

## Toxoplasmosis among schizophrenic patients in Al-Rashad Teaching Hospital

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### الخلاصة

أظهرت الدراسات أن مرضى الفصام لديهم نسبة تعرض للإصابة بداء المقوسات. يهدف البحث لمعرفة العلاقة بين داء المقوسات ومرضى الفصام وعلاقة التيستوستيرون بداء القطط مقارنة بالأشخاص الأصحاء. أجريت هذه الدراسة على (100) شخصا مصابين بالفصام تم اختيارهم من مرضى مستشفى الرشاد التعليمي و(25) شخصا اعتمدوا كعينة ضابطة ، للفترة من الأول من تشرين الأول عام 2009 إلى نهاية آذار من عام 2010. جميع العينات كانت من الذكور فقط وأعمارهم بين 20 – 55 سنة. كل العينات فحصت باستخدام تقنية الامتزاز المناعي المرتبط بالأنزيم (الايذا) للتحري عن الأضداد المناعية لداء المقوسات للأجسام المضادة ( IgG ) و (IgM) وكذلك تم قياس نسبة الهرمون الذكري لجميع العينات. أظهرت النتائج أن الإصابة بداء المقوسات للأجسام المضادة نوع (IgG) أو (IgM) أو (IgG) مع (IgM) من (63) مريضا كانت النتيجة الموجبة للأجسام المضادة (IgG) هي (49) و(6) موجب (IgM) و(4) موجب لكلا النوعين (IgG و IgM) بينما بالنسبة للأشخاص الأصحاء كانت النتيجة هي (4) للأجسام المضادة (IgG) و(0%) للأجسام المضادة (IgM). يتبين أن نسبة خطر الاصابه بالفصام خمسة مرات أكثر للأشخاص ذوي النتائج الموجبة لفحص داء المقوسات المزمن مقارنة بالنتائج السلبية لنفس الفحص. وأيضا وجود فرق معنوي بالنسبة لداء المقوسات المزمن لمرضى الفصام وبمستوى (1.1) مقارنة مع الأشخاص الأصحاء . بينما أظهرت النتائج عدم وجود فرق معنوي بالنسبة لداء المقوسات الحاد لمرضى الفصام(0.483) مقارنة مع الأشخاص الأصحاء (0.472) (p-value= 0, 82) تم قياس نسبة التيستوستيرون لجميع العينات وأظهرت النتائج وجود فرق معنوي (6.1) لمرضى الفصام مقارنة مع الأشخاص الأصحاء (4.6). (p-value= 0.001) كذلك كان الفرق معنويا بالنسبة لمعدل تركيز التيستوستيرون لمرضى الفصام لداء المقوسات المزمن الموجب حيث كانت النتيجة (7.1) بينما للفحص السالب (5.1) . أما في داء المقوسات المزمن والحاد فلم يكن هناك فرق معنوي لمرضى الفصام والأشخاص الأصحاء من ناحية المنطقة السكنية، التدخين، تناول الكحول، المستوى التعليمي، وجود قطه في البيت والحالة الزوجية.

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## Abstract

**Background;** Studies showed that people with schizophrenia and other mental disorders have a higher incidence of exposure to *T.gondii*. The aim of the present paper is to estimate the rate of toxoplasmosis in schizophrenic patients.

**Methods;** A total of (125) serum samples were studied. (100) patients from AL- Rashad Teaching Hospital compared with (25) healthy person as a control group; during the period from October 1, 2009- March 31, 2010. All were male of age (20-55 years). Serum samples were tested by using ELISA *Toxoplasma* technique for Ab. detection (IgG and IgM) in addition to the serum testosterone concentration.

**Results;** The results showed that 49% schizophrenics have IgG positive *Toxoplasma*, 6% have positive IgM and 4% have both IgG and IgM positive *Toxoplasma*. The risk of having schizophrenia in subjects with positive IgG Ab is 5 times higher than negative IgG Ab persons. The mean IgG Ab. titer was higher (1.1) in schizophrenics. The serum testosterone concentration was significant (6.1) in schizophrenics & was significantly higher in schizophrenics with positive IgG Ab. (7.1). No associations were found between toxoplasmosis and residence, smoking, alcohol consumption, educational level, history of contact with cats, or marital status.

**Conclusion;** Schizophrenics have IgG positive *Toxoplasma*, high IgG Ab titre & serum testosterone concentration.

**Key words.** Toxoplasmosis. Schizophrenics. Ellisa technique

## Introduction

*Toxoplasma gondii* is a parasite that infects most genera of warm-blooded animals, including humans, but the primary host is the cat. Animals are infected by eating infected meat, ingestion of food contaminated with oocyst in the faeces of cat that has itself recently been infected, or by transmission from mother to fetus<sup>[1]</sup>. *T. gondii* holds notoriety as the pathogen that causes the disease toxoplasmosis in humans. Infants and immune compromised hosts are readily infected with the pathogen & show accelerated symptoms, but it is interesting to observe that the pathogen is generally docile in healthy individuals with

a competent immune system <sup>[2, 1]</sup>.third of the world population has Toxoplasma infection, though this is the latent form of the disease & is non-fatal <sup>[3]</sup>.The microbe preferentially encysts itself within the tissues of the brain and the central nervous system (CNS) of the host, causing loss of normal cognitive brain function, impaired judgment, peripheral neuropathy, slowed reflexes<sup>[4, 5]</sup>. Sexual replication leads to production of oocysts which are passed in cat faeces and sporulate in soil <sup>[6]</sup>.Recently, there has been renewal of interest in infectious causation of psychiatric disorders, and one of the organisms which have received special attention, is T.gondii. This is primarily because of its wide prevalence and special affinity for brain tissue. Estimate is that 30-60 % of infected patients are infected with T. gondii <sup>[7]</sup>.During the 1980s and 1990s a number of scientists reported that T. gondii changed the behavior of mice & rats. Infected mice have increased activity & show increased aggressive behavior,& rats show a marked decrease in their natural fear of cat odors <sup>[7, 8]</sup>, changes that tend to make these rodents more likely to be eaten by a cat. Rodents infected with T. gondii have increased dopamine levels,(a neurotransmitter that is associated with novelty-seeking and neurotic behavior)<sup>[8]</sup>.Women seem to be more intelligent, outgoing, conscientious, sexually promiscuous, and kind; changes in men seem to cause opposite trends. All patients tend to be more prone to feelings of guilt <sup>[9, 10]</sup>. Studies showed that schizophrenic have a higher incidence of exposure to T. gondii than healthy control.. Antipsychotic drugs commonly show activity against T. gondii parasites, and infected rodents show reduced behavioral changes when treated with these drugs <sup>[11]</sup>.

### **Aim of the study**

Studying the rate of toxoplasmosis and the relationship between toxoplasmosis and testosterone hormone among schizophrenic male patients in Baghdad.

### **Materials and Methods**

This study was performed during the period October1,2009-March31,2010.Sera sample was collected from(100)patients in Al-Rashad Teaching Hospitals & from (25) normal persons as control from

hospital staff. *Toxoplasma* IgG, IgM & testosterone hormone level was measured by ELISA technique, the patients were asked about contact with cats, residence, smoking, alcohol consumption, education & marital status. Informed consents were taken.

## Results

The study revealed that (63) examined by ELISA technique showed seropositive results (IgG or IgM or both). Table(1) shows that, out of (63), 49(49%) schizophrenic are IgG positive for *Toxoplasma*, & 6(6%) are positive IgM and 4 (4%) are both IgG and IgM positive for *Toxoplasma*. while in control only 4 (16%) are IgG positive for *Toxoplasma*. The risk of having schizophrenia in subjects with positive IgG Ab is 5 times higher than in negative IgG Ab patients.

**Table 1:- The rate of positive serum anti-Toxoplasma Ab.**

	Control		Cases		significance	
	No.	%	No.	%	P-Value	
Positive serum Anti- <i>Toxoplasma</i> IgG Ab	4	16	49	49	0.003	Significant
OR = 5						
95% CI for OR = (1.6 - 15.8)						
Positive serum Anti- <i>Toxoplasma</i> IgM Ab	0	0	6	6	0.6	Not significant
Positive serum Anti- <i>Toxoplasma</i> (both IgM and IgG Ab)	0	0	4	4	0.58	Not significant

**Table 2:- The rate of toxoplasmosis & serum testosterone concentration. among schizophrenics according to age (years).**

Cases		Age groups/Year				significance	
		20-29	30-39	40-49	≥50	P Value	
Positive serum Anti- <i>Toxoplasma</i> IgG Ab	N	2	18	11	18	0.49	Not significant
	%	28.6	48.6	44	58.1		
Positive serum Anti- <i>Toxoplasma</i> IgM Ab	N	0	2	1	3	0.71	Not significant
	%	0	5.4	4	9.7		
High serum testosterone concentration	N	1	8	1	1	0.05	significant
	%	14.3	21.6	4	3.2		

Table (2), shows a significant difference, for serum testosterone concentration. the highest positive rates were in age groups(30-39)(21.6%),.

**Table 3: The mean serum anti-*Toxoplasma* Ab. titer &serum testosterone concentration among studied groups.**

Studied groups		No.	Range	Mean	SD	Std Error	P Value
Positive serum Anti- <i>Toxoplasma</i> IgG Ab	Control Schizophrenia	25 100	(0.05 - 1.479) (0.153- 2.873)	0.556 1.1	0.343 0.744	0.069 0.074	0.001
Positive serum Anti- <i>Toxoplasma</i> IgM Ab	Control Schizophrenia	25 100	(0.159- 0.664) (0.185 1.609)	0.472 0.483	0.149 0.219	0.03 0.022	0.82
High serum Testosterone concentration	Control Schizophrenic	25 100	(2.1 - 12.8) (1.5 - 12.5)	4.6 6.1	2.2 2.3	0.44 0.23	0.003
Total	125						

In table (3) the mean IgG Ab titer was significantly higher(1.1)in schizophrenics than control(0.556)( $P < 0.01$ ). While the mean serum testosterone concentration. was highly significant (6.1) in schizophrenic than control (4.6) ( $P < 0.01$ ).

**In table (4) the mean serum testosterone concentration was significantly higher in schizophrenics positive IgG Ab.(7.1)than IgG Ab. negative cases(5.1)**

Studied group for serum testosterone conc.		No.	Range	Mean	SD	Std Error	P Value	significance
Positive Anti- <i>Toxoplasma</i> IgG Ab	Control	21	(2.1-12.8)	4.6	2.4	0.51	0.89	Not significant
	negative	4	(3.1-5.9)	4.4	1.4	0.68		
	Schizophrenia	51	(2.5-7.2)	5.1	1.1	0.15	0.001	Highly significant ( $P < 0.01$ )
	positive	49	(1.5-12.5)	7.1	2.8	0.4		
Positive Anti- <i>Toxoplasma</i> IgM Ab.	Control	25	(2.1-12.8)	4.6	2.2	0.4	--	
	negative	0	0	0	0	0.44		
	Schizophrenia	94	(1.5-12.1)	6	2.2	0.23	0.22	Not significant
	positive	6	(2.5-12.5)	7.2	3.4	1.11		

## Discussion

This study showed that in (100) schizophrenics examined by ELISA , 49 (49%) of them are seropositive to Toxoplasma IgG Ab.& 6 (6%) positive to Toxoplasma IgM Ab .This result is supported by other study in Turkey which showed that the seropositivity for anti-Toxoplasma IgG Ab in schizophrenic(66%)was significantly higher than among healthy volunteers. While IgM titer was positive for only 1 individual in the schizophrenic & negative in the control<sup>[12]</sup>.subjects with positive IgG Ab. were significantly higher in schizophrenics(49%)than control(16%).While the results stated by Mehrzad Saraei in Iran where serum of 104 inpatient schizophrenics &114 control were examined. IgG and IgM Ab. to T.gondii were detected using (ELISA) showed 55.3% of the cases and 50.9% of the controls were seropositive for IgG specific Ab. to T. gondii. <sup>[13]</sup>.Our results are not compatible with this study for IgM Ab. 6 (6%) has Toxoplasma IgM Ab. while 14.6% of the cases and 20% of the controls were seropositive for IgM Ab. to T.gondii. Also from Iranian patients serum samples of 230 of schizophrenic &230 of a control group were examined for Toxoplasma Ab.(IgG, IgM) by Ellisa method.

Data analysis was statistically significant.41(17.8%)out of 230cases &17(7.3%)out of 230 control were Ab. positive. There were no differences between age groups & both genders<sup>[14]</sup>.The results is agreed with the assays performed with researchers blind to case/comparison status in the Toxoplasma serology lab at the Palo

Alto medical foundation research institute, from the 186 samples tested,55 were positive on the screen agglutination test. For the schizophrenic spectrum disorders,25 of 63 (39.7%) were positive; for the comparison subjects,30 of 123(24.4%) were positive. <sup>[15]</sup>.

The seroprevalence of IgG Ab. by the Sabin-Feldman dye test among the 55 subjects who screened positive on the screen agglutination test was 18 of 63(28.5%) of the schizophrenic spectrum disorders &22 of 123(17.9%) of the 123 comparison subjects. The prevalence of high Toxoplasma IgG Ab.titers was greater for schizophrenia spectrum disorders than for comparison subjects<sup>[16]</sup>.

We found that the individuals with first episode schizophrenia had significantly increased levels of IgG, IgM, and IgA, Ab. to Toxoplasma,

as compared to control subjects.<sup>[17]</sup>The general results are in accordance with that reviewed by Torrey and Yolken & they showed that seropositivity to *T.gondii* in children is associated with mental retardation & attention deficits.<sup>[18]</sup>

In the current study the risk of having schizophrenia among subjects with positive IgG Ab. is 5 times higher than negative IgG Ab. The results agreed with other study in China. These results suggest that schizophrenic symptoms may be caused by *T.gondii* infection, some researchers consider that the higher incidence of *T.gondii* in schizophrenics may be due to their lower senses, incapability of self-dependence & weak function of cell immunity,<sup>[19]</sup>The clinical& epidemiological studies mentioned above showed that there are some positive correlation between *T.gondii* infection& pathological effect on patients. Probably this is due to the following, First, seroprevalence investigation in various regions of China indicates there is a positive correlation between *T.gondii* infection and psychosis. This confirmed the results of Yolken & his colleagues who found that individuals with first episode schizophrenia had increased levels of IgG, IgM, & IgA Ab. to *Toxoplasma*.<sup>[20]</sup>Second *T.gondii* has a high affinity for brain<sup>[21]</sup>. Result showed glial cells are the targets contracted by *T.gondii*. Flegel J.et.al., suggests *T.gondii* has high affinity to brain by interacting with specific genes may induce functional changes in it<sup>[21, 22]</sup>.Third, studies indicated that any changes in the neurotransmitter levels could induce changes in personality profile<sup>[19]</sup>.In the Temperament & Character Inventory Questionnaire, Hosak et al<sup>[23]</sup> indicated that shifts in personality factors correlated with concentration of particular neurotransmitters in brain tissue and *T.gondii* produced an increase in dopamine concentration<sup>[22]</sup>. Researchers found that of the 180 schizophrenics 7% were infected with *Toxoplasma* prior to their diagnosis, compared to 5% in the 532 healthy recruits. Thus, people exposed to *Toxoplasma* had a 24 % higher risk of developing schizophrenia.<sup>[24]</sup>Several lines of indirect evidences suggest that subjects with latent infection of *T. gondii* have a higher concentration of testosterone than uninfected controls<sup>[25]</sup>.*Toxoplasma*-infected subjects have a higher level of testosterone. the behavioral changes induced by *T.gondii* could be side effects of the organism's increase in testosterone

in order to impair the cellular immunity of the host & thus increase the chances of surviving in the host organism.<sup>[26,]</sup>The increased level of testosterone in men could be explained by a positive association between testosterone & dopamine that increases in response to local inflammatory processes in the infected brain.<sup>[27,21]</sup>In this study the mean serum testosterone concentration was significantly higher in schizophrenics with positive IgG Ab.(7.1)than IgG Ab. negative cases(5.1).The mean serum testosterone concentration. was(4.4)in control with positive IgG Ab compared to(4.6) in IgG Ab. negative control. The mean serum testosterone concentration. was higher in those with positive IgM Ab.(7.2)than IgM Ab. negative cases (6) but the difference failed to reach the level of statistical significance. No associations were noted between toxoplasmosis & rural residence, smoking, alcohol consumption, educational level, history of contact with cats, marital status In conclusion schizophrenics have IgG positive Toxoplasma, high IgG Ab titre & serum testosterone concentration. further studies are recommended to study association between schizophrenia & toxoplasmosis using large sample size.

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