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Original Article

A study of eosinophilia and helminths in migrant sub-Saharan patients in a primary care center (Madrid, Spain)

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Abstract: We determine the association between eosinophilia and certain parasites diagnosed by serology in patients of subsaharan origin of a Primary Care Center from Madrid region, Spain. It was implemented a complete protocol for migrant patient to study eosinophilia and realized serology tests for parasites detection. All variable and data were evaluated by statistical methods. A total of 184 patients with eosinophilia were included in the study, 115 patients (62.5%) were seronegative for helminths and 69 were seropositive. *Strongyloides stercoralis* (55.07%), *Schistosoma* spp (39.13%) and *Toxocara canis* (20.29%) were the most prevalent helminths immunodetected in the study. So, 49 patients (26.6%) had abdominal pain, 50 patients (27.17%) had problems related with skin conditions and 38 patients (20.65%) had respiratory disorder, symptoms not related with the helminth parasites detected. Regarding number of parasites by patient, one specie was identified in 49 patients (26.63%) and two or more was identified in 20 patients (10.86%). Eosinophilia was resolved in 91.4% of parasite serpositive patients after received one specific adequate antiparasitic treatment, but this was resolved in 98.3% after received two tratments, and 100% after the third. The results obtained allow us to make some reflections on the difficulty of managing these patients in the Primary Care Center and on whether to diagnose and treat individuals from endemic areas, with or without eosinophilia and being asymptomatic or not, given the benefit it has for the individual and public health, as possible to minimize any chance of transmission.

Key words: Eosinophils, Migrants, Helminths, Primary Care Health.

1. Introduction

Eosinophilia is defined as an abnormal increase of eosinophils in peripheral blood and it is a condition that occurs relatively frequently in clinical practice. This immune response is associated with various pathologies, among others: allergic reactions, helminth parasites, gastrointestinal, hematological and lung disorders, and others like post-irradiation, bacterial infections, post-family hereditary pathologies or neoplastic disorders [1,2].

There is no consensus on the values considered normal in the eosinophil count in peripheral blood (absolute and relative), so in our study we defined eosinophilia as a number of more than 0.5 x 109 eosinophils/ l (500 cells/ul in blood), or more than 4% in relative value [3, 4].

Eosinophilia is a common finding in immigrants which can indicate asymptomatic latent infection wich could lead to chronic disease and/or long-term complication [5]. In relation to subsaharan patients from tropical and subtropical areas, parasitoses are the main cause of

eosinophilia, being the prevalence of intestinal parasites in migrants ranges from 29% to 81%, depending on the country of origin. A number of parasitic characteristics that influence it, such as the number worms housed, adaptation of the parasitic species, life cycle of the worm, age of the process, re-infection and/or superinfection, intercurrent infectious processes and treatment with corticosteroids or anthelmintic treatment among others [1,6-7].

The subsaharan migration in Spain has been quantitatively limited and discontinuous [8]. In 2014 the number of people from this source, according to the National Institute of Statistics, reached 199.900 which corresponds to 22.4% of the total African migration and accounts for 4% of all migration into our country. The Spanish regions with the highest percentage of migrants from subsaharan countries registered in 2014 were Catalonia (33.43%), followed by Madrid (17.03%), Andalusia (16.39%) and Valencia (10.35%). These Autonomous Communities account for 77.2% of the total subsaharan migrants within the Spanish State.

Migrants are generally young and healthy individuals, but those who came from developing countries may have latent infectious that need to be identified and treated. However there are a potentially generating aspects of the inequalities that affect this, such as the administrative difficulties to obtain their own Social Security Card; difficulties in their clinical history due to ethnic, cultural differences and problems with language; difficulties in diagnosis because they have non-autochthonous diseases, difficulties in the treatment as some treatments are not available in pharmacies and last difficulties in the epidemiological control [5, 9-13]. This makes the management of these patients in the Primary Care Center difficult and complicated.

The basis of this study is the relationship between parasites and their influence on eosinophils in the blood of patients attended in a spanish Primary Care Center, since helminths are the group of parasites that trigger frequently the eosinophil increase in the subsaharan migration. Due to many times mild peripheal eosinophilia may be the only clue to detect helminths and recent studies suggest that relative eosinophilia is frequently associated with helminthic infection in migrant children from tropical and sub-tropical areas, so it seems logical a thorough parasitological study in this group of patients [14, 15].

Primary Care Health Centers are essential in carrying out the initial and comprehensive review of the health status of this population. We need to know about imported infectious diseases because of people move and flow from developing countries to European countries, in order to minimize the potential risk of several diseases.

2. Patients and Methods

The study was conducted at the Center for Primary Health Care "Brújula" located in Torrejon de Ardoz, Community of Madrid, Spain, during the period between 2012 and 2014. The study was reviewed and approved by the ethical committees and informed consent was obtained from patients. The inclusion critera were: i) patients from sub-saharian origin, ii) attended in primary care consultation for any reason and iii) give the informed consent.

In our study, primary care physician implemented a complete protocol for migrant patient to study eosinophilia; it was designed to evaluate in every patient: medical history, epidemiologycal data (age, gender, country of origin, time sincde arrival to Spain, epidemiological risk factor), physical examination and several laboratory tests that includes complete blood count (absolute and relative eosinophil cell count included), biochemistry (including renal and liver function tests) and viral serology (HBV, HCV, HIV), performed routinely in the laboratory assigned to the center.

Tests and serology for parasites detection was realized in the Serologic Diagnosis of Parasitic Diseases Unit National Microbiology Center, Institute of Health Carlos III, (ISCIII).

For this, serum sample from each patient was referred to ISCIII to carry out the tests for specific IgG antibodies against the parasites. Commercial kits were used acording the manufacturer's instructions for the following parasites: Strongyloides spp (Strongyloides stercolaris IgG ELISA Diagnostic Kit, DRG, Marburg, Alemania), Toxocara spp. (Toxocara canis IgG ELISA Diagnostic Kit Novalisa TM Inmunodiagnostica GmbH, Alemania); Cysticercosis (Taenia solium IgG ELISA Diagnostic Kit Novalisa TM) and Schistosoma spp (Schistosoma mansoni IgG ELISA Diagnostic Kit

Novalisa TM). The following parasites were detected by techniques "in house" performed in the laboratory: Trichinella spp (Trichinella IgG Indirect immunofluorescent antibody test (IFAT), Fasciola spp (Fasciola hepatica IgG1 capture ELISA, lymphatic filariosis (Filarias total IgG and isotipes IgG1, IgG3 and IgG4 ELISA, Onchocercosis disease (Onchocerca total IgG and isotipes IgG1, IgG3 and IgG4 ELISA, Hydatidic disease (Echinococcus granulosus total IgG and isotipes IgG1 and IgG4 ELISA. 16-20

3.1. Variable data

All data (epidemiological, clinical and laboratorial variables) were collected on a laboratory notebook in which appeared the variables of each patient. A case was considered positive when the result was positive in serological test. Once identified patients with positive results against the tested helminths, they were given a proper treatment if they agreed to it, and after a period of time, it underwent a new identical to the initial serological test to check their negativization. In this study the tests described were conducted to obtain an accurate diagnosis, at an elevation of eosinophils and/μμμor presence of clinical symptoms.

3.2. Statistical analyses

The SPSS 20 statistical package was used for data analyses. Continuous variables were expressed as mean values and standard deviation, and categorical variables as number of cases and percentages. Cualitative variables were used, as Chi-Square Pearson or Fisher test, Relative Risk (RR) or Odds Ratio (OD) as required.

As cuantitative variables, T-Student or ANOVA were used. Results were considered statistically significant if P value was < 0.05. 21,22

3.3. Ethics

All the procedures followed in this text were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and regional) and with the Helsinki Declaration of 1975, as revised in 1983.

3. Results

The number of patients treated in this center during this period were 16.834, of whom 389 were from subsaharan origin, who were considered as the target population that represents 2.3% of all patients looked after at the Health Center. Subsaharan patients were of both sexes and different ages. During the period of study we lost cases as the result of change of address or Autonomous Community, return to their country of origin, rejection of treatment or once received it, do not performed the follow-up analytical control due to the possible loss of the right to health care, etc. Endly our final population and samples were 184 patients (47,30%).

Patient's baseline characteristics are shown in the Table I. In this sense It must be highlighted that 57.1% of the patients are women and the average age of our series was 38.4 years. The youngest patient studied was 14 years and the oldest, 85 years. The average total time of residence in Spain was 7.49 years, with a maximum of 41 years of residence. Of all the subsaharan Africa countries of origin of immigrants, Equatorial Guinea (32.6%), followed by Nigeria (31.0%) and Ghana (11.4%) are the major sources as can be seen in **Table II**.

Table I. Epidemiological data of Subsaharan migrant patients.

Variable	**N** [(1)]	**%**[(2)]
Sex		
Men	79	42,93
Women	105	57,07
Age (years old)		
≤19	8	4,35
19-65	172	93,48
65	4	
Median (IRQ)	38,4 (14-85)	2,17
Time of residence in Spain, years (IRQ)*	7,5 (2-41)	
Travel to their origin country		
No	108	58,70
Yes	8	4,35
Indeterminad	68	36,96

(1) (N=184)

(2) % respect to the total patients

IRQ: Interquartile range

*In individuals to travel to their origin countryconsidering the time of residence from the date of their last return to Spain.

With respect to the number an percentage of basal eosinophils of the 184 patients, 89 patients (48.37%) had eosinophilia. The average number of eosinophils in our entire population was 288 μl in absolute (range 86-400; SD 285) and 5.1% (range 1.9-7.5; SD 4.2) in relative values.
From the total sample 69 patients (37.5%) showed positive serology to parasitosis and 115 (62.5%) were seronegative. With regard to the parasites diagnosed by serology in 69 patients, the results are also showed in **Table II**.

Table II. Parasites diagnosed by serology in sub-Saharan patients.

Parasite	**N** [(1)]	**N/Total patients** [(2)]	**N/Patients with positive serology** [(3)]
Strongyloides stercoralis	38	20,65	55,07
Schistosoma spp	27	14,67	39,13
Toxocara canis	14	7,61	20,29
Lymphatic filariasis	5	2,72	7,25
Taenia solium	5	2,72	7,25
Oonchocerca volvulus	4	2,17	5,80
Echinococcus granulosus	1	0,54	1,45
Trichinella spp	0	0,00	0,00
Fasciola hepática	0	0,00	0,00

(1) Number of patients with parasites

(2) % among the 184 patients

(3) % among the 69 patients with positive serology

So the parasites that were diagnosed more frequently were, firstly, S. stercoralis, which appears in 38 patients (55.07%), followed by Schistosoma spp identified in 27 patients (39.13%), T. canis identified in 14 patients (20.29%) and T. solium in 5 patients (7.25%), O. volvulus in 4 patients (5.80%), and E. granulosus in 1 patient (1.45%); F. hepatica and Trichinella spp were not detected in any patient. From the 184 patients under study, 60 (32.60% of the total) came from Equatorial Guinea, endemic area for S. stercoralis; of these, 20 showed positive serology to it (28.99% of the 69 parasitized patients and 33.33% of the 60 parasitized patients from Equatorial Guinea).

Other microbiological diagnoses identified during the study, which could be related to several symptons (abdominal pain, skin conditions and respiratory disorder), are shown in **Table III**. We have not found significative relation between the serological diagnostic basal eosinophilia, parasites, age, sex or infections with VIH, VHB, VHC.

Table III. Relation of symptons and different variables in sub-Saharan patiens studied.

	Abdominal pain			**Skin disorders**			**Respiratory problems**		
Variable	**n**	**%**	**P**	**n**	**%**	**P**	**n**	**%**	**P**
Sex									
Men	18	22,78	NS*	22	27,85	NS*	13	16,46	NS*
Women	31	29,54		28	26,67		25	23,81	
Age									
≤19 years	3	37,50	NS**	2	25,00	NS**	2	25,00	NS**
19-65 years	46	26,74		47	27,33		36	20,93	
≥65 years	0	0,00		1	25,00		0	0,00	
Basal eosinophilia									
No	23	24,21	NS*	23	24,21	NS*	15	15,79	NS*
Yes	26	29,21		27	30,34		23	25,84	
Serology of tisular parasites									
No	35	30,43	NS*	29	25,22	NS*	27	23,48	NS*
Yes	14	20,9		21	30,43		11	15,94	
Parasites in feaces									
No	19	31,15	NS**	21	34,43	NS¨**	16	26,23	NS**
Yes	1	9,09		2	18,18		2	18,18	
Not realized	29	25,89		27	24,11		20	17,86	
VIH									
No	27	28,42	NS**	28	29,47	NS**	21	22,11	NS**
Yes	3	27,27		4	36,36		1	9,09	
Not realized	19	24,36		18	23,08		16	20,51	
VHB									
No	11	25,58	NS*	12	27,91	NS*	12	27,91	NS**
Yes	22	28,95		20	26,32		14	18,42	
Not realized	16	24,62		18	27,69		12	18,46	
VHC									
No	29	26,85	NS**	31	28,70	NS**	27	25,00	NS**
Yes									
Not realized	18	26,09		17	24,64		10	14,49	
Total	**49**	**26,63**		**50**	**27,17**		**38**	**20,65**	

***Chi-Square Test**

**** Fisher Test**

Respect the consideration of the basal eosinophilia as a diagnostic test (test problem) to detect tissue parasites identified by serology (reference test), the results observed in **Table IV** suggest that basal eosinophil parameter could be used as a diagnostic test because it shows a high negative predictive value (75.80%).

Table IV. Basal association between eosinophilia with or without parasites diagnosed by serology in sub-Saharan patients.

	Without tisular parasites			**With tisular parasites**			
Basal eosinophilia	**media**	**mediana**	**P25-75**	**media**	**mediana**	**P25-75**	**P [(1)]**
Eosinophils/µl	220	146	77-300	403	300	158-600	≤0,001
Eosinophils (%)	3,99	2,50	1,80-5,00	6,87	7,10	3,20-9,70	≤0,001

P25-P75= Interquartilic range

N= Number of patients

[(1)] U Mann-Whitney test

The association between basal eosinophilia and the number of parasites detected by serology is showed in the **Table V**. In 115 patients (62.5%) no one agent was identified, one in 49 cases (26.63%) and more than one in 20 cases (10.86%).

Table V. Basal association between eosinophilia as a continuous variable (eosinophils/µl) and % eosinophils with tissue parasitosis diagnosed by serology as a categorical variable.

		Basal eosinophils	
Nº Tissular helminths		**Eosinophils/µl**	**Eosinophis (%)**
	media	220	3,99
Nº parasites (n=115)	**mediana**	146	2,50
	P25-75	77-300	1,80-5,00
	media	325	5,72
With one parasite (n=49)	**mediana**	241	5,20
	P25-75	122-479	1,90-8,60
	media	593	9,68
More than one parasite	**mediana**	587	9,30
(n=20)	**P25-75**	333-666	8,15-10,40
	p*	≤0,001	≤0,001

P25-P75= Interquartilic range

N= number of patients

*Kruskal-Wallis

In addition, with regard to treatment, of the 69 patients with a positive result for parasitosis: three refused to be treated, 5 did not return to start treatment and 3 could not be submitted to analytical control after treatment. Finally were treated and evaluated 58 patients, who were given ivermectin in the case of Strongyloides spp and filaria; praziquantel for Schistosoma spp and Taenia spp; and albendazole for Toxocara spp. There was no real positive for Trichinella spp, Fasciola hepatica and Echinococcus spp and patients were not treated. It has been defined as a cure to the situation in which after administration of the specific treatment, a negative result was obtained in

the serological test carried out later. So, 91.4% of patients that received the first treatment showed complete resolution of the parasitosis diagnosed and eosinophilia; those who received the second treatment, complete resolution was seen in 98.3% and after the third treatment, complete resolution of eosinophilia was seen in 100%.

4. Discussion

In this study, carried out in a Primary Care Health, we have found a relation between "to have eosinophilia in peripheral blood and to have parasitosis" [23]. The exhaustive data from the clinic history of the patients of this study has allowed us to obtain some value information of diseases in asymptomatic patients. Prevalent rates between the presence of parasites and eosinophila range 14%-64%, but others proposed a 75.9% of helminths or 77%, though it seems that frequency and distribution of parasites depends on the countries of origin of the migrants [5, 23-26].

A limitation of this study is that no all the helminths produce eosinophilia at the same level and most of the serology tests are not positive until 4-12 weeks after primo-infection [1, 23-24]. In this sense the results could be negative, but it is posible to have some parasitoses, although most of the migrants had been living in Spain for more than three months.

We have found diarrhea, abdominal pain, gastroenteritis, skin disorders (eccem, prurit, micosis, dermatitis) and respiratory disorders (allergy, asthma, dermatitis, rinitis…) in a same way that other authors did [27]. In fact we have tried to evaluate these associations with VIH, VHB, VHC serology, helmiths serology with sociodemographic variables and eosinophilia, but we have not found any significative relation among them.

In the same manner we have not found significative relation between sex and parasitism. It is possible that the time that migrants are in our country, so high (7.49 years media), may act as a "remedy" to eliminate some parasites after to have had a good hygiene, feed and health care [24, 28-29].

The most frquent parasite found in our study was Strongyloides spp, followed by Schistosoma spp, and the hookworm Toxocara spp. However other studies conclude that filariosis is the most prevalent parasitosis but others found most prevalent the presence of schistosomosis or geohelminthiasis [5,25,26,30]. Such differences could be explained by the distinct geographical origin of patients and the geographical region in which the study was carried on.

In serology we must taken into account the possibility to find cross-reactions as others authors have been proposed, being Strongyloides spp the parasite that more frequent was associated to poliparasitoses [24,25].

There are some controversy in relation to both diagnosis and treatment. Regarding how to deal with the migrant population from endemic areas of parasitosis, application of protocols to diagnose parasitic disease in migrant population has been questioned. According to some authors, this should not be systematic and indiscriminate, but it would have to conduct serological testing in patients presenting a risk factor. Others consider it should perform analytical screens even in asymptomatic migrants since some say that all migrants and travelers returning with eosinophilia, especially those from endemic areas, should be investigated, since 21% to 33% of them are asymptomatic and the interpretation of indirect diagnosis methods to detect Strongyloides spp, are complicated especially in case of poliparasitism

In contrast, some experts argue administration of empirical treatment with ivermectin, albendazole and praziquantel. In fact, eosinophilia is resolved in over 90% of the patients treated empirically. For this, it is proposed a systematic evaluation of these patients because of none of the parasitic drugs has a 100% efficacy [14,25].

It seems logical that in migrants suspect helmintiasis and/or eosinophilia need protocols based on geographical risk of exposure. A systematic screening protocol could be applied for asymptomatic patients, including Strongyloides spp and Schistosoma spp serologies and others as HVI, HVB and HVC [14].

During the development of this research, it was significant the promulgation of Royal Decree-Law 16/2012 that affected the model of the National Health System and the right to health

care in Spain was denied to a large number of migrants, aged over 18 years, without Social Security Card. The health care would be dispensed only in emergencies, serious illness or accident and pregnancy, childbirth and postpartum. The inmediately consequence was the no diagnostic or treatment of the migrant population, so diseases as tuberculosis or VHI infections were out of the health system with the subsequent individual and colective problems.

Looking these results it looks logical to carry out studies to people that comes from endemic areas of parasitoses in order to prevent possible transmissions. So, the present study revealed that is neccesary to increase in Primary Care Health the evaluation of tropical diseases of migrant population, related with the origin country, time from the arrival to our country, visiting friends and relatives, social situation and conditions of life [30-33].

Conflicts of interest: Any author has no potential conflicts.

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