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Toxoplasma infection and epilepsy: A case-control study in Iran

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Abstract

Epilepsy is one of the most important neurological diseases with prolonged morbidity and cerebral toxoplasmosis is one of the main cause's aquired epilepsy in developing countries. In this study, we aimed at investigating the frequency of *Toxoplasma* infection among patients with cryptogenic epilepsy and the epidemiological factors associated with disease. Eighty five patients with cryptogenic epilepsy and 85 healthy subjects were studied. Anti-*Toxoplasma* antibody status was determined in all serum samples, using ELISA technique. The frequency of *Toxoplasma* infection was found to be significantly higher in epilepsy patients as compared to the healthy control (14.1%, 4.7%, respectively) (P=0.036). There was no significant difference between cryptogenic epilepsy patients and healthy control in age, education, gender and residency (P>0.05). This study indicates that *Toxoplasma* infection is a risk factor for epilepsy in Iran.

INTRODUCTION

Toxoplasma gondii (*T. gondii*) is an obligate intracellular protozoan that infects numerous species of mammals and birds. The infection produces cysts containing trophozoites in various human tissues particularly in muscles and brain. Cerebral toxoplasmosis occurs in two clinical setting. During pregnancy it produces congenital toxoplasmosis in the fetus which is characterized by developmental delay, intracranial classification, chorioretinitis and seizures. In immunocompromized patients, cerebral toxoplasmosis produces non specific sign and symptoms of intracranial mass lesion and seizure.[1] Focal neurological deficits occurred in 69% and seizure in 29%.[2]

Epilepsy is defined as recurrent seizures that are not the immediate result of an acute cerebral insult.[3] Approximately 30% of epilepsy is associated with parasitic diseases (helminthiasis) in developing countries. Poor sanitation and the consumption of contaminated foods, including vegetables and undercooked meat, are cause of infection.[4] Several parasitic infections such as malariasis, cysticercosis, toxocariasis and toxoplasmosis can cause not only acute symptomatic seizure that also remote symptomatic epilepsy.[5] Most of these are easily detected by cerebrospinal fluid (CSF) analysis, serum testing and MRI.[6] *T. gondii* can form dormant cysts in the brain, which are microscopic and undetectable with MRI routine CSF analysis. In the state dormant of parasite, brain cysts form is not associated with clinical symptoms; however, with immunosuppression of the host, reaction of the bradyzoites into tachyzoites causes the potentially lethal disease, toxoplasmosis.[7] In previous reports the rate of serpositivity for anti-*Toxoplasma* antibodies has been reported to be 20% in USA, 80% in France and 52% in Turkey.[8-10] The seroprevalence rates of *T. gondii* in human were reported to be between 9.1% and 86.3% in Iran.[11] A positive immunoglobulin- titer reflects the persistence of parasites in the central nervous system.[12] Tissue cysts containing bradyzoites may spontaneously rupture releasing parasites that caused antibody titers to be detected.[13]

To our knowledge, the seroprevalence of *T. gondii* infection in the epilepsy patients has not been previously reported in Iran. Here, we presented the results of *T. gondii* serologic testing (ELISA) on sera of patients with cryptogenic epilepsy and healthy controls. The objective of the study was to investigate whether toxoplasmosis was an aetiology factor among the epilepsy patients and the epidemiological factors associated with the infection in patients attending the Neurology Division, Shohady-e-Ashayer Hospital in Khorram Abad, Iran.

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METHODS

Study region

Khorram Abad (48º 21', 30º 43') is the largest city in Lorestan province in western Iran with 540,000 inhabitants. This area is humid with mean rainfall of 525 mm/yr and the maximum mean yearly temperature of 7.2 ºC, hence creating conditions for dispersion of parasites and parasitic disease.

Patients

The study was conducted between January and December 2010. Eighty five patients with cryptogenic epilepsy were selected from the patients who were followed up in the Neurology Division of Shohady-e-Ashayer Hospital. These patients had evaluation of their clinical history, cranial imaging such as computed tomography (CT) scans or magnetic resonance imaging (MRI). The seizure type were defined accordingly the ILAE 1981 criteria. The control groups consisted of 85 volunteers from among health care workers and the relatives of the patients with comparable epidemiological characteristic and without history of previous seizures. The demographic and life style information was obtained through a survey questionnaire. The study was carried out after being approved by Ethics Committee of Lorestan University of Medical Sciences. Three mL venous blood was taken under sterile conditions from each subject in the both group and the sera of these blood samples were separated by centrifuge at 2500 rpm, aliquot, and store at -20ºC until analyses were carried out.

Serological assay

Anti-*Toxoplasma* antibodies were detected by a commercial Enzyme-Linked Immunosorbent Assay (ELISA) kit (Diaplus Inc, Toxo IgG, USA) as described by the manufacture in the test's instruction.

Statistical analysis

The 15.0.0 version of SPSS for windows package program was used. All epidemiological, clinical and laboratory information were tested for their association between with toxoplasmosis. Data were analyzed for significant differences by the χ^2 test and were considered significant at (P<0.05).

RESULTS

Of the 85 epilepsy patients who participated in the study, 55 (64.7%) were male and 30 (35.3%) were female. Their age range was between 8 and 62 (24.1±16.1) years. Of the 85 subjects in the control group, 57 (67.1%) were male and 28 (32.9%) were female. They were between 7-59 years of age (23.2±10.6).

Neuroradiologic findings (CT scan or cranial MRI examination) were normal in 78.8% (n=67) of the epilepsy patients and 5.8% (n=5) in the control group. On the basis of the 1981 ILAE classification, of the 85 epilepsy patients, 70 patients (82.4%) had partial seizure; out of whom 53 had secondary generalization and 17 without secondary generalization.

Twelve epilepsy patients (14.1%) had positive anti-*Toxoplasma* antibodies, as compared to 4 (4.7%) among the control group. This was statistically significant (P=0.036, Table 1). Of the 12 patients with positive anti-*Toxoplasma* antibodies, 8 (66.7%) were male.

There was no significant difference between epilepsy patients and control group in terms of mean age, age group, gender and residency. However, there were significantly more students among the epilepsy patients, whereas there was more workers among the control group (Table 2). There was no predominance of urban or rural

Table 1: Seroprevalence of antibodies to *Toxoplasma gondii* in the epilepsy patients and control

	Epilepsy patients		Control		Total	χ^2
	No.	(%)	No.	(%)		
Seronegative	73	85.9	81	95.3	154	4.416
Seropositive	12	14.1	4	4.7	16	
Total	85	100	85	100	170	

P-value=0.036

Table 2: Epidemiological and demographic characteristics of epilepsy patients and control

Factor	Epilepsy patients		Control group		Total	Statistical (*P*-value)
	No.	(%)	No.	(%)		
Sex						
Male	55	64.7	57	67.1	112	0.740
Female	30	35.3	28	32.9	58	
Age group (years)						
1-19	42	49.4	38	44.7	80	0.281
20-39	28	32.9	34	40.0	62	
40-59	12	14.1	13	15.3	25	
≥60	3	3.5	0	0.0	3	
Education						
No School	13	15.3	21	24.7	34	0.402
Some high	15	17.7	6	7.1	21	
High school	40	47.1	32	37.6	72	
Some college graduate school	27	31.8	26	30.6	53	
Occupation						
Student	37	45.1	22	26.2	59	0.003
Worker	26	31.7	38	45.2	64	
Other	22	23.2	25	28.6	47	
Residency						
Rural	67	78.8	70	82.4	137	0.561
Urban	18	21.2	15	17.6	33	

population among our seropositive patients. Of the 12 seropositive patients, there were 7 out of 67 (10.4%) from the rural area, and 5 out of 18 (27.8%) from the urban area which was not statistically significant (*P*=0.171). There was significantly higher proportion of students among the seropositive subjects. Of the 12 seropositive patients, 8 out of 37 (21.6%) were students, versus 4 out of 48 (8.3%) were workers and others (*P*=0.02).

DISCUSSION

Epilepsy is an important health problem in the developing countries. The higher frequency of partial seizure in these countries compared with that in developed countries could be an indication of the higher incidence of symptomatic epilepsy secondary to cortical damage.[14] There were only few reports of previous studies to investigate the relationship between toxoplasmosis and epilepsy. To our knowledge, ours was the first case-control study on toxoplasmosis and epilepsy from Iran. Previous studies have reported that anti-*Toxoplasma* antibodies in epilepsy patients was between 31 and 59%.[3,6,10] Stommel *et al*[6] suggested that chronic *T. gondii* infections with brain cysts may be a cause of cryptogenic epilepsy. The authors thought that the cryptogenic epilepsy population could be more susceptible to the parasitic infection, for reasons unrelated to epilepsy, or due to intrinsic immunologic differences that predispose them to epilepsy. In this study, the frequency of *Toxoplasma* infection in epileptic patients was 14.1%, significantly higher than the healthy controls (4.7%). However, as the reported prevalence of toxoplasmosis in the general population in Iran ranged from 9.1 to 86.3%, the relatively low frequency of *Toxoplasma* infection in our control group required cautious interpretation.

Of the 12 epilepsy patients seropositive to *T. gondii*, 8 (66.7%) were males. However, this was not higher than the overall proportion of the male epilepsy patients of 64.7%. Toxoplasmosis is seen more frequently among young adults and older adults probably due to more frequent contact and consumption of contaminated food and poor hygiene. The relatively gradual increase in seroprevalence associated with age suggested that soil exposure, which is greatest during the childhood years, may not be the principal

mechanism by which persons are exposed to *T. gondi*.[15] In the present study, the epilepsy patients consisted of various age group from children to elderly, age ranging between 8 and 62 years. The seropositivity was not affected by age, though there were significantly more seropositive epilepsy patients who were students.

A main finding of the study was the lack of significant difference between seroprevalence in the rural population compared with the urban population to *T. gondii*. This is consistent with report by Akyol *et al*[3], suggesting that population from both the urban and rural area are equally exposed to the parasite.

In conclusion, our findings further corroborate some recent observations of an association between toxoplasmosis and epilepsy. *Toxoplasma* could increase the risk of epilepsy that results from central nervous system infection.

DISCLOSURE

Conflict of interest: None of the authors have any conflict of interest to disclose

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