

Investigation of Serological Results of Patients with Suspected Toxoplasmosis Admitted to the ELISA Laboratory of Uludağ University Hospital between 2002-2008

Uludağ Üniversitesi Hastanesi ELISA Laboratuvarına 2002-2008 Yılları Arasında Toxoplasmosis Şüphesi ile Başvuran Hastaların Serolojik Sonuçlarının Değerlendirilmesi

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ABSTRACT

Objective: The aim of this study is to investigate the distribution of anti-*Toxoplasma gondii* IgG and IgM antibodies in patients with suspected toxoplasmosis referred to the Uludağ University Medical School, Department of Medical Microbiology Enzyme-Linked Immunosorbent Assay (ELISA) laboratory over a 72-month period (March 2002-December 2008).

Methods: The samples were analyzed using VIDAS (BioMérieux, France) IgG-avidity tests and the fluorescent enzyme-linked assay (ELFA) technique.

Results: Results showed that the prevalence of anti-*T. gondii* IgG and IgM among women (29.2% and 2.02%, respectively) was higher than that of men (21.2% and 1.7%, respectively). The seroprevalence of anti-*T. gondii* IgG was 30.7% in childbearing-aged women, with rates ranging from 35.8% and 27.4% over the years. Avidity was found to be high, borderline, and lower (81.9%, 10.2%, and 7.9%, respectively) in the fertile age group of 166 women receiving the IgG avidity test.

Conclusion: Although the study data may not reflect our entire province, it virtually turns out that the risk of toxoplasmosis must be seriously taken into account, particularly when approaching some risk groups, such as seronegative women of fertile age, pregnant women, and immunocompromised patients. (*Turkiye Parazitoloj Derg* 2014; 38: 141-6)

Key Words: *Toxoplasma gondii*, ELISA, IgG avidity

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ÖZET

Amaç: Bu çalışma, Uludağ Üniversitesi Tıp Fakültesi Tıbbi Mikrobiyoloji Anabilim Dalı ELISA laboratuvarına 72 aylık (Mart 2002 - Aralık 2008 tarihleri arasında) dönemde başvuran toksoplazmoz şüpheli hastalarda anti-*Toxoplasma gondii* IgG ve IgM antikorlarının dağılımını belirlemek amacıyla yapılmıştır.

Yöntemler: Örnekler VIDAS (BioMérieux, France) IgG-avidite testi ve Fluorescent Enzyme-Linked Assay (ELFA) tekniği ile çalışılmıştır.

Bulgular: Kadınlarda anti-*T. gondii* IgG ve IgM prevalansının (sırasıyla %29,2 ve %2,02) erkeklerdekinden (sırasıyla %21,2 ve %1,7) daha yüksek olduğu belirlenmiştir. Doğurgan dönemdeki kadınlarda anti-*T. gondii* IgG seroprevalansının %30,7 olduğu ve oranların %35,8 ile %27,4

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arasında deđiřtiđi izlenmiřtir. IgG avidite testi alıřılmıř dođurgan dnemdeki 166 kadının %81,9’unda yksek, %10,2’sinde řpheli sınırlar iinde, %7,9’unda dřk avidite deđerlerine sahip olduđu saptanmıřtır.

Sonu: alıřma verileri ilimizin tamamını yansıtmasına rađmen zellikle dođurgan dnemdeki seronegatif kadınlar, gebe kadınlar ve immnkompromize hastalar gibi risk gruplarında toksoplazmozun gzardı edilmemesi gerektiđi dřnlmřtr.
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Anahtar Szckler: *Toxoplasma gondii*, ELISA, IgG- avidite

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INTRODUCTION

Toxoplasmosis is a disease caused by an obligate intracellular protozoan, namely *Toxoplasma (T. gondii)*, which can infect all nucleated cells (1). Toxoplasmosis is transmitted by eating raw or undercooked meat containing tissue cysts that comprise *T. gondii* or water and food contaminated with oocyst feces of cat/feline or by means of transplacental passage to the fetus from an infected mother (2). Contamination with blood or solid organ transplantation has also been reported (2, 3). *T. gondii* has a wide variety of hosts, so that it can infect all mammalian and avian species. Infection may have an acute course of development, or it may remain in many tissues in the form of latent cysts over many years, mainly including the reticuloendothelial system, muscle, eye, and brain tissues, or may result in congenital infection, anomalies, and abortion through transplacental passage to the fetus from an infected mother (4, 5). Toxoplasmosis is a zoonotic infection that occurs without any symptoms or with a self-limiting flu-like clinical appearance or local lymphadenopathy in subjects with intact immune resistance. However, it may cause fatal outcomes in immunocompromised subjects, infected fetuses, or newborns (6). Early detection of the infection allows for treatment. Currently, diagnosis is possible via direct and indirect methods. Direct methods include detection of *T. gondii* DNA in body fluid samples by using polymerase chain reaction (PCR), isolation of the organism with mice inoculation, cell culture, ophthalmic tests, and radiological examinations (4, 7), while indirect methods employ serological tests in detecting *T. gondii*-specific antibodies. The most commonly used indirect methods to detect *T. gondii*-specific antibodies, such as IgG and IgM, are the ELISA test, the Sabin-Feldman dye test, the indirect fluorescent antibody test (IFAT), and agglutination tests (8). Serological tests are useful in diagnosing both an acute and a previous infection. The ELISA is widely used for diagnosis because of its high sensitivity and specificity, low cost, and ease of practice (9). In this study, using the blood serum of patients admitted to the Uludag University Health Center of Practice and Research for follow-up and/or control, we analyzed the presence of anti-*T. gondii* IgM and IgG antibodies and the association between the anti-*T. gondii* IgG avidity test and IgG positivity by employing the fluorescent enzyme-linked assay (ELFA).

METHODS

Anti-*T. gondii* IgG, anti-*T. gondii* IgM, and IgG avidity results of the samples obtained from 10,295 patients with suspected toxoplasmosis between March 2002 - December 2008 sent to the Uludag University Medical School, Department of Medical Microbiology ELISA laboratory were evaluated retrospectively. Serologic tests for toxoplasmosis were analyzed using VIDAS (BioMrieux, France) kits and the ELFA technique based on recommendations of the manufacturer.

Statistical analysis

The statistical analysis of the data was performed using the SPSS 13.0 statistical package (SPSS Inc. Chicago, IL, USA). The Pearson chi-square test was used to analyze categorical data. The significance level was defined as $\alpha=0.05$.

RESULTS

Out of the 10,295 patients, of whom 7242 (70.3%) were females and 3053 (29.7%) were males, 2761 (26.8%) patients had anti-*T. gondii* IgG and 202 (1.9%) patients had anti-*T. gondii* IgM. The IgG positivity rate was found to be 29.2% in women and 21.2% in men, while IgM positivity was 2.02% and 1.7% in women and men, respectively. A significant correlation was found between the seropositivity rate of anti-*T. gondii* IgG antibody and gender ($p<0.001$) (Table 1).

Analysis of *toxoplasma* seroprevalence associated with age groups indicated that IgG ($p<0.001$) and IgM ($p=0.013$) seropositivity increased with age in men and women, respectively. Taking the 0-9 age group as a reference, inspection of the results from the tendency point of view reveals that the maximum IgG and IgM seropositivity was observed in the 50-59 age group both in men and women, with 7.18 (51.1%) and 1.98 (3.4%) odds ratios. The incidence of IgG-seropositive men increased with increasing age, from 12.7% in 0-9 years old to 50.3% in ≥ 60 years old ($p<0.001$). However, the same can not be pronounced for women of any age. The incidence is quite steady, around 30%, with slight deviation over ages, demonstrating a prominent difference between opposite genders of IgG seropositivity. As for the incidence of IgM seropositivity, no significant deviation was observed for either gender. However, the incidence in men >49 years old exhibits a dramatic fall off relative to the average (Table 2).

The rate of anti-*T. gondii* IgG positivity was 30.7% in 5073 women of fertile age (15-39 years), and the seroprevalence ranged from 27.4% to 35.8% over the years. No significant year-dependent differences in seroprevalence were found in women of child-bearing age ($p= 0.156$) (Table 3).

Avidity was found to be high in 136 (81.9%), borderline in 17 (10.2%), and low in 13 (7.9%) patients in this age group of 166 women receiving the IgG avidity test (Table 4).

DISCUSSION

The seroprevalence of toxoplasmosis varies in many countries and even in different regions within a country, depending on the differences in socioeconomic situation, development levels, climate, and geography, which has been reported to range between 20%-70% (10). In Greece, which is in the same climate zone as Turkey, the IgG seroprevalence was reported to be 37%, 29%, and 24% in 1984, 1997, and 2004, respectively. Researchers

Table 1. Prevalence of IgG and IgM *Toxoplasma gondii*-specific antibodies by gender at a tertiary hospital, Bursa, Turkey

Gender	n (%)	IgG-positive n (%)	IgG-negative n (%)	IgM-positive n (%)	IgM-negative n (%)
Female	7242 (70.3)	2115 (29.2)	4239 (58.5)	150 (2.07)	6459 (89.2)
Male	3053 (29.7)	646 (21.2)	1763 (57.7)	52 (1.7)	2762 (90.4)
Total, n (%)	10295 (100)	2761 (26.8)	5931 (57.6)	202 (1.9)	9221 (89.6)
p		<0.001	0.549	0.249	0.056

IgG: the value of immunoglobulin G; IgM: the value of immunoglobulin M

Table 2. Distribution of anti-*T. gondii* IgG and anti-*T. gondii* IgM antibodies by age group in female and male from a tertiary hospital of Bursa, Turkey, 2002-2008

Male						Female				
IgG (+)			IgM (+)			IgG (+)		IgM (+)		
Age groups (year)	n (%)	OR	Age groups (year)	n (%)	Age groups (year)	n (%)	Age groups (year)	n (%)	OR	
0-9 (n=1023)	130 (12.7)	1.00	0-9 (n=1132)	21 (1.8)	0-9 (n=833)	288 (34.6)	0-9 (n=928)	16 (1.7)	1.00	
10-19 (n=312)	60 (19.2)	1.64	10-19 (n=373)	8 (2.1)	10-19 (n=955)	329 (34.5)	10-19 (n=1118)	34 (3.0)	1.79	
20-29 (n=308)	89 (28.9)	2.79	20-29 (n=308)	8 (2.6)	20-29 (n=888)	294 (33.1)	20-29 (n=1027)	14 (1.4)	0.79	
30-39 (n=245)	115 (46.9)	6.08	30-39 (n=249)	7 (2.8)	30-39 (n=996)	342 (34.3)	30-39 (n=1232)	14 (1.1)	0.66	
40-49 (n=170)	76 (44.7)	5.55	40-49 (n=170)	5 (2.9)	40-49 (n=840)	257 (30.6)	40-49 (n=939)	23 (2.4)	1.43	
50-59 (n=180)	92 (51.1)	7.18	50-59 (n=180)	1 (0.5)	50-59 (n=690)	191 (27.7)	50-59 (n=507)	17 (3.4)	1.98	
≥60 (n=175)	88 (50.3)	6.95	≥60 (n=175)	2 (0.6)	≥60 (n=1144)	415 (36.3)	≥60 (n=858)	32 (3.7)	2.21	
p-value	<0.001		0.257			0.460		0.013		

IgG: the value of immunoglobulin G; IgM: the value of immunoglobulin M

have related this decreasing trend to socioeconomic development (11). Although serological tests used for routine diagnosis of toxoplasmosis have high sensitivity, their specificity varies depending on the individual test used. Many researchers have found consistencies between the ELISA and the gold standard Sabin-Feldman dye test (12, 13). Toxoplasmosis is classified as Group C in the classification of the nationally notifiable diseases in Turkey, and prevalence data are obtained by studies conducted in certain regions. IgG and IgM seropositivity has been reported as 24%-62.5% and 0.4%-4.8% in patients pre-diagnosed with toxoplasmosis in Turkey (14, 15). This difference may be attributed to the size of the working groups, socio-demographic characteristics, and habits, as well as the climatic characteristics and test sensitivity. The test results of patients with suspected toxoplasmosis fail to reflect the seroprevalence in the society. Evaluation of hospital record data generally portrays higher rates of seropositivity. It may be observed that test results from laboratories in the same region or in a laboratory in different time periods vary to a great extent. IgG and IgM seropositivity determined in this study, regardless of sex (26.8% and 1.9%, respectively), showed that the prevalence of toxoplasmosis significantly decreased compared to the study conducted by Kilitcugay et al. (14) in the same hospital 20 years ago (62.5% and 4.8%, respectively). The decrease in prevalence can be associated with the relative socioeconomic improvement, increased observance of general hygiene rules, and differences in test

sensitivity. Many studies have investigated the relationship between *T. gondii* seroprevalence and gender both in Turkey and in the world. In a study conducted in Brazil, IgG seropositivity was found to be 63.4% in women and 79% in men (16). In a United States study, the seroprevalence was found to be 23.3% and 21.8% in women and men, respectively (17). Similar to the results from different regions of Turkey, IgG and IgM seroprevalence was found to be 29.2% and 2.07% in women and 21.2% and 1.7% in men, respectively (12, 18-21). This may be attributed to the fact that as opposed to men, women contact contaminated raw food and are at a higher risk of exposure to oocysts disseminated by cats during household chores and gardening work. Despite this, Miman et al. (22) in Afyon Province and Demirci et al. (23) in Isparta found that IgG seropositivity was higher in men than in women. Although both research teams found higher seropositivity in men than in women, they reported that this difference had no significance. It is known that *T. gondii* seropositivity increases with age (10). In a study conducted in Brazil, the seroprevalence, which was found to be 39.7% in the 0-9 age group, was reported to reach 83% after 40 years of age (24). Increases in *T. gondii* seropositivity with age have been reported in various studies conducted in the US and Croatia (25, 26). In a study conducted in Samsun, Turkey, IgG seroprevalence was reported as 8.31% and 20.5% in children and adults, respectively, and IgM seroprevalence was reported as 0.85% and 1.05% in children and adults, respectively (21). It has also been reported

that IgG seroprevalence increases with age among women of fertile age (27-29). The results of the present study, including the age-dependent increase in *T. gondii* seropositivity in both men (IgG) and women (IgM), regardless of the latter being of fertile age, and the fact that most of the cases with seropositivity of both sexes were from the age group of ≥ 40 years show that there is a risk of *T. gondii* infection in every life period. Because of transplacental transmission from the mother to fetus and increased seropositivity with age, the detection of *T. gondii* antibody in newborns gains significance. Nuhoglu et al. have found *T. gondii* IgG antibody and *T. gondii* IgM antibody in 32.96% and 1.1%, respectively, in their study conducted using cord blood of healthy newborns (30). Kuk et al. have found *T. gondii* seropositivity to be 33.14% and 31.9% in women and newborns, respectively, which are close figures (20). In this study, *T. gondii* IgG seropositivity was higher in women of fertile age (30.7%) than in neonates (16.5%). The possible reason for *T. gondii* IgG seropositivity in neonates in the study may be that they were born from mothers with suspected toxoplasmosis. The results of *T. gondii* IgG seropositivity obtained in this study for women of fertile age (ranging from 27.4% to 35.8%) are in line with results reported elsewhere in the country. This may stem from the fact that soci-

eties living in various parts of the country have similar sociocultural and socioeconomic structures (30). The IgG avidity tests that have been in practical use in recent years allow reliable differentiation between acute primary infection, reactivation, and/or re-infection in a single serum sample. This differentiation has clinical significance, especially in pregnant women and immunocompromised patients. IgG antibodies against the antigen on first exposure during the primary infection show low avidity in the first weeks and then acquire gradually higher avidity with increased maturity (31). However, it is reported that the avidity test may be used as a confirmatory test in pregnant women for toxoplasmosis, and it is not suitable for decision-making (32). In a study conducted in Izmir, Turkey in pregnant cases, 83.3% of IgM-positive pregnant women had low avidity, and 59.7% of IgM-negative pregnant women had high avidity. The researchers report that evaluation of the IgG avidity test together with IgM and IgA antibodies in the differentiation of acute infection from prior infection would be useful (33). In the study they conducted in Kayseri, Yazar et al. found that 70.8% of 695 pregnant women with *T. gondii* IgG antibodies had high avidity, 24.5% of them had borderline avidity, and 4.7% of them had low avidity; they emphasize the importance of the IgG avidity test in pregnant women with anti-*T. gondii* IgG positivity and IgM seronegativity to determine the risk of congenital toxoplasmosis (34). In Kuwait, out of 119 patients with *T. gondii* IgG, positivity in 31 patients (13.8%) was found for IgM antibodies, and low avidity was identified in only 9 of these patients (29%), and it was concluded that previous infection was recent in these patients. On the other hand, 61.3% of patients with IgM positivity showed high avidity (35). In their study conducted in Mexico, Alvarado et al. identified *T. gondii* IgG positivity and *T. gondii* IgM positivity in 36 (8.2%) and 10 (2.3%) out of 439 pregnant women, respectively, and reported that high avidity in pregnant women with IgM antibody supports chronic infection (36). In the present study, however, out of 166 women of fertile age having an IgG avidity test, 38 (22.9%) had IgM positivity, of whom 8 (21.05%) had low avidity, suggesting a recent previous infection, while 24 (63.1%) had high avidity, suggesting a chronic infection. Due to the fact that *T. gondii* IgG seronegativity was found as high as 61.6% in the study, which is an indication of no previous exposure of women of fertile age to *T. gondii*, we consider that this population should be informed about the possible transmission of toxoplas-

Table 3. Distribution of anti-*T. gondii* IgG antibodies with respect to years in women of childbearing age from a tertiary hospital of Bursa, Turkey, 2002-2008

Years	Anti- <i>T. gondii</i> IgG positive	
	n	n (%)
2002	703	222 (31.6)
2003	839	247 (29.4)
2004	740	222 (30.0)
2005	851	252 (29.6)
2006	682	187 (27.4)
2007	402	144 (35.8)
2008	856	285 (33.2)
Total, n	5073	1559 (30.7)
p:0.156 IgG: the value of immunoglobulin G		

Table 4. Distribution of IgG and IgM compared to IgG avidity patterns in women of childbearing age from a tertiary hospital of Bursa, Turkey, 2002-2008

IgG Avidity	IgG positive, IgM positive n (%)	IgG positive, IgM negative n (%)	IgG positive, IgM equivocal n (%)	IgG positive n (%)
High Avidity (≥ 0.3) 136/166 (81.9)	24 (17.6)	93 (68.4)	4 (2.9)	15 (11.02)
Low Avidity ($0.2 \leq$) 13/166 (7.9)	8 (61.6)	3 (23)	0 (0.0)	2 (15.4)
Borderline (0.2-0.3) 17/166 (10.2)	6 (35.4)	8 (47.0)	0 (0.0)	3 (17.6)
Total, n (%)	38 (22.9)	104 (62.7)	4 (2.4)	20 (12.0)
IgG: the value of immunoglobulin G; IgM: the value of immunoglobulin M				

mosis and infection risks during the period of pregnancy. Similar to the results of studies conducted, particularly in western Turkey, the present study found *T. gondii* IgG positivity (26.8%).

CONCLUSION

Although the study data may not reflect our entire province, it virtually turns out that the risk of toxoplasmosis must be seriously taken into account, particularly when approaching some risk groups, such as seronegative women of fertile age, pregnant women, and immunocompromised patients.

Informed Consent: Informed consent was not obtained due to the retrospective nature of this study.

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Hakem Değerlendirmesi: Dış bağımsız.

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