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Research Article

Study of Anti-*Toxoplasma* IgG and IgM Seropositivity Among Subjects Referred to the Central Laboratory in Tabriz, Iran, 2013 - 2014

Mohammad Fatollahzadeh,¹ Rasool Jafari,^{1,*} Fereshteh Mohammadi,¹ Nasrin Ghayemmaghammi,² Shabnam Rezvan,² Mehdi Parsaii,² Sedigheh Sarafraz,² Shadab Sadeghpour,³ Saber Alizadeh,² and Marzieh Safari⁴

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Abstract

Background: Toxoplasmosis is one of the most widespread parasitic infections worldwide. The infection is mostly benign, although severe disease can be expected in immunocompromised/suppressed individuals and infants who are infected during pregnancy. **Objectives:** The aim of the present study was to determine the anti-*Toxoplasma* IgG and IgM seroprevalence in subjects who were referred to the Central Laboratory in Tabriz, Iran, for the diagnosis of toxoplasmosis.

Methods: This retrospective cross-sectional study was carried out among 6393 individuals who were referred to the central laboratory, Tabriz University of Medical Sciences, Tabriz, Iran, from March 2013 to January 2014. The subjects were referred from different areas of East Azerbaijan province. The quantitative determination of anti-*Toxoplasma* IgG and IgM was performed using an antibody capture chemiluminescence immunoassay. The other available variables, including sex and age, were also recorded and analyzed. **Results:** In total, 1910 (29.87%) out of 6393 subjects were found to be infected with *Toxoplasma* gondii. In terms of the seropositivity, 1871 (32.42%) out of 5770 and 128 (2.14%) out of 5965 subjects were anti-*Toxoplasma* IgG and IgM seropositive, respectively. In addition, 103 (1.69%) out of 5828 subjects were equivocal with regard to anti-*Toxoplasma* IgM, while 57 (0.97%) out of 6068 individuals were equivocal with regard to anti-*Toxoplasma* IgG. The mean concentration of anti-*Toxoplasma* IgM was observed to be higher in male subjects than in females (P = 0.016).

Conclusions: Based on the findings of the present study, the frequency of *Toxoplasma* infection is high in the studied population, although it is fairly close to the findings of reports from the other areas of Iran.

Keywords: Immunoglobulin M, Immunoglobulin G, Iran, Toxoplasma gondii

1. Background

Toxoplasmosis is generally a benign parasitic infection affecting humans and other warm-blooded animals that is caused by *Toxoplasma gondii*, a widespread zoonotic protozoon parasite (1). The infection is considered to be a life-threatening disease in immunocompromised and immunosuppressed individuals such as AIDS patients and organ transplant recipients (2). Furthermore, the infection can cause severe consequences for the fetus during pregnancy, sometimes resulting in abortion or central nervous system and vision disorders after delivery (3).

Cats and other felids are known to be the parasite's definite hosts. *T. gondii* invades the intestinal wall of the definite host so that the sexual reproduction of *Toxoplasma* can take place. The oocysts are the result of that sexual reproduction and they are shed with feces by the cat into

the environment. Oocysts are one source of human infection, since they can be ingested with contaminated food and soil. Once inside the intermediate host, for instance, a human, the parasite develops self-limiting acute toxoplasmosis, followed by the chronic phase in which tissue cysts are produced. Tissue cysts in meat are another source of human infection when undercooked meat or kebob is consumed by humans (4-6).

The infection is mostly asymptomatic or characterized by negligible symptoms so that people do not commonly notice the infection, although it can be problematic during pregnancy. The transplacental transmission of *T. gondii* following maternal infection results in the birth of a child with congenital toxoplasmosis, including retinochoroiditis, hydrocephalus, convulsions, and intracerebral calcification. The risk of congenital transmission is high during the third trimester of pregnancy, yet the risk of symp-

¹Department of Parasitology and Mycology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, IR Iran

 $^{^2}$ Department of Parasitology, Central Laboratory, Tabriz University of Medical Sciences, Tabriz, IR Iran

³School of Medicine, Najafabad Branch, Islamic Azad University, Isfahan, IR Iran

⁴Department of Microbiology and Virology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, IR Iran

^{*}Corresponding author: Rasool Jafari, Department of Parasitology and Mycology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, IR Iran. Tel: +98-9143084002, E-mail: rasooljafariii@gmail.com

tomatic congenital infection is low following delivery. The risk of symptomatic congenital toxoplasmosis is high in cases of maternal infection close to the time of gestation (i.e., first and second trimesters); however, the risk of transmission to the fetus is low during this period. Routinely, maternal infections are detected through serological screening tests such as anti-*Toxoplasma* IgM and IgG avidity tests (3-7).

Patients with T-cell defects, for example, due to hematologic malignancies (Hodgkin's disease and other lymphomas), AIDS, and intentional immunosuppressive therapy, may develop toxoplasmic encephalitis, myocarditis, and pneumonitis. These consequences of toxoplasmosis are life-threatening if they are not recognized promptly and treated properly. Toxoplasmosis in immunocompromised and immunosuppressed patients usually results in the recrudescence of a chronic infection that is acquired prior to the suppression of the immune system; however, it may also occur due to an acute infection that was acquired more recently (2).

Different prevalence rates have been reported in different regions of Iran, but most previous studies have been carried out among people with a higher risk of toxoplasmosis, including premarital women, pregnant women, neonates, and immunocompromised/suppressed patients (8-11).

2. Objectives

The aim of the present study was to determine the frequency of anti-*Toxoplasma* IgM and IgG seroprevalence among those people referred to the central laboratory, Tabriz University of Medical Sciences, Tabriz, Iran, for the diagnosis of *T. gondii* infection.

3. Methods

This retrospective cross-sectional study was carried out on the recorded data of 6393 people from different areas of East Azerbaijan province who were referred to the Central Laboratory, Tabriz University of Medical Sciences, Tabriz, Iran, for the diagnosis of *Toxoplasma* infection. Data from March 2013 to January 2014 were included in the study. The available variables, including sex and age, were also recorded. In terms of the sex distribution, 6339 (99.17%) subjects were female and 53 (0.83%) were male. In total, 6068 subjects had tested for anti-*Toxoplasma* IgM, while 5828 had tested for anti-*Toxoplasma* IgG, although the majority of subjects had undergone both tests.

The quantitative determination of anti-Toxoplasma IgG and IgM was performed using antibody capture chemiluminescence immunoassay (CLIA) kits (LIAISON® Toxo IgM

and IgG, DiaSorin S.P.A., Italy). The kits were applied in a LIAISON (DiaSorin, Germany) device. The tests were performed automatically by the device based on the manufacturer's instructions. Samples with anti-*Toxoplasma* IgM and IgG concentrations below 6 AU/mL were regarded as negative, those between 6 and 8 AU/mL as equivocal, and those equal to or higher than 8 AU/mL were considered positive.

The data were recorded and analyzed with SPSS v.16 software (SPSS Inc., Chicago, IL, USA) using the Kolmogorov-Smirnov, Mann-Whitney, and Chi-square tests.

4. Results

A total of 6393 people were included in this study. Among them, 1910 (29.87%) subjects were infected with *T. gondii*. In terms of the seropositivity, 1871 (32.42%) out of 5770 individuals were anti-*Toxoplasma* IgG seropositive, while 128 (2.14%) out of 5965 humans were anti-*Toxoplasma* IgM seropositive (Table 1). Furthermore, 103 (1.69%) out of 5828 subjects were equivocal with regard to anti-*Toxoplasma* IgM, while 57 (0.97%) out of 6068 were equivocal with regard to anti-*Toxoplasma* IgG. The mean concentration of anti-*Toxoplasma* IgM was observed to be significantly higher in male subjects than in females (P = 0.016) (Table 2).

Of the 6393 subjects studied, 83 (1.29%) were seropositive for both anti-*Toxoplasma* IgM and IgG, while 45 (0.74%) were seropositive solely for anti-*Toxoplasma* IgM. The mean age of the seropositive subjects is displayed in Table 3.

5. Discussion

T. gondii is one of the main concerns during pregnancy, as well as in patients with an impaired immune system and those undergoing immunosuppressive therapy. Infection with T. gondii occurs worldwide, yet a higher prevalence is observed in temperate zones (8). In the present study, a fairly large number of people referred to the Central Laboratory, Tabriz University of Medical Sciences, Tabriz, Iran, were studied over 11 months. The studied subjects had been referred to the central laboratory from different areas of East Azerbaijan province. The overall prevalence was 29.87%, which can be attributed to the high representation (99.17%) of females in the studied population. Based on the results of the present study, the prevalence of T. gondii infection in the studied population is close to that found in reports from nearby regions (12); however, the prevalence in other parts of the country has been reported to range from 12% to 86%. The prevalence of toxoplasmosis is higher in the humid regions of northern Iran

Table 1. Odds Ratio Estimates for Anti-Toxoplasma IgG and IgM Among the Sexes

	Ig	IgG		OR	95% CI	P Value
	Positive	Negative				
Sex						
Male	16	35	51	0.95	0.526, 1.724	0.502
Female	1855	3864	5719	1		
Total	1871	3899	5770			
Sex	IgM (Positive)	IgM (Negative)				
Male	3	41	44	3.392	1.037, 11.103	0.068
Female	125	5796	5921	1		
Total	128	5837	5965			

Table 2. Mean Anti-Toxoplasma IgG and IgM Serum Concentrations Among the Sexes

Variable/Sex	N	Mean	St. Deviation	St. Error Mean	Mean Rank	Z	P Value
IgM							
Female	125	18.7	22.876	2.046	63.28	-0.403	0.016
Male	3	83.83	72.035	41.589	115.33		
IgG							
Female	1855	91.28	97.347	2.26	933.846	-1.428	0.063
Male	16	141.15	137.653	34.413	1185.687		

Table 3. Mean Age Among the Anti-Toxoplasma IgG and IgM Seropositive Subjects

Age Mean	N	Mean	Min (Year)	Max (Year)	St. Deviation	St. Error Mean
IgG						
Positive	1870	29.74	0.41	72	6.437	0.148
Borderline	57	28.33	0.33	55	7.752	1.026
IgM						
Positive	128	26.75	5	45	6.375	0.563
Borderline	103	27.37	7	44	5.949	0.586

(reviewed by Daryani et al. 2014) (8). A very small proportion (0.74%) of the studied population tested positive solely for anti-*Toxoplasma* IgM, which indicates an acute infection, although 83 (1.29%) subjects tested positive for both IgM and IgG, which can be either an acute or a newly switched chronic infection. In total, 128 IgM-positive individuals were observed in the present study.

The results of the present study indicate the lower prevalence of the infection in the studied population from north-western Iran when compared to other reports from the same region. For instance, the prevalence has been reported to be 71.61% and 54.13% in pregnant women, while it has been found to be 25.9% in high school girls (13, 14).

In the present study, a considerable number of the studied cases were equivocal with regard to the seropositivity, since 103 (1.69%) and 57 (0.97%) individuals were equivocal for anti-*Toxoplasma* IgM and IgG, respectively. The number of doubtful results in relation to IgM was twice that for IgG. Considering the fact that a large proportion of the studied population comprised females of childbearing age, these equivocal results, especially with regard to IgM, make it difficult to determine whether it is recent infection or a chronic infection. In this situation, performing an anti-*Toxoplasma* IgG avidity test (15) or repeating the initial test might prove helpful.

5.1. Conclusions

Based on the findings of the present study, the prevalence of *Toxoplasma* infection is high in the East Azerbaijan province of Iran, although it is fairly close to that found in reports from other parts of the country. Furthermore, an anti-*Toxoplasma* IgG avidity test can be suggested for pregnant women based on the considerable number of borderline results found in the IgM tests in the present study.

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References

- Hill DE, Chirukandoth S, Dubey JP. Biology and epidemiology of Toxoplasma gondii in man and animals. *Anim Health Res Rev.* 2005;6(1):41–61. [PubMed: 16164008].
- Weiss LM, Dubey JP. Toxoplasmosis: A history of clinical observations. Int J Parasitol. 2009;39(8):895–901. doi: 10.1016/j.ijpara.2009.02.004. [PubMed: 19217908].
- Kieffer F, Wallon M. Congenital toxoplasmosis. Handb Clin Neurol. 2013;112:1099-101. doi: 10.1016/B978-0-444-52910-7.00028-3. [PubMed: 23622316].
- 4. Schluter D, Daubener W, Schares G, Gross U, Pleyer U, Luder C. Animals are key to human toxoplasmosis. *Int J Med Microbiol.* 2014;**304**(7):917–29. doi:10.1016/j.ijmm.2014.09.002. [PubMed: 25240467].
- Torrey EF, Yolken RH. Toxoplasma oocysts as a public health problem. *Trends Parasitol*. 2013;29(8):380-4. doi: 10.1016/j.pt.2013.06.001. [PubMed: 23849140].
- Elmore SA, Jones JL, Conrad PA, Patton S, Lindsay DS, Dubey JP. Toxoplasma gondii: epidemiology, feline clinical aspects, and prevention. *Trends Parasitol*. 2010;26(4):190-6. doi: 10.1016/j.pt.2010.01.009. [PubMed: 20202907].

- 7. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. Clin Microbiol Infect. 2002;8(10):634–40. [PubMed: 12390281].
- 8. Daryani A, Sarvi S, Aarabi M, Mizani A, Ahmadpour E, Shokri A, et al. Seroprevalence of Toxoplasma gondii in the Iranian general population: a systematic review and meta-analysis. *Acta Trop.* 2014;137:185–94. doi:10.1016/j.actatropica.2014.05.015. [PubMed: 24887263].
- Rostami A, Keshavarz H, Shojaee S, Mohebali M, Meamar AR. Frequency of Toxoplasma gondii in HIV Positive Patients from West of Iran by ELISA and PCR. *Iran J Parasitol*. 2014;9(4):474–81. [PubMed: 25759728].
- Ahmadpour E, Daryani A, Sharif M, Sarvi S, Aarabi M, Mizani A, et al. Toxoplasmosis in immunocompromised patients in Iran: a systematic review and meta-analysis. J Infect Dev Ctries. 2014;8(12):1503-10. doi: 10.3855/jidc.4796. [PubMed: 25500647].
- Alavi SM, Jamshidian R, Salmanzadeh S. Comparative study on toxoplasma serology among HIV positive and HIV negative illicit drug users in Ahvaz, Iran. Caspian J Intern Med. 2013;4(4):781-4. [PubMed: 24294474].
- Rasouli S, Sadaghian M, Jafari R. Prevalence of human toxoplasmosis and related risk factors using Electrochemiluminescence (ECLIA) method in West Azarbaijan Province, Iran, 2010. Int J Biosci. 2014;4(8):124–30.
- Rajaii M, Aliparasti MR, Nagilli B, Almasi S, Asle-Rahnamaie-Akbari N. Comparison of immunofluorescence and enzyme-linked immunosorbent assay and immunoglobulin G avidity techniques for screening of anti: Toxoplasma antibodies among single serum sample pregnant women in Tabriz, Iran. *Indian J Pathol Microbiol*. 2015;58(1):40-4. doi: 10.4103/0377-4929.151183. [PubMed: 25673590].
- Fallah E, Rasuli A, Shahbazi A, Ghojazadeh M, Khanmohammadi M, Hamzavi F, et al. Seroprevalence of Toxoplasma Gondii Infection among High School Girls in Ajabshir from East Azarbaijan Province, Iran. J Caring Sci. 2014;3(3):205-10. doi: 10.5681/jcs.2014.022. [PubMed: 25276764].
- Lappalainen M, Hedman K. Serodiagnosis of toxoplasmosis. The impact of measurement of IgG avidity. Ann Ist Super Sanita. 2004;40(1):81-8. [PubMed: 15269456].