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Original Article

Clinical and Laboratory Findings among Patients with Toxocariasis in Medic Medical Center, Ho Chi Minh City, Vietnam in 2017-2019

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Abstract

Background: Human toxocariasis is prevalent in many countries but this disease has been rarely reported from Vietnam. We aimed to investigate the clinical and laboratory findings and assess possible association between these findings in patients with toxocariasis in Vietnam.

Methods: A prospectively study, between October 2017 and June 2019 was performed involving 120 toxocariasis patients at Medic Medical Center, Ho Chi Minh City, Vietnam. The diagnosis of toxocariasis was established based on clinical, laboratory (eosinophilia, raised IgE concentration) and serological (positive *Toxocara* IgG ELISA test) evaluation as well as the exclusion of other helminthic coinfection.

Results: The most frequently reported manifestation was of skin (n = 93, 77.5%), including urticarial (n= 69, 57.5%) followed by neurologic, gastrointestinal and pulmonary signs/symptoms. Hepatic involvement occurred in 8.3% of the patients. No significant relationship between clinical findings and laboratory parameters was found except the higher values of eosinophil count and IgE concentration among patients with liver involvement. There was a significant relationship between eosinophil count and IgE concentration ($r=0.389$, $P<0.001$). Serological findings did not show a correlation with clinical and other laboratory findings.

Conclusion: Our data revealed a wide range of clinical symptoms/signs and a high incidence of skin manifestations in patients with toxocariasis. Eosinophil count and IgE concentration are valuable markers for the evaluation of the disease.



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Introduction

Toxocariasis is a zoonotic disease caused by some nematode species (ascarids), *Toxocara canis* or *T. cati*, that routinely infect dogs or cats around the world (1). Humans become infected with these ascarids by ingesting embryonated eggs from soil/water or infective larvae in improperly cooked tissues of paratenic hosts. In aberrant hosts such as human *Toxocara* larvae fail to develop to mature adult worms but, instead, they wander throughout the body and cause damage to the tissues they enter (1).

The clinical symptoms are variable and non-specific because the larvae can invade a wide range of organs. Human toxocariasis may be asymptomatic or manifested as syndromes known as visceral larva migrans (VLM), ocular larva migrans (OLM), neurotoxocariasis and covert or common toxocariasis (CT) (2).

The definite diagnosis of human toxocariasis can be made by the detection of larvae or larval DNA from tissue or body fluid samples (2). Sampling tissue biopsies or fluid samples can be extremely difficult, so a diagnosis of human toxocariasis has mostly relied on the use of immunological techniques. Enzyme-linked immunosorbent assay (ELISA) based on *Toxocara* excretory-secretory (TES) antigens from infective-stage larvae have been widely used for serodiagnosis of human toxocariasis (2, 3). However, immunodiagnostic tests are not capable of distinguishing between current and past infection so some other tests have been used to support the diagnosis (4). Among non-specific laboratory indices, the increase in the blood eosinophil count and the concentration of serum total IgE are the most prominent (5). There have been many studies on laboratory feature of patients with toxocariasis but the association between them has only been partially investigated (6, 7).

Vietnam is a country in Southeast Asia with a hot and humid climate which is favorable for

the transmission of *Toxocara* and other helminths (8, 9). People living there are frequently infected with *Toxocara* (10, 11) but data on the clinical or laboratory features of Vietnamese patients is limited.

We aimed to add data on the sociodemographic pattern, clinical presentation, laboratory profile of human toxocariasis in Vietnam then to assess any possible association between clinical and laboratory findings in these patients.

Materials and Methods

Study design

This prospective study was carried out at the Medic Medical Center, Ho Chi Minh City, Vietnam during October 2017 and June 2019. All patients visiting the center with clinical symptoms/signs suspected of helminthiasis were screened for infection. Criteria for inclusion were subjects more than 5 years old and diagnosed as toxocariasis. Criteria for exclusion were pregnant women, subjects exhibiting hepatic or renal dysfunction, having acute diseases or concurrent parasitic diseases.

Data collection

Information about the demographic features and risk factors were collected based on a case record form (CRF). Biological examinations composed of blood cell counts, standard tests of blood biochemistry, abdominal ultrasound and computed tomography (CT), chest X-ray and CT, brain magnetic resonance imaging (MRI). Total serum IgE concentrations were measured using the Elecsys and Cobas 8000 (Roche) analyzers. The stool samples were collected and examined for intestinal helminths. ELISA tests for some infection common in Vietnam (cysticercosis, fascioliasis, strongyloidiasis, gnathostomiasis and amebiasis, toxocariasis) were performed using Cortez

Diagnostics Inc. following the manufacturer's instructions.

Definition

Participants aged 6 to 17 yr were classified as children and those 18 years and older were classified as adults (12). The hemoglobin cut-off of 120 g/L for women and children or 130 g/L for men was used to identify anemia (13). Leukocytosis was identified as > 10000 cells/ μL . Peripheral eosinophilia was defined as blood eosinophil count of >500 cells/ μL and those with >1500 cells/ μL was classified as marked eosinophilia (14). Increased IgE concentration was considered when the value was over 130 IU / mL. Patients with multiple low-echoic or low-density lesions found upon hepatic sonography or CT was considered having liver involvement (15). Lung parenchymal involvement was defined when diffuse multiple nodular infiltrations were found upon a CT scan. Patients having symptoms or signs compatible with active toxocariasis, a positive result of the *Toxocara* ELISA, eosinophilia, raised IgE concentration and a negative result for other parasitic coinfection were diagnosed as toxocariasis (16).

Statistical analysis

Data analysis was performed by a statistics package SPSS 16.0 (SPSS-IBM Company).

The relationships among laboratory data, organ involvements, and symptoms were analyzed by Mann–Whitney test. The Pearson correlation coefficient was used to measure the strength of a linear association between different laboratory parameters. *P*-value less than 0.05 was considered statistically significant.

Ethical consideration

This research is part of thesis work for the fulfillment of Doctor of Philosophy in Health Studies at the National Institute of Malaria, Parasitology and Entomology (NIMPE) of Vietnam and obtained clearance from the ethical committee of the NIMPE. Written or verbal consent was obtained from all subjects or their parents/guardians (on behalf of their children). All persons with positive results of parasitic infection were provided with drug treatment at the center.

Results

Table 1 summarizes the demographic characteristics of the participants. There were 120 patients aged from 14 to 70 year old involved in the current study with the majority was female (62.5%).

Table 1: Demographic characteristics of the study population (N=120)

Variable		N	Percentage (95%CI)
Age (yr)	Mean \pm SD	41 \pm 15	
	Range	14 - 70	
Gender	Male	45	37.5 (28.7 – 46.3)
	Female	75	62.5 (53.7-71.3)
Occupation	Farmers	35	29.2 (20.9 – 37.4)
	Other	85	70.8 (62.6 – 79.1)
Level of education	Primary school	20	16.7 (9.9 – 23.4)
	Secondary school	85	70.8 (62.6 – 79.1)
	College/university	15	12.5 (6.5 – 18.5)
Risk factors	Ownership dogs or cats	61	50.8 (41.8 – 59.9)
	Soil contact	56	46.7 (37.6 – 55.7)
	Eating fresh vegetables	17	14.2 (7.8 – 20.5)
	Eating undercooked meat	10	8.3 (3.3 – 13.4)

A significant proportion of participants owned dogs and/or cats. Soil contacts were present among 46.7% of the patients. A small proportion of patients had a habit of eating fresh vegetables or undercooked meat.

Clinical characteristics are given in Table 2. The predominant signs/symptoms were of skin (77.5%) followed by the manifestation of nerve, abdomen and pulmonary. Hepatic involvement occurred in 8.3% of the patients.

Table 2: Clinical characteristics of the study population (N=120)

<i>Organisation involved</i>	<i>Symptoms/signs</i>	<i>N</i>	<i>Percentage</i>
Cutaneous manifestation	Chronic urticaria	69	57.5 (48.5 – 66.5)
	Pruritus	30	25.0 (17.1 – 32.7)
	Erythematous rash	22	18.3 (11.3 – 25.4)
	Hypodermic nodules	12	10.0 (4.6 – 15.5)
		42	35.0 (26.3 – 43.7)
Neurologic disorders	Headache	32	26.7 (18.6 – 34.7)
	Dizziness	20	16.7 (9.9 – 23.4)
	Sleep disorder	11	9.2 (3.9 – 14.4)
Respiratory disorders		26	21.7 (14.2-29.1)
	Dry cough	18	15.0 (8.5 – 21.5)
	Chest pain	7	5.8 (1.6 – 10.1)
	Difficult breathing	4	3.3 (0.1 – 6.6)
	Wheezing	3	2.5 (0.3 – 5.3)
Digestive disorders		38	31.7 (23.2 – 40.1)
	Abdominal pain	28	23.3 (15.7 – 31.0)
	Loss of appetite	20	16.7 (9.9 – 23.4)
	Diarrhoea	18	15.0 (8.5 – 21.5)
	Liver involvement	10	8.3 (3.3 – 13.4)

There were 16.7% of patients having leucocytosis. All the participants had a high eosinophil count and only 8.3% of them showed marked eosinophilia. The mean value

of serum IgE concentration was 764.7 IU/ml (ranging from 135 to 3.000 IU/ml). There were some patients with mild anemia (Table 3).

Table 3: Laboratory characteristics of the study population (N=120)

<i>Laboratory parameters</i>		<i>N</i>	<i>Percentage</i>
Red blood cell (1000 cells / μ L)	Mean \pm SD	4,716.85 \pm 541.526	
	Range	3870 – 7050	
Haemoglobin levels (g/L)	Mean \pm SD	14.195 \pm 1.296	
	Range	11.4 - 17.9	
Anemia		3	2.5 (0.3 – 5.3)
Leukocytes (cells / μ L)	Mean \pm SD	8.331 \pm 1.904	
	Range	4.810 - 12.770	
Leucocytosis		20	16.7 (9.9 – 23.4)
Eosinophile (cells / μ L)	Mean \pm SD	919 \pm 491	
	Range	518 - 3.350	
Eosinophilia		120	100
Marked eosinophilia		10	8.3 (3.3 – 13.4)
Anti- <i>Toxocara</i> spp. IgG (OD)	Mean \pm SD	1.51 \pm 0.85	
	Range	0.36 - 3.50	
IgE concentration (IU / mL)	Mean \pm SD	764.7 \pm 630.6	
	Range	135 - 3.000	
Raised total IgE		120	100

Results in Table 4 showed that IgE concentration and eosinophil count were significantly

higher in patients with liver involvement than in those without hepatic lesion ($P < 0.05$).

Table 4: The value of peripheral blood eosinophil count, serum IgE, and IgG ELISA OD in patients having different organ involvement

Symptoms/ signs	Laboratory parameters	Present of symptoms		P-value
		Yes	No	
Chronic urticaria	Eosinophils (cells / μ L)	911.74 \pm 458.11	928.22 \pm 536.27	0.834
	IgE concentration (IU / mL)	781.89 \pm 658.91	741.38 \pm 595.81	0.610
	OD value	1.40 \pm 0.78	1.65 \pm 0.92	0.155
Pruritus	Eosinophils (cells / μ L)	866.17 \pm 522.81	776.47 \pm 348.50	0.109
	IgE concentration (IU / mL)	561.62 \pm 289.25	832.36 \pm 697.07	0.151
	OD value	1.33 \pm 0.75	1.60 \pm 0.86	0.051
Erythematous rash	Eosinophils (cells / μ L)	862.73 \pm 495.97	931.32 \pm 491.24	0.276
	IgE concentration (IU / mL)	756.62 \pm 735.79	766.48 \pm 608.78	0.533
	OD value	1.46 \pm 0.76	1.52 \pm 0.87	0.914
Hypodermic nodules	Eosinophils (cells / μ L)	881.42 \pm 179.73	945.11 \pm 507.44	0.069
	IgE concentration (IU / mL)	577.66 \pm 354.94	785.45 \pm 651.87	0.399
	OD value	1.34 \pm 1.02	1.52 \pm 0.83	0.280
Headache	Eosinophils (cells / μ L)	998.53 \pm 598.48	889.73 \pm 445.63	0.158
	IgE concentration (IU / mL)	749.86 \pm 583.13	770.06 \pm 650.11	0.689
	OD value	1.53 \pm 0.82	1.49 \pm 0.87	0.680
Dizziness	Eosinophils (cells / μ L)	1019.25 \pm 509.07	898.64 \pm 487.13	0.081
	IgE concentration (IU / mL)	814.83 \pm 725.04	754.64 \pm 613.59	0.866
	OD value	1.34 \pm 0.61	1.54 \pm 0.89	0.576
Sleep disorder	Eosinophils (cells / μ L)	726.82 \pm 154.21	938.11 \pm 508.94	0.237
	IgE concentration (IU / mL)	613.14 \pm 238.70	800.15 \pm 647.32	0.053
	OD value	1.47 \pm 0.87	1.51 \pm 0.85	0.895
Dry cough	Eosinophils (cells / μ L)	935.00 \pm 484.19	915.87 \pm 494.19	0.988
	IgE concentration (IU / mL)	574.42 \pm 385.12	798.25 \pm 660.27	0.210
	OD value	1.67 \pm 0.79	1.48 \pm 0.86	0.252
Abdominal pain	Eosinophils (cells / μ L)	1072.25 \pm 672.41	872.02 \pm 413.91	0.256
	IgE concentration (IU / mL)	974.99 \pm 879.12	700.66 \pm 522.45	0.346
	OD value	1.47 \pm 0.79	1.51 \pm 0.87	0.963
Loss of appetite	Eosinophils (cells / μ L)	937.20 \pm 449.34	915.05 \pm 500.64	0.902
	IgE concentration (IU / mL)	757.64 \pm 766.75	766.08 \pm 604.27	0.660
	OD value	1.29 \pm 0.72	1.55 \pm 0.87	0.267
Diarrhea	Eosinophils (cells / μ L)	928.61 \pm 622.73	864.06 \pm 445.35	0.081
	IgE concentration (IU / mL)	1098.75 \pm 916.22	705.72 \pm 551.21	0.106
	OD value	1.59 \pm 0.88	1.49 \pm 0.85	0.643
Liver involvement	Eosinophils (cells / μ L)	1574.60 \pm 928.08	859.12 \pm 385.68	0.011*
	IgE concentration (IU / mL)	1097.14 \pm 792.01	734.45 \pm 609.33	0.038*
	OD value	1.59 \pm 0.85	1.49 \pm 0.85	0.638

Figure 1 presents a significant association between IgE concentration and eosinophil count ($r=0.389$, $P<0.001$). The relation between OD value and serum IgE concentration

or eosinophil count was not statically significant ($r=0.134$, $P=0.146$ and $r=0.010$, $P=0.916$ respectively).

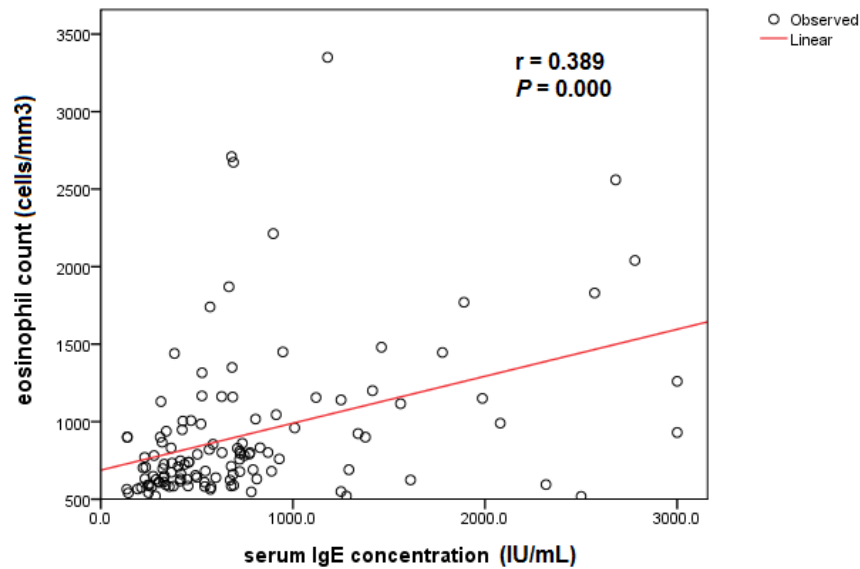


Fig. 1: The correlation between serum IgE concentration and eosinophil count

Discussion

The demographic characteristics and related factors

The study population was comprised of 120 subjects and females were more affected (62.5% of the patients). Epidemiological studies have revealed no association between gender and risk of infection (17) so the majority of female in the current study may present the differences in care consultation rates among genders (18). Most of the patients were adult which was consistent with some other surveys in Asia (11, 19, 20). A significant proportion of participants owned (50.8%) dogs or/and cats (25.0%) that was a proven risk factor for *Toxocara* infection (21). Soil contacts were present among 46.7% of the patients. *Toxocara* eggs are extremely resistant and may remain viable in the soil for a long time, therefore, the risk of ingestion of infective eggs from the contaminated soil is possible even if there is no recent presence of dogs or cats (22). About 29.2% of the patients were farmers and the remaining patients were students, workers, employees or small traders. The role of living in rural areas is now not so important, as

toxocariasis has been observed more frequently in the urban environment (23).

Clinical characteristics

The most frequently documented symptoms/signs were cutaneous manifestations followed by neurologic, gastrointestinal and respiratory symptoms that were commonly involved in patients with toxocariasis (24-26). For the pleomorphism of the clinical manifestations of toxocariasis the frequency of symptoms/signs is different among various reports (25, 27, 28). The predominance of skin manifestations in our patients could be because symptoms such as pruritus, rash, etc. were easily recognized and prompted people to consult doctors early. In some cases, cutaneous manifestations are the only signs indicating human toxocariasis (29). The respiratory symptoms reported in the study were dyspnea, wheezing, nonproductive cough and chest pain that were common in toxocariasis and presented mild infection (2). More severe respiratory tract involvement is uncommon and appears only among those with very heavy infection (30). Gastrointestinal symptoms such as abdominal pain, anorexia, nausea, vomiting, diarrhoea were observed in 31.7%

patients which were compatible with Ain Tiewsoh JB' findings (35.7%) (25). There were ten (8.3%) patients with liver involvement that may present the more severe form of toxocariasis among the participants. The neurological manifestations found in the participants included headache, dizziness and sleep disturbance which has been described by several authors (1, 28).

Laboratory characteristics

The immune responses to *Toxocara* larvae characterized by the Th2 response which is generally accepted as the responsible mechanism leading to two of the most notable clinical features of larva migrans, eosinophilia and the IgE hyperglobulinemia (31). Among helminthic causes of eosinophilia *Toxocara* maybe the most common and eosinophilia is considered a classic criterion of VLM (26). The level of eosinophilia in some patients with toxocariasis may be very pronounced, with counts as high as 15,000-100,000 cells/ μ L (14). Eosinophilia and raised total IgE presented in all patients, however, the level of eosinophilia in the current study was mild (average eosinophil count of 919 cells / μ L) and only 8.3% of patients had marked eosinophilia. The mild level of eosinophilia may suggest the light infection (32) and compatible with mild symptoms/signs in the participants. Serum IgE levels are alternative marker assisting in the diagnosis of a current *Toxocara* infection. The raised IgE concentration is a less effective marker than eosinophilia (33, 34) but could be very helpful for the diagnosis of toxocariasis in case of sequestration of eosinophils in infected tissues and the peripheral eosinophil count may not fully reflect the true infectious (26).

Leukocytosis presented in a minority of the patients (16.7%). Leukocytosis has not been considered as a diagnostic marker for toxocariasis because the leukocyte counts could be dependent on many other factors (16). Anemia was documented in only 2.5% patients

and all of them had mild anemia which in line with other reports (25), (28).

Correlation between clinical symptoms and laboratory indices

The correlation between clinical symptoms and the level of IgE production or eosinophilia have been reported in some study (35). The only association found in the current study was higher values of IgE concentration and eosinophil count in patients with hepatic involvement. *Toxocara* was the most common cause of eosinophilic liver abscess (36). The size of the infection is proportional to the amount of trapping or arresting larvae in the liver (37) so the existence of an association between higher values of IgE and eosinophil count in patients with liver involvement is explainable. The lack of relationship between other clinical signs/symptoms and other laboratory indices may suggest the low level of infection among the participants. The magnitude of immune response is proportional to the intensity of infection (38) and only in those with severe lesion such as liver involvement, the response become significant.

Similarly to other findings (39), (4) we have found no correlation between the IgG titers and clinical manifestations. IgG-ELISA is the most useful test in serodiagnosis of human toxocariasis; however, the significant of the titers of ELISA IgG OD value is not clear. Although patients with strong clinical evidence of toxocariasis have very high ELISA values, some patients with important infections have lower values and some asymptomatic patients have high titers (40).

Correlation between different laboratory parameters

There was a significant relation between eosinophil count and IgE concentration but no relationship between IgG and other parameters was found. The association between intensity of IgE response and the level of eosinophilia have been reported (6, 7, 28). The absence of a relationship between the level of

anti-*Toxocara* antibodies and eosinophilia or IgE concentration in the current study was consistent with some previous findings. Studies in Iran, Sri Lanka and Brazil did not document a statistically significant correlation between eosinophilia and *Toxocara* seropositivity (3, 41, 42). A little correlation between IgG and IgE in the sera of patients with symptomatic toxocariasis was reported (43). Taylor et al found 27% of toxocariasis patients with high titers of IgG had normal eosinophil counts (24). The lack of correlation between IgG and other markers of serological response may be due to the difference in persistence time of these markers. IgG antibodies can persist for a long time while IgE and eosinophil count significantly decreases after the treatment (4, 44).

Conclusion

This research has revealed that Vietnamese patients have a wide range of clinical symptoms/signs that mainly present mild forms of toxocariasis. Given the fact that most patients have cutaneous manifestation, the authors propose the inclusion of this clinical entity in the differential diagnosis of patients with eosinophilia and cutaneous symptoms. The positive association between IgE concentration and eosinophil count and hepatic involvement suggests these two parameters are valuable markers for the evaluation of the disease. Further studies to ascertain the contribution of this parasitic disease to the overall morbidity and efforts to increase the awareness of toxocariasis in the community are needed.

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Conflict interest

The authors declare that they have no conflict interests.

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