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Spectrum of Imported Infectious Diseases: A Comparative Prevalence Study of 16,817 German Travelers and 977 Immigrants from the Tropics and Subtropics

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Abstract. The aim of this study was to assess the spectrum of imported infectious diseases (IDs) among patients consulting the University of Munich, Germany, between 1999 and 2014 after being in the sub-/tropics. The analysis investigated complete data sets of 16,817 diseased German travelers (2,318 business travelers, 4,029 all-inclusive travelers, and 10,470 backpackers) returning from Latin America (3,225), Africa (4,865), or Asia (8,727), and 977 diseased immigrants, originating from the same regions (112, 654 and 211 respectively). The most frequent symptoms assessed were diarrhea (38%), fever (29%), and skin disorder (22%). The most frequent IDs detected were intestinal infections with species of *Blastocystis* (900), *Giardia* (730), *Campylobacter* (556), *Shigella* (209), and *Salmonella* (183). Also frequently observed were cutaneous larva migrans (379), dengue (257), and malaria (160). The number of IDs with significantly elevated proportions was higher among backpackers (18) and immigrants (17), especially among those from Africa (18) and Asia (17), whereas it was lower for business travelers (5), all-inclusive travelers (1), and those from Latin America (5). This study demonstrates a large spectrum of imported IDs among returning German travelers and immigrants, which varies greatly based not only on travel destination and origin of immigrants, but also on type of travel.

INTRODUCTION

The number of international travels worldwide has increased from 25 million in 1950 to 626 million in 1999, and to 1,133 million in 2014. In addition to the traditional favorite destinations of Europe and North America, many new destinations have emerged, especially in subtropical and tropical countries.[1] In 2014, about 18.2 million individuals traveled from Germany to destinations outside of Europe. Out of them, 1.5 million traveled to Latin America, 2.8 million to Africa, and 7.8 million to Asia.[2]

Beside the growth of international travelers, the global number of immigrants (including migrant workers and forcibly displaced persons) is constantly increasing. The global number of international migrant workers was 179 million in 1999 and 232 million in 2014.[3] According to United Nations High Commissioner of Refugees, in 1999, 37 million individuals were forcibly displaced, whereas this number increased to approximately 60 million in 2014. Among them, it is estimated that 19.5 million are refugees and another 1.8 million are asylum seekers. In 2013, Germany became the country hosting the highest absolute number of asylum seekers, with over 173,000 new asylum applications registered in 2014.[4]

The increasing number of international travelers and immigrants has, and continues, to lead to new health challenges, especially in terms of infectious diseases (IDs).[5] Growing mobility means there is an increased potential of travelers acquiring IDs and importing these "exotic" diseases to their home countries, especially those traveling to sub-/tropical regions.[6] As IDs are becoming a more prominent global issue,[7] a broader differential diagnostic thinking is paramount for assessing returning travelers.[8]

In recent years, various publications have shown that international travelers and immigrants enlarge the spectrum of imported IDs. Studies performed by GeoSentinel Surveillance analyzed large samples of more than 7,600 migrants and 82,800 travelers, with data collected from more than 40 sites on six continents, although none of these studies compared imported IDs among travelers and immigrants with a sample size as large as this study.[9–14] EuroTravNet is a European network that has collected data from more than 15 European sites and published studies with sample sizes of up to more than 900 migrants and 32,000 travelers.[15–17] As multicenter studies, these networks analyzed data of a highly heterogeneous international population, and consequently the comparability between the different study groups, such as type of travel or immigrants, was limited. Furthermore, the data presented in these studies were highly descriptive.

In these studies it was shown that a greater proportion of immigrants who had been visiting friends and relatives (VFRs), had serious, potentially preventable travel-related illnesses when compared with tourists. They also showed that migrant patients have acute illnesses or chronic conditions related to exposure in their country of origin.[9,10] Several studies have shown that the most prevalent symptoms among travelers and immigrants were diarrhea, fever, and skin disorders.[6,11,18–20] In some studies that compared travelers with immigrants whose purpose of travel was VFR, the risk of acute diarrhea was higher among travelers, whereas the risk for malaria and viral hepatitis was higher among VFRs.[21]

The findings mentioned above were considered when patients consulted the Department of Infectious Diseases and Tropical Medicine (DITM) of the University of Munich, Germany. The results of these consultations showing the spectrum of imported IDs were published recently.[22–27] The aim of the present cross-sectional study was to evaluate differences in the spectrum of imported IDs 1) between German travelers returning from the sub-/tropics and immigrants originating from the sub-/tropics; 2) between different sub-/tropical travel destinations and origins of immigrants, respectively, divided into Latin America, Africa, and Asia; and 3) between the different types of German travelers, differentiated into business travelers, all-inclusive travelers, and backpackers. The study was performed using the data from a large number of patients who consulted the University of Munich,

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Germany, between 1999 and 2014 after being in the sub-/tropics. All 17,794 patients were diagnosed and treated at a single study site. Consequently, all patients were subject of the same standardized process, allowing for maximal comparability of the data between the study groups.

MATERIALS AND METHODS

Database. A database from the DITM has been collecting data on sociodemographics (sex, age, origin, and profession), travel (duration of travel, destination, and type of travel), clinical history and symptoms, diagnostics, and—if applicable—diagnosis of individuals consulting its outpatient department for treatment or medical checkup. From January 1999 through December 2014, the database registered 38,059 individuals with complete data sets. Out of them, 22,588 (59.35%) individuals had symptoms after traveling to the sub-/tropics (Latin America, Africa, or Asia), 7,514 (19.74%) individuals did not have symptoms and had not recently traveled to the sub-/tropics, 4,810 (12.64%) individuals had symptoms but had not recently traveled to the sub-/tropics, and 3,147 (8.27%) individuals did not have symptoms after traveling in the sub-/tropics. The symptoms presented here are those from patients' first consultation at DITM after being in the sub-/tropics.

Study design. In this study, all patients consulted the DITM, at which time the data of the independent variables (exposure as sociodemographics and travel) and dependent variables (outcomes as symptoms, diagnostics, and diagnosis) were assessed simultaneously: transversal study or cross-sectional study. The independent variables were not influenced by the study design: noninterventional or observant study. The results of the study were presented in terms of prevalences of imported IDs among different study groups: prevalence study.

Study groups of German travelers. Of the 22,588 patients returning from traveling in the sub-/tropics, 19,581 (86.69%) were of German origin (defined as born in Germany). Among them, 2,318 (11.84%) were business travelers (defined as such who were primarily on travel because of business or related issues), 4,029 (20.58%) were all-inclusive travelers (defined as such whose travel was not organized by themselves including package holiday), and 10,470 (53.47%) were backpackers (including low-budget and adventure travelers). The remaining 2,764 (14.12%) patients comprised a miscellaneous group of students, scientists, missionaries, volunteers, and other persons with activities during travel not being clearly defined. Of these 2,318 business travelers (BU), 388 (16.74%) had traveled to Latin America (BU-LA), 848 (36.58%) to Africa (BU-AF), and 1,082 (46.68%) to Asia (BU-AS). Of the 4,029 all-inclusive travelers (AL), 799 (19.33%) had traveled to Latin America (AL-LA), 1,567 (38.89%) to Africa (AL-AF), and 1,683 (41.77%) to Asia (AL-AS). Of the 10,470 backpackers (BA), 2,058 (19.66%) had traveled to Latin America (BA-LA), 2,450 (23.40%) to Africa (BA-AF), and 5,962 (56.94%) to Asia (BA-AS). These nine groups (BU-LA, BU-AF, BU-AS, AL-LA, AL-AF, AL-AS, BA-LA, BA-AF, and BA-AS) were defined as study groups, comprising altogether 16,817 diseased German travelers returning from the sub-/tropics (Table 1).

Study groups of immigrants. The term "immigrant" in this study refers to persons VFRs and forcibly displaced persons (including asylum seekers) of non-German origin (defined as born outside of Germany) and their family members. Of the 22,588 patients returning from the sub-/tropics, 3,007 (13.31%) patients were diseased immigrants, including 842 (3.73%) patients of African origin, 830 (3.67%) of West-European origin, 511 (2.26%) of East-European origin, 421 (1.86%) of Asian origin, and 233 (1.03%) of Latin American origin, 146 (0.65%) from United States or Canada, and 24 (0.11%) from Oceania. Of the 233 patients of Latin American (LA) origin, 112 (48.07%) had traveled from Latin America as immigrants to Germany (IM-LA), while of the 842 patients of African (AF) origin, 654 (77.67%) had traveled from Africa as immigrants to Germany (IM-AF), and of the 421 patients of Asian (AS) origin, 211 (50.12%) had traveled from Asia as immigrants to Germany (IM-AS). These three groups (IM-LA, IM-AF, and IM-AS) comprised altogether 977 diseased immigrants originating from the sub-/tropics (Table 1).

Study population and IDs. The study population comprised 17,794 patients: 16,817 diseased German travelers returning from the sub-/tropics (divided into nine study groups) and 977 diseased immigrants originating from the sub-/tropics (divided into three study groups). The study identified 36 imported IDs which had a sample size of > 10 cases: eight viral, eight bacterial, nine protozoal, seven helminthic, and four ectoparasitic IDs. These 36 IDs comprised 4,198 laboratory-confirmed cases with complete data sets. Only exact laboratory-confirmed IDs were considered in this study. Clinically suspected or probable cases were not included.

Data analysis. The database of the DITM was the source of all data analyzed in this study. The descriptive analysis was performed by Excel Worksheet (Microsoft, Redmond, WA). The aim of this study was to evaluate associations between the 12 different study groups (independent variable) and the risk for any imported ID (dependent variable). Bivariate approximative test (χ^2 test) and exact test (Fisher's test) were conducted using EpiInfo, version 3.3.2 (Centers for Disease Control and Prevention, Atlanta, GA) and Stata software, version 9.0 (Stata Corporation, College Station, TX) for comparing the proportion of any variables in a certain study group with the overall proportion of the same variable: comparative prevalence study. Significant differences were defined as $P < 0.05$.

Ethical considerations. Ethical clearance for the study protocol was provided by the Ethical Committee of the Medical Faculty at the University of Munich, Germany. Clinical and laboratory data were used only from patients who provided written informed consent, or in the case of minors, had a general written informed consent from the legal caretakers.

RESULTS

Sociodemographic data. Data from 17,794 patients fulfilled the inclusion criteria and were therefore included in this study (study population). Of them, 9,114 (51.2%) were female, whereas this proportion differed significantly in 12 study groups. The proportion of females was significantly higher among all-inclusive travelers (AL-LA: 57.3%, $P < 0.01$; AL-AF: 58.5%, $P < 0.01$; AL-AS: 56.5%, $P < 0.01$), among IM-LA (68.8%, $P < 0.01$), and among BA-AS (53.6%, $P < 0.01$).

The age range was 4 months to 91 years, with a median of 35.0 years, and an interquartile range (IQR) of 27.7–46.9 years. In all three regions, the study groups with the highest median

TABLE 1

Spectrum of imported IDs among diseased German travelers (business travelers, all-inclusive travelers, and backpackers) after returning from the sub-/tropics, and among diseased immigrants originally from these regions

Destination/home region	LA				AF				AS				All
Sample size	3,337				5,519				8,938				17,794
Proportion (%)	18.75				31.02				50.23				100
Origin (place of birth)		Germany		LA		Germany		AF		Germany		AS	All
Sample size		3,225		112		4,865		654		8,727		211	17,794
Proportion (%)		18.12		0.63		27.34		3.68		49.04		1.19	100
Type of travel/immigrant	BU	AL	BA	IM	BU	AL	BA	IM	BU	AL	BA	IM	All
Study groups: 12	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	All
Sample size	388	779	2,058	112	848	1,567	2,450	654	1,082	1,683	5,962	211	17,794
Proportion (%)	2.18	4.38	11.57	0.63	4.77	8.81	13.77	3.68	6.08	9.46	33.51	1.19	100
%	100	100	100	100	100	100	100	100	100	100	100	100	100
Demographic data													
Sex: female	174	446	1,072	77	334	916	1,276	213	373	951	3,195	87	9,114
%	44.85	57.25	52.09	68.75	39.39	58.46	52.08	32.57	34.47	56.51	53.59	41.23	51.22
P value	0.01*	< 0.01*	0.40	< 0.01*	< 0.01*	< 0.01*	0.36	< 0.01*	< 0.01*	< 0.01*	< 0.01*	< 0.01*	NA
Age: median (years)	36.00	36.32	31.48	34.58	38.54	40.07	35.09	37.00	39.75	42.78	32.02	38.92	35.00
Interquartile range	29.05; 46.72	28.57; 49.56	25.84; 41.11	27.18; 43.03	31.03; 48.59	30.39; 55.34	27.63; 47.33	29.49; 43.62	32.19; 49.51	31.23; 56.33	26.44; 42.46	29.08; 47.01	27.70; 46.94
Travel data													
Duration: median (days)	21	14	28	NA	21	14	21	NA	18.5	14	25	NA	21
Interquartile range	7; 90	14; 21	17; 49		10; 120	10; 15	14; 28		7; 60	14; 21	21; 35		14; 30
Symptoms													
Diarrhea	138	268	813	34	317	683	924	103	484	577	2,436	45	6,822
%	35.57	34.40	39.50	30.36	37.38	43.59	37.71	15.75	44.73	34.28	40.86	21.33	38.34
P value	0.26	0.02*	0.25	0.08	0.56	< 0.01*	0.49	< 0.01*	< 0.01*	< 0.01*	< 0.01*	< 0.01*	NA
Fever	102	197	447	21	258	421	814	299	313	494	1,624	81	5,071
%	26.29	25.29	21.72	18.75	30.42	26.87	33.22	45.72	28.93	29.35	27.24	38.39	28.50
P value	0.33	0.042*	< 0.01*	0.02*	0.20	0.13	< 0.01*	< 0.01*	0.75	0.41	< 0.01*	< 0.01*	NA
Skin disorders	86	184	563	33	136	309	498	96	179	426	1,373	49	3,932
%	22.16	23.62	27.36	29.46	16.04	19.72	20.33	14.68	16.54	25.31	23.03	23.22	22.10
P value	0.97	0.29	< 0.01*	0.06	< 0.01*	0.02*	0.02*	< 0.01*	< 0.01*	< 0.01*	0.03*	0.69	NA
Nausea	65	141	336	19	132	315	456	84	197	282	1,148	19	3,194
%	16.75	18.10	16.33	16.96	15.57	20.10	18.61	12.84	18.21	16.76	19.26	9.00	17.95
P value	0.53	0.91	0.04*	0.79	0.06	0.02*	0.36	< 0.01*	0.82	0.18	< 0.01*	< 0.01*	NA
Arthralgia	42	103	222	21	93	165	272	108	147	219	670	40	2,102
%	10.82	13.22	10.79	18.75	10.97	10.53	11.10	16.51	13.59	13.01	11.24	18.96	11.81
P value	0.054	0.21	0.13	0.02*	0.43	0.10	0.24	< 0.01*	0.06	0.11	0.09	< 0.01*	NA
Viral IDs (8)	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	ALL
Dengue fever	7	9	32	2	3	2	4	3	19	33	136	7	257
%	1.80	1.16	1.55	1.79	0.35	0.13	0.16	0.46	1.76	1.96	2.28	3.32	1.44
P value	0.55	0.49	0.65	0.68†	< 0.01*	< 0.01*	< 0.01*	0.03*	0.38	0.06	< 0.01*	0.02*	NA
Mononucleosis	2	0	5	1	1	2	9	0	5	1	24	0	50
%	0.52	0	0.24	0.89	0.12	0.13	0.37	0	0.46	0.06	0.40	0	0.28
P value	0.30†	0.18†	0.73	0.27†	0.73†	0.32†	0.38	0.26†	0.23†	0.09†	0.03*	1.00†	NA
HIV infection	1	0	1	1	2	2	1	10	3	1	8	0	30
%	0.26	0	0.05	0.89	0.24	0.13	0.04	1.53	0.28	0.06	0.13	0	0.17
P value	0.48†	0.64†	0.25†	0.17†	0.65†	1.00†	0.11†	< 0.01†*	0.43†	0.36†	0.43	1.00†	NA
Cytomegalovirus infection	4	1	3	1	0	4	2	0	4	2	5	0	26
%	1.03	0.13	0.15	0.89	0	0.26	0.08	0	0.37	0.12	0.08	0	0.15
P value	< 0.01†*	1.00†	1.00†	0.15†	0.63†	0.28†	0.57†	1.00†	0.07†	1.00†	0.12	1.00†	NA

(continued)

TABLE 1
Continued

Destination/home region	LA				AF				AS				All
Herpes simplex	0	0	2	0	0	4	0	2	1	3	7	0	19
%	0	0	0.10	0	0	0.26	0	0.31	0.09	0.18	0.12	0	0.11
P value	1.00†	1.00†	1.00†	1.00†	1.00†	0.08†	0.10†	0.15†	1.00†	0.42†	0.76	1.00†	NA
Chronic hepatitis C	1	0	2	0	0	0	1	3	0	1	10	0	18
%	0.26	0	0.10	0	0	0	0.04	0.46	0	0.06	0.17	0	0.10
P value	0.33†	1.00†	1.00†	1.00†	1.00†	0.40†	0.50†	0.03†*	0.62†	1.00†	0.047*	1.00†	NA
Chikungunya	1	2	1	2	1	2	1	0	2	3	3	0	18
%	0.26	0.26	0.05	1.79	0.12	0.13	0.04	0	0.18	0.18	0.05	0	0.10
P value	0.33†	0.19†	0.71†	< 0.01†*	0.59†	0.67†	0.50†	1.00†	0.30†	0.24†	0.13	1.00†	NA
Herpes zoster	1	0	1	0	2	2	2	0	3	2	3	0	16
%	0.26	0	0.05	0	0.24	0.13	0.08	0	0.28	0.12	0.05	0	0.09
P value	0.30†	1.00†	1.00†	1.00†	0.18†	0.65†	1.00†	1.00†	0.07†	0.66†	0.21	1.00†	NA
Bacterial IDs (8)	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	ALL
Campylobacter spp. infection	4	11	44	1	21	22	62	5	37	47	300	2	556
%	1.03	1.41	2.14	0.89	2.48	1.40	2.53	0.76	3.42	2.79	5.03	0.95	3.12
P value	0.02*	< 0.01*	< 0.01*	0.27†	0.31	< 0.01*	0.08	< 0.01*	0.57	0.41	< 0.01*	0.07	NA
Shigellosis	3	7	23	1	14	16	29	5	17	12	81	1	209
%	0.77	0.90	1.12	0.89	1.65	1.02	1.18	0.76	1.57	0.71	1.36	0.47	1.17
P value	0.63†	0.46	0.79	1.00†	0.19	0.55	0.96	0.32	0.21	0.06	0.11	0.52†	NA
Salmonellosis	1	11	10	0	8	17	24	3	16	18	71	4	183
%	0.26	1.41	0.49	0	0.94	1.08	0.98	0.46	1.48	1.07	1.19	1.90	1.03
P value	0.20†	0.28	< 0.01*	0.63†	0.80	0.82	0.80	0.14	0.13	0.86	0.13	0.17†	NA
Rickettsiosis	0	0	0	0	4	18	60	1	1	0	3	0	87
%	0	0	0	0	0.47	1.15	2.45	0.15	0.09	0	0.05	0	0.49
P value	0.27†	0.03†*	< 0.01*	1.00†	1.00†	< 0.01*	< 0.01*	0.38†	0.054	< 0.01*	< 0.01*	0.63†	NA
Typhoid fever	0	0	0	0	0	0	2	1	1	1	10	0	15
%	0	0	0	0	0	0	0.08	0.15	0.09	0.06	0.17	0	0.08
P value	1.00†	1.00†	0.24†	1.00†	1.00†	0.64†	1.00†	0.43†	0.61†	1.00†	< 0.01*	1.00†	NA
Paratyphoid fever	0	0	0	0	0	0	0	0	1	0	9	1	11
%	0	0	0	0	0	0	0	0	0.09	0	0.15	0.47	0.06
P value	1.00†	1.00†	0.63†	1.00†	1.00†	0.61†	0.38†	1.00†	0.50†	0.62†	< 0.01†*	0.12†	NA
Syphilis	0	0	0	0	1	0	1	4	2	1	1	1	11
%	0	0	0	0	0.12	0	0.04	0.61	0.18	0.06	0.02	0.47	0.06
P value	1.00†	1.00†	0.63†	1.00†	0.42†	0.61†	1.00†	< 0.01†*	0.14†	1.00†	0.11†	0.12†	NA
Tuberculosis	0	0	0	1	0	0	0	4	0	0	2	4	11
%	0	0	0	0.89	0	0	0	0.61	0	0	0.03	1.90	0.06
P value	1.00†	1.00†	0.63†	0.07†	1.00†	0.61†	0.38†	< 0.01†	1.00†	0.62†	0.24†	< 0.01†	NA
Protozoal IDs (9)	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	ALL
Blastocystis hominis infection	18	22	92	6	58	72	103	32	48	73	368	8	900
%	4.64	2.82	4.47	5.36	6.84	4.59	4.20	4.89	4.44	4.34	6.17	3.79	5.06
P value	0.70	< 0.01*	0.20	0.88	0.02*	0.38	0.04*	0.84	0.34	0.16	< 0.01*	0.40	NA
Giardiasis	5	18	81	2	22	31	77	17	41	40	392	4	730
%	0.88	2.18	3.60	1.61	1.88	1.87	2.71	2.22	2.86	2.24	6.10	1.74	3.64
P value	< 0.01*	< 0.01*	0.69	0.33†	0.02*	< 0.01*	< 0.01*	0.048*	0.59	< 0.01*	< 0.01*	0.10	NA
Malaria	2	3	2	0	20	8	38	68	2	0	13	4	160
%	0.52	0.39	0.10	0	2.36	0.51	1.55	10.40	0.18	0	0.22	1.90	0.90
P value	0.59†	0.12	< 0.01*	0.63	< 0.01*	0.09	< 0.01*	< 0.01*	0.01*	< 0.01*	< 0.01*	0.12†	NA
Entamoeba spp. infection	3	2	14	0	10	6	14	9	11	11	50	0	130
%	0.77	0.26	0.68	0	1.18	0.38	0.57	1.38	1.02	0.65	0.84	0	0.73
P value	0.76†	0.11	0.78	1.00†	0.12	0.09	0.32	0.048*	0.25	0.70	0.23	0.41†	NA

(continued)

TABLE 1
Continued

Destination/home region	LA				AF				AS				All
Cryptosporidiosis	1	1	10	0	2	4	4	1	0	1	29	0	53
%	0.26	0.13	0.49	0	0.24	0.26	0.16	0.15	0	0.06	0.49	0	0.30
P value	1.00†	0.73†	0.10	1.00†	1.00†	1.00†	0.19	1.00†	0.08†	0.06	< 0.01*	1.00†	NA
Cyclosporiasis	2	2	7	0	0	0	0	0	5	5	16	0	37
%	0.52	0.26	0.34	0	0	0	0	0	0.46	0.30	0.27	0	0.21
P value	0.19†	0.68†	0.19†	1.00†	0.42†	0.07†	0.01*	0.65†	0.07†	0.39	0.21	1.00†	NA
Cutaneous leishmaniasis	3	0	4	0	2	0	4	0	3	1	3	2	22
%	0.77	0	0.19	0	0.24	0	0.16	0	0.28	0.06	0.05	0.95	0.12
P value	0.01†*	0.62†	0.31†	1.00†	0.28†	0.25†	0.53†	1.0†	0.15†	0.72†	0.048*	0.03†*	NA
Dientamoeba fragilis infection	0	1	1	0	0	2	1	0	3	2	7	1	18
%	0	0.13	0.05	0	0	0.13	0.04	0	0.28	0.12	0.12	0.47	0.10
P value	1.00†	0.55†	0.71†	1.00†	1.00†	0.67†	0.50†	1.00†	0.09†	0.69†	0.63	0.19†	NA
Trichomoniasis	0	1	3	0	2	1	1	0	1	1	4	0	14
%	0	0.13	0.15	0	0.24	0.06	0.04	0	0.09	0.06	0.07	0	0.08
P value	1.00†	0.47†	0.21†	1.00†	0.14†	1.00†	0.71†	1.00†	0.58†	1.00†	0.79†	1.00†	NA
Helminthic IDs (7)	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	ALL
Cutaneous larva migrans	2	22	81	2	6	18	27	3	7	46	165	0	379
%	0.52	2.82	3.94	1.79	0.71	1.15	1.10	0.46	0.65	2.73	2.77	0	2.13
P value	0.03*	0.17	< 0.01*	1.00†	< 0.01*	< 0.01*	< 0.01*	< 0.01*	< 0.01*	0.07	< 0.01*	0.03†*	NA
Schistosomiasis	0	1	3	0	9	0	18	28	0	0	7	0	66
%	0	0.13	0.15	0	1.06	0	0.73	4.28	0	0	0.12	0	0.37
P value	0.41†	0.37†	0.07	1.00†	< 0.01†*	0.01*	< 0.01*	< 0.01†*	0.03†*	< 0.01*	< 0.01*	1.00†	NA
Hookworm (*Necator* and *Ancylostoma* spp.) infection	0	0	7	0	1	0	4	4	0	0	7	0	23
%	0	0	0.34	0	0.12	0	0.16	0.61	0	0	0.12	0	0.13
P value	1.00†	0.62†	< 0.01*	1.00†	1.00†	0.26†	0.55†	< 0.01†*	0.40†	0.16†	0.75	1.00†	NA
Acariasis	0	0	3	0	0	0	3	4	1	0	8	3	22
%	0	0	0.15	0	0	0	0.12	0.61	0.09	0	0.13	1.42	0.12
P value	1.00†	0.62†	0.74†	1.00†	0.62†	0.25†	1.00†	< 0.01†*	1.00†	0.26†	0.78	< 0.01†*	NA
Trichuriasis	1	0	2	0	2	0	3	3	2	2	3	2	20
%	0.26	0	0.10	0	0.24	0	0.12	0.46	0.18	0.12	0.05	0.95	0.11
P value	0.36†	1.00†	1.00†	1.00†	0.25†	0.25†	0.75†	0.04†*	0.35†	0.71†	0.08	0.02†*	NA
Strongyloidiasis	0	0	1	0	0	0	2	9	0	0	2	0	14
%	0	0	0.05	0	0	0	0.08	1.38	0	0	0.03	0	0.08
P value	1.00†	1.00†	1.00†	1.00†	1.00†	0.63†	1.00†	< 0.01†*	1.00†	0.64†	0.16†	1.00†	NA
Oxyuriasis	0	0	0	0	2	3	1	0	2	0	4	1	13
%	0	0	0	0	0.24	0.19	0.04	0	0.18	0	0.07	0.47	0.07
P value	1.00†	1.00†	0.39†	1.00†	0.13†	0.10†	1.00†	1.00†	0.19†	0.63†	1.00†	0.14†	NA
Ectoparasitic IDs (4)	BU-LA	AL-LA	BA-LA	IM-LA	BU-AF	AL-AF	BA-AF	IM-AF	BU-AS	AL-AS	BA-AS	IM-AS	ALL
Myiasis	0	0	25	0	1	1	2	1	0	0	1	0	31
%	0	0	1.21	0	0.12	0.06	0.08	0.15	0	0	0.02	0	0.17
P value	1.00†	0.65†	< 0.01†*	1.00†	1.00†	0.52†	0.30†	1.00†	0.26†	0.11†	< 0.01*	1.00†	NA
Scabies	2	1	3	0	3	0	1	1	2	2	7	0	22
%	0.52	0.13	0.15	0	0.35	0	0.04	0.15	0.18	0.12	0.12	0	0.12
P value	0.08†	1.00†	0.74†	1.00†	0.08†	0.25†	0.35†	0.56†	0.39†	1.00†	0.87	1.00†	NA
Tungiasis	1	0	6	0	1	2	4	0	0	1	1	0	16
%	0.26	0	0.29	0	0.12	0.13	0.16	0	0	0.06	0.02	0	0.09
P value	0.30†	1.00†	< 0.01†*	1.00†	0.54†	0.65†	0.26†	1.00†	0.62†	1.00†	0.02*	1.00†	NA

(continued)

TABLE 1
Continued

Destination/home region	LA				AF				AS				All
Pediculosis/phthiriasis	1	0	5	0	0	0	0	1	1	3	0		11
%	0.26	0	0.24	0	0	0	0	0.09	0.06	0.05	0		0.06
P value	0.22†	1.00†	< 0.01†*	1.00†	1.00†	0.61†	0.38†	1.00†	0.50†	1.00†	0.76†	1.00†	NA
All cases of 36 IDs listed	66	115	474	20	198	239	505	221	241	311	1,763	45	4,198
%	17.01	14.76	23.03	17.86	23.35	15.25	20.61	33.79	22.27	18.48	29.57	21.33	23.59
P value	< 0.01*	< 0.01*	0.52	0.15	0.86	< 0.01*	< 0.01*	< 0.01*	0.29	< 0.01*	< 0.01*	0.49	NA
Number of IDs with significantly elevated proportions in any study group	2	0	5	1	3	1	3	11	0	0	10	5	41

AF = Africa; AL = all-inclusive traveler; AS = Asia; BA = backpacker; BU = business traveler; HIV = human immunodeficiency virus; ID = infectious disease; LA = Latin America; NA = not applicable.
* Significant differences were defined as $P < 0.05$.
† Fisher's exact χ^2 test.

age was that of all-inclusive travelers (LA: 36.3 years; AF: 40.1 years; AS: 42.8 years), followed by business travelers (LA: 36.0 years; AF: 38.5 years; AS: 39.8 years), immigrants (LA: 34.6 years; AF: 37.0 years; AS: 38.9 years), and the lowest age was that of backpackers (LA: 34.6 years; AF: 37.0 years; AS: 38.9 years) (Table 1).

Travel data. Among the 16,817 diseased German travelers returning from the sub-/tropics, the range of travel duration was 1 day to 35 years, with a median of 21 days, and an IQR of 14–30 days. In all three regions, the study groups with the highest median of travel duration were those of backpackers (LA: 28 days; AF: 21 days; AS: 25 days), followed by business travelers (LA: 21 days; AF: 21 days; AS: 18.5 days), and the lowest duration of travel was that of all-inclusive travelers (LA: 14 days; AF: 14 days; AS: 14 days) (Table 1).

Clinical data. In the database, 15 different symptoms were registered systematically. The most documented symptoms were diarrhea (38.3%), fever (28.5%), skin disorders (22.1%), nausea (18.0%), and arthralgia (11.8%). The proportion of patients with certain symptoms differed immensely: while diarrhea was significantly more frequent among AL-AF, BU-AS, and BA-AS, fever was significantly more frequent among BA-AF, IM-AF, and IM-AS. Overall, arthralgia was found significantly more frequently among immigrants (LA: 18.8%; AF: 16.5%; AS: 19.0%) (Table 1).

Frequently imported IDs. In the study population, 36 IDs were documented in more than 10 laboratory-confirmed cases. Among the 12 most frequent IDs, six were intestinal infections with *Blastocystis* (*N* = 900), *Giardia* (*N* = 730), *Campylobacter* (*N* = 556), *Shigella* (*N* = 209), *Salmonella* (*N* = 183), and *Entamoeba* (*N* = 130) spp. The remaining six frequently documented IDs were cutaneous larva migrans (*N* = 379), dengue fever (*N* = 257), malaria (*N* = 160), rickettsiosis (*N* = 87), schistosomiasis (*N* = 66), and cryptosporidiosis (*N* = 53) (Table 1).

Overview of data analysis. During the analysis of the data from 17,794 patients, 36 IDs were documented in more than 10 laboratory-confirmed cases, comprising a total of 4,198 (23.6%) cases. This proportion was significantly elevated among African immigrants (33.8%) and backpackers from Asia (29.6%), whereas it was significantly reduced among all three study groups of all-inclusive travelers (AL-LA: 14.8%; AL-AF: 15.3%; AL-AS: 18.5%), BU-LA (17.0%), and backpackers from Africa (20.6%) (Table 1).

The proportions of the 36 defined IDs were compared among the 12 different study groups. Of the 432 associations, 42 associations were found with significantly lower proportions of any of these 36 IDs in any of these 12 study groups, whereas 41 associations were found with significantly elevated proportions (Table 1). Concerning type of travel, the latter 41 associations were mostly found among backpackers (18), followed by immigrants (17), business travelers (5), and all-inclusive travelers (1). Concerning travel destination or home region, respectively, these 41 associations were mostly found among travelers or immigrants, arriving from Africa (18), followed by Asia (15) and LA (8) (Table 2).

Rarely imported IDs. Of the 38,059 individuals with complete data sets in the DITM database, more than 110 IDs were found to be associated (or at least suspected to be associated) with travel or migration from the sub-/tropics. Among them, 17,794 (46.75%) patients fulfilled the inclusion criteria (see above: Study population and IDs). In this study population,

TABLE 2

Overview of imported IDs with significantly elevated proportions among diseased German travelers (business travelers, all-inclusive travelers, and backpackers) after returning from the sub-/tropics, and among diseased immigrants originally from these regions

Destination/home region	Latin America				Africa				Asia			
Origin (place of birth)	Germany			Latin America	Germany			Africa	Germany			Asia
Type of travel/immigrant	Business traveler	All-inclusive traveler	Backpacker	Immigrant	Business traveler	All-inclusive traveler	Backpacker	Immigrant	Business traveler	All-inclusive traveler	Backpacker	Immigrant
ID (listed in order as in Table 1)	Cytomegalovirus infection	–	Cutaneous larva migrans	Chikungunya	*Blastocystis hominis* infection	Rickettsiosis	Rickettsiosis	HIV infection	–	–	Dengue fever	Dengue fever
	Cutaneous leishmaniasis	–	Hookworm (N. and A. spp.) infection	–	Malaria	–	Malaria	Chronic hepatitis C	–	–	Mononucleosis	Tuberculosis
	–	–	Myiasis	–	Schistosomiasis	–	Schistosomiasis	Syphilis	–	–	Chronic hepatitis C	Cutaneous leishmaniasis
	–	–	Tungiasis	–	–	–	–	Tuberculosis	–	–	*Campylobacter* spp. infection	Ascariasis
	–	–	Pediculosis/ phthiriasis	–	–	–	–	Malaria	–	–	Typhoid fever	Trichuriasis
	–	–	–	–	–	–	–	*Entamoeba* spp. infection	–	–	Paratyphoid fever	–
	–	–	–	–	–	–	–	Schistosomiasis	–	–	*Blastocystis hominis* infection	–
	–	–	–	–	–	–	–	Hookworm (N. and A. spp.) infection	–	–	Giardiasis	–
	–	–	–	–	–	–	–	Ascariasis	–	–	Cryptosporidiosis	–
	–	–	–	–	–	–	–	Trichuriasis	–	–	Cutaneous larva migrans	–
	–	–	–	–	–	–	–	Strongyloidiasis	–	–	–	–
Number of IDs with significantly elevated proportions in any study group	2	0	5	1	3	1	3	11	0	0	10	5
			8				18				15	

HIV = human immunodeficiency virus; ID = infectious disease; A. = *Ancylostoma*; N. = *Necator.*

36 IDs were analyzed, which had a sample size of > 10 cases. Among the IDs excluded from the data analysis, the following travel or migration associated IDs of interest were found. Viral IDs: chronic hepatitis B (16), varicella (14), hepatitis A (10), influenza (9), acute hepatitis B (2), and hepatitis E (2). Bacterial IDs: *Streptococcus* pharyngitis (12), infections with *Yersinia* (9) and *Chlamydia* (7) spp., leprosy (5), relapsing fever (1), and melioidosis (1). Protozoal IDs: toxoplasmosis (8), mucocutaneous leishmaniasis (7), visceral leishmaniasis (4), and Chagas disease (1). Helminthic IDs: taeniasis (12), loa loa filariosis (10), and onchocerciasis (6). Ectoparasitic IDs: cimicosis (6). Fungal IDs: mycetoma (3).

DISCUSSION

So far, this is the largest observational study on the assessment of imported IDs seen in returning travelers and immigrants consulting a single study site. The study was performed with data from 17,794 patients who consulted the University of Munich, Germany, between 1999 and 2014 after being in the sub-/tropics.

Most travelers came from destinations in Asia, followed by Africa and Latin America, as seen in comparable former studies.[12–14] The most immigrants were of African origin, followed by those of Asian and Latin American origin, as also seen in a previous multicenter study.[10] Regardless of the travel destination, most travelers were backpackers, followed by all-inclusive travelers and business travelers. The proportion of females was significantly highest in all-inclusive travelers, and significantly lowest among business-travelers. Among the immigrants, the proportion of females was significantly higher among those from Latin America, while it was significantly lower among those from Africa and Asia. Median age was highest among all-inclusive travelers, followed by business-travelers, immigrants, and backpackers. The median travel duration was 21 days, whereas it was longer among backpackers and shorter for all-inclusive travelers. Most travelers who stayed longer than 90 days in the sub-/tropics were found among the business travelers.

The most frequent travel-associated symptom and the second-most frequent migration-associated symptom was diarrhea: its proportion was significantly elevated among all-inclusive travelers returning from Africa as well as business travelers and backpackers returning from Asia. Among the first two study groups, the majority of travelers' diarrhea lasted only a few days with mild symptoms. In contrast to that, several intestinal pathogens such as *Campylobacter* spp., *Blastocystis hominis*, *Giardia lamblia*, and *Cryptosporidium* spp. were found significantly more frequently among backpackers returning from Asia, but not in any other study group, except *B. hominis*, which was significantly higher among business travelers from Africa.

Although *B. hominis* may only serve a complement of other enteric pathogens by causing diarrhea, its intestinal detection can be used as an indicator for the hygienic conditions of a travelers' or immigrants' environment.[20] Based on this, it seems that travelers in Asia are more often faced with low hygienic conditions, as also typhoid fever and paratyphoid fever were found to be significantly more frequent only among backpackers returning from Asia.

The symptom most frequently associated with migration and second-most frequently with travel was fever. Its proportion was significantly elevated among backpackers from Africa as well as immigrants from Africa and Asia. Among the first study group, rickettsiosis was found significantly more frequently than among all-inclusive travelers returning from Africa (almost all patients had traveled to South Africa). Additionally, malaria and schistosomiasis were found significantly more frequently than among business travelers from Africa. Rickettsiosis, malaria, and schistosomiasis were the only three IDs which showed an elevated prevalence among more than one study group who had been to Africa. This is an important finding concerning pre-travel consultations for individuals who plan to travel to Africa, as these three IDs can be avoided by having knowledge about their methods of transmission.

Beside fever, arthralgia was also reported significantly more frequently among diseased African immigrants. This might be partially caused by the 11 IDs which were found significantly more often in this study group. Of them, four IDs were found to be significantly elevated only among African immigrants: Human immunodeficiency virus infections, syphilis, intestinal infection with *Entamoeba* spp., and strongyloidiasis. Beside African immigrants, hookworm infections had significantly elevated prevalence among backpackers from Latin America. Walking barefoot seems to be the principal risk factor, as the prevalence for cutaneous larva migrans was also significantly elevated in this study group. Furthermore, beside African immigrants, chronic hepatitis C had a significantly elevated prevalence among backpackers from Asia. This finding could be explained by a large number of these travelers having been pierced or tattooed during travel to Asia. Furthermore, a certain number of intravenous drug users among these travelers can be assumed, but representative data on this risk factor are missing. Three IDs were significantly more prevalent among African and Asian immigrants only: tuberculosis, ascariasis, and trichuriasis. These IDs might be "typical" IDs for immigrants, as they showed low prevalence among travelers.

The fifth most frequently found symptom was arthralgia, which was reported significantly more often by immigrants from Latin America and Asia. The only ID, which was significantly more prevalent among immigrants from Latin America was chikungunya. This finding was surprising as this ID has been present in the Americas only since 2013.[28] However, the sample size was extremely low, with only 18 cases in this study. Like chikungunya, dengue is one of the most emerging IDs worldwide. Besides immigrants from Asia, this study found significantly elevated prevalence of dengue among backpackers from the same continent. This is an important finding concerning pre-travel consultations, as knowledge about protection from mosquito bites is essential. Backpackers from Asia also showed a significantly elevated proportion of mononucleosis, probably due to the fact that this group comprises mostly young travelers.

Skin disorder was the third most frequently reported symptom in the study population. Its prevalence was significantly elevated among backpackers returning from Latin America and Asia, as well as all-inclusive travelers returning from Asia. In the latter study group, however, no ID was found with significantly elevated prevalence, so it was assumed that these travelers have no specific risk for any ID. The most frequently defined dermatological ID was cutaneous larva migrans, which was found significantly more frequently among backpackers returning from Latin America and Asia. The four most

detected ectoparasitic ID were myiasis, scabies, tungiasis, and pediculosis/phthiriasis. Myiasis, tungiasis, and pediculosis/phthiriasis were significantly more frequent among backpackers returning from Latin America only. This is also an important finding concerning pre-travel consultation.

Among immigrants, except cutaneous leishmaniasis, the proportions of skin disorders were not significantly elevated. Middle East countries are endemic for cutaneous leishmaniasis, and this study found this among the immigrants from this region. Besides this study group, cutaneous leishmaniasis was surprisingly found to be significantly more frequent among business travelers from Latin America. This statement is based on only three cases, although all three persons stayed for professional reasons for several months in rural areas in Latin America, where the risk for bites by infected phlebotomines is elevated. Furthermore, the proportion of cytomegalovirus infections was found to be higher in this study group. It can be assumed that this is a result of this group having more intimate or sexual contacts with native population but exact data on this are missing.

Concerning herpes simplex and herpes zoster, no risk group was identified in this study. This fact allows for the assumption that these two dermatological IDs are not associated with travel or migration, as the respective virus exists ubiquitous. Finally, neither shigellosis, salmonellosis, cyclosporiasis, intestinal infections with *Dientamoeba fragilis*, trichomoniasis, oxyuriasis, nor scabies were identified as a specific risk for any of the study groups.

As explained above, out of the large study population of 17,794 individuals, this study documented 36 IDs that occurred in more than 10 laboratory-confirmed cases, comprising a total of 4,198 (24%) cases. This proportion was significantly the highest among African immigrants and backpackers returning from Asia. Based on this, it can be assumed that these two study groups are at higher risk, while the risk is lowest for all-inclusive travelers. The present study found 41 associations with significantly elevated proportions of any ID in any of the 12 study groups. Of the 36 IDs, none had significantly elevated prevalence among all-inclusive travelers returning from Latin America, or among business travelers and all-inclusive travelers returning from Asia. Overall, 18 IDs with significantly elevated prevalence were detected among backpackers, 17 among immigrants, five among business travelers, and only one among all-inclusive travelers. Divided by region, the most associations were found among travelers or immigrants from Africa (18), followed by Asia (15) and Latin America (8). Divided by study group, the most associations were found among African immigrants (11), followed by backpackers returning from Asia (10), immigrants from Asia (5), and backpackers returning from Latin America (5).

This study has some limitations. It has a cross-sectional design, and as such, all data on independent variables (e.g., travel and migration) and dependent variables (e.g., ID) were collected at the same day of consultation at the DITM. Consequently, only limited data on the clinical status before travel or before migration were available through patient interviews. Additionally, no follow-up data, such as duration of IDs, which developed after consultation of the DITM, could be collected. Furthermore, the data analysis assessed associations between independent and dependent variables, but their causal interpretation was limited. As our study was neither population based nor related to the totality of German travelers and immigrants to Germany, and a certain part of the presented cases were referred to the DITM, a specialized center of imported IDs, no absolute data on the number of travelers or immigrants were available. Consequently, no exact calculations on relative risk could be provided by this study. However, in contrast to the other studies using large numbers of patients, which were multicentric,[9–17] this study provides uniformity in patient referral patterns, consistency in coding of diagnoses by clinicians, and central laboratory reference facilities.[22–27] As all patients were subject of the same standardized process, maximal comparability of the data was possible in this comparative prevalence study.

CONCLUSION

The general findings of this study allow for the conclusion that the risk for any ID is higher among immigrants originating from Africa and Asia than among German travelers returning from the same regions. Immigrants from Africa were found to have the highest frequency of imported IDs. For immigrants from Latin America, no clear differences were found compared with German travelers returning from this region.

Concerning the type of travel, it can be concluded that German backpackers were at higher risk for any ID, while the risk was lower among German business travelers and the lowest for German all-inclusive travelers. Considering travel destination, backpackers from Asia showed high proportions for several IDs, mainly those causing diarrhea, as well as dengue. The overall risk for acquiring any ID was higher among travelers and immigrants from Africa and Asia, whereas it was lower for those from Latin America.

This study demonstrates a largely differing spectrum of imported IDs between returning German travelers and immigrants, not only highly depending on travel destination and origin of immigrants, but also on the type of travel. These findings will support clinicians treating diseased travelers returning from the sub-/tropics and diseased immigrants originating from the sub-/tropics.

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