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Toxocariasis and Toxoplasmosis in Children with Idiopathic Epilepsy in Mid-Region of the Nile Delta, Egypt: Prevalence and Risk Factors

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A B S T R A C T

Epilepsy is one of the most common and important neurological disorders among children especially in developing countries. *Toxoplasma gondii* (*T. gondii*) is an intracellular protozoan capable of forming cysts in the brain of chronically infected humans. Moreover, the larvae of *Toxocara canis* (*T. canis*) can locate in the central nervous system leading to several neurological disorders. This study was undertaken to identify the prevalence and risk factors of toxocariasis and toxoplasmosis in children with idiopathic epilepsy. This study was conducted on 150 children aged 2−15 years, including 100 children suffering from idiopathic epilepsy and 50 apparently healthy children as a control group. All children were submitted to clinical questionnaire. They were tested for the presence of anti-*Toxocara* IgG by ELISA and western blotting, and for presence of anti-*Toxoplasma* IgG and IgM by ELISA and avidity test. The frequency of *Toxocara* infection in epileptic patients was 13% versus 4% of the healthy group by ELISA. By western blotting technique, Anti-*Toxocara* IgG antibodies were detected in 7 (53.8%) of ELISA positive children in epileptic children group, whereas the serum samples of all ELISA-positive normal children were negative. Contact with dogs is the main risk factors for toxocariasis. Regarding *T. gondii*, by ELISA, 74 (74%) epileptic children had anti-*T. gondii* antibody, 59 had *Toxoplasma* IgG only, 3 cases had *Toxoplasma* IgM only, and 12 cases had both *Toxoplasma* IgG and IgM. Moreover, 20 (40%) normal children had positive results. Residence, contact with cats, contact with soil, and drinking unfiltered water are important risk factors for toxoplasmosis. There was significant association between toxoplasmosis and idiopathic epilepsy. Despite being statistically insignificant, the association between *Toxocara* infection and epilepsy still needs further investigation.

Introduction

Childhood epilepsy is one of the most important neurological disorders in both developing and developed countries. Epilepsy has an impact on both mental and physical health of children. Epileptic children may suffer from behavioral disorders, psychiatric disorders, and social isolation due to social stigmatization (Baca *et al.,* 2011; Camfield and Camfield, 2015). The underlying cause of epilepsy is unknown in more than 60 % of epileptic patients in spite of development of advanced diagnostic methods (Bell *et al.,*

2014). Infectious agents are implicated in its etiology. Several epidemiological studies have investigated the role of some helminths and protozoa such as *Taenia sollium*, *Toxocara*, *Plasmodium*, and *Toxoplasma* in causing epileptic attacks (Sander and Perucca, 2003; El-Tantawy *et al.,* 2013).

Toxocariasis is one of the most commonly reported zoonotic infections in the world. It is a helminthic disease caused by two species of the ascarid nematodes *Toxocara canis* (*T. canis*) and to a lesser extent *T. cati* (Macpherson, 2013). Toxocariasis carries a major health risk especially in the developing countries due to untreated and uncontrolled definitive hosts, poor hygiene, geophagia, lower education levels, and poverty which provide ideal transmission opportunities (Oryan *et al.,* 2010; Congdon and Lloyd, 2011). Children are more susceptible to this infection because they handle contaminated soil (Figueiredo *et al.,* 2005).

Toxocariasis can be classified as visceral larva migrans, ocular larva migrans, covert toxocariasis and neurotoxocariasis (Fan *et al.,* 2013).The larvae of *Toxocara* can reach the central nervous system (CNS) causing a variety of neurologic disorders. Toxocariasis has been suggested as a co-factor for epilepsy (Nicoletti *et al.,* 2008).

Another parasitic infection which is thought to be associated with epilepsy is toxoplasmosis. Toxoplasmosis is caused by obligate, intracellular, parasitic protozoan called *Toxoplasma gondii* (*T. gondii*). It is one of the most common parasitic infections in humans and other warm-blooded animals with worldwide distribution. It is estimated to cause infection in one-third of the world's human population (Tenter *et al.,* 2000; Dubey and Jones, 2008). After acute toxoplasmosis, the infection becomes latent and becomes encysted especially in the central nervous system and in the muscle tissues for the life of the infected host (Dubey and Jones, 2008; Miller *et al.,* 2009). It has several clinical manifestations ranging from asymptomatic infection to multiorgan involvement (Montaya and Liesenfeld, 2004).

Cerebral toxoplasmosis can cause seizures and intracranial mass lesions (Zibaei *et al.,* 2011). The latent form of *T. gondii* is a common and dormant infection affecting the brain and has the potential to cause epilepsy (Yazar *et al.,* 2003). However, a few data are available concerning seroprevalence of *T. canis* infection and the association between this infection, and toxoplasmosis with idiopathic epilepsy in Egypt.

The aim of this study was to identify the prevalence and risk factors of toxocariasis and toxoplasmosis in children with idiopathic epilepsy in Mid-Region of the Nile Delta, Egypt.

Materials and Methods

Subjects

This study was carried out in the period from July 2016 to July 2017. The nature of the study was explained to one of the parents or the legal guardian of the child. Informed consents were obtained, and ethics committee approved the protocol in compliance with the current standard laws.

This study was conducted on 150 children 2‒15 years old including 100 children suffering from idiopathic epilepsy, as evidenced by history, normal general and neurological examination, and normal Magnetic resonance imaging (MRI) of the brain, who were attendants of Paediatric Neurology Unit of Tanta University Hospital (epileptic group) and 50 apparently healthy children as a control group.

Methods

All children were subjected to history taking through a questionnaire including personal data; risk factors for *Toxocara* and *Toxoplasma* as contact with animals (dogs and cats), contact with the soil, and consumption of undercooked meat or unfiltered water; current complaints with special inquiry on fever, lymphadenopathy, skin lesions, other neurological manifestations, and eye manifestations; history of the present illness including onset, progress of their current disease, received treatment, and investigations. Careful physical and neurological examinations were done for all the participants.

Three milliliters venous blood sample was taken from epileptic and normal children under sterile condition. One ml of blood was collected in EDTA tube to be used for determination of total leucocytic count and differential leucocytic count for calculation of absolute eosinophilic count according to Dacie and Lewis (1992). Eosinophilia was categorized into mild (600−1500 cells/mm^3), moderate (1500−5000 cells/mm^3) and high (more than 5000 cells/mm^3) (Singh *et al.,* 2009). The other 2 ml of blood was centrifuged at 2000 rpm for 10 min; the separated serum was kept at -20ºC in sterile aliquots and labeled with the child name and number for the serological tests. Haemolyzed samples were not used to prevent any potential error in test results.

Tests for anti-*Toxocara* IgG antibodies

The separated serum samples were used for detection of anti-*Toxocara* IgG by Enzyme-linked immunosorbent assay (ELISA). Anti-*Toxocara* antibodies (IgG) were detected by a commercial ELISA kit (Diagnostic Automation/Cortez Diagnostics, Inc., California, USA) according to the manufacturer's instructions.

Positive cases with anti-*Toxocara* IgG with ELISA were reexamined with western blotting technique for confirmation relied also upon a commercial kit (LDBIO Diagnostics, Lyon − France) following the manufacturer's guidance.

Tests for anti-*Toxoplasma* antibodies

The separated serum samples were used for detection of anti-*Toxoplasma* IgG and IgM by ELISA. Enzyme-linked immunosorbent assay test (Institut Virion\Serion GmbH, Germany) was used for screening of all the samples fo anti- *T. gondii* IgG and IgM antibodies according to the manufacturer's instructions. Positive cases with anti- *Toxoplasma* IgG and IgM were re-examined with *Toxoplasma* IgG avidity test using The "DS-EIA-ANTI-TOXO-G-AVIDITY" kit (DSI S.r.1.Saronno (VA), Via A.Volonterio, 36a, 21047, Italy).

Statistical analysis

The data were analyzed statistically using SPSS version 22.0 software (IBM, Armonk, NY, United States of America). Qualitative data were expressed as frequency and percentage. Chi-square test and Fisher's test were used as tests of significance. The values of $P<0.05$ were considered to be statistically significant.

Results and Discussion

Demographic data in epileptic and normal participants

In epileptic children group, 58 (58%) were males and 42 (42%) were females, and the normal children group consisted of 24 males (48%) and 26 females (52%). The participants' ages ranged from 2 to 15 years. The differences were statistically insignificant as shown in table 1.

Seroprevalence of *T. canis*

Enzyme-linked immunosorbent assay (ELISA)

According to ELISA results, 13 (13%) epileptic children had anti-*Toxocara* IgG antibody. Out of the 50 normal children, 2 (4%) had positive results and the difference was statistically insignificant (*P* >0.05) as shown in table 2.

Western blotting technique

Serum samples from *Toxocara* ELISA-positive cases were investigated using western blotting. Anti-*Toxocara* IgG antibodies were detected in 7 (53.8%) of ELISA-positive children in epileptic children, whereas the serum samples of all ELISA-positive normal children were negative by western blotting. There was no statistically significant difference between epileptic and normal children (*P*>0.05) as shown in table 2. The positive western blotting strips which indicate the presence of specific anti-*Toxocara* IgG in the samples showed at least two or more bands of low molecular weight between 24 and 35 kDa as shown in figure 1.

Regarding eosinophilia in seropositive cases, 6 cases (85.7%) had high eosinophilia and 1 (14.3%) case had moderate eosinophilia. There was significant association between eosinophilia and toxocariasis (*P*<0.05).

Risk factors of toxocariasis in epilepsy

There were no statistically significant differences between seropositive and seronegative epileptic groups regarding age, gender, residence, contact with soil, eating undercooked meat. Regarding the role of contact with dogs as a risk factor for toxocariasis in epilepsy, there was significant difference between both groups (*P*<0.05) as shown in table 3. It was found that children who were exposed to dogs were at 6 times higher risk of developing toxocariasis (OR, 6.442; 95% CI, 1.175−35.307).

Seroprevalence of *T. gondii*

Enzyme-linked immunosorbent assay

There was statistically significant difference in *T. gondii* IgG antibodies between epileptic and normal children (*P*<0.05). According to ELISA results, 74 (74%) children with idiopathic epilepsy had anti-*T. gondii* antibody. Of the 74 seropositive epileptic children, 59 had *Toxoplasma* IgG only, 3 cases had *Toxoplasma* IgM only, and 12 cases had both *Toxoplasma* IgG and IgM. Out of the 50 normal children, 20 (40%) had positive results as shown in table 4.

By using the avidity test for patients seropositive with *T. gondii* IgG and IgM antibodies, all tested positive sera showed high avidity.

Risk factors for toxoplasmosis in epilepsy

Regarding the role of residence, contact with cats, contact with soil, and drinking unfiltered water as risk factors for toxoplasmosis in epilepsy, there was significant difference between different groups (*P*<0.05); whereas, there were no statistically significant differences concerning the age, gender or consumption of undercooked meat between different groups as shown in table 5.

It was found that epileptic children who lived in rural areas were at 23 times higher risk of developing toxoplasmosis (OR, 23.852; 95% CI, 6.403−88 .852). Epileptic children drinking unfiltered water were at 15 times higher risk of developing toxoplasmosis (OR, 15.225; 95% CI, 4.961−46.728).

Types of seizures in seropositive epileptic children

Out of 74 epileptic children who were seropositive with toxoplasmosis, 49 cases (66.2%) had generalized seizures, 16 cases (21.6%) had focal seizures, and 9 cases (12.2%) had absence epilepsy. There was statistically significant difference between the different types of seizures as shown in table 6. Out of 7 epileptic children seropositive with toxocariasis, 5 cases (71.4%) had generalized seizures, 1 case (14.3%) had focal seizures, and 1 case (14.3%) had absence epilepsy. There was statistically significant difference between the different types of seizures as shown in table 6.

Table.1 The demographic data in epileptic and normal participants

Factors	Epileptic children (n=100)		Normal children (n=50)		Total (n=150)		χ^2	P
	n	%	n	%	n	%		
Age groups (years)								
2− <6	45	45	25	50	70	46.7		
6− <10	40	40	18	36	58	38.7	0.513	**0.776**
10−15	15	15	7	14	22	14.6		
Gender								
Male	58	58	24	48	72	48	1.345	**0.247**
Female	42	42	26	52	78	52		
Residence								
Rural	59	59	28	56	87	58	0.123	**0.726**
Urban	41	41	22	44	63	42		

Table.2 Seroprevalence of *T. canis* in epileptic and normal children

	Epileptic children (n=100)		Normal children (n=50)		Total (n=150)		χ^2	P
	n	%	n	%	n	%		
Seropositive with ELISA only	13	13	2	4	15	10	3.000	**0.083**
Seropositive with ELISA and western blotting	7	7	0	0	7	4.7	3.671	**0.055**

Table.3 Summary of risk factors to toxocariasis in epileptic patients

Risk factors	Seropositive (7)		χ^2	P
	n	%		
Age 2− <6 (45)	0	0	5.572	0.062
6− <10 (40)	3	7.5		
10−15 (15)	4	26.7		
Gender Male (58)	5	8.6	0.552	0.458
Female (42)	2	4.8		
Contact with dogs Yes (n=31)	5	16.1	5.752	0.016*
No (n=69)	2	2.9		
Contact with soil Yes (n=68)	7	10.3	3.542	0.060
No (n=32)	0	0		
Eating raw or undercooked meat Yes (n=21)	2	9.5	0.263	0.610
No (n=79)	5	6.3		
Residence Rural (59)	4	6.8	0.011	0.918
Urban (41)	3	7.3		

Table.4 Seroprevalence of *T. gondii* antibodies (IgG and IgM) in epileptic and normal children

	Epileptic children (n=100)		Normal children (n=50)		Total (n=150)		χ^2	P
	n	%	n	%	n	%		
T. gondii IgG only	59	59	14	28	73	48.7	12.820	**0.001***
T. gondii IgM only	3	3	3	6	6	4	FE	**0.635**
T. gondii IgM and IgG	12	12	3	6	15	10	1.333	**0.249**

Table.5 Summary of risk factors to toxoplasmosis in epileptic patients

Risk factors	Seropositive (74)		χ^2	P
	n	%		
Age			2.763	0.251
2− <6 (45)	30	66.7		
6−<10 (40)	33	82.5		
10−15 (15)	11	73.3		
Gender			0.923	0.337
Male (58)	45	77.6		
Female (42)	29	69		
Eating raw or undercooked meat (n=21)	18	85.7	1.902	0.169
No (n=79)	56	70.9		
Contact with cats (n=58)	49	84.5	7.893	0.005*
No (n=42)	25	59.5		
Unfiltered water (n=63)	58	92	28.881	0.001*
No (n=37)	16	43.2		
Contact with soil (n=68)	62	91.1	32.587	0.001*
No (n=32)	12	37.5		
Residence	56	94.9	32.391	0.001*
Rural (59)				
Urban (41)	18	43.9		

*Significant (P <0.05)

Table.6 The distribution of *T. gondii* and *T.canis* antibodies in patients with different types of seizures

Types of seizures	*T. gondii* (n=74)		χ^2	P	*T. canis* (n=7)		χ^2	P
	n	%			n	%		
Generalized	49	66.2	55.502	0.001*	5	71.4	6.862	**0.037***
Focal	16	21.6			1	14.3		
Absence	9	12.2			1	14.3		

*Significant (P <0.05)

Figure.1 *T. canis* western blotting strips Strip one: positive control; Strips (2-5): positive Strip; (6): negative
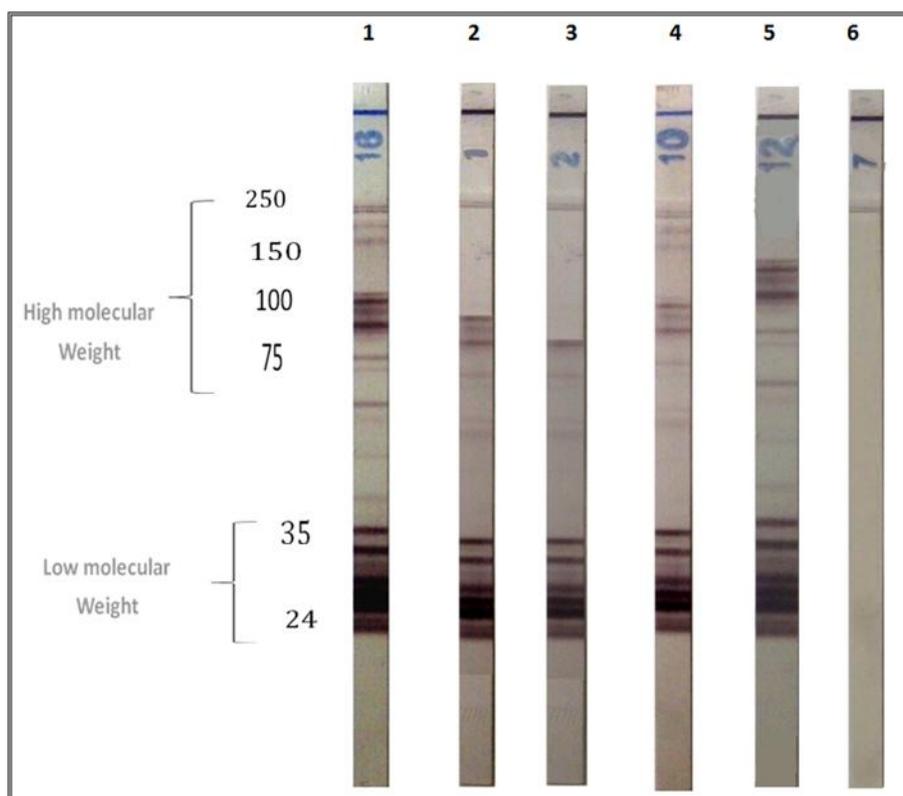
Epilepsy is one of the most common neurological diseases affecting almost 1 % of people worldwide (Thurman *et al.,* 2011). Epidemiological studies have suggested presence of an association between helminthic infections and epilepsy especially in the developing countries (Wanger and Newton, 2009). Regarding toxocariasis*,* the migrating *T. canis* larvae can reach the human brain causing epileptic foci (Despommier, 2003). Also, *T. gondii* can form dormant brain cysts which have the potential to cause epilepsy (Stommel *et al.,* 2001). However, such studies are lacking in our geographical location.

In the current study, we found that the frequency of *Toxocara* infection in epileptic patients was 13% versus 4% of the healthy group by ELISA. This finding has a scientific significance despite being statistically insignificant ($P > 0.05$). By western blotting,

anti-*Toxocara* IgG antibodies were detected in 7 (53.8%) of ELISA positive children in epileptic children group, whereas the serum samples of all ELISA-positive normal children were negative ($P > 0.05$). In accordance with these findings, Zibaei *et al.,* (2013) found that the frequency of *Toxocara* infection in epileptic patients was 11.8%, scientifically higher than the healthy group (3.5%).

Also, Eraky *et al.,* (2016) found no statistically significant difference between epileptic cases and healthy controls ($P>0.6$) as anti-*Toxocara* IgG antibodies were detected in 4 epileptic children (3 cases (7.5%) in cryptogenic and only 1 case (3.3%) in non-cryptogenic groups), and 2 seropositive cases (10%) only were found in the control subjects. The latter study has the limitation of the small sample size as there were 70

epileptic children and 20 healthy ones only involved in the study.

Many epidemiological studies have been carried out in different locations to investigate the presence of possible association between epilepsy and *T. canis* seropositivity. A significant association has been reported in many studies. In Burundi, Nicoletti *et al.,* (2007) reported that anti- *T. canis* antibodies were found in 114 epileptic patients (59.7%) and in 97 controls (50.8%). In a study done in Italy, the authors reported that anti-*T. canis* antibodies were found in 38 epileptic patients (16.4%) and in 13 controls (6.6%) giving a crude OR of 2.85 (Nicoletti *et al.,* 2008). In Iran, Allahdin *et al.,* (2015) found that 28 (19.85%) epileptic patients and 2(1.38%) of healthy people had anti-*Toxocara* antibodies by ELISA ($P<002$). Zibaei *et al.,* (2013) concluded that toxocariasis is a risk factor for epilepsy in Iran.

The current study showed the positive western blotting strips, which indicate the presence of specific anti-*Toxocara* IgG in the samples, with at least two or more bands of low molecular weight between 24 and 35 kDa. These results are similar to those reported in two studies in Iran as the authors have tested anti-*Toxocara* positive samples with western-blotting method and confirmed the presence of low molecular weight bands in the zone of 24-35 kDa as positive test (Zibaei *et al.,* 2013; Allahdin *et al.,* 2015).

Some pathogenic mechanisms have been proposed to explain the mechanisms of epileptogenesis in toxocariasis. *Toxocara* larvae could stimulate formation of a granulama around them. An acute granulomatous reaction can cause acute symptomatic seizures, and then may leave after resolution fibrous scars and chronic granulomatous lesions which may lead to epilepsy (Wagner and Newton, 2009). In

addition, the increases of the blood brain barrier permeability and the proinflammatory cytokines production due to the presence of *Toxocara* spp. larvae in the brain may be responsible for neuronal damage (Fan *et al.,* 2015). Similar physiopathological mechanisms have been suggested to be responsible for the epileptogenesis due to neurocysticercosis (Nash *et al.,* 2015). Also, presence of autoantibodies against neuronal elements may play a role in some types of epilepsies (Ganor *et al.,* 2005). The autoimmune nature of epilepsy may be explained by the presence of antibodies to a major excitatory neuro-transmitter in the CNS (Levite and Ganor, 2008) and it was found that toxocariasis stimulates autoantibodies production (Obwaller *et al.,* 2004).

Othman *et al.,* (2010) reported that experimental *T. canis* infection induced several alterations in the brains of infected animals including increased expression of pro-inflammatory cytokines and nitric oxide, neurotransmitter profile disturbances, and astrogliosis. The authors concluded that neurotransmitters level changes especially decreased GABA may explain increased incidence of seizures in children infected with *Toxocara*.

In helminthic infection, moderate to severe eosinophilia occurs as a part of pathophysiologic response to this infection (Klion and Nutman, 2004). It has been recognized that *Toxocara* infection is one of the causes of eosinophilia in the peripheral blood and eosinophilic infiltration in internal organs (Kwon *et al.,* 2006). A significant association between eosinophilia and infection by *T. canis* was observed in our study as reported by others (Kwon *et al.,* 2006; Karadam *et al.,* 2008).

As regards association of *T. canis* with the age, gender, residence, contact with soil, and

eating raw or undercooked meat in this study, there was no statistically significant difference between both groups regarding these factors. In partial accordance with these findings, Zibaei *et al.,* (2013) did not observe any significant difference between either of the seropositive and seronegative patients regarding age and residence in their investigations on adult epileptic patients. In the contrary, El-Tantawy *et al.,* (2013) found that the rate of *Toxocara* infection in epileptic patients was high in the age group 5−10 years, in male patients, seroprevalence of *Toxocara* has been reported in rural areas higher than urban areas in other studies of epilepsy.

Concerning the gender, our result is in accordance with Khademvatan *et al.,* (2014) who found that Anti-*Toxocara* antibodies were detected in 17.14% of females and 12.3% of males with schizophrenia disorder and there was no significant difference between gender and positive serology. As regards to the association between toxocariasis and contact with soil, this finding is in accordance with Akyol *et al.,* (2007) who found that there was no significant relationship between pica and *Toxocara* seropositivity rates in cryptogenic epileptic patients. On the contrary, in Ahvaz in southwestern Iran, a study showed high rates of soil infection in many parts of this city (46.5%) and this may be as a risk factor for toxocariasis (Khademvatan *et al.,* 2014). As regard to eating raw or undercooked meat, El-Sayed and Ismail (2012) found that seropositivity for *T. canis* was detected in 30.5% of schizophrenic patients with history of raw food intake and 9.7% of schizophrenic patients with no history of raw food intake and the difference was statistically significant. Our results may be due to diet changes with age, eating the raw or undercooked meat in the adulthood may increase the risk of exposure to the parasite.

In respect to association of toxocariasis with contact with dogs, the current study showed a high percentage of children with a history of contact with dogs among seropositive group (71.4%), while a lesser percentage was observed in seronegative group (27.9%) and there was a significant difference between the two groups (*P*<0.05). Also, children who were exposed to dogs were at 6 times higher risk of developing toxocariasis (OR, 6.442; 95% CI, 1.175−35.307). This is in accordance with Fernando *et al.,* (2007) who reported that children who were in contact to puppies less than 3 months at home were at 17 times higher risk of developing toxocariasis (OR, 17.51; 95% CI, 5.67−56.57). On the contrary, El-Tantawy *et al.,* (2013) found that there was no significant relationship between animal contact and *Toxocara* seropostivity rates in children with cryptogenic epilepsy.

The current study showed that the most common type of seizures among epileptic children who were seropositive with toxocariasis was the generalized one (71.4%) and there was statistically significant difference between the different types of seizures. On the contrary, Nicoletti *et al.,* (2008) concluded that there was significant association between toxocariasis and epilepsy and a stronger association was found with the partial epilepsy. Akyol *et al.,* (2007) found that there was no significant difference between the focal and generalized epilepsy groups regarding seropositivity rate for *T. canis*.

In the current study, patients and control sera were investigated for toxoplasmosis. There was association between *Toxoplasma* seropositivity and idiopathic epilepsy as there was statistically significant difference in *T. gondii* IgG antibodies between epileptic and normal children (*P*<0.05). Our results are consistent with many studies in which the authors reported that the level of *T. gondii*

IgG antibodies showed a statistically significant high value in children with epilepsy (El-Tantawy *et al.,* 2013; Ngoungou *et al.,* 2015). Stommel *et al.,* (2001) suggested that chronic toxoplasmosis with brain cysts may cause cryptogenic epilepsy. In contrast, other studies found that there was no association between epilepsy and toxoplasmosis (Allahdin *et al.,* 2015; Babaie *et al.,* 2017a).

The current study showed that there was no statistical difference between seroprevalence of IgM in epileptic and healthy children (*P*>0.05). This finding is in accordance with the study of Yazar *et al.,* (2003) which IgM antibodies were negative in all of the studied epileptic groups. Using the avidity test for patients who have both *T. gondii* IgG and IgM antibodies, IgG antibodies of high avidity were detected in 100% of these sera confirming past infection. This pointed to the possible role of latent toxoplasmosis rather than the recently-acquired infection in seizure disorders.

Many mechanisms could explain the association between toxoplasmosis and epilepsy. Recent evidence indicates that the dormancy of *T. gondii* in the brain is not true as the parasite has a dynamic status within the cysts (Watts *et al.,* 2015) which can alter the function of the neurons by modulation of neurotransmitters such as GABA (Brooks *et al.,* 2015), noradrenaline (Gatkowska *et al.,* 2013), serotonin (Gatkowska *et al.,* 2013), dopamine (Babaie *et al.,* 2017b), glutamate (Kannan *et al.,* 2016) and nitric oxide (Tonin *et al.,* 2014; Dincel and Atmaca 2015). Moreover, *T. gondii* can increase pro-inflammatory cytokines level in the serum (Bottari *et al.,* 2015). Therefore, modulation of neurotransmitters profile and increased cytokine levels might be the causes of increased seizure susceptibility by *T. gondii*. Alternatively, the parasite itself is involved in epileptogenesis through rupture of the cysts leading to neuronal injury, or indirectly by immune system activation leading to inflammation and tissue necrosis (Babaie *et al.,* 2017a).

The current study showed that there was no significant difference between different groups regarding age, gender, and consumption of undercooked meat. This result regarding the age was in accordance with Alvarado-Esquivel *et al.,* (2006) who did not detect any association between prevalence of toxoplasmosis and the age of psychiatric patients. On the contrary, Babaie *et al.,* (2017a), in their investigations on adult epileptic patients, found that the IgG titer of *T.gondii* significantly increased (*P* < 0.001*)* with age and the authors found that consumption of undercooked meat was highly correlated with *Toxoplasma* infection (*P* < 0.001). concerning the gender, our resulte were in accordance with Babaie *et al.,* (2017a) found that there was no correlation between the gender and seropositive rate of *T. gondii* infection in epileptic patients (*P* = 0.61).On the contrary, other studies showed that the seropostivity of toxoplasmosis in epileptic patients were more in males than females (El-Tantawy *et al.,* 2013; Eraky *et al.,* 2016).

The study showed that there was significant association between the residence and prevalence of *Toxoplasma*. This finding may be attributed to exposure to soil and cat feaces. This is in accordance with many studies that showed that the risk for developing toxoplasmosis in epileptic patients is higher in rural than in urban areas (El-Tantawy *et al.,* 2013; Eraky *et al.,* 2016). On the other hand, there are studies which did not find any association between residence and *Toxoplasma* prevalence in epileptic patients (Akyol *et al.,* 2007; Zibaei *et al.,* 2011).

The current study showed a statistically significant difference between both groups. Our observation is consistent with that of Eraky *et al.,* (2016) who found that there was significant correlation between *Toxoplasma* infection and positive history of contact with cats among epileptic patients, as 5 out of the 8 anti-*Toxoplasma* seropositive cases (62.6%) gave positive history for contact with animals. Also, in a study done by Meng *et al.,* (2015), the authors found that raising cats at home seemed to be a main risk factor. On the contrary, El-Tantawy *et al.,* (2013) found that there was no significant relationship between animal contact and *Toxoplasma* seropostivity rate in children with cryptogenic epilepsy.

In respect to the association of toxoplasmosis with source of water, the current study showed that epileptic children drinking unfiltered water were at 15 times higher risk of developing toxoplasmosis (OR, 15.225; 95% CI, 4.961 −46 .728). This may be explained as the general network supply of water in our cities is generally not well treated. To our knowledge, there was no available study investigating this risk factor in epileptic patients. However; in a study in Cameroon, the authors reported a higher prevalence (75.58%) in people having the general network supply as a source of drinking water (Njunda *et al.,* 2011). Using concentration of water via Fluoropore® membranes followed by bioassay in Brazil, *T. gondii* were isolated and implicated in a large waterborne outbreak (de Moura *et al.,* 2006). Okwuzu *et al.,* (2015) reported that source of water and drinking unpasteurized cow milk were risk factors of toxoplasmosis.

The current study showed that contact with soil is an important risk factor for toxoplasmosis as there was significant difference between seropositive and seronegative groups in epileptic children. Likewise, Allahdin *et al.,* (2015) found that

contact with soil and cat may increase the chance of infection in epileptic patients. Moreover, Gyang *et al.,* (2015) who investigated the seroprevalence and risk factors of toxoplasmosis among primary schoolchildren, reported that the high seroprevalence of *T. gondii* in children was attributed to their frequent contact with contaminated soil. On the contrary, Babaie *et al.,* (2017a) found that there was no significant difference between seropositive and seronegative groups in epileptic patients regarding contact with soil (*P*=0.062). The latter finding may be due to the age of participants as they were adult persons (<30 − >50 years old).

The current study showed that out of 74 epileptic children who were seropositive for toxoplasmosis, 66.2% had generalized convulsions, 21.6% had focal convulsions, 12.2% had absence epilepsy and there was statistically significant difference between the different types of convulsions. These findings are in accordance with Eraky *et al.,* (2016) who found that 12.5% of cases had focal convulsions and 87.5% of cases had generalized convulsions. On the contrary, Akyol *et al.,* (2007) found that there was no significant difference between types of seizures (focal and generalized) regarding *T. gondii* seropositivity rate. Cerebral toxoplasmosis has been reported to cause seizures by producing diffuse encephalitis or localized lesions (Neto and De Bittencourt, 1996).

In conclusion, the current study highlighted the association between toxoplasmosis and idiopathic epilepsy.

As regards toxocariasis, there was no statistically significant difference in *Toxocara* seropositivity between patient and control group; however toxocariasis should be considered a latent risk factor especially in

rural localities. Moreover, it identified the epidemiological variables and risk factors associated with toxoplasmosis and toxocariasis which are key steps for raising the public awareness and for implementation of different levels of prevention and control strategies.

Acknowledgments

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