

TOXOPLASMOSIS AMONG SCHIZOPHRENIC PATIENTS

By

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ABSTRACT

Background: A variety of neurologic symptoms, including in-coordination, tremors, head-shaking, and seizures, have been described in sheep, pigs, cattle, rabbits, and monkeys infected with *T. gondii*. Up to a third of the world's human population is estimated to carry a *Toxoplasma* infection.

Objective: Studying the possible association between *Toxoplasma gondii* infection and schizophrenia by using ELISA technique for detection of *Toxoplasma* IgG and IgM.

Subjects and Methods: The study was carried out at Psychiatry Department, Al-Azhar University Hospital (New-Damietta) from July 2014 to January 2015. The study included 100 schizophrenic patients. Another hundred normal persons of the same age and sex, without psychosis or symptoms and signs suggesting toxoplasmosis were selected as a control group. All persons were subjected to detailed history taking, laying stress on risk factors of toxoplasmosis (such as contact with cats, eating undercooked meat and contact with the soil) and manifestations of schizophrenia. The separated serum was stored frozen at (-20°C) until used for estimation of *Toxoplasma* Specific IgG and IgM titers.

Results: The prevalence of toxoplasma infection detected either by IgM or IgG was significantly higher in schizophrenic patients (28.0%, 58.0% respectively). Patients with toxoplasmosis were significantly younger, and incidence decreased with increased age. Risk factors and family history of schizophrenia were significantly higher in study group. Considering positive cases, those factors and family history were not significantly increased. Even eating undercooked meat and family history of schizophrenia were significantly lower.

Conclusion: Results of the present study shed light on the prevalence of toxoplasmosis in schizophrenic patients and revealed that toxoplasmosis was significantly higher in those patients when compared to control group. Thus, schizophrenia may be linked to this infection. However, a future large scale randomized studies were needed to confirm this association.

Keywords: *Toxoplasma gondii*; schizophrenia

INTRODUCTION

Toxoplasmosis is a parasitic disease caused by protozoan *Toxoplasma gondii* (Ryan and Ray, 2004). The parasite infects most genera of warm-blooded animals, including humans, but primary host is the felid (cat) family. Infection occurs by eating infected meat, or ingesting water, soil, or food that has come into contact with infected animal's

fecal matter. Transmission can occur from infected mother to fetus during pregnancy. This is why physicians recommended that pregnant woman do not clean litter boxes or eats under-cooked meat products (Dubey, 2005). About one third of world's human population is estimated to carry a *Toxoplasma* infection (Montoya and Liesenfeld, 2004).

The parasite can cause encephalitis and neurological diseases, and can affect

the heart, liver, inner ears, and eye (**Bin Dajem and Almushait, 2012**). Research has also linked toxoplasmosis with attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), and schizophrenia. Numerous studies found a positive correlation between latent toxoplasmosis and suicidal behavior in humans (**Ling et al., 2011; Pedersen et al., 2012; Zhang et al., 2012 and Coccaro et al., 2016**). Research related to the effects of toxoplasmosis on personality and mental health was awarded the 2014 Nobel Prize in Public Health (**Cook et al., 2015**).

The aim of this work was to study the possible association between *Toxoplasma gondii* infection and schizophrenia by using ELISA technique for detection of *Toxoplasma* IgG and IgM.

MATERIALS AND METHODS

The study was carried out at Psychiatry Department, Al-Azhar University Hospital (New-Damietta) from July 2014 to January 2015. The study included 100 patients with symptoms and signs of schizophrenia and fulfilling the inclusion criteria that included hallucinations, voices that converse with or about the patient, disorganized speech and behavior, agitation and delusions. Negative symptoms included poverty of speech, flattened affect, loss of sense of pleasure, lack of will or drive, and social withdrawal. A hundred normal persons of the same age and sex, without schizophrenia or symptoms and signs suggesting toxoplasmosis were selected as a control group. *The study protocol was explained for all included subjects and an informed consent for participation in the study was obtained.* All the studied persons were subjected to detailed history taking, laying stress on risk factors of toxoplasmosis

such as contact with felids, eating undercooked meat and contact with the soil and manifestations of schizophrenia. Blood sample was withdrawn aseptically via venipuncture. The separated serum was stored frozen at -20°C until used for estimation of *Toxoplasma* specific IgG and IgM titers.

Statistical analysis: The collected data were tabulated and statistically analyzed using statistical package for social science (SPSS) version 16.0 (SPSS Inc. USA); running on IBM compatible personal computer. Qualitative (categorical) data were represented as relative frequency (n) and percent (%) distribution. For comparison between groups, Chi square (X^2) test was used. Quantitative data were represented as arithmetic mean and standard deviation (SD). For comparison between two groups, the student t-test was used. For interpretation of results, p value ≤ 0.05 was considered significant.

RESULTS

In the present work, both study and control groups were comparable as regarding sex, age and residence. There was male predominance in the study group (60.0%). The mean age in study group was 34.25 compared to 35.20 in control group. In addition, there was rural area predominance in study group (71.0% were of rural area). On the other hand, there was significant increase of risk factors (contact with cats, eating undercooked meat and contract with soil) in study group when compared to control group (56.0%, 14%, 39% vs 0.0%, 0.0%, 0.0% respectively). In addition, there was significant increase of family history of schizophrenia in study group when compared to control group (28.0% vs 0.0% respectively). Positive IgG for toxoplasma significantly increased in study group (58.0%) vs (13.0%) in control group. Similarly, there was a significant

increase of positive IgM for toxoplasma in study group when compared to control group (28.0% vs 4.0% respectively-Table 1).

In cases with positive IgM, positive cases were mostly males, but the difference was statistically non-significant. Positive cases significantly increased in third decade (53.6%) when compared to fourth, fifth or sixth decades (35.7%, 7.1% and 3.6% respectively). In addition, positive IgM cases were significantly related to rural area (67.9%). Contact with cats increased, but the

difference was non-significant; while, eating undercooked meat was significantly lower in positive IgM cases (14.3%), and contact with soil was distributed equally. Family history of schizophrenia was not significantly different. Looking at distribution of different variables in cases positive for IgG, positive cases were significantly in younger age, and incidence decreased with increasing age. Also, rural area significantly increased, and both eating undercooked meats and family history of schizophrenia were significantly lower (Table 2).

Table (1): Comparison between control and study groups as regards to studied variables.

Variables		Control group	Study group	Test	P value
Sex (No.%)	Males	59(59.0%)	60(60.0%)	0.02	0.88
	Females	41(41.0%)	40(40.0%)		
Age (years)		35.20±10.31	34.25±9.51	0.67	0.49
Residence	Rural	70 (70.0%)	71(71.0%)	0.01	0.99
	Urban	30(30.0%)	29(29.0%)		
Risk factors	Contact with cats	0(0.0%)	56(56.0%)	200.0	<0.001
	Eating undercooked meat	0(0.0%)	14(14.0%)		
	Contact with soil	0(0.0%)	39(39.0%)		
Family history of schizophrenia		0(0.0%)	28 (28.0%)	32.55	<0.001
Positive IgG for toxoplasma		13(13.0%)	58(58.0%)	44.21	<0.001
Positive IgM for toxoplasma		4(4.0%)	28(28.0%)	21.41	<0.001

Table (2): Distribution of studied variables positive for IgM and IgG in study group

Variables		Positive IgM (no=28)	P value	Positive IgG (no=58)	P value
Sex	Males	17(60.7%)	0.25	36(62.1%)	0.06
	Females	11(39.3%)		22(37.9%)	
Age (years)	Third decade	15(53.6%)	<0.001	27(46.6%)	0.001
	Fourth decade	10(35.7%)		18(31.0%)	
	Fifth decade	2(7.1%)		11(19.0%)	
	Sixth decade	1(3.6%)		2(3.4%)	
Residence	Rural	19(67.9%)	0.05	42(72.4%)	0.001
	Urban	9(32.1%)		16(27.6%)	
Contact with cats	Yes	15(53.6%)	0.71	32(55.2%)	0.43
	No	13(46.4%)		26(44.8%)	
Eat undercooked meat	Yes	4(14.3%)	<0.001	7(12.1%)	<0.001
	No	24(85.7%)		51(87.9%)	
Contact with Soil	Yes	14(50.0%)	1.0	23(39.7%)	0.12
	No	14(50.0%)		35(60.3%)	
Family history of Schizophrenia	Positive	13(46.4%)	0.71	12(20.7%)	<0.001
	Negative	15(53.6%)		46(79.3%)	

DISCUSSION

In many studies conducted in different parts in the world, the percentage of seropositive schizophrenic cases for Toxoplasmosis. IgG and IgM were higher than other apparently healthy persons. They were 40%, 53% and 67.7% positive cases for *Toxoplasma* IgG in the studies conducted by **Tamer et al. (2008)** in Turkey, **Sabah and Mahfoth, (2009)** in Iraq and **Alipour et al. (2011)** in Iran respectively, while there were 5% and 16% positive for *Toxoplasma* IgM in the studies conducted by **Tamer et al, (2008)** in Turkey and **Fadheelah et al. (2011)** in Iraq.

The previous data and findings drew our attention to the aim of the present study which was the significance and importance to study prevalence of toxoplasmosis among schizophrenic patients. The resulting data revealed that there was statistically non-significant difference between cases and control group regarding sex, age and residence. The consumption of undercooked meat was found to be associated with an increased and significant incidence of toxoplasmosis among the study group. Regarding family history of schizophrenia, there was a statistically significant increase in positive cases among the study group in comparison to no positive family history among the control group. History of cat contact was highly significant among IgG positive cases and among IgM positive cases in comparison to control group. Third decade was the most common age in both cases and controls (45.0% of cases and 42.0% of controls were in the third decade). There was no statistical significance

difference of age in cases when compared to controls. The obtained results coincided with that obtained by **Alipour et al. (2011)** and **Khademvatan et al. (2014)**.

As regard age and seropositivity, we found that positive IgM cases were in third decade, 35.7% in fourth decade, 7.1% in fifth decade and 3.6% in sixth decade. The positive IgG cases were 46.6% in third decade, 31.0% in fourth decade, 19.0% in fifth decade and 3.4% in sixth decade. Both IgM and IgG were statistically significant in third and fourth decades of age. The obtained results coincided with that obtained by **Sabah and Mahfoth (2009)**

In the present study, there were 58% with positive IgG and 42% with negative IgG in the patient group, while in the control group there were 13.0% IgG positive and 87.0% IgG negative and there was statistically significant increase in positive cases in the study group in comparison to control group. These results were slightly higher than that obtained by **Tamer et al. (2008)** who found that IgG seropositivity was 40%, which may be attributed to the geographical distribution of studied cases and controls, sensitivity and specificity of the used materials. However, the obtained results coincided with that obtained by **Sabah and Mahfoth (2009)** in Iraq and **Alipour et al., (2011)** in Iran.

Regarding toxoplasmosis IgM, there were statistically significant increases in positive cases among the study group in comparison to the control group. These results are close to those obtained by **Fadheelah et al. (2011)** in Iraq.

As regard sex, the majority of positive IgG and IgM cases were males, but the

difference was statistically insignificant. As regard residence, both IgG and IgM were statistically significant higher in rural areas than urban areas. The obtained results coincided with that obtained by **Sabah & Mahfoth (2009)**, and **Elsheikha et al. (2016)**.

The findings and results of the present study should alert physicians and psychiatrists that toxoplasmosis should be suspected in patients presenting with schizophrenia.

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التوكسوبلازما لدي مرضي الفصام

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خلفية البحث: في الحيوانات (مثل الأغنام، الخنازير، الماشية، الأرانب والقروذ) التي أصيبت بالتوكسوبلازما وجد أن هناك مجموعة من الأعراض العصبية المختلفة مثل عدم الإتران، والرعدة، وهز الرأس، والتشنجات. وقد وجد أن حوالي ثلث سكان العالم الثالث يحملون طفيل التوكسوبلازما.

الهدف من البحث: صممت الدراسة الحالية بهدف تقييم الإرتباط المحتمل بين العدوي بالتوكسوبلازما وبين إضطراب الفصام بإستخدام تقنية الإليزا لإكتشاف الأجسام المضادة من النوع (جي) و (إم) (العدوي الحادة والمزمنة).

المرضي وطرق البحث: أجريت الدراسة الحالية بقسم الطب النفسي (مستشفى طب الأزهر بدمياط - جامعة الأزهر). في الفترة من يوليو 2014 إلي يناير 2015. وقد اشتملت الدراسة 100 مريض من مرضي الفصام. كما تم تضمين 100 شخص من الأصحاء من نفس المجموعة العمرية والنوع كمجموعة ضابطة. وقد تم أخذ التاريخ المرضي بصورة مفصلة، مع التركيز علي عوامل الخطورة بالنسبة للإصابة بالتوكسوبلازما، مثل الاحتكاك بالقطط، وأكل لحم غير مطهو بصورة كاملة، والاحتكاك بالترربة)، بجانب أعراض الفصام. وقد تم استخلاص المصل من عينات الدم، عند درجة حرارة -20 درجة مئوية، حتي وقت قياس الأجسام المضادة للتوكسوبلازما. ولم يتم إضافة أي مادة حافظة لعينة المصل لتجنب تثبيط تفاعلات الإنزيمات.

النتائج: معدل إنتشار عدوي التوكسوبلازما سواء الإصابة الحادة أو المزمنة كان أعلى بصورة يعتد بها من الناحية الإحصائية لدي مرضي الفصام مقارنة بالمجموعة الضابطة. وبالنسبة للمرضي المصابين بالتوكسوبلازما كانوا أصغر في العمر بدرجة يعتد بها إحصائيا، ووجد أن معدل الإصابة بالتوكسوبلازما يقل مع تقدم العمر. ووجد أن عوامل الخطورة للإصابة والتاريخ العائلي الموجب، للتوكسوبلازما كانت أكثر لدي مجموعة الدراسة مقارنة بالمجموعة الضابطة.

الاستنتاج: ألقت نتائج الدراسة الضوء علي معدل الإصابة بالتوكسوبلازما لدي مرضي الفصام، ووجد أن معدل الإصابة أكثر بدرجة يعتد بها إحصائيا لدي هؤلاء المرضي مقارنة بالمجموعة الضابطة. ولذلك فثمة إرتباط بين إضطراب إالفصام والإصابة بالتوكسوبلازما، ولذلك يوصي بدراسات مستقبلية علي نطاق واسع لتأكيد أو نفي تلك العلاقة.