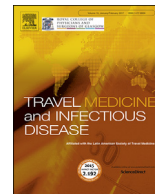




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Helminthic infections in returning travelers and migrants with eosinophilia: Diagnostic value of medical history, eosinophil count and IgE

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ABSTRACT

Objectives: Eosinophilia in travelers and migrants returning from the tropics is often associated with invasive helminthic infections. Total IgE is considered a useful additional diagnostic parameter; however, both parameters are also increased in various other non-helminthic diseases.

Methods: We retrospectively evaluated travelers and migrants seen at our department between September 2007 and May 2014. Patients with an absolute eosinophil count ≥ 500 cells/ μ L were considered for further analyses.

Results: Among 6618 returned travelers and migrants, 154 (2.3%) had a total eosinophil count ≥ 500 cells/ μ L. Of these, 71 patients (46%) were diagnosed with helminthic infection. In an additional 62 patients (40%) with eosinophilia a final diagnosis was found, including non-helminthic infections in 34 patients and non-infectious causes in 28 patients, while in 21 patients (14%) no diagnosis was made. Patients with helminthic infections had higher eosinophil counts than travelers and migrants with other diagnoses (median 981 vs. 710 cells/ μ L; $p = 0.001$), while total IgE levels ($n = 70$; 172 vs. 152 kU/l; $p = 0.731$) were similar in both groups.

Conclusion: Eosinophil count but not total IgE levels are associated with helminthic infections in returning travelers and migrants with eosinophilia. Our results do not support the use of total IgE to differentiate helminthic infections from other causes of eosinophilia in this population.

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Abbreviations: Immunoglobulin, Ig; T-helper cell type 2, Th2; interleukin, IL; visiting friends and relatives, VFR; positive predictive value, PPV; eosinophilic granulomatosis with polyangiitis, EGPA.

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1. Introduction

Eosinophilia is a complex immune-mediated response to a diverse set of factors. Activated eosinophils migrate to inflammation sites and release a differentiated set of cationic proteins from their granula [1]. These cytotoxic proteins are a mainstay in the host defense against invasive helminthic infections. However, blood eosinophilia, which is commonly defined as an absolute eosinophil count ≥ 450 or ≥ 500 cells/ μ L, is also seen in patients with allergic disorders, vasculitis, malignant diseases, autoimmune disorders, skin diseases, endocrine conditions, primary immunodeficiencies, drug reactions, and, occasionally, even in some non-helminthic infections like coccidioidomycosis or sarcocystosis [2–4]. Another

definition of eosinophilia considers a relative eosinophil count $\geq 5\%$ of all leukocytes [5].

The prevalence of eosinophilia is highly dependent on the patient population and ranges between 0.1 and 1.5% in the general European and Northern American population, and between 5 and 31% in migrants, and somewhere in between in returning travelers [6,7]. Male travelers and travelers with longer stays in endemic countries are more likely to present with eosinophilia. Regarding destinations, most patients with eosinophilia had returned from sub-Saharan Africa, followed by South- and Southeast Asia and Latin America [8–16]. The probability of identifying a specific diagnosis correlates with the level of the eosinophil count. Often a conclusive diagnosis cannot be found [9,10,17]. Invasive helminthic infections are an important cause of blood eosinophilia in returning travelers and migrants. Prevalence rates strongly depend on several factors (e.g. travel destination, diagnostic methods, etc.) [8,9,11,15–18]. Migrants, especially from West and Central Africa, have a higher prevalence up to 76% [19,20]. The relative risk of helminthic infection is about 12-fold higher compared to the risk of allergic diseases in patients with eosinophilia from tropical and subtropical helminthes-endemic regions [21]. Several studies reported that about 35% of travelers with eosinophilia caused by helminthic infections are asymptomatic [8,9]. In migrants from tropical and subtropical helminthes-endemic regions the number of asymptomatic patients with helminthes-related eosinophilia is considerably higher with a prevalence of up to 81% [10,15]. Gastrointestinal symptoms, fatigue and skin lesions are the most common clinical signs in those travelers and migrants that become symptomatic with eosinophilia [9,10].

Eosinophils play an important role in the fight against invasive helminthic infections, but the positive predictive value for the detection of helminthic infections in returning travelers or migrants strongly depends on the context – it will be higher in populations with higher prevalence of helminthic infections [9,17]. It has been suggested that the total immunoglobulin E (IgE) might be an additional helpful laboratory parameter for the diagnosis of helminthic infections, although it is unspecific and elevated total IgE levels are also found in other disease entities such as atopic diseases [22–24]. The presence of helminthes induces a T-helper cell type 2 (Th2) immune response with a mainly interleukin-4 (IL-4) mediated increase of IgE antibodies [25,26]. Patients with intestinal helminthes have elevated serum levels of IL-4 and total IgE [27]. The latter is suggested to reflect the level of Th2 cell activation [28]. Elevated total IgE levels show a positive correlation with helminthes egg loads, whereas anti-helminthic treatment decreases total IgE levels [29–31]. Some studies reported higher total IgE levels in patients with helminthic infections compared to patients with atopic diseases or when co-infected with helminthes [32,33]. IgE levels are commonly elevated in patients with eosinophilia and vice-versa and both parameters are considered as diagnostic biomarkers for helminthic infections [34,35].

Diagnostic evaluation of blood eosinophilia is often challenging and clear guidelines are missing [22]. The aim of our study was to describe patients with eosinophilia presenting to a travel clinic and to evaluate whether demographic factors, the eosinophil count, or total IgE levels are predictive of a final diagnosis of a helminthic disease.

2. Materials and methods

2.1. Study setting and design

We retrospectively evaluated all patients seen at our in- or outpatient department between September 2007 and May 2014. Patient data were retrieved from the clinical database of the

University Medical Centre Hamburg-Eppendorf. Every patient presenting to our department received a standardized questionnaire. The questionnaire consisted of questions on age, sex, country of birth, country of residence, as well as the travel destinations and durations of the last five years. It is used to inform the medical consultation and this information is included in the patient file. All other clinical data (laboratory values, symptoms, and diagnoses) were retrieved from the electronic patient file. For further analysis only patients with an absolute eosinophil count ≥ 500 cells/ μ l on at least one visit at our clinic were considered.

2.2. Definition of a helminthic infection

The diagnostic workup of returning travelers and migrants with eosinophilia is guided by accredited, in-house standard operating procedures in the diagnostic department of the Bernhard Nocht Institute for Tropical Medicine, the national Reference Centre for Tropical Infections. Stool microscopy is performed in all patients using the formol-ether-concentration technique, as is serology against strongyloides using an enzyme-linked immunosorbent assay (ELISA) with specific strongyloides extracts as antigens. If the patient is returning from a bilharziosis-endemic region or a filaria-endemic region (mainly Sub-Saharan-Africa) a schistosoma-serology or a filarial serology is performed using ELISAs with crude schistosoma or filarial antigen extracts as well as indirect immunofluorescence (IIFs) using histological sections of respective helminths. If the eosinophil count is higher than 1500 eosinophils/ μ l stool samples are also analyzed for nematode larvae using the Baermann technique. A final diagnosis of a helminthic infection was either defined by direct detection of helminths/eggs in stool samples or by indirect detection using serology in combination with a clinical response to specific therapy, or typical presentation and travel history with exclusion of other possible etiologies. Eosinophil count was determined by microscopy of peripheral blood smears in the clinical laboratory for tropical medicine at the Bernhard-Nocht-Institute, Hamburg. Total IgE levels were determined in the central laboratory of the University Medical Centre Hamburg-Eppendorf with levels <100 kU/L as the normal reference values.

2.3. Statistical methods

All data were collected in accordance with legal requirements regarding data protection and medical confidentiality. Retrieved data were pseudonymized and entered into an Excel spreadsheet, version 2016 (Microsoft, Mountain View, California), and further analyzed by STATA IC/13.1 (StataCorp LP, College Station, Texas, USA). Characteristics of travelers were described by their absolute and relative counts for categorical variables, and by the median and the range for non-normally distributed continuous variables. For the exploratory analyses comparing travelers with a confirmed helminthic infection to travelers with other diagnoses, an association with categorical variables was tested by a chi-square test, while an association with non-normally distributed continuous variables was tested by the Wilcoxon rank-sum test. To allow for confounding effects, a multivariate logistic regression model was built. We included variables, which showed any association ($p = 0.1$) with being diagnosed with a helminthic infection in the univariate analyses. Eosinophil count was grouped into two categories with a threshold of 1500/ μ l. This threshold is commonly used to differentiate mild from moderate to severe eosinophilia and is part of the diagnosis of hyper eosinophilia [36,37]. The final destinations were regrouped to lower the number of subgroups into sub-Saharan Africa, South- and Southeast Asia, and other (including all other destinations). Similarly travel type was regrouped into non-visiting friends and relatives (VFR) returning traveler, VFR returning

traveler, immigrants, and others (including all other travel types: foreign visitors and expatriates).

3. Results

During the surveillance period 8354 returned travelers and migrants were seen at our in- or outpatient clinic. A total of 1736 patients had to be excluded. Of those, a differential blood count was absent/not performed in 1732 patients and data of four patients were recorded twice (Fig. 1).

Out of 6618 returned travelers and migrants who fulfilled inclusion criteria 154 patients (2.3%) were identified with a total eosinophil count ≥ 500 cells/ μ L. Baseline characteristics at presentation are listed in Table 1. Most of the patients with eosinophilia were seen at the outpatient clinic (94%). The median eosinophil count was 762 cells/ μ L at presentation. The male:female ratio was 1.6:1 and the median age was 33 years. The majority of patients returned from sub-Saharan Africa (43%) and Southeast Asia (31%). Reasons for travelling were mainly travel unrelated to visiting friends and relatives (mostly for touristic reasons) (72%), followed by migrants (13%), and VFR (10%). Gastrointestinal symptoms (36%) were the most common clinical presentation reported followed by fatigue (25%), and skin lesions (23%); multiple answers were possible (Table 2). Fever (12%), respiratory symptoms (9%), and/or neurological disorders (7%) were less frequently reported. Nineteen returning travelers and migrants (12%) were asymptomatic and eosinophilia was detected coincidentally.

Seventy-one patients (71/154, 46%) with an eosinophil count ≥ 500 cells/ μ L were diagnosed with helminthic infections. The most common helminthic infection was schistosomiasis (29/71), followed by strongyloidiasis (12/71), and infections with *Ascaris lumbricoides* (6/71), *Ancylostoma duodenale* (5/71), *Loa loa* (4/71), or cutaneous larva migrans (4/71). Other helminths were less frequently detected including *Echinococcus granulosus* (2/71), *Fasciola hepatica* (2/71), *Dirofilaria immitis* (1/71), *Dracunculus*

medinensis (1/71), *Enterobius vermicularis* (1/71), *filariasis* (unspecified) (1/71), *Gnathostoma spinigerum* (1/71), *Hymenolepis nana* (1/71), and *Opisthorchis* species (1/71). In further 62 patients (62/154, 40%) with eosinophilia a final diagnosis was found including non-helminthic infections in 34 (34/154, 22%) patients and non-infectious causes in 28 patients (28/154, 18%), while in 21 patients (21/154, 14%) no diagnosis was made. Final diagnoses of all 154 patients with an eosinophil count ≥ 500 cells/ μ L are listed in Table 3.

Patients with confirmed helminthic infections had significantly higher eosinophil counts than travelers with other diagnoses (median 981 vs. 710 cells/ μ L; $p = 0.001$). There was no difference in the eosinophil count between non-helminthic infections and other non-infectious diagnoses. 70 patients have been tested for IgE. There was no difference in baseline characteristics between patients tested for IgE and those not tested (Supplementary Table S1). Of 70 patients with data on IgE levels, the median IgE was 158 kU/L (range 4–5000). Elevated IgE (>100 kU/L) was found in 43 (61%). Twenty-four out of 43 patients with elevated IgE were diagnosed with a helminthic infection, compared to 15 out of 27 with normal IgE levels, thereby not showing an association between elevated IgE and helminthic infections ($p = 0.983$). Similarly, absolute IgE levels did not differ between the two groups (172 kU/L in those with a helminthic infection vs 152 kU/L in those without, $p = 0.731$). Additionally there was no correlation between the eosinophil count and IgE level (Fig. 2).

Age, sex, and duration of travel were not associated with final diagnosis of helminthic infection. However the travel region and the type of traveler are major factors which influence the risk of a helminthic infection. The vast majority of migrants (18/20) with eosinophilia had a final diagnosis of helminthic infection, while less than half of returning travelers (47/78) had a final diagnosis of helminthic infection. Helminthic infections were found more often in travelers returning from sub-Saharan Africa than from other tropical regions (Table 4). To adjust for any confounding effects, we

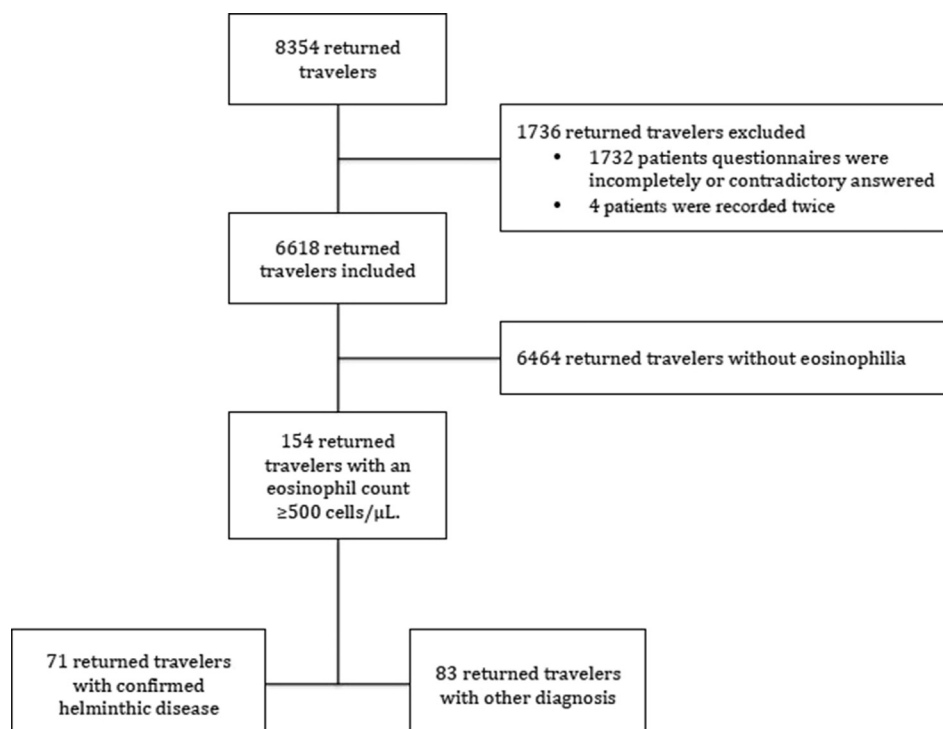


Fig. 1. Flow chart of returned travelers with eosinophilia, September 2007 to May 2014.

Table 1
Baseline characteristics of patients presenting with eosinophilia.

n	154
Sex	
Male	94 (61%)
Female	60 (39%)
Age, years	
Median (range)	33 (5–77)
Type of traveler	
Returning traveler (non-VFR)	111 (72%)
Returning traveler (VFR)	15 (10%)
Immigrant	20 (13%)
Foreign visitor	6 (4%)
Expatriate	3 (2%)
Type of clinic visit	
Outpatient	144 (94%)
Inpatient	10 (6%)
Region of travel	
Sub-Saharan Africa	66 (43%)
South and Southeast Asia	47 (31%)
Central and South America	12 (8%)
Europe	11 (7%)
Middle East	7 (5%)
Oceania	2 (1%)
Northern Africa	2 (1%)
Northern America	1 (1%)
Multiple regions	6 (4%)
Eosinophil count (cells/ μ l)	
Median (range)	762 (500–15100)
IgE, kU/L [n = 70]	
Median (range) [normal <100]	158 (4–5000)

Values represent no. (%).

VFR: Visiting friends and relatives. n: Number. IgE: Immunoglobulin E.

Table 2
Diagnostic categories of patients presenting with eosinophilia (n = 154).^a

Presenting complaint	n (%)
Gastrointestinal tract	55 (36%)
Fatigue	38 (25%)
Skin	35 (23%)
Laboratory abnormalities ^b	22 (15%)
Fever	19 (12%)
Screening	19 (12%)
Respiratory tract	14 (9%)
Neurological	10 (7%)
Other ^c	26 (17%)

n: Number.

^a More than one item per patient possible.^b Other than eosinophilia.^c Items accounting for less than 5% were subsumed under "other".**Table 3**
Final diagnoses of 154 patients presenting with eosinophilia.

Final diagnosis	n (%)
Patients diagnosed with helminthic infections (n = 71)	
Schistosomiasis ^a	29 (19%)
- Diagnosis by serology	- 16
- Diagnosis by microscopy: <i>Schistosoma mansoni</i>	- 10
- Diagnosis by microscopy: <i>Schistosoma haematobium</i>	- 3
<i>Strongyloides stercoralis</i>	13 (8%)
<i>Ascaris lumbricoides</i>	6 (4%)
<i>Ancylostoma duodenale</i>	5 (3%)
Cutaneous larva migrans	4 (3%)
<i>Loa loa</i>	4 (3%)
<i>Echinococcus granulosus</i>	2 (1%)
<i>Fasciola hepatica</i>	2 (1%)
<i>Dracunculus medinensis</i>	1 (<1%)
<i>Enterobius vermicularis</i>	1 (<1%)
<i>Filaria</i> spp.	1 (<1%)
<i>Gnathostoma spinigerum</i>	1 (<1%)
<i>Hymenolepis nana</i>	1 (<1%)
<i>Opisthorchis</i> spp.	1 (<1%)
Patients with other diagnoses (n = 83)	
Unknown cause	21 (14%)
Traveler's diarrhea	13 (8%)
Atopic disease	12 (8%)
- Atopic eczema	- 5
- Urticaria	- 2
- Not specified	- 2
- Contact dermatitis	- 1
- Chronic sinusitis	- 1
- Nutrient deficiencies	- 1
<i>Blastocystis hominis</i>	7 (5%)
Asthma bronchiale	4 (3%)
Inflammatory bowel disease	4 (3%)
Hypereosinophilic syndrome	3 (2%)
Malignant disease	3 (2%)
<i>Dientamoeba fragilis</i>	2 (1%)
<i>Entamoeba histiolytica</i>	2 (1%)
Malaria (1 <i>M. falciparum</i> , 1 <i>M. vivax</i>)	2 (1%)
<i>Sarcocystis</i> spp.	2 (1%)
<i>Borrelia recurrentis</i>	1 (<1%)
Dengue virus	1 (<1%)
Drug reaction	1 (<1%)
EGPA	1 (<1%)
<i>Giardia lamblia</i>	1 (<1%)
Psoriasis vulgaris	1 (<1%)
Pyoderma	1 (<1%)
Sepsis of unknown focus	1 (<1%)

EGPA: Eosinophilic granulomatosis with polyangiitis.

^a Including three patients with Katayama fever.

built a multivariate model, which confirmed the strong association between travelling to sub-Saharan Africa and being diagnosed with a helminthic infection, as well as between immigrants and being diagnosed with a helminthic infection (Table 5).

4. Discussion

We describe a cohort of returning travelers and migrants with eosinophilia in which approximately half of patients could be diagnosed with a helminthic infection. Our study results showed that exposure variables (such as the type of traveler and the destination), as well as the eosinophil count are associated with helminthic infections in returning travelers and migrants with eosinophilia, but IgE levels are not.

When helminthic disease is confirmed, treatment is often simple, safe and cost-effective. Diagnostic work-up, however, is often complex and requires highly specialized laboratory resources and

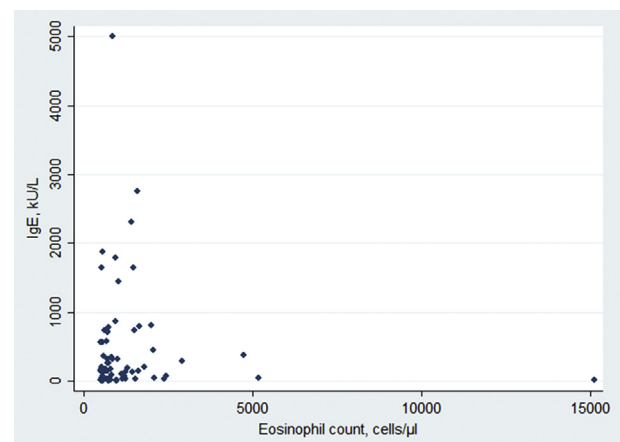
**Fig. 2.** Association of total IgE level and eosinophil count (n = 70; $R^2 = 0.006$; $p = 0.543$).

Table 4

Association of patient characteristics and diagnosis of a confirmed infection.

	Confirmed helminthic infection ^a	Other diagnosis	p value
n	71	83	–
Eosinophil count (cells/μl)			
median (range)	981 (508–15100)	710 (400–4851)	0.001 ^c
IgE (kU/L), ^b normal: <100			
median (range)	172 (4–5000)	152 (11–1870)	0.731 ^c
Age (years)			
median (range)	30 (13–74)	36 (5–77)	0.386 ^c
Sex, n (%)			
Male	41 (58%)	53 (64%)	0.438 ^d
Female	30 (42%)	30 (36%)	
Type of traveler			
Returning traveler (non-VFR)	41 (58%)	69 (83%)	<0.001 ^d
Returning traveler (VFR)	6 (8%)	9 (11%)	
Immigrant	18 (25%)	2 (2%)	
Foreign visitor	3 (4%)	3 (4%)	
Expatriate	3 (4%)	0 (0%)	
Region of travel			
Sub-Saharan Africa	41 (58%)	25 (30%)	0.021 ^d
South and Southeast Asia	19 (27%)	28 (34%)	
Central and South America	3 (4%)	9 (11%)	
Europe	2 (3%)	9 (11%)	
Middle East	4 (6%)	3 (4%)	
Oceania	0 (0%)	2 (2%)	
Northern Africa	0 (0%)	2 (2%)	
Northern America	0 (0%)	1 (1%)	
Multiple regions	2 (3%)	4 (5%)	
Travel duration (months) ^e			
median (range)	1 (0–23)	1 (0–24)	0.583 ^c

Values represent median or no. (%).

VFR: visiting friends and relatives. n: Number. IgE: Immunoglobulin E.

^a Included schistosomiasis, strongyloidiasis, ascariasis, ancylostomiasis, larva migrans cutanea, loiasis, echinococcosis, fasciola, dirofilariasis, dracunculus, enterobius, filariasis, gnathostomiasis, hymenolepsis, opisthorchiasis.^b n = 70 contributed total IgE values (39 with helminthic infections, 31 with other diagnoses).^c p-value obtained by Wilcoxon rank-sum test.^d p-value obtained by chi-square test.^e Foreign visitors and immigrants were dropped for this analysis; n = 131.**Table 5**

Multivariate analysis of the association between patient characteristics and diagnosis of a helminthic infection.

Variable	Crude OR	Adjusted OR ^a
Eosinophilia		
500–1500/μl	1.00	1
>1500/μl	4.21 (1.74–10.21)	5.89 (2.12–16.41)
Travel type		
Non-VFR returning traveler	1.00	1.00
VFR returning traveler	1.12 (0.37–3.38)	0.96 (0.27–3.40)
Immigrant	15.15 (3.34–68.64)	16.78 (3.32–84.85)
Other	3.37 (0.80–14.19)	3.64 (0.73–18.06)
Travel destination		
Other	1.00	1.00
South and Southeast Asia	1.85 (0.75–4.57)	2.83 (0.96–8.30)
Sub-Saharan Africa	4.47 (1.91–10.48)	6.28 (2.25–17.52)

VFR: visiting friends and relatives. OD: Odds ratio.

^a Adjusted for eosinophilia, travel type and travel destination.

clinical know-how. Patients with eosinophilia returning from the tropics may benefit from consulting an expert in tropical medicine, since helminth infection is the most common reason for blood eosinophilia in this patient population ranging from 14 to 67% depending on the study population (migrants > travelers) and study design [8,9,11,15–18,38], as is the case in our study (46%). In contrast to other studies we could find a final diagnosis in the vast majority of patients with eosinophilia (86%; 133/154 patients). This might be due to the pre-selected population of mostly ill-returned travelers and migrants presenting to a specialized travel clinic and a standardized work-up of patients.

Prospective studies in un-selected migrants and refugees showed that the majority of patients with eosinophilia are asymptomatic [10,15]. However, we only identified 19 asymptomatic patients (12%), who presented for screening after returning from the tropics – while the majority of patients presenting to our travel clinic had some post-travel symptoms. Hence asymptomatic travelers and migrants with eosinophilia are underrepresented in our study, thereby limiting generalizability to the overall population of travelers and migrants.

Almost all migrants with eosinophilia (18 of 20 migrants) had helminthic infections with schistosomiasis (19%) and strongyloidiasis (8%) being the most common. Both of these are associated with deleterious health effects (e. g. portal hypertension, bladder cancer, hyperinfection syndrome). Similar results of species distribution with a predominance of schistosomiasis and strongyloidiasis were reported by other studies [8,15]. Our data were collected before the present migration movements to Europe emerged. Hence, the pathogen distribution might have changed since our study population differs from the present refugees who are predominately from Syria, Afghanistan, and Somalia. Currently, there are no commonly accepted European guidelines available for the diagnostic work-up of travelers and migrants presenting with eosinophilia. Based on epidemiological data on imported diseases, some experts recommend structured screening programs guided by the geographic history and cardinal symptoms [22]. The British Infection Society guidelines group recommends stool microscopy and strongyloides serology in all travelers returning from the tropics and additionally, terminal urine microscopy and serology for schistosomiasis in those returning from Africa [39], however, this

recommendation has not been systematically evaluated so far.

Patients with confirmed helminthic infection had higher eosinophil counts than travelers with other diagnoses. It remains unclear, if this might be due to a diagnostic bias, since a higher eosinophil count may encourage physicians for a more aggressive diagnostic approach. However, similar results concerning eosinophilia and helminths were also shown by Schulte and colleagues who reported highest eosinophil counts (mean, 1545 eosinophils/ μ L) in patients with helminthic infections [9]. Whether the final diagnosis of the patients in our study is at the same time the cause of their eosinophilia cannot be determined with certainty in all cases. The association of the final diagnosis and eosinophilia is thought to be causal for patients diagnosed with a helminthic infection, infections with *Blastocystis hominis*, *Dientamoeba fragilis*, and *Sarcocystis* (in the case of man being the dead-end host), as well as systemic diseases (such as eosinophilic granulomatosis with polyangiitis/EGPA). However, the real cause of eosinophilia may have been missed in other patients (such as those with traveler's diarrhea or those infected with *Giardia lamblia*).

We could not find any association between IgE levels and a final diagnosis of a helminthic infection. Furthermore, total IgE levels and eosinophil count appear not to have any correlation. Several studies have shown that in a more general population (including patients with and without eosinophilia), eosinophilia and elevated total IgE are associated with each other [34,35]. For example, Belhassen-Garcia and colleagues reported a significant correlation between eosinophilia and hyper-IgE in migrant children with helminthic infections coming from Sub-Saharan Africa, Northern Africa or Latin America, however, hyper-IgE prevalence (56.8%) was twice the eosinophilia prevalence (22.9%), hence pointing to interindividual differences in IgE and eosinophil levels. Interestingly, the positive predictive value (PPV) for helminthic infection was significantly higher for eosinophilia in this population – which would be in line with our findings of a reduced diagnostic value of total IgE in the work-up of helminthic infections [35].

We could show that in the work-up of returning travelers and migrants with eosinophilia, IgE levels do not add a relevant diagnostic benefit to differentiate patients in whom helminths are expected. The main determinants of a final diagnosis of a helminthic infection are the travel destination (especially Sub-Saharan Africa) and the type of travel (especially migrants). Hence, in the absence of appropriate guidelines for the diagnostic work-up of eosinophilia in travelers and migrants, proper history taking seems to have more benefit than additional laboratory parameters (such as total IgE) to guide further diagnostic methods such as stool microscopy and serological investigations.

Conflicts of interest

JPC currently holds a position as medical director at Takeda International AG, Vaccine Business Unit, Zurich, Switzerland. All other authors declare they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.tmaid.2017.09.001>.

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Table S1

Association of patient characteristics and determination of IgE

	IgE tested	IgE not tested	<i>p</i> value
n	70	84	-
Eosinophil count (cells/ μ l)			0.272
- median (range)	817 (509-15100)	730 (500-4851)	
Age (years)			0.485
- median (range)	31 (11-74)	35 (5-77)	
Sex, n (%)			0.567
- Male	41 (59%)	53 (63%)	
- Female	29 (41%)	31 (37%)	
Type of traveler			0.640
- Returning traveler (non-VFR)	50 (71%)	60 (71%)	
- Returning traveler (VFR)	5 (7%)	10 (12%)	
- Immigrant	11 (16%)	9 (11%)	
- Foreign visitor	2 (3%)	4 (5%)	
- Expatriate	2 (3%)	1 (1%)	
Region of travel			0.431
- Sub-Saharan Africa	30 (43%)	36 (43%)	
- South and Southeast Asia	19 (27%)	28 (33%)	
- Central and South America	5 (7%)	7 (8%)	
- Europe	4 (6%)	7 (8%)	
- Middle East	3 (4%)	4 (5%)	
- Oceania	2 (3%)	0 (0%)	
- Northern Africa	2 (3%)	0 (0%)	
- Northern America	1 (1%)	0 (0%)	
- Multiple regions	4 (6%)	2 (2%)	
Travel duration (months) [§]			0.932
-median (range)	1 (0-23)	1 (0-24)	