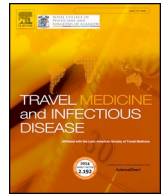




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Infectious disease symptoms and microbial carriage among French medical students travelling abroad: A prospective study

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ABSTRACT

Background: In France, no previous studies have focused specifically on health problems among medical students during internships abroad including the clinical symptoms suggestive of infectious diseases and the acquisition of pathogen carriage.

Methods: Clinical follow up and qPCR based respiratory, gastrointestinal and vaginal pathogen carriage before and after travel were prospectively assessed in a cohort of medical students departing from Marseille, France.

Results: 134 students were included. 73.9%, 38.8% and 5.0% of students reported gastrointestinal, respiratory and vaginal symptoms, respectively. The acquisition rate of Enteropathogenic *Escherichia coli* (EAEC) and Enteropathogenic *E. coli* (EPEC) was 53% and 41%, respectively. The acquisition of respiratory viruses was low but associated with persisting symptoms, while bacterial acquisition ranged from 3.3% for *Streptococcus pyogenes* to 15.0% for *Haemophilus influenzae*. *Gardnerella vaginalis* and *Atopobium vaginae* acquisition rates were 7.7% and 14.3% respectively. Five students (5.1%) had molecular quantification criteria for bacterial vaginosis on return.

Conclusion: This preliminary study demonstrates that besides the known risk of gastrointestinal and respiratory infections and associated changes in intestinal and respiratory microbiota, medical students abroad may also experience changes in vaginal microbiota leading, in some cases, to clinical symptoms or the acquisition of bacterial vaginosis, which may be asymptomatic.

1. Introduction

In 2018, French people undertook an estimated 24.5 million trips to French Overseas territories, mainly in Europe and, to a lesser extent, Africa, America and Asia [1]. International travellers are exposed to the acquisition of pathogens associated with travel, with a potential risk to the community or the hospital population upon return, whether or not they are symptomatic while travelling. This has been extensively described, by example, among French Hajj pilgrim travelling to Mecca, Saudi Arabia [2,3]. A significant proportion of medical students from high-income countries participate in usually self-organised, but also arrange through faculty partnership or commercial volunteer

placement organizations, clinical electives abroad - also known as international medical electives or global health electives [4]. Electives typically last between one and three months. As an example, Work the World, an Australian organization, placed 15,000 medical students since 2005 [5]. Destination may be in developed countries, but low and middle-income countries are becoming popular destinations. International medical electives are generally clinical immersion experiences, but younger medical students may also participate to humanitarian missions unrelated to clinical activities [4]. In addition to the clinical placements themselves, many students add cultural side trips and wilderness or other adventures to their itineraries [4]. The motivations of students are to improve their medical knowledge by clinical

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experience, to help people living in conditions of extreme poverty and to discover new cultures and ways of life.

Health risks for medical students while on electives abroad are a subject which concerns the medical profession. There is, however, little recent data about infectious diseases among medical students doing part of their studies abroad [6–8]. In one Australian survey, 64% of students experienced some sort of health problems, of which travellers' diarrhoea was the most common (40%) and 12.5% contracted upper respiratory tract infection (including influenza) [6]. In a Dutch study, 65% students reported diarrhoea, 33% constipation, 29% skin infections and wounds, and 11% respiratory tract infections [7]. In a Swedish study, 69% of students reported diarrhoea [8].

In France, no previous studies have focused specifically on health problems among medical students during internships abroad. The purpose of this study was to investigate the prevalence of clinical symptoms suggestive of infectious diseases and to document the acquisition of pathogen carriage among French medical students undertaking an internship abroad.

2. Materials and methods

2.1. Study design

A monocentric prospective cohort survey was conducted between June and August 2018 among medical students from the Faculty of Medicine of Aix Marseille University, France, who were planning to undertake an internship abroad during the summer months. Recruitment was done on a voluntary basis, during their vaccination and pre-travel consultation at the Institut Hospitalo-Universitaire Méditerranéenne Infection, which is on the Marseille University medical campus. Participants were asked to sign a written informed consent form and to complete an inclusion questionnaire covering demographic data, intended travel dates and destination, and history of chronic illness. Vaccination status following consultation was recorded. All participants received advice regarding the prevention of traveller's diarrhoea (hand hygiene and safe food and water habits) and the usefulness of personal preventive measures against insect bites (mosquito bed net and repellent) and warnings regarding rabies risks. Travellers to malaria-endemic zones were prescribed malaria chemoprophylaxis. Participants were invited to self-collect throat, nasal, faecal and vaginal samples during the week preceding departure and during the week following their return to France. Samples were collected using commercial rigid cotton-tipped swab applicators (Medical Wire & Equipment, Wiltshire, United Kingdom) and placed in viral transport media (Sigma Virocult®, Wiltshire, United Kingdom). For nasal sampling, participants were trained to insert the swab into one nostril (about 2 cm). For pharyngeal sampling, participants introduced the swab into the oral cavity and gently rubbing the tonsillar pillars several times. For rectal sampling, participants introduced the swab into the rectum through the anus (about 3 cm). For vaginal sampling, participants placed the swab in the vagina (about 3 cm) avoiding touching the skin and vulva with the swab and gently rubbed the inner walls several times. Samples were returned to our institute by participants for processing. Students were also provided with a return questionnaire addressing the exact place where the internship took place, the type of activities conducted, tourism and travel to other countries during the internship period, housing conditions, contact with children and animals, and symptoms and treatment during the stay. Influenza-like illness (ILI) was defined as the association of cough, sore throat and subjective fever [9]. Diarrhoea was defined by at least three loose or liquid stools per day.

3. Microbiological methods

3.1. Identification of respiratory pathogens

3.1.1. Respiratory specimens

DNA and RNA were extracted from the respiratory samples using the EZ1 Advanced XL (Qiagen, Hilden, German) with the Virus Mini Kit v2.0 (Qiagen) according to the manufacturer's recommendation.

3.1.1.1. Identification of respiratory virus. One-step simplex real-time quantitative RT-PCR amplifications were performed using Multiplex RNA Virus Master Kit (Roche Diagnostics, Meylan, France) for influenza A, influenza B, human rhinovirus, metapneumovirus, respiratory syncytial virus and internal controls MS2 phage [10]. LightCycler® 480 Probes Master kit (Roche diagnostics) was used for adenovirus according to the manufacturer's recommendations. Human coronavirus (HCoV) and human para-influenza virus (HPIV) were detected by one-step duplex quantitative RT-PCR amplifications of HCoV Gene Kit (REF: 71–045, BioMérieux, Marcy l'Etoile, France), according to the manufacturer's recommendations.

3.1.1.2. Identification of respiratory bacteria. Real-time PCR amplifications were carried out using LightCycler® 480 Probes Master kit (Roche diagnostics) according to the manufacturer's recommendations. The *SHD* gene of *Haemophilus influenzae*, *nucA* gene of *Staphylococcus aureus*, *phoE* gene of *Klebsiella pneumoniae*, *lytA* *CDC* gene of *Streptococcus pneumoniae* and *hypothetical protein* gene of *Streptococcus pyogenes* [11] were amplified with internal DNA extraction controls TISS, as previously described.

3.2. Identification of gastrointestinal pathogens

3.2.1. Gastrointestinal specimens

DNA was extracted by semi-automated extraction, as previously described [12]. The automated procedure using the EZ1 Advanced XL (Qiagen) with the DNA Tissue Kit (Qiagen) according to the manufacturer's recommendation.

3.3. Identification of gastrointestinal virus

One-step simplex real-time quantitative RT-PCR amplifications were performed using Multiplex RNA Virus Master Kit (Roche Diagnostics) for adenovirus, rotavirus, norovirus, astrovirus, and internal controls MS2 phage [13].

3.4. Identification of gastrointestinal bacteria and parasites

Real-time PCR amplifications were carried out using LightCycler® 480 Probes Master kit (Roche diagnostics) according to the manufacturer's recommendations. The *mapA* gene of *Campylobacter jejuni*, *ipaH* gene of *Shigella* spp/EIEC (enteroinvasive *Escherichia coli*), *invA* gene of *Salmonella* spp, *stx1* and *stx2* genes of enterohemorrhagic *E. coli* (EHEC), *EAF* and *EAE* genes of enteropathogenic *E. coli* (EPEC), *pCVD432* gene of enteroaggregative *E. coli* (EAEC) [14] and *Twhip2* gene of *Tropheryma whipplei* [15] were amplified with internal DNA extraction controls TISS. The *Hsp70* gene of *Cryptosporidium parvum/hominis* and *18S* genes of *Entamoeba histolytica* and *Giardia lamblia* were used to detect parasites [16].

3.5. Identification of vaginal pathogens

3.5.1. Vaginal specimens

Two hundred microliters of each homogenised vaginal suspension was used for DNA purification with the QIAamp DNA Mini Kit (Qiagen) using the EZ1 Advanced XL (Qiagen) which was modified as described elsewhere [17].

3.6. Identification of vaginal bacteria and parasites

Real-time PCR amplifications were carried out by using LightCycler® 480 Probes Master kit (Roche diagnostics) according to the manufacturer's recommendations. The *hypothetical protein* gene of *Chlamydia trachomatis*, *fusA* gene of *Mycoplasma genitalium* [18], *porA* gene of *Neisseria gonorrhoeae* [19], repeated sequence of *Trichomonas vaginalis* [20], *ftsY* gene of *Mycoplasma hominis*, *16S* gene of *Atopobium vaginae* and *Cpn60* gene of *Gardnerella vaginalis* [21] were amplified with internal DNA extraction controls TISS.

3.7. Amplification procedure and thresholds

All quantitative real-time PCR to detect respiratory, gastrointestinal and vaginal pathogens were performed using a C1000 Touch™ Thermal Cycle (Bio-Rad, Hercules, CA, USA). Negative control (PCR mix) and positive control (DNA from bacterial strain or RNA from viral strain) were included in each run. Positive results for bacteria or virus amplification were defined as those with a cycle threshold (CT) value ≤ 35 . Bacterial vaginosis was defined by an *A. vaginae* DNA load $\geq 10^8$ copies/mL (CT ≤ 21) and/or a *G. vaginalis* DNA load $\geq 10^9$ copies/mL (CT ≤ 18), as previously reported [21].

3.8. Statistical analysis

Differences in the proportions were assessed using chi-squared test or the two-sided Fisher exact test when appropriate. The acquisition of pathogens was defined as negative before travel and positive when returning from the internship abroad. To evaluate the potential acquisition of pathogen carriage, we used the McNemar's test to compare their prevalence before and after travel. We used the Fisher's exact test to evaluate the relation between prevalence of pathogens carriage on return and clinical symptoms. Percentages and 95% confidence interval (95%CI) estimations and comparisons were carried out using STATA version 14. A p-value of ≤ 0.05 was considered statistically significant.

4. Ethics

The protocol was approved by our Institutional Review Board (2019–006). It was performed in accordance with the good clinical practices recommended by the Declaration of Helsinki and its amendments. All participants gave a written informed consent.

5. Results

5.1. Characteristics of study participants

A total of 134 students agreed to participate and answered the return questionnaire, 75.4% of students were female. The median age was 21 years (ranging from 19 to 23 years) (Table 1). Most participants (74.6%) were students in their second year of medical studies and were

Table 1
Demographics.

Variables		n (N = 134)	%
Gender	Female	101	75.4
	Male	33	24.6
Age (years)	Median	21	
	Interquartile Range	20–22	
	Range	19–23	
Study year (medical cursus)	Second year	100	74.6
	Fourth year	34	25.4
Country of birth	Metropolitan France	129	96.3
	Overseas French territories	2	1.5
	Others ^a	3	2.2

^a One Vietnam, one Algeria and one Mexico.

Table 2

Primary destination country (where the internship took place).

Variables	N = 134	%
Vietnam	35	26.1
India	27	20.1
South India	16	11.9
North India	11	8.2
Peru	25	18.7
Madagascar	12	9.0
Tanzania	10	7.5
Senegal	7	5.2
Brazil	6	4.5
Indonesia	3	2.2
Argentina	2	1.5
Cambodia	2	1.5
Japan	2	2.2
Canada	1	0.8
Chile	1	0.8
Ecuador	1	0.8

taking part in a non-medical humanitarian mission. The remaining participants were in their fourth year and were assigned to different departments of medicine or surgery for clinical training (Supplementary Table S1).

The immunological status of participants before travel is described in Supplementary Table S2. In total, 23.1% were vaccinated against influenza and only 0.8% against invasive pneumococcal infections. The majority were vaccinated against hepatitis A (88.8%) and typhoid fever (78.8%). 11.2% of them were prescribed antimalarial prophylaxis.

Four (3%) students had a chronic respiratory disease and two (1.5%) used long-term corticosteroids.

The primary travel destinations for internships were in South East Asia (30.6%), South America (25.4%), Africa (21.6%), South Asia (20.2%) and North America (0.8%). The top primary destination countries were in Vietnam (26.1%), India (20.2%), Peru (18.7%) and Madagascar (9.0%) (Table 2). The mean travel duration was 44.7 days \pm 10.3 days (ranging from 27 to 65 days). Accommodation conditions were judged as being “very clean” by 14.9% of students, “clean” by 44% and “very basic” by 41%. 80.6% of the participants had contact with local children and 47.8% with animals. During their stays, 97.8% also travelled as tourists in the country of primary destination and 28 (20.9%) visited other countries. The top additional destination countries were Laos (29.6%), Bolivia (25.0%), Cambodia (17.9%), Thailand (10.7%) and Argentina (10.7%).

5.2. Clinical features and detection of pathogens

5.2.1. Respiratory infections

A total of 52/134 (38.8%) students reported at least one respiratory symptom (Fig. 1) during their stay. The mean time between arrival at the travel destination and the onset of symptoms was 20.7 days \pm 1.8 days. Rhinitis was the most prevalent symptom (31.3% of all participants), followed by a sore throat (27.6%) and a cough (23.1%). Only 7.5% of students reported febrile respiratory symptoms and 1.5% ILL. Only five students received antibiotics and one was hospitalised for respiratory tract infection symptoms. The persistence of respiratory symptoms upon return was reported by 7.5% individuals.

A total of 120 (89.6%) individuals provided respiratory paired swabs (before and after travel). A proportion of 9.2% acquired viruses and 15.0% bacteria. The most common virus acquired was human rhinovirus (6.7%), followed by coronavirus HKU1 (1.7%) and respiratory syncytial virus (1.7%). Bacterial acquisition rates were slightly higher, ranging from 3.3% for *S. pyogenes* to 15.0% for *H. influenzae* (Table 3).

5.2.2. Gastrointestinal infections

A total of 99 (73.9%) students reported gastrointestinal symptoms;

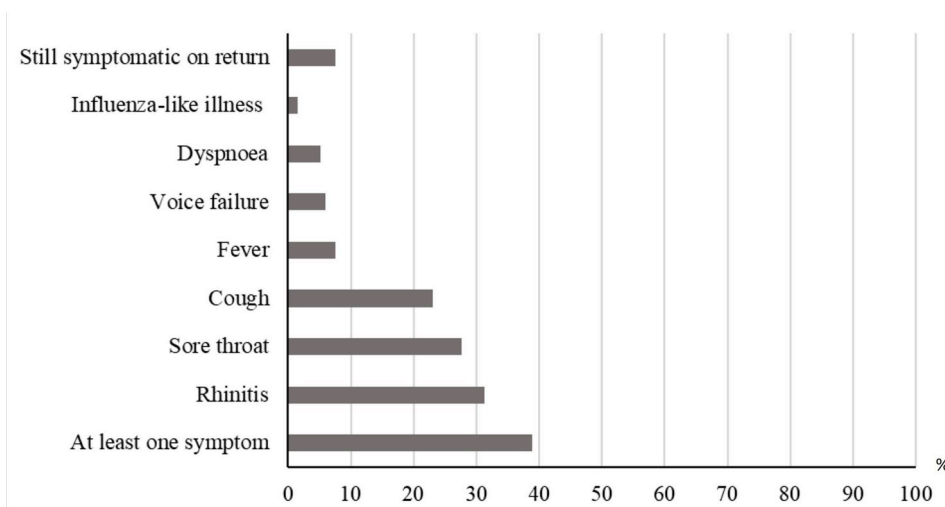


Fig. 1. Prevalence of respiratory symptoms (%).

all during travel and just one following return. The mean time between arrival at the travel destination and the onset of symptoms was 16.4 days ± 1.3 days. Abdominal pain and diarrhoea were the most frequent symptoms with prevalence of 53.7% and 52.2%, respectively, followed by nausea (29.1%) and constipation (20.9%). Only four students (3.0%) received antibiotics for gastrointestinal symptoms. 7.5% of participants were still symptomatic on returning to Marseille, France (Fig. 2).

A total of 117 (87.3%) participants provided paired rectal swabs. Only two students (1.6%) acquired a virus (adenovirus). Bacterial acquisition rates were higher, notably for EAEC (53.0%) and EPEC (41.0%). Additionally, 4.3% individuals acquired *C. jejuni* and 2.6% *G. lamblia* (Table 4).

5.2.3. Vaginal infections

Of the 101 female students, five (5.0%) reported vaginal symptoms such as leucorrhoea, during their stay, of whom one took antibiotics for this purpose. Two students (2%) were still symptomatic on returning to France.

Table 3
Prevalence of respiratory pathogens.

Variables	Before travel		After travel		Acquisition		p*
	n = 120	%	n = 120	%	n = 120	%	
Viruses							
Adenovirus	1	0.8	0	0	0	0	0.32
Coronaviruses	0	0	2	1.7	2	1.7	0.16
Coronavirus HKU1	0	0	2	1.7	2	1.7	0.16
Coronavirus 229E	0	0	0	0	0	0	NA
Coronavirus NL63	0	0	0	0	0	0	NA
Coronavirus OC43	0	0	0	0	0	0	NA
Influenza A	0	0	0	0	0	0	NA
Influenza B	0	0	0	0	0	0	NA
Metapneumovirus	0	0	0	0	0	0	NA
Parainfluenza virus	0	0	0	0	0	0	NA
Respiratory syncytial virus	0	0	2	1.7	2	1.7	0.16
Rhinovirus	4	3.3	10	8.3	8	6.7	0.06
At least one virus	5	4.2	13	10.8	11	9.2	0.03
Bacteria							
<i>Haemophilus influenzae</i>	78	65.0	76	63.3	18	15.0	0.75
<i>Klebsiella pneumoniae</i>	15	12.5	21	17.5	15	12.5	0.22
<i>Staphylococcus aureus</i>	39	32.5	33	27.5	11	9.2	0.26
<i>Streptococcus pneumoniae</i>	3	2.5	9	7.5	9	7.5	0.08
<i>Streptococcus pyogenes</i>	1	0.8	5	4.2	4	3.3	0.05
At least one bacterium	93	77.5	93	77.5	18	15.0	1.0

* p-value: before versus after travel, McNemar's test.

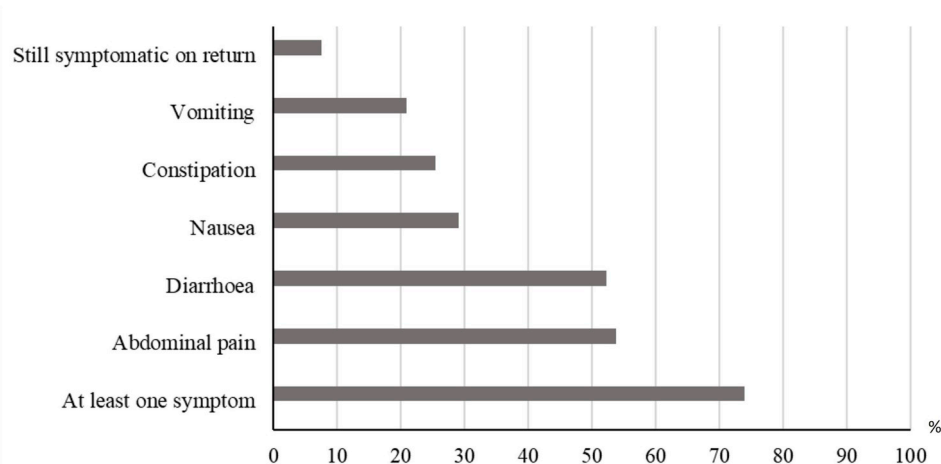


Fig. 2. Prevalence of clinical gastrointestinal symptoms (%).

diarrhoea and the prevalence of gastrointestinal pathogens upon return (Supplementary Table S4). Of the five students who reported vaginal symptoms, only one was positive for *A. vaginae* and *G. vaginalis* on return but did not have molecular criteria for bacterial vaginosis.

6. Discussion

In 2018, 60% of second year medical students in France were females [22]. According to data of the Aix Marseille Faculty of Medicine, 247 (60.1%) and 242 (62.1%) of the students were females in the second and fourth year respectively, in 2018. In our study, female students accounted for 101 (74.6%) of participants, which is consistent with previous studies showing that more females participate in study abroad programmes than males [7,8] while the proportion of female among students who did not participate to elective abroad was 58.2%. Given the young age of the participants, the prevalence of chronic diseases was low. The duration of the stays abroad was in the same range as that in other recent studies conducted on medical students [7,8]. The most frequent destinations were developing countries including Vietnam, India and Peru and most students took part in long-term humanitarian missions, including in relatively remote areas with poor sanitary conditions, being immersed in local population and in frequent contact with children and animals.

Table 4

Prevalence of gastrointestinal pathogens.

Pathogens	Before travel		After travel		Acquisition		p*
	N = 125	%	N = 126	%	N = 117	%	
Viruses							
Adenovirus	0	0	2	1.6	2	1.7	0.16
Astrovirus	0	0	0	0	0	0	NA
Norovirus	0	0	0	0	0	0	NA
Rotavirus	0	0	0	0	0	0	NA
Bacteria							
<i>Campylobacter jejuni</i>	2	1.6	5	4.0	5	4.3	0.26
Enteraggregative <i>Escherichia coli</i>	5	4.0	68	54.0	62	53.0	< 0.0001
Enterohemorrhagic <i>E. coli</i>	3	2.4	3	2.4	1	0.9	0.32
Enteropathogenic <i>E. coli</i>	24	19.2	63	50.0	48	41.0	< 0.0001
<i>Salmonella</i> spp	0	0	3	2.4	3	2.6	0.08
<i>Shigella</i> spp/EIEC	0	0	4	3.2	4	3.4	0.05
<i>Tropheryma whipplei</i>	1	0.8	1	0.8	0	0	NA
Parasites							
<i>Cryptosporidium parvum/hominis</i>	0	0	0	0	0	0	NA
<i>Entamoeba histolytica</i>	0	0	0	0	0	0	NA
<i>Giardia lamblia</i>	0	0	3	2.4	3	2.6	0.32
At least one pathogen	33	26.4	98	77.8	65	55.6	< 0.0001

* p-value: before versus after travel, McNemar's test.

Table 5

Prevalence of vaginal microorganisms.

Microorganisms	Before travel N = 93 (%)	After travel N = 99 (%)	Acquisition N = 91 (%)	p *
Bacteria				
<i>Atopobium vaginae</i>	20 (21.5)	23 (23.2)	13 (14.3)	0.68
<i>Atopobium vaginae</i> (CT < 21)	0	1 (1.0)	1 (1.1)	NA
<i>Chlamydia trachomatis</i>	1 (1.1)	1 (1.0)	1 (1.1)	1.0
<i>Gardnerella vaginalis</i>	30 (32.3)	27 (27.3)	7 (7.7)	0.25
<i>Gardnerella vaginalis</i> (CT < 18)	0	5 (5.1)	5 (4.4)	NA
<i>Mycoplasma genitalium</i>	0	0	0	NA
<i>Mycoplasma hominis</i>	2 (2.2)	2 (2.1)	1 (1.1)	1.0
<i>Neisseria gonorrhoeae</i>	0	0	0	NA
Parasites				
<i>Trichomonas vaginalis</i>	0	0	0	NA
At least one pathogen	47 (50.5)	45 (45.5)	11 (12.1)	0.34

* p-value: before versus after travel, McNemar's test.

More than seven students out of ten reported gastrointestinal symptoms (notably diarrhoea, abdominal pain and nausea-vomiting which is suggestive of gastroenteritis). This result is in line with other studies conducted on medical students abroad, confirming that despite

reinforced pre-travel advice, travellers' diarrhoea was highly frequent among medical students who were fully aware of the means of preventing it [6–8]. In a large five-year study conducted among European travellers, pre-travel advice was not associated with lower rates of traveller's diarrhoea, suggesting that current preventive strategies should be revised [23]. We observed a low rate of EAEC (4.0%) but a relatively high rate of EPEC (19.2%) carriage in asymptomatic students before travel, in marked contrast with recent findings describing rates of 1–2% in pre-travel stools of Finish travellers using a validated qPCR multiplex assay [24]. High rates of both EAEC (17.5%) and EPEC (14.0%) were also observed in asymptomatic Hajj pilgrims departing from Marseille to Saudi Arabia [25]. Such high rates of EPEC in both asymptomatic medical students and an older Muslim population from Marseille at baseline warrants further investigation in different populations, to better understand the local epidemiology of EPEC in southern France. Nevertheless, we documented a dramatically high acquisition rate of EAEC (53.0%) and EPEC (41.0%) among medical students, as documented in other recent studies conducted in different populations of international travellers [25–31]. This acquisition of *E. coli* is worrying and deserves further investigation aimed at evaluating antibiotic resistance in these bacteria, since one study conducted in medical students revealed a 35% acquisition rate of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* [8]. We found no significant association between diarrhoea and *E. coli* carriage in our study, in contrast with other studies where EAEC has been reported to be frequently associated with diarrhoea in travellers returning from various geographical areas [25–29]. This may be explained either by asymptomatic colonisation or by prolonged nucleic acid shedding in the absence of viable pathogens. Also, the onset of gastro-intestinal symptoms occurred early during the trip, while sampling was performed on return, several weeks later. Sampling at the time of the onset of symptoms should be performed in future studies.

Respiratory symptoms (mostly rhinitis and pharyngitis) affected 38.8% of medical students, compared with 11–12.5% in other studies conducted on medical students [6,7] and 28% in a cohort of Australian travellers returning from Asia (mostly tourists) [32]. The higher rate of respiratory symptoms in our study may have resulted from the frequent contact which students had with children. We found a significant association between viral carriage on return and persisting respiratory symptoms, while no association was found with bacterial carriage, suggesting that most respiratory infections were indeed due to viruses. The most common virus acquired was human rhinovirus (6.7%) while the influenza virus was not detected. Studies conducted among ill international travellers to tropical and sub-tropical areas suffering respiratory tract infection symptoms in association with fever showed that influenza viruses were isolated in 14.2–24.7% of cases [33,34]. The small number of patients with febrile respiratory tract infections in our cohort is a likely explanation for the lack of detection of the influenza virus.

In our results, a total of 10 (9.4%) female students reported vaginal symptoms or acquired bacterial vaginosis based on molecular quantification criteria during their stay. The acquisition of *A. vaginalis* and *G. vaginalis* was detected in 14.3% and 7.7% of female students, respectively. To our knowledge, there have been no previous studies addressing the prevalence of *A. vaginalis* and *G. vaginalis* in international travellers. Our results suggest that international travel may be associated with changes in vaginal microbiota leading, in some cases, to clinical symptoms or the acquisition of bacterial vaginosis, which may be asymptomatic, and which warrants further investigation in larger numbers of travellers.

Our study has some limitations including its monocentric design and its small sample size. Nevertheless, this preliminary study demonstrates that besides the well known risk of gastrointestinal and respiratory infections and changes in intestinal and respiratory microbiota, medical students abroad (and most likely other international travellers) may also experience changes in vaginal microbiota and vaginal symptoms

which opens up a new research area in travel medicine. Further studies including larger numbers of students are needed to investigate the potential risk factors for clinical infections and modifications of microbiota. Despite students were asked for other symptoms overall, we cannot exclude that some symptoms were not reported, notably sexually transmitted infection or blood-borne infection symptoms. Also, we did not ask students for sexual contacts whilst overseas. It should be noted that non-infectious disease risk were not addressed in this study. Finally, the sample size was too small to address the potential effect of destination on symptoms and changes in microbiota.

The trend towards studying abroad fosters intercultural exchanges. However, students have a higher exposure to infectious diseases. Although most of their respiratory and gastrointestinal symptoms were self-limiting, 7.5% of students still had symptoms on return, which could be a source of infection for their family members and patients.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tmaid.2019.101548>.

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