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Seroprevalence and Correlation between Toxoplasmosis and Schizophrenic Patients in Sulaymaniyah City, Iraq

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Abstract

Toxoplasma gondii is an intracellular protozoan that causes a disease known as toxoplasmosis; both sexes are affected by the parasite. The main severe symptoms of toxoplasmosis are the danger of infection of the CNS. Early exposure to multiple agents of infections was correlated with the subsequent development of schizophrenia.

In this study two laboratory Serodiagnosis tests (LAT and ELISA) were used on a total of 45 sera samples (20 females and 25 males) of schizophrenic patients that were collected from the mental health care unit, Sulaymaniyah teaching hospital. The study showed that 38(84%) of cases were positive for anti-*Toxoplasma* and 7(16%) of cases were negative for anti-*Toxoplasma* antibodies by LAT while 28(62%) were tested by the ELISA method showing seropositive results (IgG) and 17(38%) showing seronegative results. Such discrepancies between schizophrenic patients and control were significant in both studies. (Chi-square) (P = 0.01)

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Although 14(35 %) cases were positive for the anti-toxoplasma antibody by LAT in control cases, and ELISA-IgG was positive for 13(33%). This study indicates that prevalence of schizophrenia in patients with antibody to *Toxoplasma gondii* is higher in comparison to the control cases, it's also possible that toxoplasma infections increase the likelihood of schizophrenia. This study is achieved to investigate or observe the correlation between the Toxoplasmosis and behavior mode of patients in Sulaymaniyah city. This study is achieved to investigate or observe the correlation between the Toxoplasmosis and behavior mode of patients in Sulaymaniyah city.

Key words: Schizophrenia, CNS, neuropsychiatric disease, *Toxoplasma gondii*, congenital abnormalies

الانتشار المصلي والعلاقة بين لداء المقوسة الكوندية ومرض الفصام الشخصي في مرضى الفصام في محافظة السليمانية / العراق

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الخلاصــة

المقوسة الكوندية هو أحد الاوالي الطفيلية التي تصيب الاحشاء الداخلية والتي تسبب بمرض داء المقوسات والتي تصيب كلا الجنسين. أن أحد الاعراض الخطرة لداء المقوسة هي أصابة الجهاز العصبي المركزي والتي تعتبر كنتيجة للتعرض للطفيلي وبأعداد كبيرة في المراحل الاولية من الاصابة. فـي هذه الدراسة أستخدمت تقنيتين في تشخيص المصول (الأليزا واللاتكس) لاستبيان نسبة الاصابة في 45 نمذج مصلي لمرضى الانفصام الشخصي والتي شملت 20 نموذج لاناث مصابات و 25 نموذج لذكوراصيبوا بداء الانفصام الشخصي وجمعت العينات من وحدة العنية المركزية لمرضى الفصام التابع للمستشفى التعليمي في السليمانية. حيث أظهرت النتائج ان 38 حالة (84%) من النماذج كانت موجبة الاصابة وأن 7 حالات (16%) كانت سالبة لالختبار المقوسة بواسطة أختبار اللاتكس بينما أظهرت النتائج وبعد أجراء أختبار ألاليزا التاكيدي أن 28 حالة (62%) كانت موجبة للاختبار وأن 17 حالة (38%) من النماذج كانت سالبة لاختبار (IgG) أظهر التحليل الاحصائي وجود فروق معنوية بين نماذج الفصام الشخصي ونماذج السيطرة وعلاقتها بداء المقوسة الكوندية وبأستخدام مربع كاي (P=

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(0.01. بالرغم من وجود حالات موجبة من ضمن نماذج السيطرة الا أنا قد سجلنا فروق معنوية بين المرضى ونماذج السيطرة والتي قدرت بـ 14 حالة (35%) موجبة للاختبار اللاتكس و13 حالة (33%) من نماذج السيطرة كانت موجبة للاختبار الاليزا.

أستنبطت الدراسة أن نسبة أنتشار الاجسام المضادة لداء المقوسة في مرضى الفصام الشخصي كانت أعلى من نسبتها في نماذج السيطرة وهذا يدل على العلاقة الرابطة بين الاصابة بداء المقوسة ومايؤول اليه للاصابة بمرض الفصام الشخصي. هذه الدراسة اجريت لبيان العلاقة بين الاصابة بداء المقوسة وبعض الاضطرابات في الدماغ.

الكلمات المفتاحيةً: مرض الفصام الشخصي، الجهاز العصبي المركزي، الامراض النفسية العصبية، المقوسة الكوندية، العاهات الخلقية.

Introduction

Toxoplasmosis is an infectious disease caused by *Toxoplasma gondii*, a parasitic protozoan that really affects around 1/3 of the entire human population. It is the most prevalent infectious disease of origin, more common than malaria, tuberculosis, and other infections and parasitic infection [1].

Early infection of pregnant women can increase the possibility of CNS congenital disorders, such hydrocephalus, microcephalus, intracerebral calcification, chorioretinitis, convulsions, and psychomotor disorders, some clinical correlations contribute to mental disorders, extreme vision deficiency, or blindness [2].

Some more study have found that encephalitis toxoplasmosis (ET) toxicity is a risk factor for conditions such as schizophrenia and mood changes [3].

Toxoplasmosis infection can change actions and the role of neurotransmitters. Early infection of humans with *T. gondii* may cause psychotic symptoms related to those exhibited by individuals with schizophrenia [4].

Subclinical infection in which the parasite is encysted within the CNS may occur in individuals infected later in the fetal growth period or in the early postnatal period. Post immunosuppression reactivation, *T. gondii* can lead to reactivate and replicate and the consequent development of brain in some individuals of psychiatric symptoms [5].

Several studies show that an elevated prevalence of schizophrenia in diagnosed individuals' family members means that genetic factors play a role in their pathology, and other candidate predisposing genes have been identified in addition to major environmental factors [6]. Such as infectious agent exposure. Specific infectious agents have not been identified linked with the development of schizophrenia. *Toxoplasma gondii* infection in humans can cause signs similar to those displayed by schizophrenic patients [1] [7].

Immune response to infections of parasites such as *T. gondii* can induce depression and several behavioural changes.

In the chronic phase of infection, Toxoplasmosis produce tissue cysts in the C.N.S for years, the neurological effects such as delusions and hallucinations are associated with stages of chronic phase [9].

Materials and Methods

Patient and Control group

A total of 45 sera samples (20 females and 25 males) The schizophrenia patients were received from the Sulaymaniyah teaching hospital's mental health care unit, and their real age from 20 to 55, whereas the control group included 40 healthy individuals evaluated from any medical disorder.

As a part of the routine diagnostic of a parasite, an antibody was performed by using LAT test then confirm by using IgG antibodies Enzyme-linked Immunosorbent assay kits (ELISA-IgG;

human biochemical and diagnostic, Germany), according to instruction described and supplied. All data were analyzed by Chi-square to find any significant comparison between the percentages of this study and relations between toxoplasmosis and Schizophrenia was investigated.

For each participating one, 5 ml of venous blood was drawn using a disposable syringe and dropped into an aliquots tube, then the sample was centrifuged (10 m./ 5000 rpm). The serum was transferred in to 3 eppendorf tubes (1 ml), which were frozen at -30°C.

The samples were tested for anti-T. gondii antibodies using two methods: the first was the Latex antibody test (LAT), and the second included the confirmation testing for IgG antibodies using Enzyme-linked Immunosorbent assay kits. (ELISA-IgG; human biochemical and diagnostic, Germany).

Results

Our findings were as follows:

Two Sero-diagnostic tests (Latex agglutination test and Enzyme-linked Immunosorbent assay for IgG) were used. The study showed that 38(84%) of cases were positive for anti-*Toxoplasma* and 7(16%) of cases were negative for anti-*Toxoplasma* antibodies by LAT in patients' group (Table 1); whereas it was 28(62%) examined by ELISA technique observed seropositive results (IgG) and 17(38%) observed seronegative results (Table 2). In both tests, the differences between schizophrenia patients and controls were significant (P 0.01). (Chi-square).

While 14 (35%) of control tested positive for anti-toxoplasma antibody by LAT, and 13 (33%) tested positive by ELISA-IgG.

Table1: The percentage of anti-*T. gondii* antibodies in 45 samples of schizophrenic Patients and 40 samples of healthy individuals (control) tested by LAT test.

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GROUP	NUMBER EXAMINED	LAT				P-VALUE	
		+ re	Percentage%	-re	Percentage%		
Schizophrenic Patients	45	38	84 %	7	16 %	0.01	SIGNIFICANT
Control	40	14	35 %	26	65 %		
Total	85	52	--	33	--		

Table 2: The percentage of anti-*T. gondii* antibodies in 45 samples of schizophrenic Patients and 40 samples of healthy individuals (control) tested by ELISA-IgG test.

GROUP	NUMBER EXAMINED	ELISA-IGG TEST				P-VALUE	
		+ re	Percentage%	-re	Percentage%		
Schizophrenic Patients	45	28	62 %	17	38 %	0.01	SIGNIFICANT
Control	40	13	33 %	27	67 %		
Total	85	41	--	44	--		

Discussion

This study revealed that in 45 schizophrenic patients examined by LAT, 38(84%) of them were positive for *toxoplasma* antibodies. and 7(16%) were negative to LAT. (Tab.1). The confirmation test by ELISA (IgG) showed that 28(62%) were positive for anti-*toxoplasma* antibodies. and 17(38%) showed seronegative to *toxoplasma* antibodies (Tab.2). The Control group showed that in 40 healthy individuals examined after confirmation by ELISA, 13(33%) were seropositive to *toxoplasma* antibodies, whereas 27(67%) showed negative results to the mentioned test (Tab.2). Statistically, this study found significant differences between schizophrenic patients and the control group in both tests ($p \leq 0.01$).

according to the current study, anti-*toxoplasma* antibodies are found in higher numbers in patients with schizophrenia than in healthy people. Antibodies against *T. gondii* are very frequent. Although of, *Toxoplasma gondii* is endemic in our country (Iraq), according to some studies performed in different parts of Iraq most of them used LAT and ELISA technique to

detection this parasite, some studies thought to use specific techniques such as Immunohistochemical IHC to detection of this parasite [9], they show high prevalence of this parasite among healthy persons, toxoplasmosis was found in many local studies among women who had a problematic pregnancy or a history of abortion [10], with greater incidence in rural persons compared to those in urban regions [9] [11] [12], this could be due to increased contact with animals.Epidemiological and serological indicators have, reinforced the suggestion that toxoplasmosis might intermediate some neurological signs such as schizophrenia [13].

In last years, serological studies on patients with schizophrenia have been performed indicating that anti- *toxoplasma* antibodies were higher in patients than healthy person.Several research' findings revealed that a variety of factors, such as geographic location, play a role of the balance between the host and the parasite is maintained by genetic variables that influence the host's sensitivity and resistance to chronic toxoplasmosis in the brain. In humans, HLA-DQ3 and DQ1 that regulate the immune responses are it is important to determine the resistance or susceptibility of the hosts to the development of cerebral toxoplasmosis, the stage (Tachyzoites, Bradyzoites or oocysts) and the methods of transmission, genotype of *T. gondii*, and of the parasite instigating the infection. The parasite genotype looks like to be an important factor influencing the outcome of clinical signs in humans. [32].

Based on variations in their DNA, *T. gondii* has been divided into three genotypes (types I, II, and III). Mice infected with type II strains developed toxoplasmic encephalitis after being treated with anti-interferon-c (IFN-c) antibody, whereas mice infected with type III strains did not. The ocular infections appear to be caused by the type I strain.[14]. A possible explanation for the association between infection and psychiatric signs could be the parasite induced dysregulation of distinct neurotransmitters. The behavioral changes may have a direct or indirect effect of *T. gondii* infection [15].. The location of the tissue cysts has been suggested to play an important role in the behavioural changes of the host [16].

An attractive hypothesis explains the effects of *T. gondii* infection on neuromodulators are based on the capability of the parasite cysts to harass dopamine metabolism. Chemical secretions such as Dopamine plays several important roles in regulating long-term of brain functions [17]. dysregulation of Dopamine is proposed to play a central role in schizophrenia, potentially in combination with glutamate metabolism. Other study achieved on mice revealed that dopamine secretion increased several folds due to enhancing the levels of k+ and tyrosine hydroxylase by *T. gondii* infection. Altered dopamine levels induced by *T. gondii* in tissue cysts in these regions of the brain could have significant harmful consequences on a variety of brain functions, possibly leading to an array of behavioural changes and possible neurological malfunctions [18].

The parasite can deliver certain effector proteins without entering the host cell, and also inhibit host cell apoptosis presumably to inhibit elimination and to survive the host´s immune response [16]. Numerous genes have been implicated in schizophrenia as have virus-related infections during pregnancy or infant period infections and toxoplasmosis or Lyme disease. Schizophrenia might thus be a “pathogenic” autoimmune disruption, caused by pathogens, genes, and the immune system acting together [19].This study confirms results by [3] [20] and [8] [21]. This data confirmed by other studies which show that the Seroprevalence of anti-toxoplasma antibodies in patient group (67.7%) was significantly higher than in the control group (37.1%) and also they showed that a significant correlation between *Toxoplasma* infection and schizophrenia ($P<0.01$) [22].In another investigation shows the highest of serological evidences such as IgG in *Toxoplasma* positive schizophrenics and major depression disorder [21].

Previous study shows that there are observed differences between women who are healthy and those who have schizophrenia ($P = 0.001$) [23], another study suggested that a relationship between chronic toxoplasmosis and schizophrenia antibodies to *T. gondii* were found to be increased in schizophrenic patients [21].

Disagreement to our study no significant difference was found in *T.gondii* IgG seropositivity between the schizophrenic patients and control group [24] [25]. They have suggested that toxoplasmosis does not have a relationship with schizophrenia. [26] Proposed that *T. gondii* infection is strongly and significantly related with generalized anxiety disorder (GAD). [27] in western of Iran has showed a relationship between chronic toxoplasmosis and psychiatric patients in general and schizophrenia and bipolar cases in particular with higher significantly frequency than in healthy individuals. In a study clarifying gene-environment overlaps in the behavioral responses to Toxoplasma infection by using a genetic animal model for depression, shows that the chronic toxoplasmosis worsen anxiety and depressive-like behavior [28].

An association showed between *T. gondii* and schizophrenia, as well as between CMV and other psychiatric complications [29]. Other study revealed that people with schizophrenia who tested positive for *Toxoplasma* infection had a nearly 5-times greater risk of death compare to control [30]. In a case–control study. they found low rate of suicide attempts in male patients with schizophrenia based on their serological tests [31].

Finally, in spite of we were unable to determine the exact date of the event toxoplasmosis in our community. Toxoplasma IgG antibodies can be found in patients as a result of congenital infection or infection acquired later in life, however we observed a statistically significant link between the serological indication of exposure to *Toxoplasma* and schizophrenia compared to healthy population.

Conclusion:

This investigation corroborates that Toxoplasma has a beneficial effect on the rate of schizophrenia, according to this study. It's reasonable to predict a link between Toxoplasma infection and schizophrenia. Our research also backs up these claims. role of toxoplasmosis in the onset of some behavioral changes.

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