's diarrhea vary in between cases. It might have an infectious cause such as bacteria, protozoa, or viruses. It also could be as a result of noninfectious cases in rare cases (Larson, 1997).

- Literature based on causes of diarrhea

Most studies support the evidence that enterotoxigenic *Escherichia coli* is the most common pathogen that cause travelers' diarrhea (Larson, 1997). But also, travelers' diarrhea can be a result of various organisms. In a case control study done in Thailand on travelers to diagnose the causes of diarrhea, among participants, the stool analyses showed that *Plesiomona*s (14%), *Vibrio* (14%), *Campylobacte*r (14%), and norovirus (12%) were frequently isolated organisms in the stool samples with a statistical significance association with diarrhea. (Bodhidatta et al., 2019). Other less common pathogens wee *Plesiomonas shigelloides*, *Aeromonas hydrophilia*, *Bacteroides fragilis*, *Arcobacter* spp, *Clostridium difficile*, *Vibrio cholerae*, and *Vibrio* parahaemolyticus. Viruses can be the cause of travelers' diarrhea in 10% of the total cases (Leung, Leung, Wong, & Hon, 2019). A study done on Koreans traveling to Southeast Asia examining the incidence of common microbial reasons. Enterotoxigenic *Escherichia coli* was

found in 36% of travelers' diarrhea cases, followed by Enteroaggregative *Escherichia coli* in 27% (Ahn et al., 2011)then *Vibrio parahaemolyticus* in 13.1%, and Norovirus in 11.5%.

A new trend of global antimicrobial resistance has been recognized in recent years. This trend makes it difficult to treat infection with resistance pathogens. Travelers to lower- and middle-income counties are in higher risk of falling ill to a antimicrobial resistance pathogens. It is advised to avoid inappropriate antibiotic use, to have access to clean water and food, to be vaccinated with the recommended vaccine based on age and travel destination, and to have access to good medical care (Frost et al., 2019). Traveler's diarrhea will remain a challenge to both travelers and health care providers despite the wide range of research done on that matter (Zaidi & Wine, 2015).

- Literature based on severity and the length of symptoms

Diarrhea occurs within the first 14 days of exposure and it will take around one day for the bacteria or viruses for their incubation period, meanwhile parasitic infections usually have longer incubation periods (DynaMed, 2018). In many cases, affected individuals will complain of watery diarrhea, loss stool or mucus or bloody stool. Other symptoms are tenesmus, fecal urgency, abdominal pain, nausea, fatigue, vomiting and fever (Leung et al., 2019).

Usually for travelers returning from their trip the symptoms are self-resolving which means patients with travelers' diarrhea usually do no need any medical intervention to treat their symptoms. They only last for a four of five days and they will be mild which means no medical intervention required. But in 2% of travelers' diarrhea cases they will have persistence in the

symptoms which will last for 2 weeks. And in rare occasions it will last for 4 months with 1% chance of occurrence (Fedor, Bojanowski, & Korzeniewski, 2019).

- Literature about seeking medical advice before traveling.

Seeking medical advice is always preferred before any travel especially when traveling to high risk countries (Steffen et al., 2015). Vaccination such as Cholera vaccination or Typhoid vaccination, showed effective result in lowering the chances of diarrheal disease occurrence in travelers (Scarpignato & Rampal, 1995).

A retrospective population-based study done in Korea on acute infectious diarrhea with the use of medically prescribed empirical antibiotics showed that the rate for antibiotic used was 46% of the whole population who received antibiotics for self-treatment of diarrhea. The used of antibiotic was not medically needed in their cases. Elderly people occupy the higher percent in comparison to other ages, and people who treated in private hospital were the ones who given the antibiotics the most. This study encourage physician to publish guidelines for travelers' diarrhea treatment in order to know the type and the need of receiving antibiotics in case of infectious diarrhea sine the majority of the cases came from viral pathogens at 59%. The result suggested that people are more likely to receive unecessary medication if they were treated in private hospitals which may question the need of the medication in the first place. On the other hand watery bacterial diarrhea resolved by itself without any treatment(Lee et al., 2019).

A Geosentinel global surveillance system in the United States showeded that people who returned from international travel and had gastrointestinal diagnoses were usually exposed to unsafe food. Others had their gastrointestinal symptoms because they did not

receive the proper prophylaxis such as vaccination or did not follow the CDC recommendation for international travel (Harvey et al., 2013). This study emphasized the importance of receiving pre-travel advice such as to use boiled, sealed, or purified beverages, to follow food safety, by paying attention to restaurant hygiene, and avoid raw food (2019, CDC). While there are a lot of published literature on the treatment of travelers' diarrhea, there is still the danger of newly emerged acute or chronic travelers' diarrhea which identify a new generation of drug resistance travelers' diarrhea pathogens (Riddle et al., 2017).

- Literature about risk factors:

A retrospective cohort study done on a tour group after salmonella outbreak happened on 7 out of 15 members, with attack rate of 46.7% of the travelers. The 7 travelers' symptoms were: nausea, vomiting, fever and diarrhea. Laboratory confirmation with PCR and bacterial cultures was done and it showed a strain of salmonella. After food history investigation all 7 members have a common breakfast meal of boiled egg which caused the food poisoning (Gao et al., 2019). Having a pre-travel medical consultation is so crucial as it shown in a retrospective cohort study that people who received medical advice less prone to develop travel related illnesses, or have less sever gastrointestinal symptoms or have shorter hospitalization period if needed (Tan, St Sauver, & Sia, 2018). A 7 years case-case analysis using 7 years of travelers' diarrhea surveillance data showed that people who are engaging in risky behaviors can possible have a lack of understanding preventive measures (Jennings et al., 2017).

The most common cause for travelers' diarrhea is fecal-oral route. This can occur as result of environmental hazard or host hazards. People traveling to developing countries are the one

who usually have the travelers having gastroenteritis symptoms because the poor strict hygiene regulations there. People traveling to sub-Saharan Africa, South America or South Asia are highest risk to develop traveler's diarrhea. And for the personal hazard factor it is shown that risky behaviors, backpacking travelers are the ones with more chances to have travelers' diarrhea (Fedor et al., 2019).

- Literatures about travelers and produce.

The main cause behind travelers' diarrhea highly dependent on the destination, food and water hygiene should be educated to the travelers to prevent many diarrheal disease (Lima, 2001). Water and food born communicable diseases were statistically significant causative factors as for travelers' diarrhea (Jung, Jang, Hwang, Park, & Son, 2019). (Stoney et al., 2017) study showed that half of the research participants with travelers' diarrhea either drank from tap water, drank unpasteurized milk or ate salad (Stoney et al., 2017). A study showed that backpacker usually have higher chances of developing travelers' diarrhea because they consume more street food. Meanwhile beach vacation like resorts have slightly lower chances of developing travelers' diarrhea (Scarpignato & Rampal, 1995). 20% to 50% of people traveling to developing countries are at risk of developing travelers' diarrhea due to fecally contaminated water or food. Other types of high-risk foods include ice cubes, uncooked Vegetables and unpeeled fruit, salads and raw or rare meat or seafood (Diemert, 2006)

- Literatures about types of diarrhea and treatment:

As of recent years, traveler's diarrhea symptoms have worsened especially with antibiotic resistant Enterobacteriace carriage in stool. After receiving antibiotics to treat their traveler's

diarrhea some travelers are then at risk for the development of multidrug resistant diarrhea. So, practitioners should prescribe for them an antibiotic for treatment instead of depending on self-treatment methods.

Travelers with diarrhea should first start with loperamide for treatment of the diarrhea, if the symptoms do not resolve or become worse, they should seek medical advice for further management to avoid using unnecessary antibiotic use. (Ericsson & Riddle, 2018). Other studies have also been interested in the effect of probiotics on Enterobacteriaceae during travel. A randomized control trail done on 61 travelers where they were taking a rectal swab before and after the trips and with one group given probiotics while the other did not. The result showed there was no statistically significant difference between the two groups. (Dall et al., 2019). Another study said it is best to stick to preventive measures such as sealed bottled water, avoiding tap water, avoiding fresh produce unless they are cooked, rather than probiotics (Barrett-Connor, 1973). There are no effective drugs to prevent travelers' diarrhea or prophylaxis against traveler's diarrhea, the most effective way is to avoid all risky practice during the travel (Barrett-Connor, 1973).

Chapter 3: Methods

Introduction:

In this day and age with the abundance of travel advertisements, websites, and applications, traveling has become more common and easier than ever before. Accommodations, transportation, and destinations in 2019 have become highly dependent on social media to advertise their services to travelers, which in turn, bring more revenue and tourism (Manoukian, 2019). Due to the increase in globalization, people tend to travel internationally more often for various reasons, including for business, education, tourism, and to visit family. The annual number of international trips for tourism exceeded 1 billion travelers in 2016. Traveler's diarrhea is considered the most common travel-related illness with up to 70% risk of occurrence in travelers (Vilkman, Pakkanen, Laaveri, Siikamaki, & Kantele, 2016). More focus on travelers' diarrhea should be made especially with the annually increasing number of travelers and the rising rate of antimicrobial resistance of many diarrheal pathogens (Frost, Van Boeckel, Pires, Craig, & Laxminarayan, 2019). In particular, travelers should be educated on high risk destinations for traveler's diarrhea, high risk activities, and how to protect travelers during travel from contracting travelers' diarrhea.

Study Design and Participants:

A longitudinal prospective study using 2 surveys, one pre-travel and the other post-travel, was conducted. A self-administered survey was given to each participant during their visit to the Emory Travelwell Center. During the pre-travel visit, each participant received a standard medical consultation appropriate for their destination. Then a post-travel survey was sent to

the patient to be self-administered online through (KoBoToolbox: https://www.kobotoolbox.org/) at home after the end of the trip.

Inclusion criteria were: 1. Adult (age ≥ 18 years old); 2. Current resident of the United State of America 3. Travel between June 30, 2018 and Jan 30,2020. The pre-travel surveys and post-travel surveys where connected by assigning a study ID number for each participant.

The surveys were tested, reviewed and validated by Infectious Disease Consultants and a Public Health specialist before sending them to the participants. Most of the questions were multiple choice.

Data Collection and Variables

The pre-travel surveys covered sociodemographic (age, gender, level of education, health conditions), travel knowledge, reason and mode of travel, type of transportation expected, and what vaccinations and other preventative measures they received before traveling. Lastly, they were also asked about their knowledge on best behaviors to prevent illness, especially food-borne illness, while traveling.

The post travel survey, which was sent 2-3 weeks after travel, covered if there was any change of mode of transportation, change in length of trip, eating habits during the trip, did they experience any illness, did they have any diarrhea and what do they think is the best practice to stay safe. Specific to diarrhea, they were also asked about their use of hand sanitizer, type of produce eaten (peel-able or not), types of beverages, any raw food consumption, any illnesses in travel companions, and if they have an advice that they think beneficial in their opinion for travelers.

Statistical Analysis:

Kobo toolbox and STATA SE 16 were used for data analysis, calculating the frequencies, percentage, means and medians to describe the sociodemographic of the study participants, common destinations, reasons for travel, diarrhea development and types of travelers behaviors (both safe and un-safe). Risk ratios were calculated to determine associations between reason for travel, destinations, risky behaviors, and adherence to preventative measure and the occurrence of traveler's diarrhea. A p-value of <0.05 was used to determine statistical significance.

Ethical Approval:

All participants who fulfilled the inclusion criteria were consented. Participants were given a thorough explanation about the theory of the study, the purpose of the study, and the process of the study including the part about them receiving post-travel surveys after they come back from the trip. Because this study included human subjects and personal health information both surveys started after receiving the Institutional Review Board (IRB) of Emory University approval.

Chapter 4: Results

Demographics and travel characteristics of participants:

Over the full study period, 422 participants completed pre-travel surveys (self-administered) with a completion rate of 100%. For the post-travel surveys (online) there were 224 completed surveys after the return of the travelers, for a response rate of (53%). Using the total number who completed the pe-travel surveys, the age ranged from 18-80 years with a mean age of 44.99 years (17.56 SD*). Fifty-eight percent of the participants were females, 45% of the participants reported having a previous illness, and 58% reported previously receiving any vaccination for travel [Table 1]. The mean duration of travel was 17 days (32.97 SD). Destination of the travelers were divided into nine regions. The most visited region was East Africa with 120 travelers visiting (28.44%), then South America visited by 82 of the participants (19.43%), then West Africa with 65 visitors (15.40%), followed by South Asia / Indian subcontinent which was visited by 41 participants (9.72%), followed by Southeast Asia with 31 visitors (7.35%), then Europe with 14 participants (3.32%). Five visitors visited East Asia (1.18%), and finally 3 travelers visited the Middle East (0.71%). Preferred accommodation was hotels that were chosen by 84.25% of the participants. Travelers' activities varied between wildlife and reserve parks 42.52%, hiking 34.44%, swimming 26.54%, sailing 6.64%, ziplining 3.79%, or no activities for 26.78% of the participants. [Table 2].

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*SD: Standard deviation

Previous knowledge and previous travelers

Ninety-two percent of the participants had traveled before and 33% of the participants developed travel-related illnesses such as fever, traveler's diarrhea, or skin disorders in their previous trips. The knowledge about travel-related illnesses showed that only 29% of travelers learned or heard about travel-related illnesses. When travelers asked to estimate their level of knowledge of travel related illness, 98% of participants responded with few reporting no knowledge (1.19%), 7% as having little extent, 45% with some extent, and 42% as having a great extent of knowledge [Table 3].

Although all participants had pre-travel advice in the clinic for the travel related to this current study, when travelers were asked about receiving pre-travel advice in their previous travels, the majority of travelers (62%) had sought pre-travel advice for their previous travels. The advice mainly was received from a physician with (59%), internet (50.47%), word of mouth (33.89%), brochure (16.11%), or travel agent (10.69%). [Table 3]

Travelers answered the best ways to prevent traveler's illnesses as the following: use of bottled water (97.63%), washing hands (95.02%) insect bite prevention (91.23%), use of hand sanitizer (82.46%), avoidance of street food (80.33%), and avoiding swimming in freshwater (66.11%) [Table 3].

Post-travel survey results:

A total of 224 people completed the post-travel survey online (53%). Most of the travelers had no unexpected change in the path of the journey (85.71%). If there was a change, it was due to

additional destinations (3.56%), shorter duration (2.22%), or longer duration (1.79%) [Table 4]. The changes occur because travelers wanted to do more sightseeing, or it was work-related changes. Other changes were airplane-related issues that varied from missing a connecting flight, airport shutdown, flight delay, or flight cancelation (0.89% for each reason).

Reported symptoms /Medical attention:

Forty-eight out of the 224 participants developed sickness during their trip (21.33%). Thirty-three people reported having diarrhea (14.67%), twelve had respiratory tract infection such as cough sore throat or runny nose(5.33 %), eleven reported having abdominal pain (4.44%), eleven participants had other symptoms such as headache, allergies or nausea (0.44% for each symptom) eight reported having a fever (3.56%), seven reported having vomiting (3.11%), and lastly three travelers reported having skin disorders(1.33%). Thirty-three of the traveling companions also got sick during the trip (14.67%).

For those who reported diarrhea, symptoms developed during the trip for 13 participants (39.39%), and 1-5 days after returning for 2 participants (6.06%). Only 3 participants sought medical attention for these symptoms (9.09%). For seeking medical care it varied from visiting a clinic in the United States by 3 participants (9.09%) and seeking medical advice in a clinic in another country 12 (36.36%). Five of those who had diarrhea received oral hydration (15.15%).

Reported diarrhea risk factors:

Bivariate (unadjusted) analyses applied to measure the relative risk between diarrhea and risky behaviors, avoidance measures, the reason for travel, and destination. Each covariate was

reported based on the risk ratio and keeping the independent variabls (diarrhea) in individual RR calculations as constant [table 5].

For the following risk factors, there was a positive relative risk between them and traveler's diarrhea but the findings were not statistically significant: eating raw produce by 166 participants (73.78%) and 27 developed diarrhea (16.27%, RR 1.50, 95% CI 0.74, 3.2); drinking freshly squeezed juices by 53 of participants (23.56%) and 9 developed diarrhea (16.98%, RR=1.81, 95% CI 0.60, 5.46); eating fresh produce which was not peeled by 38 participants (46.34%) and 7 developed diarrhea (18.54%, RR 1.19, 95%CI 0.64, 2.22). On the contrary consuming ice had a negative risk ratio with traveler's diarrhea but was not statistically significant (RR 0.93, 95% CI 0.59, 1.48). Also, eating street food by 48 participants (21.33%) and 7 developed diarrhea (14.58%, RR 1 , 95%CI= 0.83 , 1.21) had a negative relative risk with no statistical significant. Contact with livestock or animals by 31 participants (13.78%) was not associated with diarrhea (RR 0.77, 95%CI 0 .12, 4.86) [Table 5].

For the avoidance measures, washing hands or using hand sanitizer was reported by 209 participants (92.89%) and out of those, 32 developed diarrheas (15.31%, RR 2.77, 95%CI 0.40, 19.1). Avoiding street food by 163 participants (72.44%) and out of those 25 did developed diarrhea (15.34%, RR 1.82, 95%CI 0.68, 1.64). The rest of avoidance measures are listed in Table 5. Interestingly, none of them were protective for diarrhea, although the adherence to these practices were not measured.

Comparing reasons for travel and occurrence of diarrhea: The reason for travel showed that tourism was the aim of the travel for 133 participants (59.11%), and 20 developed diarrhea (15.04%, RR 1.19 95%CI 0.38, 3.64). While the relative risk was positive, it was not statistically

significant. The following reasons for travel had negative relative risks and were statistically significant; Business travel for 51 participants (22.67% of total), and 5 reported having diarrhea (9.80%, RR 0.11, 95% CI= 0 .04, 0.27); Research and education: 24 participants (10.67%) and out of those 5 also reported having diarrhea (20.83%, RR 0.277, 95%CI 0.10, 0.75). Lastly, 28 participants (12.44%) traveled for volunteering and humanitarian work, and 3 reported having diarrhea (16.67%, RR 0.217, 95% CI= 0 .08, 0.57).

For destination, there was a positive association between traveling to North Africa and East Africa with diarrhea but it was not statistically significant. East Africa, it was the destination for 76 participants (33.78%), and 11 developed diarrhea (14.47%, RR 0.98, 95%CI= 0.31, 3.08); North Africa was the destination for 3 travelers (1.33%) and 2 did report having diarrhea (66.67%, RR 11.59, 95%CI = 0.87- 153). The following destinations had negative relative risks and no statistically significance: South America was the destination for 49 participants (12.78%), and 7 developed diarrhea (14.29%, RR 0.97, 95% CI= 0.27, 3.34); Southern Africa was the destination for 16 participants (7.11%), and 2 had diarrhea (12.50%, RR 0.82, 95%CI 01.4 ,4.81). [Table5].

Chapter 5: Discussion

The purpose of this study was to assess the correlation between traveler's diarrhea with risky behaviors, following preventive measures, the reason for travel, and the destination of travel. We found among all reported travel-related illness, diarrhea was the highest disease reported among the study population (N*=33, 14.67%). This proportion is lower than the result found by (Stoney et al., 2017) where they reported 30% of travelers' diarrhea in the study population. It is also lower than (Gao et al., 2019) where they reported 46% rate of travelers' diarrhea in the study group. Since all the participants in this group received the same medical advice and anticipatory guidance on preventing traveler's diarrhea, this could explain our overall low percentage of diarrhea.

This study found a positive relative risk between some risky behaviors and developing travelers' diarrhea. These risk factors were eating raw produce, drinking freshly squeezed juices, eating fresh produce did not have thick peel [table 5]. While the results did not prove statistically significant, the positive relative risks of these behaviors support the literature by Stoney et. al and Diemert et. al about these factors and supports CDC recommendations to follow safety measures in eating and drinking by paying attention to hygiene in any type of food consumed (2019, CDC).

On the other hand, when looking at the associations between preventative measures taken and risk of diarrhea, there was a positive relative risk with no statistically significant association between washing hands or using hand sanitizer and using avoiding street food [table 5]. According to CDC washing hand is highly recommended before food consumption and if not available an effective sanitizer can be used when hands washing is not available (CDC,

2019). As for Barr & Smith et. al study in preventing acute diarrhea they recommended adequate hands washing (Barr & Smith, 2014). This is likely not a true association as the majority of participants reported hand washing, and we were not able to determine how adherent participants were to this.

Surprisingly our study shows no significant correlation between some of the preventive measures such as avoiding fresh produce that did not have thick peel or washing produce before consumption. Also, there was no statistical significant between consuming ice in beverages or eating the raw or undercooked meat. This finding goes against the line of Diemert et al & Jung et al., 2019 results. The lack of association could be due to the low response from our study. Washing fruit before eating was actually associated with diarrhea, which may signify that the travelers were not using clean water, or they had a false sense of security by washing the fruit. It also may be that they did not always adhere to these measures. Future studies with a likert scale could help explore these relationships better.

For the reason of travel, only tourism show positive a relative risk albeit no statistical significant association with travelers' diarrhea [table 5]. In the reviewed study by Fedor et al., they mentioned that people who have more planned activities such as hiking have a higher risk of developing traveler's diarrhea due to more exposure to hazardous environmental factors. The travelers who did not have any traveler's diarrhea mostly did not have any activities during their trip such as when traveling for business or have good compliance with the advice received for their trip. Therefore, this seemed to be in line with prior studies. Our study shows that business travel seems to be protective and it was statistically significant.

Only 6 participants out of 33 that developed travelers' diarrhea sought medical advice. Our finding supports the result of Fedor et al. because most travelers' diarrhea is self-resolving and does not require medical intervention unless it becomes persistent.

For the preventive measures, it showed there was a high awareness level in the study population since there was a lower relative risk of diarrhea with many of the preventative measures s such as drinking from bottled water, washing hands or using hand sanitizer and use effective insect repellant. Our study showed 43.71% of the participant had great knowledge about the travel-related illness and anticipated a high use of preventive measures during trave and the majority of participants practiced good preventative measures.

In terms of destination, Fodor et al. found that traveling to sub-Saharan Africa, South America or South Asia are the highest risks to develop traveler's diarrhea. Meanwhile, our study found that traveling to East Africa, and South America had the highest number of reported diarrhea cases (N=11, N= 7 respectively). This can be due to a larger number of travelers to the mentioned regions (N=76, N=49 respectively), and the remaining regions had lower numbers of travels. Although East Africa had no statistical significant result, South America had a positive risk ratio which increases the risk of developing diarrhea, and requires further study. [Tab5].

Two hundred and twelve of the participants found the pre-travel advice beneficial (94.22%). Our study had an average age of 44.9 and the majority of the participants had a graduate university degree at 68.72%. This could also be a contributing factor to having good compliance with safety/preventive measures and knowledge. Also, all of our participants

received pre-travel medical advice though Emory TravelWell Center. This result emphasizes the recommendation of (Steffen et al., 2015) which is having a medical consultation before any trip.

The review (Harvey et al., 2013) highly recommended pre-travel counseling and sticking to preventive measures including receiving needed vaccination in case of traveling to high risk regions, following the CDC recommendation for international travel, and avoiding risky behaviors.

For the study limitations, there was a recall bias. We are depending on participants reporting their symptoms which can be subjected to either over or under-reporting, and we received low response rate (53%) for the post-travel survey which can affect the founded result. The study was highly dependent on the response of the participants to measure the association between the outcome and other variables. Receiving the response required sending multiple emails as a reminder, phone calls or recording a voice massage.

Conclusion and recommendation:

The findings from this study that diarrhea disease is the most commonly reported travel-related illness and is consistent with previous studies. Lower-income countries is a risk factor for developing traveler's diarrhea due to a relative reduced availability of lack of clean water and food, which has also been reported in previous studies. Practicing good hygiene strategy during travel is a preventive factor against developing diarrhea as seen in our results. Having pre-travel advice or counseling is highly suggested to lower the chances of developing travelers' diarrhea,

and may have been a driving factor in the overall low proportion of travelers reporting diarrhea in our study.

Traveler's diarrhea will continue to be challenging for both travelers and health care providers. Future work should involve a larger study sample size especially for the post travel surveys. And depend on medical records for those who return from their travel to seek medical advice for a better response rate and lowering the bias changes in reporting symptoms.

Chapter 6: Public health implications

With the globalization that currently the world experience, traveling become so important in every aspect of life. Travelers' diarrhea considers attack rates range from 30% to 70% of travelers. This high percentage can but a burden on the traveler's health, finance, and their families. The importance of preventive measures lies behind following clear public health rules to lower the burden of traveler's diarrhea (Gorbach, 1985). Increasing the awareness of public health among travelers is important to lower the percentage of travelers' diarrhea and to maintain good health during the travelers (Korzeniewski, 2017). Although travelers' diarrhea was recognized more than 35 years ago (Gorbach, 1985), it remains a public health challenge that needs to addressed to better prevent it (Zaidi & Wine, 2015).

N*: Number

Tables:

Table 1: Demographics of the participants.

	Observation	mean	Standard deviation	Minimum	Max
Age	422	44.99	17.57	18	80
age group	**Frequency**		**Percent**		
18-35 years	135		31.99%		
36-55 years	166		39.34%		
>55 years	121		28.67%		
Participants Genders					
Female	247		58.53%		
Male	175		41.47%		
Total	422		100.00%		

Education level	**Frequency**	**Percent**	**Cumulative**
Primary School	1	0.25	15.76
Some Secondary school	5	1.23	20.20
Secondary school	12	2.95	18.97
Some university	44	10.48	31.03
University graduate	279	68.72	99.75
Other	63	15.52	15.52
Refused	1	0.25	16.01
Unknown	1	0.25	99.51
Total	406	100.00	

Diseases	**Observation**	**Percent**
Hypertension	55	13.03%
Immune condition	20	4.74%
Cancer	18	4.27%
Irritable bowel syndrome	12	2.84%
Diabetes Mellitus	14	3.32%
Asthma	21	4.98%

Table 2: Transportation taken by the travelers , Accommodation, Reason Of The Trip, Destination, Activities. The tables done on a study population of 224 participants. The number and percentages for the period of travel ranging from high to low.

	Frequency	Percent
Airplane	208	49.29
Car	147	34.53
Bus	48	11.37
Train	21	4.98
Boat	26	6.16
Cruise-Ship	3	0.71

Accommodation Type	**Frequency**	**Percent**
Hotel	353	84.25%
Family housing	42	10.02%
Camping	40	9.48%
Other	248	100%

Reason of travel	**Frequency**	**Percent**
Tourism	245	58.19%
Business	91	21.625
Visiting family or friend	45	10.68%
Research	34	8.08%

Length of the trip	**Number of participants**	**Mean**	**Standard Deviation**	**Minimum**	**Maximum**
	420	17.63	32.97	1	455

Destination	**Frequency**	**Percent**
East Africa	120	28.44%
South America	82	19.43%
West Africa	65	15.40%
South Asia / Indian subcontinent	41	9.72%
South Africa	39	9.24%
Southeast Asia	31	7.35%
Europe	14	3.32%
East Asia	5	1.18%
Middle East	3	0.71%

Activity type	**Observation**	**Percent**
Sailing	28	6.64%
Hiking	145	34.44%
Swimming	112	26.54%
Wildlife parks	179	42.52%
Ziplining	16	3.79%
No activities	113	26.78%

Table 3: knowledge, preventive measures taken by the participants, and other information about travel history. The total number of the participants is 224.

Extent of awareness of travel preventive measures	Observation	Percent
Great extent	184	43.71
Some extent	193	45.85
Little extent	33	7.84%
Very little	1	0.24%
None	5	1.19%
Planned Preventive measures	**Observation**	**Percent**
Use of Bottled water	412	97.63%
Washing hands	401	95.02%
Insect prevention measures	385	91.23%
Use of hand sanitizer	348	82.46%
Avoiding street food	339	80.33%
Avoiding freshwater swimming	279	66.11%
	Observations	**Percent**
Following pre-travel advice while traveling abroad previously be travelers	158	37.44%
Thinking following pre-travel advice beneficial.	211	50%
Traveled before this trip.	391	92.87%
Previously receive vaccination for previous trip.	237	58.81%

Table4: changes in destination and reported illnesses. Other symptoms*: headache, allergies, or nausea

Reported illnesses	Observation	Percent
Any illness	48	21.33%
Sick travel companion	33	14.67%
Diarrhea	33	14.67%
3 or more loose stool	21	9.33%
Other symptoms*	11	4.87%
Abdominal pain	10	4.44%
Fever	8	3.56%
Vomiting	7	3.11%
Skin rash or disorders	3	1.33%
Bloody diarrhea	1	0.44%
Sick contact	17	7.56%
When symptoms started	**Observation**	**Percent**
Symptoms started during the trip	17	7.56%
Symptoms started within 1-5 days of the trip	4	1.78%
Place of medical attention	**Observation**	**Percent**
Clinic in the U. S	3	9.09%
Another clinic location	12	36.36%
Type of medical intervention	**Observation**	**Percent**
Received oral hydration	6	2.67%

Table5: The number of reported diarrhea cases according to each category, the reported risk ratio, 95%confident interval and P-value. M: number of participants who answered with no to the question.

	Number	Percent	Reported Diarrhea(N)	Reported Diarrhea (%)	Risk ratio	95% CI	p-value	Total responders
Risky Behaviors								
Ate raw produce	166	73.78%	27	16.27%	1.50	0.74 -3.2	P= 0.331	224 M=1
Consumed ice in beverages	83	36.89%	13	15.80%	0.93	0.59 - 1.48	P= 0.712	224 M=1
Drank freshly squeezed juice	53	23.56%	9	16.98 %	1.81	0.60 - 5.46	P= 0.29	224 M=112
Ate street food	48	21.33%	7	14.58%	1.00	0.83 – 1.21	P= 0.872	224 M=1
Ate fresh produce was not peeled	38	46.34%	7	18.54%	1.19	0.64 – 2.22	P=0.76	82 M=143
Contact with livestock or animals	31	13.78%	7	22.58%	0.77	0 .12 - 4.86	P= 0.787	224 M=112
Ate raw or undercooked meat	5	2.2%	2	40%	0.21	0.03 - 1.36	P=0.101	224 M=112
Drank tap water	17	7.56%	2	11.76 %	0.98	0.89 – 1.08	P=0.9	224 M=1
Had new Sex partner	3	1.33%	1	33.33%	0.30	.025 - 3.47	P=0.607	224 M=112
Avoidance Measures.								
Washed hands or used hand sanitizer	209	92.89%	32	15.31%	2.77	0.40 - 19.1	P= 0.45	224 M=16
Avoided street food	163	72.44%	25	15.34%	1.82	0.68 - 1.64	P=0.737	224 M=62
Used effective Insect repellant *	160	71.11	23	14.37%	0.96	0 .48- 1.89	P= 1	224 M=65
Avoided fresh produce did not have thick peel	69	57.50%	13	18.8%	1.623	0.75 – 3.52	P=0.171	224 M=105
Washed produce before consumption	44	53.66%	4	9.1%	3.10	0.87 - 11.1	P=0.081	224 M=143
Reason for travel								
Tourism	133	59.11%	20	15.04%	1.188	0.38 - 3.64	P=0.763	224 M=87
Business	51	22.67%	5	9.80%	0.108	0 .04 - 0.27	P<0.05	224 M=174
Research/ Education	24	10.67%	5	20.83%	0.277	0.10 - 0.75	P= 0.011	224 M=201
Volunteering/ humanitarian work	28	12.44%	3	16.67%	0.217	0 .08 - 0.57	P= 0.002	224 M=197A
Destination								
East Africa	76	33.78%	11	14.47%	1.31	0.31 - 3.08	P=0.677	224 M=1
South America	49	21.78%	7	14.29%	0.97	0.27 - 3.34	P=0.957	224 M=1
North Africa	3	1.33%	2	66.67%	11.59	0.87- 153	P= 0.063	224 M=1
South Asia/ Indian Subcontinent	18	8.00%	2	11.11%	0.773	0.13 - 4.46	P=0.774	224 M=1

Southern Africa	16	7.11%	2	12.50%	0.828	0.14 - 4.81	P=0.834	224 M=1

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