Seroepidemiological Study of *Toxoplasma gondii* Infection among Psychiatric Patients in Mashhad, Northeast of Iran

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**Abstract**

**Background:** Psychiatric patients have an increased risk of some infections like toxoplasmosis. Investigations on *Toxoplasma gondii* infection among psychiatric patients have been limited in Mashhad, Northeast of Iran. In this case-control study, prevalence of T. gondii was investigated by serological method.

**Methods:** This case-control study was performed among psychiatric patients admitted to Avicenna Hospital in Mashhad, Northeast of Iran. Three hundred and fifty inpatients and 350 controls were examined in 2012-2013 for detection of IgG and IgM antibodies against *T. gondii* in their blood sera by ELISA. Sociodemographic and clinical manifestations of the patients were obtained.

**Results:** Anti-*T. gondii* IgG antibodies was found in 164 (46.85%) of 350 psychiatric inpatients and 120 (34.28%) of 350 controls. Seventeen (4.85%) of psychiatric individuals and 3 (0.85%) of control group were IgM+/IgG indicating acute form of toxoplasmosis. There were no statistically significant differences between the case and control groups. In patient group, schizophrenic patients had the highest positive rate (46.28%) and bipolar mood disorder had the second most prevalent rate (20%). Of 162 schizophrenia patients, 65 (40.1%) had latent infection which was higher than that observed in controls.

**Conclusion:** The prevalence of *T. gondii* infection among psychiatric patients suffering from schizophrenia was more in Mashhad, compared with control group.
Introduction

Psychiatric patients are in high risk of some infections, not only because of their life style; however, it could be a common etiologic process. The relationship between infectious diseases and psychiatric disorders has rooted in the epidemiologic surveys that reports high co-morbidity of these conditions (1-3). Some infections have been declared to play a role in the etiology of some major psychiatric problems (4, 5).

Toxoplasma gondii, is one of the obligate intracellular protozoan parasite in the phylum Apicomplexa with a worldwide distribution in a wide variety of intermediate hosts including humans and other mammals (6). Humans may become infected through with ingestion of oocysts in cat feces, or by eating meat of infected animals (7). Primary acute toxoplasmosis may be developed in each trimester of pregnancy and causes severe damage to the foetus (8, 9). Subsequently, usually acquired infections are asymptomatic but in some patients presented by ocular and central nervous system manifestations. T. gondii may affect dopamine levels into the brain, causing in alterations in CNS (10). Earlier investigations observed that latent Toxoplasma infection might affect behavior (11), perhaps being a contributory, or even causative, factor in some psychiatric disorders, including depression, anxiety and schizophrenia (1, 10, 12-14).

Several factors affect prevalence of toxoplasmosis including age, rural or urban setting, socioeconomic criteria and nutritional habit (15). Furthermore, seroprevalence of infection rates vary from 10% to 70% in Asia (16), 24% to 57.5% in two Iranian populations (17, 18). It is estimated to be about 50% in Iran; therefore, toxoplasmosis continues to be a public health problem in Iran (19). In Northeast of Iran, there is no data about seropositive of T. gondii infection from health and patients suffer from psychiatric problems, and there is no information about risk factors between T. gondii antibodies and psychiatric disorders.

The aim of this investigation was to check the prevalence of antibodies against T. gondii in patients with psychiatric and mood disorders and in a matched group of control subjects.

Materials and Methods

This case-control study was performed in 2013 between two populations: psychiatric/mood disorders patients and control group. Since Dec 2011 to Mar 2012, all patients referred to the only Avicenna Hospital in Mashhad, Northeast of Iran, were invited to enroll in this study. The patients had been diagnosed clinically by psychiatrics. All psychiatric patients were included in the study based on the following inclusion criteria: 1) psychiatric inpatients, 2) aged >16 yr, 3) consent to participate in the study. During the study period, 350 psychiatric disorders patients were hospitalized. The age range of the population was 16-75 (35±11.61) yr old. All patients had no family history of schizophrenia, no evidence of immunodeficiency or other immunologic abnormalities, no history of head trauma, previous meningitis/encephalitis and brain surgery.

Sampling

Three hundred and fifty healthy volunteers were selected as control group. They were screened for the absence of physical and psychiatric disorders and matched to patients according to sex, socioeconomic status, and age (38±13.2 yr old), matched with study group (P>0.05).

The Research Ethical Committee of Mashhad University of Medical Sciences, Iran, approved this study. All participants signed informed consent form.

Serological examination

A sample of 5 ml blood was collected from each psychiatric patients and control; then serum separated by centrifugation at 1000 r.p.m. and stored at -20 °C. All samples labeled by blind numbers unrecognized to other col-
leagues in this study. The levels of specific IgG and IgM antibodies to *T. gondii* in the serum samples were measured using a commercial enzyme immunoassay kit (Pishtaz Teb Diagnostics, Tehran, Iran). The IgG and IgM antibody titers were read at optical density (OD) of 490 nm using automatic ELISA reader (Spectra, Molecular Devices, USA). ELISA cut off for positive and negative results were 10IU/ml. The results below that considered as negative and upper than that considered as positive.

SPSS software ver. 16.0 was used for statistical analysis. The relative proportions were calculated with a confidence interval of 95%. Possible associations were identified using the Chi-Square and Fisher’s exact statistical tests at a significant level of 5%.

Statistical analysis

Socio-demographic data including age, birthplace, residence, marital status, occupation, educational level and socio-economic level were obtained from all patients. Clinical data including blood transfusion or transplant history; and behavioral data including animal contacts, cat attender, consumption of meat (raw or undercooked lamb, beef, goat, chicken, sea food and bird), unpasteurized dairy products, contaminated water, improper washed raw vegetable or fruits, contact with soil (gardening or agriculture), were obtained. Clinical diagnosis was confirmed by means of the Structured Clinical Interview as mentioned in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria (20).

Table 1: Seroprevalence of anti-*T. gondii* IgG/IgM antibodies in psychiatric patients and controls according to age groups and gender

| Age group (yr) | Controls | Psychiatric patients |
|---------------|----------|----------------------|
|               | IgG+ No. % | IgM+ No. % | No. tested | IgG+ No. % | IgM+ No. % | No. tested |
| 10-20         | 0 (0.58)   | 2 (0.58)   | 9           | 6           | 1 (0.28)   | 9 (2.58)   |
| 21-30         | 2 (0.58)   | 20 (5.72)  | 56          | 50          | 5 (1.43)   | 44 (12.58) |
| 31-40         | 0 (0.28)   | 33 (9.43)  | 45          | 40          | 5 (1.43)   | 45 (12.85) |
| 41-50         | 1 (0.28)   | 36 (10.29) | 46          | 39          | 5 (1.43)   | 13 (3.72)  |
| 51-60         | 0 (0.28)   | 16 (4.58)  | 24          | 11          | 1 (0.28)   | 13 (3.91)  |
| 61-70         | 0 (0.28)   | 6 (1.72)   | 7           | 1           | 0 (0.28)   | 1 (0.47)   |
| 71-80         | 0 (0.28)   | 4 (1.14)   | 0           | 0           | 0 (0.28)   | 1 (0.47)   |
| Total Together| 3 (0.85)   | 117 (33.42)| 180         | 170         | 17 (4.85)  | 147 (42)   |

Results

The number of male individuals were 263 (75.1%) and 170 (48.6%) in patient group, respectively. More than 74% of the patients were citizens of Mashhad. The anti *T. gondii* IgG+/IgM+ antibody was positive in 46.85% and 34.28% of both case and control group, respectively. The seroprevalence of latent *T. gondii* infection in the populations studied according to age groups and gender. As you can observe the prevalence of the infection in both patients and controls increased with age (Table 1).

There were no statistically significant differences in any of the case and control groups. However, the patients in middle age groups in control group showed higher rates of IgG+ seroprevalence (P=0.002). According to psychiatric diagnosis based on DSM-IV criteria schizophrenic patients had the highest positive rate (46.28%) and by Chi square test, there is significant difference between IgG and IgM positives in pa-
tients and control group; \( P=0.019 \) and \( P=0.001 \), respectively. Patients with bipolar mood disorder were the second most prevalent group (20%). Table 2 shows the seroprevalences of \( T. \) gondii infection in the inpatients according to their psychiatric disorder. The highest prevalence of latent \( T. \) gondii infection in schizophrenics was found in patients aged 21-30 yr old (Table 3).

**Table 2**: Clinical diagnosis and seroprevalence of anti-\( T. \) gondii IgG/ IgM antibodies in 350 psychiatric disorders

| Disorder Category         | Clinical Diagnosis               | Patients studied | Patients with anti-\( T. \) gondii IgG+ | Patients with anti-\( T. \) gondii IgM+ |
|---------------------------|----------------------------------|------------------|-----------------------------------------|----------------------------------------|
| Personality disorders     | Personality disorder             | 6 (1.71)         | 3 (0.85)                                | 0                                      |
| Anxiety disorders         | Posttraumatic Stress Disorder    | 15 (4.28)        | 4 (1.14)                                | 0                                      |
| Developmental disorders   | Mental retardation               | 6 (1.71)         | 2 (0.58)                                | 0                                      |
| Psychotic disorders       | Schizoaffective                   | 24 (6.9)         | 10 (2.85)                               | 1 (0.28)                               |
| Psychotic disorders       | Schizophrenia                     | 162 (46.28)      | 65 (18.57)                              | 9 (2.56)                               |
| Psychotic disorders       | Delusional Disorder              | 8 (2.28)         | 4 (1.14)                                | 0                                      |
| Developmental disorders   | Mental disorder                   | 24 (6.85)        | 8 (2.28)                                | 1 (0.28)                               |
| Mood disorders            | Bipolar Affective Disorder       | 70 (20)          | 33 (9.42)                               | 5 (1.42)                               |
| Mood disorders            | Major Depressive Disorder        | 35 (10)          | 18 (5.13)                               | 1 (0.28)                               |
| Total                     |                                  | 350 (100)        | 147 (42)                                | 17 (4.85)                              |

**Table 3**: Seroprevalence of anti-\( T. \) gondii IgG antibodies in schizophrenic patients according to age groups

| Age groups (yr) | No. Tested | Positive No. | %  |
|-----------------|------------|--------------|----|
| 10-20           | 10         | 2            | 20 |
| 21-30           | 50         | 23           | 46 |
| 31-40           | 56         | 21           | 37.5 |
| 41-50           | 31         | 13           | 41.3 |
| 51-60           | 12         | 5            | 41.6 |
| 61-70           | 3          | 1            | 33.3 |
| Total           | 162        | 65           | 40.1 |

**Discussion**

*Toxoplasma gondii* is one of the most widespread protozoan parasites of humans (9), although, prevalence between different populations varies according to different geographical regions. In a previous study on HIV patients in Mashhad, the IgG and IgM anti-*Toxoplasma* antibodies were estimated 38.01% and 2.5%, respectively (21).

In the present study, the prevalence of \( T. \) gondii infection was 46.85% and 34.28% in psychiatric inpatients and control individuals, respectively. The present results correspond with the result of the other places of Iran (22-26) and some reports in the world (27-31). However, some of them are in contrast (12, 15, 25, 32-35). This difference could be due to our method for selection of population study. Furthermore, the healthy individuals in our control group were the relatives of the patients’ group revealed that the higher prevalence of toxoplasmosis in psychiatric and schizophrenic patients showed associations between \( T. \) gondii infection and schizophrenia as other researchers have reported (1, 12-14). Patients with schizophrenia have insufficient hygiene and self-care skills, and they have a greater tendency to pica and coprophagia. The prevalence of anti-\( T. \) gondii IgM antibody was not
significantly high in patients in comparison to the control group.

One of the most important aspects of studies on seropositivity of toxoplasmosis in psychiatric patients not be estimated was the initiation of exposure. Indeed, we could not identify either of infection acquired as early as birth time or months/yr later. This is because anti-psychotic and bipolar disorder drugs are able to inhibit the growth of *T. gondii* (36).

In addition, environmental exposures have been recognized as a risk to increase the rate of toxoplasmosis. Among behavioral characteristics, known factors associated with *T. gondii* infection such as consumption of untreated water, unwashed raw fruit or vegetable and direct contact with cat played the important role for parasite transmission in our population study.

**Conclusion**

The prevalence of *T. gondii* infection in patients with psychiatric disorder especially those suffering from schizophrenia were more in Mashhad compared with control group. Therefore, measuring antibody titer in such patients could be helpful to identify the infection and start treatment in proper time.

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**References**

1. Alvarado-Esquivel C, Urbina-Alvarez JD, Estrada-Martinez S et al. *Toxoplasma gondii* infection and schizophrenia: a case control study in a low *Toxoplasma* seroprevalence Mexican population. Parasitol Int. 2011; 60(2): 151-5.
2. De Hert M, Wampers M, Van Eyck D et al. Prevalence of HIV and hepatitis C infection among patients with schizophrenia. Schizophr Res. 2009; 108(1-3): 307-8.
3. Nakamura Y, Koh M, Miyoshi E, Ida O, et al. High prevalence of the hepatitis C virus infection among the inpatients of schizophrenia and psychoactive substance abuse in Japan. Prog Neuropsychopharmacol Biol Psychiatry. 2004; 28(3): 591-7.
4. Brown AS. Prenatal infection as a risk factor for schizophrenia. Schizophr Bull. 2006; 32(2): 200-2.
5. Wang HL, Wang GH, Li QY, Shu C, Jiang MS, Guo Y. Prevalence of *Toxoplasma* infection in first-episode schizophrenia and comparison between *Toxoplasma*-seropositive and *Toxoplasma*-seronegative schizophrenia. Acta Psychiatr Scand. 2006; 114(1): 40-8.
6. Wastling J, Heap S, Ferguson D. *Toxoplasma gondii*—keeping our guests under control. Biologist (London). 2000; 47(3): 234-8.
7. Tenter AM, Heckerth AR, Weiss LM. *Toxoplasma gondii* from animals to humans. Int J Parasitol. 2000; 30(12-13): 1217-58.
8. Kravecz JD, Federman DG. Toxoplasmosis in pregnancy. Am J Med. 2005; 118(3): 212-6.
9. Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet. 2004; 363(9425): 1965-76.
10. Flegr J. How and why *Toxoplasma* makes us crazy. Trends Parasitol. 2013; 29(4): 156-63.
11. Flegr J. Effects of *Toxoplasma* on human behavior. Schizophr Bull. 2007; 33(3): 757-60.
12. Hamidinejat H, Ghorbanpoor M, Hosseini H, Alavi SM, Nabavi L, Jalali MH, et al. *Toxoplasma gondii* infection in first-episode and inpatient individuals with schizophrenia. Int J Infect Dis. 2010; 14(11): e978-81.
13. Henriquez SA, Brett R, Alexander J, Pratt J, Roberts CW. Neuropsychiatric disease and *Toxoplasma gondii* infection. Neuropsychopharmacol Biol Psychiatry. 2009; 16(11): 122-33.
14. Tamer GS, Durdar D, Yalug I, Caliskan S, Yazar S, Aker A. The schizophrenia and *Toxoplasma gondii* connection: infectious, immune or both? Adv Ther. 2008; 25(7): 703-9.
15. Alvarado-Esquivel C, Sifuentes-Alvarez A, Narro-Duarte SG et al. Seroepidemiology of *Toxoplasma gondii* infection in pregnant women in...
a public hospital in northern Mexico. BMC Infect Dis. 2006; 6:113.
16. Guy E, Dubey JP and Hill DE. *Toxoplasma gondii*. Smith IJ and Robertson HV, In: Food-borne Protozoan Parasites. Nova Biomedical. 2012: 167-188
17. Hashemi HJ, Saraci M. Seroprevalence of *Toxoplasma gondii* in unmarried women in Qazvin, Islamic Republic of Iran. East Mediterr Health J. 2010; 16(1): 24-8.
18. Sahali-Moghadam A, Hafizi A. A serological study on *Toxoplasma gondii* infection among people in south of Tehran, Iran. Korean J Parasitol. 2009; 47(1): 61-3.
19. Assmar M, Amirkhani A, Piazak N, Hovanesian A, Kooloobandi A, Etessami R. Toxoplasmosis in Iran. Results of a seroepidemiological study. Bull Soc Pathol Exot. 1997; 90(1): 19-21.
20. First M SR, Gibbon M, Williams J. Structured clinical interview for DSM-IV axis I disorders (SCID-1), clinician version American Psychiatric Press. Washington, DC. 1997.
21. Shafiei R, Riazi R, Sarvghad MR, Galian Mehdi S, Mehdizadeh A, Haja M. Prevalence of IgG and IgM anti-*Toxoplasma gondii* antibodies in HIV positive patients in northeast of Iran. Iran J Pathology. 2011; 6(2): 68-72.
22. Ahmad D, Mehdi S, Sayed HH, Sayed AK, Shirzad G. Serological survey of *Toxoplasma gondii* in schizophrenia patients referred to Psychiatric Hospital, Sari City, Iran. Trop Biomed. 2010; 27(3): 476-82.
23. Khademvatan S, Khajeddin N, Izadi S, Yousefi E. Investigation of anti-Toxocara and anti-*Toxoplasma* antibodies in patients with schizophrenia disorder. Schizophr Res Treatment. 2014; 2014: 230349.
24. Saraci-Sahnesarai M, Shamloo F, Jahani Hashemi H, Khabbaz F, Alizadeh SA. Relation between *Toxoplasma gondii* infections and schizophrenia. IJPCP. 2009; 15(1): 3-9.
25. Fata A, Elahi R, Berenji F, Zare R, Ghabouli MJ, Ashrafi Abyaneh H. Evaluation of Immuno- fluorescence antibody (IFA) and Immuno-peroxidase Test (IPT) among 200 pregnant women for toxoplasmosis. Med J Mashhad Univ Med Sci. 2001; 44: 16-21.
26. Sarkari B, Shafiei R, Zare M, Sohrabpour S, Kasraian L. Seroprevalence and molecular diagnosis of *Toxoplasma gondii* infection among blood donors in southern Iran. J Infect Dev Ctries. 2014; 8(4): 543-7.
27. Boronow J, Dickerson F, Stallings C, Lee B, Origoni A, Yolken RH. HSV-1. CMV and *Toxoplasma* serology predict cognitive deficits in schizophrenia. Schizophr Res. 2002; 53: 85.
28. Leveke FM, Gerth CW, Koethe D, Klosterkotter J, Ruslanova I, Krivogorsky B, et al. Antibodies to infectious agents in individuals with recent onset schizophrenia. Eur Arch Psychiatry Clin Neurosci. 2004; 254(1): 4-8.
29. Nascimento FS, de Rosalmeida Dantas C, Netto MP et al. Prevalence of antibodies to *Toxoplasma gondii* in patients with schizophrenia and mood disorders. Schizophr Res. 2012; 142(1-3): 244-5.
30. Quying L, Xiaonian L. Li L. The control study of schizophrenia and affective disorders and *Toxoplasma* infections. Acta Academiae Medicinae Beiji. 1999; 20: 223-5.
31. Torrey EF, Yolken RH. *Toxoplasma gondii* and schizophrenia. Emerg Infect Dis. 2003; 9(11): 1375-80.
32. Cetinkaya Z, Yazar S, Gecici O, Namli MN. Anti-*Toxoplasma gondii* antibodies in patients with schizophrenia—preliminary findings in a Turkish sample. Schizophr Bull. 2007; 33(3): 789-91.
33. Gu H, Yolken RH, Phillips M, Yange F, Bilder RM, Gilmore JH. Evidence of *Toxoplasma gondii* infection in recent-onset schizophrenia [abstract]. Schizophr Res. 2001; 49(2 Suppl: 1: 53.
34. Yolken RH, Bachmann S, Ruslanova I et al. Antibodies to *Toxoplasma gondii* in individuals with first-episode schizophrenia. Clin Infect Dis. 2001; 32(5): 842-4.
35. Alipour A, Shojae S, Mohebal E, Tehranidoost M, Abdi Masoleh F, Keshavarz H. *Toxoplasma gondii* infection in schizophrenia patients: a comparative study with control group. Iran J Parasitol. 2011; 6(2): 31-7.
36. Jones-Brando L, Torrey EF, Yolken R. Drugs used in the treatment of schizophrenia and bipolar disorder inhibit the replication of *Toxoplasma gondii*. Schizophr Res. 2003; 62(3): 237-44.