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Eosinophils and Parasitic Infections

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Abstract

Background: Eosinophils dysregulate immune responses associated with malignancies, allergic and parasitic diseases especially helminthic infections, though it is infrequently observed with protozoan diseases.

Objective: The aim of the present study was to evaluate and compare the percentage of eosinophils in different parasitic diseases at Baqiyatallah Hospital, Tehran, Iran.

Materials and Methods: One hundred and 72 samples were obtained from 74 and 98 patients with helminthic and protozoan diseases respectively and evaluated. Direct wet mount and formalin ether concentration were used for intestinal parasites identification. Scotch tape test and serological methods were utilized for diagnosis of *Enterobius vermicularis* and tissue parasites respectively. Eosinophils were counted and six or more percentages were considered as eosinophilia.

Results: In general, in 34 out of 74 helminthic infections (45.9%) and 5 out of 98 protozoan infections (5.1%), an eosinophil level equal or more than 6% was observed. The rate of eosinophilia in helminthic infections were 13/18 (72.2%), 7/11 (63.6%), 3/10 (30%), 2/3 (66.7%), 1/9 (11.11%), 5/13 (38.5%), 3/4 (75%) in the patients with fasciolosis, strongyloidiasis, hymenolepiasis, hookworm infection, enterobiasis, echinococcosis, and trichostrongyliasis, respectively. Concerning the protozoan infections, 3/26(11.5%) and 2/20(10%) of the individuals suffering from giardiasis and blastocystosis showed an eosinophil level higher than normal range, respectively.

Conclusion: As expected, helminthic infections especially fasciolosis and strongyloidiasis were the most important infections correlated with eosinophilia. According to available reports, eosinophilia higher than normal range in giardiasis and blastocystosis is not unexpected.

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Background

Eosinophils, a group of white blood cells (WBCs) in human and some other animals, were discovered by Paul Ehrlich using eosin dye.[1] The normal percentage of eosinophils in the peripheral blood is 3%–5% and the increase of these types of granulocytes known as "eosinophilia" happens when absolute eosinophil count exceeds the normal range (350–500/mm^3).[2,3]

Hypereosinophilia is observed either due to the clonal expansion of eosinophils via a somatic mutation or in response to the secretion of exogenous type 2 cytokines such as interleukin-3 (IL-3), interleukin-5 (IL-5), and granulocyte-macrophage colony-stimulating factor (GMCSF).[4]

Some new studies have proposed the contribution of eosinophils in the pathogenesis of various diseases. Atopic diseases, drug hypersensitivity reactions, connective tissue disorders, malignancies, rarely hypereosinophilic syndromes, monogenic disorders of immune deficiency, pulmonary infections, and eosinophilic gastroenteritis are examples of different disorders in which eosinophilia is observed.[5-8]

Eosinophils dysregulate immune responses related to allergic diseases, such as asthma. Furthermore, this group of immune cells is often conceptualized as destructive end-stage effector mainly related to parasitic diseases especially helminthic infections such as intestinal and tissue nematode infections.[6,7] One of the most important laboratory findings in many helminthic infections such as toxocariasis, fasciolosis, ascariasis, hookworm infection, and strongyloidiasis is the high rate of peripheral blood eosinophilia.[9-15]

Moreover, there are some reports about the presence of eosinophilia in protozoan infections such as isosporiasis, sarcocystosis, and dientamoebiasis.[16-18]

To the best of our knowledge, the level of eosinophils

in different parasitic diseases less has been evaluated, particularly in Iran. Therefore, the aim of the present study was to evaluate and compare the percentage of eosinophils in different parasitic diseases at Baqiyatallah hospital, Tehran, Iran.

Materials and Methods

In this cross-sectional study, the samples from 172 patients including 74 cases suffering from helminthic infections and 98 cases with protozoan diseases were evaluated. The samples from the patients who had other types of diseases were excluded. Moreover, in order to attain more accurate results, only one parasite was considered. WBC count and levels of eosinophils were assessed for all 172 cases.

Helminthic infections included fasciolosis, hydatidosis, hymenolepiasis, taeniasis, ascariasis, enterobiasis, trichostrongyliasis, hookworm infection, and strongyloidiasis, amoebiasis, giardiasis, toxoplasmosis, blastocystosis and malaria, cutaneous and visceral leishmaniasis were among the protozoan infections (the number of samples is shown in Table 1).

Most of the samples were obtained from the patients referred to the laboratory of Baqiyatallah Hospital, whereas some of the fascioliasis, hydatidosis, trichostrongyliasis, strongyloidiasis, leishmaniasis and malaria samples were obtained from the patients referred to Tehran University of Medical Sciences (Tehran, Iran), Pasteur Institute (Tehran, Iran), and two private medical laboratories in Lahijan and Amol, Iran.

The samples were prepared by direct wet mount and formalin ether concentration for the diagnosis of the intestinal parasites, scotch tape test for the diagnosis of *Enterobius vermicularis,* and serologic tests for the assessment of tissue parasites including *Fasciola* spp., *Echinococcus granulosus*, and *Toxoplasma gondii*.

Eosinophils were counted by Sysmex KX-21 automated hematology analyzer (Japan) and rechecked manually. Eosinophils with the counts of 6% or more were considered as eosinophilia.[2,3]

Results

Our results showed that 34 out of 74 (45.9%) samples of helminthic infections and 5 out of 98 (5.1%) samples of protozoan infections had an eosinophil level equal or more than 6%. The rate of eosinophilia in different helminthic infections including fasciolosis, strongyloidiasis, hymenolepiasis, hookworm infection, enterobiasis, echinococcosis, and trichostrongyliasis were 13/18 (72.2%), 7/11 (63.6%), 3/10 (30%), 2/3 (66.7%), 1/9 (11.11%), 5/13 (38.5%), and 3/4 (75%), respectively. Eosinophil count was not higher than normal range in four patients with taeniasis and two other patients with ascariasis. In all the patients infected with eight pathogenic and non-pathogenic protozoa including *Entamoeba histolytica*, *Giardia lamblia*, *T. gondii*, *Blastocystis hominis*, *Entamoeba coli*, *Endolimax nana*, *Plasmodium* spp., *Leishmania (tropica or major*) and *Leishmania infantum*, only 3/26 (11.5%) and 2/20 (10%) of the individuals suffering from giardiasis and blastocystosis showed an eosinophil level higher than normal range, respectively (Table 1 and Figure 1).

Discussion

The number of eosinophils increases in different disorders.[5-8] Parasitic diseases especially tissue helminthic infections are among the major problems in this context.[9-18]

Table 1. The Prevalence of Eosinophilia in Individuals With Different Parasitic Infections

Name of Parasites	No. of Patients (Male/Female)	Range of Age	No. Patients with Eosinophilia (Male/Female)	Percentage of Patients with Eosinophilia (Male/Female)
E. granulosus	13 (7/6)	19-67	5 (2/3)	38.5 (15.4/23.1)
Fasciola spp	18 (7/11)	27-63	13 (4/9)	72.2 (22.2/50)
S. stercoralis	11 (8/3)	12-59	7 (5/2)	63.6 (45.4/18.2)
E. vermicularis	9 (4/5)	3-25	1 (0/1)	11.11 (0/11.11)
T. orientalis	4 (2/2)	8-38	3 (1/2)	75 (25/50)
T. saginata	4 (3/1)	9-53	0 (0/0)	0 (0/0)
A. lumbricoides	2 (2/0)	16,31	0 (0/0)	0 (0/0)
H. nana	10 (7/3)	8-45	3 (2/1)	30 (20/10)
Hook worms	3 (2/1)	16-42	2 (2/0)	66.7 (66.7/0)
E. histolytica	6 (3/3)	20-69	0 (0/0)	0 (0/0)
G. lamblia	26 (17/9)	3-62	3 (2/1)	11.5 (7.7/3.8)
T. gondii	5 (2/3)	8-23	0 (0/0)	0 (0/0)
B. hominis	20 (10/10)	4-80	2 (2/0)	10 (10/0)
E. coli	5 (3/2)	20-69	0 (0/0)	0 (0/0)
E. nana	3 (2/1)	7-46	0 (0/0)	0 (0/0)
Plasmodium spp	10 (6/4)	14-61	0 (0/0)	0 (0/0)
Leishmania (tropica or *major)*	19 (13/6)	10-63	0 (0/0)	0 (0/0)
Leishmania infantum	4 (4/0)	12-17	0 (0/0)	0 (0/0)

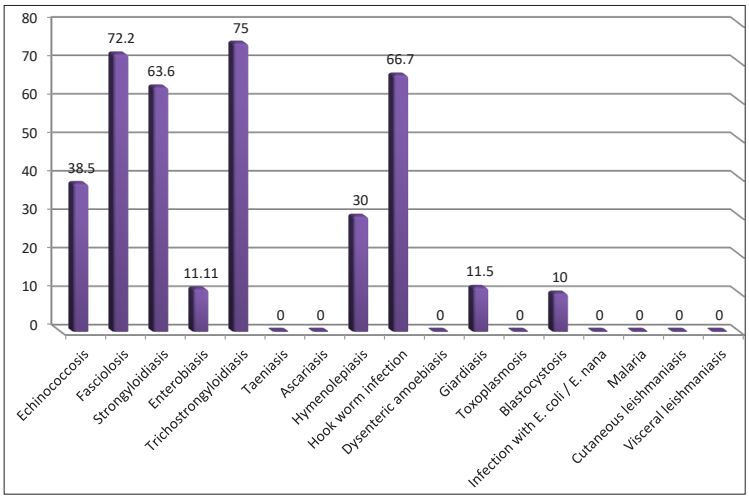

Figure 1. The Frequency of Eosinophilia(%) in Different Parasitic Infections.

In this study, the percentage of eosinophils was evaluated in the patients infected with different pathogenic/non-pathogenic parasites, and the worms examined were: *Fasciola* spp., *Strongyloides stercoralis*, *Hymenolepis nana*, *Hookworms*, *E. vermicularis*, *Echinococcus granulosus*, *Trichostrongylus orientalis, Taenia saginata* and *Ascaris lumbricoides*.

Fasciolosis is one of the most common zoonotic infections in Iran and in some parts of the world. The largest epidemic of fasciolosis occurred in north of Iran (Guilan) during two previous decades and an emerging infection was also observed in Kermanshah, Iran.[19,20] In the present study, in 72.2% of 18 patients infected with *Fasciola* spp., the percentage of eosinophils was greater than or equal to 6%. Karahocagil et al detected 24 patients with fasciolosis from 92 individuals with a history of watercress ingestion. Eosinophilia was observed in 17 persons (70.8%), which is similar to our results but the average percentage of eosinophils was 30.8±25.7,[10] whereas mean eosinophil count was 7.6% (6%-14%) in our study. The eosinophilia was seen in 19/20 (95%) of the patients suffering from fasciolosis in a hospital in Spain.[21] In another study in our country, eosinophilia greater than 30% was reported in Guilan (75%) and Kermanshah (42%).[19] Considering the fact that fasciolosis is directly affected by worm's burden, the lower percentage of eosinophils in our study might relate to lower intensity of infection, although the phase of disease may also contribute as an important factor in this regard.

About 100 million people in endemic areas of the world are infected by *S. stercoralis*, displaying different clinical symptoms such as eosinophilia.[15] In this investigation, 7/11 (63.6%) of the patients infected with *S. stercoralis* had eosinophil count higher than normal range. In a study carried out by Ashrafi et al, 150 patients with an elevated level of eosinophils were evaluated. Their results showed that 63 (42%), 9 (6%) and 1 (0.7%) of them were infected by *S. stercoralis*, *Fasciola* spp. and *Trichostrongylus* spp.[14] In another study in which 76 individuals with proven strongyloidiasis were evaluated, 82.6% had eosinophilia.[22] Some researchers have demonstrated the main role of eosinophilia in the diagnosis of *S. stercoralis* and reported this parameter as a good indicator of infection with this worm among farm workers on the Mediterranean Coast of Spain; however, all these studies have simply kept the count of eosinophil which is not a sufficient determining factor in the diagnosis of *S. stercoralis*.

In our study, 3/10 (30%) of the patients with hymenolepiasis showed elevated percentage of eosinophil. Ajami and Rafiei also reported an increase in the percentage of eosinophils in the patients infected with *H. nana* in comparison with that in the control group; however, the difference was not significant.[25] The results of a study demonstrated that *H. nana* oncosphere-derived molecules cause the intestinal eosinophilia in mice and can induce eosinophilia up to 15% in about 7% of the infected individuals.[26,27]

According to many researches, eosinophil counts were prominent in the patients infected with *Hookworms*.[28, 29] In the present study, 2 out of 3 (66.7%) patients infected with *Hookworms* had eosinophilia.

The percentage of eosinophil was only elevated in 1 out of 9 (11.11%) cases infected with *E. vermicularis*. Although it is claimed that *E. vermicularis* is an almost harmless intestinal helminth and could play a role in educating the immune system, it can sometimes cause eosinophilia.[30] The relationship between trichostrongyliasis and different intensities of eosinophilia has been proven.[27, 31] In the same vein, 3 out of 4 (75%) patients with trichostrongyliasis, in our study, had elevated eosinophilia. Elevation of eosinophil level to about 52% of leukocytes/mm^3 in blood was found in a patient with trichostrongyliasis in France.[32]

Cystic echinococcosis (CE) is a frequent infectious disease among different animals as well as humans in Middle East as an endemic area[33]. Although it is believed that eosinophilia is seen in less than one quarter of the

cases of hydatid cyst,[27] 38.5% (5/13) of our cases were identified with eosinophilia.

Protozoan infections infrequently cause peripheral eosinophilia. The intestinal coccidian like *Isospora belli* and *Sarcocystis hominis*[16,17] can be related with eosinophilia. Furthermore, there are some reports about the relationship between malaria (*Plasmodium falciparum*) and eosinophilia.[34]

Among the patients infected with protozoa in our study, only few cases of giardiasis and blastocystosis showed an eosinophil count higher than normal range respectively.

Various studies on *Blastocystis* have recently been flourished.[35,36] Our results showed that 2/20(10%) of the individuals infected with *Blastocystis hominis* had an increased percentage of eosinophils.

Some of the studies in the field of *Giardia* and eosinophilia are the case reports[37,38] and there are no considerable number of studies conducted on larger sample sizes in this regard. In a study carried out by Ashrafi et al, only 2.7% of the patients with high percentage of eosinophils had giardiasis.[14] In our study, 3 out of 26 (11.5%) persons infected with *G. lamblia* showed higher percentage of eosinophils.

In this study, the percentage of eosinophils was compared between the individuals with parasitic infections. Generally, our findings are in line with a lot of available results on parasitic diseases and eosinophilia. The *Fasciola* spp. and *S. stercoralis* as the most important helminthic infections that cause tissue exposure showed higher levels of eosinophilia among helminthic infections. A few number of the patients infected with *G. lamblia* and *B. hominis* as protozoan diseases also showed high eosinophil counts. Eosinophilia could be a useful marker especially in the diagnosis of *Fasciola* spp. and *S. stercoralis* in helminthic infections, and in this particular context *G. lamblia* and *B. hominis* should be further noticed.

Authors' Contributions

Study concept and running tests: MR; Analysis and interpretation of data: MR and TM; Drafting the manuscript: TM, KK.

Ethical Approval

This study was approved by the Ethics Committee of Baqiyatallah University of Medical Sciences (Ethical code number: IR.BMSU.REC.1396.535)

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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