

Seroprevalence of toxoplasmosis in women admitted to an education and research hospital in eastern anatolia after the syrian crisis

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Abstract

Aim: Toxoplasmosis caused by *Toxoplasma gondii*, is a zoonotic disease which is generally asymptomatic. However, it causes serious symptoms in pregnant women and immunocompromised individuals. About one third of the people worldwide are seropositive. Due to the civil war in Syria, Turkey has been home to more than 4 million refugees. This unexpected increase in the Syrian population in particular increases the risk of infectious diseases. The aim of this study was to evaluate the prevalence of *Toxoplasma gondii*, anti-toxoplasma IgG and IgM antibodies in local and Syrian women, who were admitted to Obstetrics and Gynecology Clinic of Malatya Education and Research Hospital, which is a tertiary care hospital in eastern part of Turkey, between January 2015 and July 2019.

Material and Methods: The anti-toxoplasma IgG and anti-toxoplasma IgM antibody values of women who were admitted to our hospital and evaluated in terms of toxoplasma, determined by using "Chemiluminescence Immunoassay (CLIA)" method, were investigated retrospectively.

Results: According to the results analyzed in a total of 11.025 women, including 743 Syrian refugees, the seropositivity of anti-toxoplasma IgG and IgM were found to be 25.8% (2.819/10.932) and 1.6% (180/11.025), respectively. Among these patients, the seropositivity of anti-toxoplasma IgG was found to be 25.3% (190/750) and the seropositivity of anti-toxoplasma IgM was found to be 2.5% (20/797) in pregnant women. Anti-toxoplasma IgG and IgM seropositivity were found to be 27.9% and 0.5%, respectively, in Syrian women. In Malatya, a city located in eastern Turkey, *Toxoplasma gondii* seropositivity was found to be common to the extent that it could not be neglected in both local women and Syrian refugees. No statistically significant difference could be found in Syrian female refugees living in Malatya in terms of carrying toxoplasma antibodies when compared with the local women. More than 70% of pregnant women were observed to be seronegative and they were at serious risk for toxoplasmosis. In particular, it was concluded that women at childbearing age, who constitute the risk group, should be made aware of the disease and serological tests should be performed routinely for toxoplasma.

Keywords: *Toxoplasma gondii*, seroprevalence, anti toxoplasma IgG, anti toxoplasma IgM, Syrian refugees

INTRODUCTION

The term TORCH is made up of the initial letters of five major congenital factors that develop during pregnancy and threaten the life. The letter 'T' is used for the disease toxoplasmosis, which is caused by *Toxoplasma gondii*, a mandatory intracellular parasite that infects warm-blooded animals, including humans. It was discovered in the tissues of the living in 1908 by two scientists named Nicolle and Manceaux during their studies on rodents of

the genus *Ctenodactylus gondii*, and one year later, the parasite was named as *Toxoplasma gondii* (1-3).

This parasite may spread through food, drinks and hands contaminated with infected cat droppings, ingestion of uncooked or undercooked meats contaminated with cysts, eating raw eggs and drinking raw milk, as well as blood transfusion from the infected donor, organ transplantation and placental transfer from infected mother to baby (4-8).

Toxoplasma gondii spreads throughout the body, including

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the brain and muscle, and it initiates an encapsulation process that protects itself from the immune response of the host, resulting in a latent infection. *T. gondii* produces tyrosine hydroxylase, a rate-limiting enzyme in dopamine production. Following the infection, *T. gondii* can receive the remaining components required for dopamine synthesis from the host cell. Cells infected with *T. gondii* may contain 350 percent more cytoplasmic dopamine as compared to uninfected cells. *T. gondii* seropositivity has been shown to be associated with schizophrenia, impulsivity and aggressiveness (9).

Although toxoplasmosis is generally latent (90%) in immunocompetent individuals, it is reported that serious complications may develop with the reactivation of chronic infection in cases with immunodeficiency such as AIDS, hematologic cancers, bone marrow and cases with transplantation of solitary organs. Toxoplasmosis can cause serious clinical conditions as a result of primary infection during pregnancy. When the primary toxoplasmosis occurs in the first or second trimester of pregnancy, the risk of it passing to the fetus is 30% on average; however this rate increases up to 90% in the last two weeks of the third trimester. The risk of fetal infection increases as pregnancy progresses, but the clinical condition is more severe in infections occurring at the early stage of pregnancy. Restriction of intrauterine growth, jaundice, hepatosplenomegaly, myocarditis, pneumonia, purpura, chorioretinitis, hydrocephalus, intracranial calcification, blindness, mental retardation, epilepsy and some other diseases may result from congenital toxoplasmosis (2,8,10,11).

Socio-economic level, eating habits, hygiene and sanitation, age, parasitic sensitivity, soil and moisture conditions of the region and cat feeding at home are the main factors affecting the seroprevalence of the parasite. Although the rate of *Toxoplasma gondii* infection observed in the world population is approximately 30%, a very small proportion of these patients have clinical symptoms. The prevalence of *T. gondii* has been reported to be minimum 5% and maximum 80%, although it *Toxoplasma gondii* varies from one country to another (3,11).

In our study, anti-toxoplasma IgG and IgM antibodies were evaluated and our plan was to contribute to the

seroprevalence data of our city and to raise awareness. Our study is important in terms of determination of seroprevalence of toxoplasmosis, awareness towards the possible consequences of the disease and taking precautions.

MATERIAL and METHODS

Toxoplasma gondii IgG and IgM antibodies of all women, who were admitted to Obstetrics and Gynecology Clinic of Education and Research Hospital Malatya a city located in eastern part of Turkey, between January 2015 and July 2019, whose blood cultures were sent to the Medical Microbiology Laboratory of the hospital, and pregnant and non-pregnant women in 14-77 age group were retrospectively included in the study. In the hospital laboratory, *T. gondii* antibodies were studied using the "Chemiluminescence immunoassay" method (Cobas 6000 V2, Roche Diagnostics, Mannheim, Germany) according to the recommendations of the manufacturer.

The study was started on July 30, 2019 with the permission of the Scientific Committee of our hospital. All necessary data were obtained from the hospital information system. In the case of more than one sample of the same case, repetitions were prevented by evaluating the latest serology results in the system.

Statistical Package for the Social Sciences (SPSS) 22 program was used for statistical analysis of the data obtained. Data were expressed as numbers and percentages. Pearson chi-square test and Yates chi-square test were used for analysing. $p < 0.05$ was considered to be significant.

RESULTS

In this study, 10.932 anti-toxoplasma IgG and 11.025 anti-toxoplasma IgM test results of approximately five years period obtained between January 2015 and July 2019, were included. The distribution of the results of the tests by age and years, is presented in Table 1.

When the number of cases was examined by age and years, a statistically significant difference was found. It was observed that the number of cases had decreased in all age groups over the years (Table 1).

Table 1. Distribution of toxoplasma antibody measurements and percentages according to age and year.

(n/row%)	Year					p
	2015	2016	2017	2018	2019	
Age range						
14-25	2.351/31.1	2.435/32.2	2.147/28.4	593/7.8	30/0.4	
26-35	3.821/34.3	3.538/31.7	2.846/25.5	871/7.8	72/0.6	
36-45	908/29.8	980/32.1	863/28.3	287/9.4	14/0.5	<0.001
46 and above	67/31.8	70/33.2	29/13.7	33/15.6	2/5.7	

(n/row%)	IgG results			Ig M results		
Age range	IgG +	IgG -	p	IgM +	IgM -	p
14-25	772/20.5	2.994/79.5	<0.001	55/1.5	3.708/98.5	0.656
26-35	1.465/26.5	4.073/73.5		98/1.8	5.469/98.2	
36-45	531/35.0	987/65.0		27/1.8	1.498/98.2	
46 and above	54/55.1	44/44.9		1/1	97/99.0	

(n/row%)	IgG results			Ig M results		
Year	IgG +	IgG -	p	IgM +	IgM -	p
2015	944/26.5	2.621/73.5	0.608	46/1.3	3.499/98.7	0.002
2016	901/25.7	2.600/74.3		52/1.5	3.444/98.5	
2017	746/25.4	2.189/74.6		57/1.9	2.875/98.1	
2018	210/24.5	648/75.5		21/2.3	900/97.7	
2019	18/31.0	40/69.0		4/6.8	55/93.2	

Table 2 shows anti-toxoplasma IgM and IgG values by age. When IgM and IgG results were analyzed according to age groups, it was observed that IgG positivity increased significantly with increasing age range ($p < 0.05$).

When all the cases were evaluated, 25.8% (2.819/10.932) of the anti-toxoplasma IgG data were positive, 74.1% (8.098/10.932) were negative and 0.1% (15/10.932) were at the greyzone and 1.6% (180/11,025) of the anti-toxoplasmic IgM data were positive, 97.7% (10.773/11.025) were negative, and 0.6% (72) were found to be at the greyzone. The change in the results of anti-toxoplasma IgG and IgM according to year is shown in Table 3 in terms of number and percentage. It was seen that IgM positivity increased significantly over the years.

Pregnant women were evaluated separately. In all pregnant women, anti-toxoplasma IgG seropositivity was 25.3% (190/750) and anti-toxoplasma IgM seropositivity was 2.5% (20/797) (Table 4).

In our study, female Syrian refugees admitted to our hospital, were also evaluated. The ratio of the number of

tests applied to the Syrian female refugees recorded in the hospital automation system, to all tests was found to be 6.8% (1.486/21.957), and seropositivity of anti-toxoplasma IgG and anti-toxoplasma IgM were found to be 27.8% (207/745) and 0.5% (4/741), respectively. Whereas, in our evaluation of local women, excluding refugee women, the seropositivity of anti-toxoplasma IgG and IgM were 25.7% (2.613/10.187) and 1.7% (176/10.284), respectively (Table 5). When Syrian women and local women were compared in terms of anti-toxoplasma IgG and IgM seropositivity rates, IgM positivity was found to be significantly higher in local women ($p < 0.05$).

	Pregnant	Positive (%)	Negative (%)	Greyzone (%)	Total
IgG	190	(25.3)	560 (74.7)	0	750
IgM	20	(2.5)	771 (96.7)	6 (0.7)	797
Total (%)	210	(13.6)	1.331 (86)	6 (0.4)	1.547

(n/row%)	IgG results			Ig M results		
	IgG +	IgG -	p	IgM +	IgM -	p
Syrian	207/27.9	536/72.1	0.190	4/0.5	734/99.5	0.022
Local	2.613/25.7	7.562/74.3		176/1.7	10.039/98.3	

DISCUSSION

Toxoplasma gondii can hold all cells and vital organs in the human body except erythrocytes. Toxoplasma infection may be acute or chronic, symptomatic or asymptomatic, but is usually asymptomatic. Within 5-23 days after ingestion of cysts or oocytes, a small number of cases may develop flu-like symptoms, lymphadenopathy and hepatosplenomegaly. Dormant cysts formed in the organ tissue after primary infection may reactivate when the immune system is suppressed and may start spreading to the central nervous system and lungs, thus causing severe neurological disorders or pneumonia. These diseases may be fatal in immunocompromised patients (12).

Congenital toxoplasmosis is known to be mostly asymptomatic, but causes permanent damage and severe defects to the fetus with chorioretinitis, cerebral calcification, hydrocephalus, severe thrombocytopenia and convulsions. Primary infection during early pregnancy can cause spontaneous abortion, stillbirth or fetal abnormalities. Detection of seronegative women before or during pregnancy and early diagnosis and treatment of infected mothers during pregnancy are effective in preventing congenital toxoplasmosis (12,13).

The prevalence of toxoplasmosis, which is widespread all over the world and is seen to be in varying rates between regions, is higher in humid and tropical regions, whereas, it is observed to be low in dry, hot areas and poles. Seroprevalence rates are 3% or less in North America and Australia, whereas, it is generally reported to exceed 50% in Europe, South America and Africa. The prevalence of *Toxoplasma gondii* has been reported to be between 5% and 80%, although it varies from one country to another (3,14).

In studies conducted on patients with suspected toxoplasmosis in our country, *Toxoplasma gondii* seropositivity rates were reported to be IgG 21%, IgM 1.2% in Bolu (14), IgG 31.01%, IgM 0.77% in Elazig (15), IgG 31.5%, IgM 1.6% in Aydin (16), IgG 37%, 1.9% in IgM in Istanbul (17), IgG 29.2%, IgM 2.02% in Bursa (18), IgG 20.6%, IgM 2.4% in Mugla (19), IgG 30.7%, IgM 0.9% in Malatya (20), and in pregnant women, the rates were reported to be IgG 41.1%, IgM 1.1% (21) in Rize, IgG 46.3%, IgM 1.8% in Adana (22), IgG 33.9%, IgM 2.5% in Kayseri (23), IgG 33.4%, IgM 2.4% in Antalya (24), IgG 47.1%, IgM 2.26% in Kahramanmaraş (25) and IgG 27.3%, IgM 1.1% in Ankara (26). When all these studies are taken into consideration, the seroprevalence of *T. gondii* is around 30% in our country.

The highest rates recorded in our country are in Sanliurfa. In a study conducted in Sanliurfa in 2012 during the three-year period between January 2007 and December 2009, Cicek et al. reported the seropositivity percentage of anti-toxoplasma IgG antibodies in pregnant and non-pregnant women to be 68.9% and 63.0%, respectively, and the seropositivity percentage of anti-toxoplasma IgM to be 2.8% and 3.0%, respectively. The reason for this was

considered to be the low socio-economic and educational level of the women living in Sanliurfa, the high prevalence of eating raw meatballs and insufficient hygienic conditions (27).

In a study conducted by Beytur et al. in 2009, IgM positivity was found to be 0.9% and IgG seropositivity was found to be 30.7% (20). In 2000, in a study conducted by Bulut et al. toxoplasma IgG positivity was found to be 39.4% and toxoplasma IgM positivity was 1.4% in women who were at the childbearing age (31). Again in Malatya in 2012, Doğan et al. conducted a study and found the antitoxoplasma IgG positivity rate to be 37.5% in pregnant women (32). In our study, anti-toxoplasma IgG seropositivity was found to be 25.8% and anti-toxoplasma IgM was found to be 1.6%.

When the five-year data of Malatya Education and Research Hospital is evaluated, *Toxoplasma gondii* seropositivity rates are below the country average in our city. It is pleasing that seropositivity rates tend to decrease in terms of anti-toxoplasma IgG values as compared to previous years. However, there is a partial increase in IgM rates. In our study, it was observed that there was a statistically significant increase in the positivity of IgM and IgG antibodies in patients with increasing age, as in other studies ($p \leq 0.05$). However, the decrease in serological screenings for toxoplasmosis in our hospital in the last one year period (approximately 7000 patients were screened in 2015, 2016, while this number has decreased to 118 in the first half of 2019) has increased the seropositivity rate to 31%. The increase in IgM antibody levels over the years may be due to the increase in the age of exposure to parasites, with increasing socio-cultural level and urbanization in our region.

The civil war in Syria has displaced millions of people since 2011 and led to a serious population movement. Many Syrians fleeing the conflict in their country, migrated to Turkey (33). In March 2019, the UN Refugee Agency reported that the majority of Syrian refugees (more than 63.3%) were registered in Turkey. For Malatya, the percentage of Syrian refugees is 3.74% of the total population when compared to the local population (34). Undoubtedly, the most frightening plausibility for our country is infectious diseases carried by the immigrants. Since the beginning of the Syrian crisis, many infectious diseases including multidrug-resistant gram-negative bacterial infections, tuberculosis, measles, cutaneous leishmaniasis, cholera and Hepatitis A have re-emerged in Turkey (35,36).

It is known that socio-economic and educational levels and hygienic conditions are very important in the spread of toxoplasma. In our study, we wanted to show the possible differences between the toxoplasma antibodies of the local women and Syrian refugees, in terms of carriage by separately categorizing the Syrian female refugees who applied to our hospital. However, when the results of the anti-toxoplasma IgG and IgM of Syrian women were examined, we found that IgM positivity was significantly higher in local women. There was no significant difference

found between local women and Syrian female refugees in terms of toxoplasma antibodies. Our study showed that the settlements of the refugees after the Syrian crisis did not pose a health threat to the spread of toxoplasmosis in our city. In the literature review, no other study was found in which Syrian refugees were evaluated for toxoplasmosis. In addition, our study is the most comprehensive study on the prevalence of toxoplasmosis in our city so far.

Between 2015-2019, the decrease in the number of tests was remarkable when the samples were evaluated by years. This was due to the change in the gynecologists and obstetricians working in our hospital and as well as the increase in the number of followed-up pregnant women. Also, whether or not the requests of physicians regarding the screening for the TORCH group tests were found to be necessary and the *Toxoplasma gondii* antibody request was removed from the panel in the hospital.

The decline in the number of cases in the following years is the weak side of our study.

CONCLUSION

Seronegative women at childbearing age, especially pregnant women (74.7% anti-toxoplasma IgG negative), at risk for congenital infection should be serologically screened for *Toxoplasma gondii*, regional and national seroprevalence rates of toxoplasmosis should be determined, and education should be provided on infection prevention.

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