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Prevalence of *Toxoplasma gondii* Infection Among Schizophrenic Patient: Probable Linked Between Toxoplasmosis and Behavior Shifting

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Abstract

Toxoplasma gondii the cause of toxoplasmosis is intracellular parasite; when primary infection occurs during pregnancy the offspring has a markedly increased risk of CNS congenital abnormalities, including microcephaly, hydrocephalus, mental retardation, convulsions, cerebral calcifications, and chorioretinitis. *Fifty-seven* patients with schizophrenia with age range 12–60 years, study group 102 subjects without schizophrenia as control group ,with age range 15–60 years. Immunofluorecent assay were used to determine qualitative and quantitative IgG tested by automated VIDAS family instruments, this assay principle combines an enzyme immunoassay method by immunocapture with final fluorescent detection (ELFA). *The* present study show significant differences between schizophrenic patient (57) group and control group (102). Through a case–control study design, 57 schizophrenic patients and 102 control subjects matched by gender, age and residence place were examined with enzyme-linked immunfluorscent assays for the presence and levels of *T. gondii* IgG antibodies. Both the seroprevalence and the level of *T.gondii* IgG antibodies were higher in schizophrenic patients (15/57; 26%) as compare with control subjects (7/102; 7%). This study suggested the hypothesis that *T. gondii* is a risk factor for schizophrenia especially in old schizophrenic patients.

Keywords

Toxoplasma gondii, Seroprevalence, Schizophrinic Patient, Hilla - Iraq

1. Introduction

Human toxoplasmosis is causes by a coccidian, *Toxoplasma gondii*, originally discovered in 1908 in a desert rodent. The principal means of acquiring the infection is by ingestion of inadequately cooked meat, primarily either beef, pork, and lamb, or by contact with feral or domestic cats [1] (Bogitsh *et al*., 2013).

T. gondii the cause of toxoplasmosis is intracellular parasite; when primary infection occurs, during pregnancy, the offspring has a markedly increased risk of CNS congenital abnormalities, including microcephaly, hydrocephalus, mental retardation, convulsions, cerebral calcifications, and chorioretinitis .Detection of Toxoplasma includes direct detection of the parasite, immunoassays for serum immunoglobulin (IgM) antibody, and elevation of maternal IgG antibody to Toxoplasma. In addition, elevation of Toxoplasma IgG may reflect primary active or reactivated infection; IgM antibody is a specific indicator of recent infection. Increased IgG may persist for years in subjects with dormant infection [2] (Fawzy & Saber, 2009).

T. gondii infects approximately 30% of the world's population, but causes overt clinical symptoms in only a small proportion of people [3] (Henriquez et al, 2009). Recent epidemiologic studies indicate that infectious agents

may contribute to some cases of schizophrenia. In animals, infection with *T. gondii* can alter behavior and neurotransmitter function. In humans, acute infection with *T. gondii* can produce psychotic symptoms similar to those displayed by persons with schizophrenia [4] (Torrey & Robert, 2003). Toxoplasma organisms have also been shown to impair learning and memory in mice, and to produce behavioral changes in both mice and rats. Of special interest are studies showing that Toxoplasma-infected rats become less neophobic, leading to the diminution of their natural aversion to the odor of cats. These behavioral changes increase the chances that the rat will be eaten by a cat, thus enabling Toxoplasma to complete its life cycle, an example of evolutionarily driven manipulation of host behavior by the parasite[4] (Torrey and Robert, 2003). Schizophrenia is a severe and debilitating psychiatric disorder that has a lifetime prevalence of 1% and is ranked as the ninth most prevalent cause of disability worldwide. It is a heterogeneous disease characterized by a diverse range of symptoms[3] (Henriquez et al., 2009). The positive symptoms (such as hallucinations and delusions).The mechanism of action by which *T.gondii* alters rodent behavior is unknown. Histopathological, immunological, and/or neuromodulatory changes are all potential candidates. While gross pathology alone is unlikely to account for the observed changes in the majority of cases, because other behavioral characteristics are left intact, multifocular lesions and/or histopathological changes in the cyst-containing regions of the brain have been observed[5] (Webster, 2006). *T.gondii* can cause manipulation in host behavior especially murder behavior in women [6].

2. Materials and Methods

2.1. Immuno-Fluorescent Assay

The detection of anti-toxoplasma IgG in serum by using enzyme linked fluorescent assay (ELFA). In present study the qualitative and quantitative IgG tested by automated VIDAS family instruments, this assay principle combines an enzyme immunoassay method by immunocapture with final fluorescent detection (ELFA). The procedure of this assay accomplished by manufacture commercial kit by Biomerieux Company (France).

2.2. Subjects

Fifty-seven patients with schizophrenia were identified in the Marjan Hospital. Academic psychiatrists made diagnosis. To evaluate the positive and negative symptoms the PANSS (positive and negative symptoms scale) was used. All patients had no family history of schizophrenia, no history of head trauma and brain surgery. Blood samples were obtained from the patients and control groups in the morning.

2.3. Control Group

The control group consisted of 102 healthy volunteers. They were evaluated to rule out any medical and psychiatric disorders.

2.4. Statistical Analysis

All statistical analyses were performed using SPSS 10.0 statistical software (SPSS Inc., Chicago, USA). Relations among the categorical variables were investigated by chi-square test. P-values more than or equal to 0.05 were considered statistically significant. All data were analyzed by chi-square at a confidence level of 95%.

2.5. Serum Collection

Five mL of blood was obtained from each of the schizophrenia patient and healthy subject by venipuncture, under sterile conditions. Serum was separated from whole blood by centrifugation at 2000 r.p.m. and was stored at -20ºC until use.

Table (1). *Comparison of Toxoplasma IgG levels in Toxoplasma positive patients and controls.*

P-value	Control (102)		Schizophrenic patient		Toxoplasma IgG level
	No.	%	No.	%	
0.0258	2	2	3	5	4-8IU/ml
0.0032	6	6	12	21	9-86IU/ml
0.0037	1	1	3	5	87-182 IU/ml

***Table* (2).** *Seroprevalence of T. gondii infection in different age of groups in schizophrenic patients and controls.*

P-value	Control No %	Seronegative IgG	Seropositive IgG	Schizophrenic patient	Age groups (years)
0.16	27(15%)	(80%) 24	(20%) 6	30	12-22
0.00	54 (4%)	(85%)11	(15%) 12	13	23-33
0.00	1 (7%)	(75%) 6	(25%) 2	8	34-44
0.00	0 (0%)	(17%) 1	(83%) 5	6	≥45
0.00	102(7%)	(74%) 42	(26%) 15	57	Total

3. Results

The difference in the seroprevalences was significant in schizophrenic patient as compare with controls in sociodemographic characteristics, gender and age of groups ($p < 0.05$) as shown in Table 1, 2. Further, no significant relationship was found among sociodemographic characteristics and gender in control ($p>0.05$), as shown in Table 3. The prevalence of *T. gondii* was higher in female

than in male in schizophrenic patient 31% (4), 23% (10) respectively (Table3). Individuals with schizophrenia had significantly increased levels of serum IgG antibodies to *T. gondii* compared with controls ($p < 0.05$). Our data show the high level of seropositive infection in age group ≥45 where percentage of infection reach 83% as compare with control ($p < 0.05$).

4. Discussion

There is little information about the association between *Toxoplasma gondii* infection and schizophrenia in Iraq. Our data support previous reports of a higher seroprevalence of *T. gondii* infection in schizophrenia patients than in controls (Table-2).

Table (3). *Diagnosis of T. gondii infection in different gender and demographic characteristics in schizophrenic patients and controls.*

P-value	Control		Seronegative		Seropositive		No. of patient (57)	Characteristics
	No.	%	No.	%	No.	%		
0.338	6	48	24	77	7	23	31	Urban
0.359	7	54	18	69	8	31	26	Rural
	0.0049				0.0094			P-value
0.287	8	12	34	77	10	23	44	Male
0.384	7	90	62	8	5	38	13	Female
	0.0042				0.0154			P-value

The present study showed a higher seroprevalence of anti *T.gondii* IgG antibodies in schizophrenia patients than in controls matched by age and gender. Our investigation confirming results by Alipour et *al*. [7] (2011b); Mokhtari and Mokhtari [8] (2006). Whereas, our data contradiction with Tanyusel, et *al.* (2010) [9] study where, there is no significant differences in schizophrenic patient and control group this might be related to the fact that few control group(40) as compare with schizophrenic patient(73). The high prevalence of toxoplasmosis in healthy individuals more than in patient may be related to the method of diagnosis (Screen Agglutination Test, Sabin-Feldman Dye and ELISA test) that have specificity and sensitivity less than ELIFA assay[10] (Brown, 2005). From our result we are found a significantly higher seroprevalence of anti-T.gondii (IgG) antibodies in schizophrenic patients than in controls matched by age, gender and residence place, this may be due socioeconomic level, and educational level. The association consistent with many previous studies[11] (Alvarado-Esquivel et al., 2011).

Torrey et *al.* [12] (2007), in their meta-analysis studies, showed the good three major problems with the plausibility of *T. gondii* being etiologically linked to schizophrenia these where, One is the fact that these studies are serological and are not based on the direct detection of Toxoplasma organisms or DNA in infected body fluids. The second is epidemiological; the seropositivity rate of *T. gondii* is very high in countries such as France and Ethiopia, yet schizophrenia has not been found to be unusually prevalent in these countries. The third problem with plausibility is that the majority of individuals with schizophrenia do not have measurable antibodies to *T. gondii*. This fact may be related to the relative insensitivity of available serological assays or to the heterogeneity of disease pathogenesis.

A comprehensive understanding of the mechanisms through which the *T. gondii* can cause schizophrenia progress or development not complete. In the following we are summarizes a possible explanation for three major problems. The use of different methods such as latex, ELISA, Sabin-Feldman Dye, IFA, ILIF and PCR each of one have different accuracy, this may lead to the different results . we are think there is a threshold level of IgG level by which the schizophrenia were development , or may be can otherwise can consider as cofactor for schizophrenia progress. Our result showed that the high level of IgG was found in more than 45 years, also the percentage of infection also high (83%). We believe that the association between serointensity with high of IgG level and schizophrenic patient. An experimental research has proven behavior change when infected by the parasite; this confirms the hypothesis of the existence of the relationship between infection and the progression of the disease [13-14] (Webster, 2007; Vyas, 2006).Also, higher rates of *T. gondii* seropositivity have been reported for several psychiatric conditions in multiple parts of the world. Patients with schizophrenia who were seropositive had significantly reduced gray-matter volume as compared with seronegative patients [15] (Hurley, 2012). In addition, many studies, including the current study has excluded the cases of people who have a family history of the disease, schizophrenia, so the results showed that the infection rate may reflect the proportion of the parasite in the progression of the disease. They also found that individuals with schizophrenia have an increased prevalence of antibodies to *T. gondii* and suggested that this, as well as genetic and environmental factors, could be associated with a large number of cases of schizophrenia.

It is possible that immune response to infection with parasite such as *T. gondii* and *Toxocara spp.* can cause depression and manipulating of behavior [16] (Al-Hassnawi & Al-Quraishi, 2014). A continuous production of proinflammatory cytokines is essential for resistance to acute and chronic infection with *T.gondii.* These cytokines have been previously implicated in triggering depression in humans [17] (Arling et *al.*, 2009). Proinflammatory cytokines, such as IL-6, IL-1B and TNF have recently been associated with psychological stress behavior [18-19] (ling et al., 2011; Al-Hassnawi and Al-Quraishi, 2013). Inflammatory mediators produced in response to *T. gondii* infection may contribute or progress to schizophrenia .In most age groups, schizophrenic patients showed higher seroprevalences of *T. gondii* infection than in controls.

5. Conclusion

Our results confirm recent findings that *Toxoplasma gondii* infection is significantly associated with schizophrenia. The results also show that *T. gondii* is significantly associated with gender, age and demographical characteristic. This finding is essential as a preliminary data in Iraq in establishing an association between *T. gondii* and schizophrenia.

Recommendation

Liaison team between serologist ,human parasitology, psychiatrist, neurologist for control and treatment control maternal exposure to toxoplasma infection to prevent the risk of schizophrenia schizophrenic patients send for screening tests and serology to exclude possible *toxoplasma gondii* infection.

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