Arrival Date: 15.04.2021 | Published Date: 25.05.2021 | 2021, Vol: 6, Issue: 12 | pp: 98-103 | Doi Number: http://dx.doi.org/10.46648/gnj.204

EVALUATION OF *Toxoplasma gondii* SEROPREVALENCE AND IGG AVIDITY TEST RESULTS AMONG CHILDBEARING-AGE WOMEN IN KARABUK PROVINCE

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ABSTRACT

Toxoplasmosis is a zoonotic infectious disease that is common worldwide and caused by the Toxoplasma gondii. Congenital toxoplasmosis is one of the major complications of this infection. The present study aimed to investigate T.gondii seroprevalence and evaluate the IgG avidity test results among childbearing- age women retrospectively. A total of 9401 samples obtained from childbearing -age (15-49 years of age) women who attended Karabuk University Training and Research Hospital between February 2016- January 2020, over the four-year, were included in the study.The Toxoplasma-IgM, Toxoplasma-IgG antibody, and Toxoplasma IgG avidity tests were analyzed chemiluminescent method by using ARCHITECT I 2000 SR immunoassay device (Abbott Laboratories, USA). Toxoplasma-IgM and Toxoplasma-IgG seropositivity were detected as 0.7% (67/9401) and 15.7% (1415/9005) respectively. A high percentage of Toxoplasma-IgM and Toxoplasma-IgG seropositivity were detected among 31-35 years of age group. The Toxoplasma seropositivity increased by age, but no statistically difference was found (P >0.05).The Toxoplasma IgG avidity was high in 45 patients (69.4%), low avidity was detected in 16 patients (22.6%) and from the remaining 6 patients were borderline (8%). The Toxoplasma IgM and IgG seropositivity rate decreased 2016 to 2020. The highest Toxoplasma IgM and IgG seropositivity were in 2016 with 1.2% and 16.8%, respectively. The T. gondi seropositivity rate was decreased from 2016 to 2020; it is probably a result of increasing awareness of the disease among patients. We think our results will contribute to the epidemiological data in our province and country and raise awareness.

Key words: Childbearing- age women, Toxoplasma IgG avidity, *Toxoplasma gondii*, Toksoplazmoz.

ÖZET

Toksoplasmoz, dünya çapında yaygın olarak görülen ve *Toxoplasma gondii*'nin neden olduğu zoonotik bir bulaşıcı hastalıktır. Konjenital toksoplazmoz, bu enfeksiyonun en önemli komplikasyonlarından biridir. Bu çalışma retrospektif olarak doğurganlık çağındaki kadınlarda *T. gondii* seroprevalansını araştırmayı ve IgG avidite testi sonuçlarını değerlendirmeyi amaçlamaktadır. Çalışmaya, Karabük Üniversitesi Eğitim ve Araştırma Hastanesi'ne Şubat 2016-Ocak 2020 tarihleri arasındaki dört yıllık süreçte başvuran doğurganlık çağındaki (15-49 yaş) kadınlardan elde edilen toplam 9401 örnek dahil edildi. Toxoplasma-IgG antikoru ve Toxoplasma IgG avidite testleri kemilüminesan yöntemle, ARCHITECT I 2000 SR immunoassay cihazı (Abbott Laboratories, ABD) kullanılarak analiz edildi. Toxoplasma-IgM ve Toxoplasma-IgG seropozitifliği sırasıyla %0,7 (67/9401) ve %15,7 (1415/9005) olarak tespit edildi. En yüksek Toxoplasma-IgM ve Toxoplasma-IgG seropozitifliği 31-35 yaş grubu kadınlarda saptandı. Toxoplasma seropozitifliğinin yaşla arttığı tespit edildi, ancak istatistiksel olarak fark bulunmadı (P> 0.05). Toxoplasma IgG avidite sonucu 45 hastada (%69,4) yüksek, 16 hastada (%22,6) düşük ve kalan 6 hastada (%8). sınırda avidite saptandı. En yüksek Toksoplazma IgM ve IgG seropozitifliği sırasıyla %1,2 ve %16,8 ile 2016 yılında saptanmış; seropozitiflik oranları 2016'dan 2020'ye azalmıştır. Bu durum; muhtemelen kadınlar arasında hastalığın farkındalığının artmasının bir sonucudur. Sonuçlarımızın ilimiz ve ülkemizdeki epidemiyolojik verilere katkı sağlayacağını ve farkındalık yaratacağını düşünüyoruz.

Anahtar Kelimeler: Doğurganlık çağındaki kadınlar, Toxoplasma IgG avidity, *Toxoplasma gondii*, Toxoplasmozis.

INTRODUCTION

Toxoplasmosis is a zoonotic infectious disease that is common worldwide and caused by the Toxoplasma gondii which is an obligate intracellular protozoan parasite. The parasite is distributed throughout the world in virtually all warm-blooded animals including humans [1]. It is estimated that one-third of the world's population is infected with T. gondii [2].

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Cats are the main source of parasite. Toxoplasma gondii has three forms: the tissue cyst, the oocyst, and the tachyzoite. Cats can be infected with any of the three forms of the parasite and release the infectious oocysts. The parasite is usually transmitted to humans through food contaminated with oocyst or undercooked meats containing tissue cysts. Also, T. gondii can transmission by transplacental route from infected mother to fetus, blood transfusion or organ transplantation from infected donors [3].

The primer infection is generally uncritical and often asymptomatic in healthy individuals. However, in pregnant women, the parasite might cross the placenta, infect the fetus, and cause mental retardation, hydrocephaly or fetal death. The infection has health-threatening in congenitally infected fetuses and immunocompromised individuals [3]. T. gondii seropositivity has been reported to vary according to age, climate, and environmental conditions, occupational groups, socioeconomic situation, etc. T. gondii seropositivity initiates in the first year, and it rises to 50–75% in adolescents [4] The prevalence of T. gondii in pregnant women has been investigated in different parts of the world and is estimated to range between 14% and 77% [5].

The diagnosis of toxoplasmosis made by showing tissue cyst forms by microscopic examination, detecting the parasite DNA by molecular methods or by determining specific antibodies against the surface antigens of the parasite by serological methods. Although the Sabin-Feldman test is accepted as a reference method, it can not be widely used in routine laboratories due to the need for live parasites, experience and challenges in application. The Enzyme-linked immunosorbent assay (ELISA) is most used method in diagnosing T. gondii infection [6]. This method, detects T. gondii IgM and IgG antibodies. Since it is highly sensitive and easy to use, it does frequently used in the laboratory diagnosis of toxoplasmosis. However, while the specific IgM positivity is interpreted in favor of acute toxoplasmosis, the persistence of IgM antibodies for months or even years and the observation of false positivity causes difficulties in diagnosis. Therefore, it is recommended to perform the T. gondii IgG avidity test to confirm a positive IgM test result by other specific methods or to determine whether the infection is in the early or late stage. This distinction has significant clinical importance, especially in pregnant women and immuncompromised patients [6].

Toxoplasma gondii seroprevalence has a global distribution, however it may be different between countries and even regions within the same country. Socio-economic level of society, eating habits, prevalence of contact with cats, climate, environment, hygiene and sanitation conditions, age, gender, ethnicity, medical history, and immunogenetic characteristics affect seropositivity rates. Therefore, epidemiological data are crucial in T. gondii infection [7].

In this study, we aimed to determine the seroprevalence of T.gondii and evaluate the IgG avidity test results among childbearing age women, who applied to Karabuk University Training and Research Hospital.

MATERIALS AND METHOD

A total of 9401 serum sample obtained from the 9401 childbearing age (15-49 years of age) women who attended Karabuk University Training and Research Hospital between February 2016- January 2020, over four-year period, were included in this cross-sectional study.Sera samples were tested for Toxoplasma-IgM and Toxoplasma-IgG antibody levels of the samples were analyzed by ARCHITECT I 2000 SR immunoassay device (Abbott Laboratories, Abbott Park, USA) with a chemiluminescent microparticle immunoassay method in accordance with the manufacturer's instructions.

Toxoplasma gondii IgM and IgG antibodies values >0.60 were considered positive, <0.50 were negative and 0.5–0.6 were considered as 'grey zone'. Toxoplasma gondii IgG avidity test was performed to only Toxoplasma-IgM positive samples. The Toxoplasma IgG-avidity test discriminates between past and recently acquired infection. The avidity index allows samples classification as low (avidity index <0.2 indicating an acute infection), borderline (avidity index 0.2–0.3) or high (avidity index >0.3) avidity. The Sabin -Feldman Test or Polymerase Chain Reaction (PCR) test was not performed in samples in which the Toxoplasma avidity test performed. The Toxoplasma-IgM and Toxoplasma-IgG test results were obtained from records in the laboratory information system and repeated patient results were excluded.

The Statistical Package for the Social Sciences (SPSS Inc., USA) version 20.0 was used for statistical analyses. Data are calculated with the numbers and percentages defined by median (minimum–maximum). Pearson Chi-Square test was used to compare between age groups and Toxoplasma IgM and IgG positivity.

The ethic approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Karabuk University (No: 2021/533).

RESULTS

The seroprevalence of T.gondii and the IgG avidity test results among 9401 childbearing- age women were investigated. Among the 9401 patients, the median age of the study population was 32 years (range 15-49 years).

Totally 9401 sera samples were evaluated, and 8729 (92.8%) of them were sent from the Gynecology and Obstetrics clinic. The distribution of the samples according to the clinics is shown in Table 1.

Table 1. The distribution of the studied samples according to the clinics [n (%)]

Clinics	n (%)
Gynecology and Obstetrics	8729 (92.8)
Pediatrics	471 (5)
Infectious Diseases	90 (0.9)
Internal Medicine	55 (0.5)
Neurology	10 (0.1)
Eye Diseases	6 (0.06)
Other Clinics	40 (0.4)
Total	9401 (100)

Totally 9401 sera samples were analyzed for Toxoplasma-IgM and 9005 serum samples were evaluated for Toxoplasma-IgG. Toxoplasma-IgM and Toxoplasma-IgG seropositivity was detected as 0.7% (67/9401) and 15.7% (1415/9005) respectively.The distribution of Toxoplasma-IgM and Toxoplasma-IgG rates were shown in Table 2.

Table 2. The distribution of Toxoplasma-IgM and IgG seropositivity [n (%)]

Test Result	Toxoplasma IgM	Toxoplasma IgG
	n (%)	n (%)
Positive	67 (0.7)	1415 (15.7)
Negative	9334 (99.8)	7590 (84.3)
Total	9401 (100)	9005 (100)

Both Toxoplasma-IgM and Toxoplasma-IgG were detected as the most common in 31-35 years. The least common group was 15-20 years. Toxoplasma-IgM positivity was not detected among women 15-20 years and 46-49 years. The difference was not statistically significant between Toxoplasma IgG and IgM seropositivity and age groups (P>0.05). The distribution of Toxoplasma-IgM and Toxoplasma-IgG seropositivity according to age groups were shown in Table 3.

Table 3. Toxoplasma-IgM and Toxoplasma-IgG seropositivity according to age groups

Test results	n (%)	n (%)
15-20	0 (0)	7 (0.4)
21-25	14 (20.8)	134 (9.5)
26-30	20 (29.9)	396 (28)
31-35	23 (34.3)	399 (28.2)
36-40	9 (13.5)	295 (20.9)
41-45	1 (1.5)	151 (10.7)
46-49	0 (0)	34 (2.3)
Total	67 (100)	1415 (100)

Toxoplasma IgG avidity test was performed to Toxoplasma-IgM positive samples. Toxoplasma-IgG was negative in five of the 67 patients who were Toxoplasma-IgM positive. Confirmatory tests showed high avidity in 43 patients, low avidity was detected in 14 patients and from the remaining 5 patients with borderline. *Toxoplasma gondii* IgG avidity test results showed in Table 4.

Table 4. *Toxoplasma gondii* IgG avidity test results [n (%)]

Avidity test results	IgG (+) and IgM (+) (n=62)
High avidity	43 (69.4)
Borderline	5 (8)
Low avidity	14 (22.6)
Total	62 (100)

In our study, we investigated Toxoplasma IgM and Toxoplasma-IgG seropositivity in samples between 2016-2020, over four-year period. The highest Toxoplasma IgM and IgG seropositivity were detected in 2016 with 1.2% and 16.8%, respectively. The Toxoplasma IgM seropositivity was detected 0.6% (15/2573), 0.5% (13/2372) and 0.4% (11/2100) in 2017, 2018 and 2019, respectively. Toxoplasma IgG seropositivity was detected 16.1% (397/2468), 15.1% (372/2470) and 14.6% (250/1714) in 2017, 2018 and 2019, respectively. The distribution of Toxoplasma-IgM and Toxoplasma-IgG seropositivity according to years is shown in Figure 1.

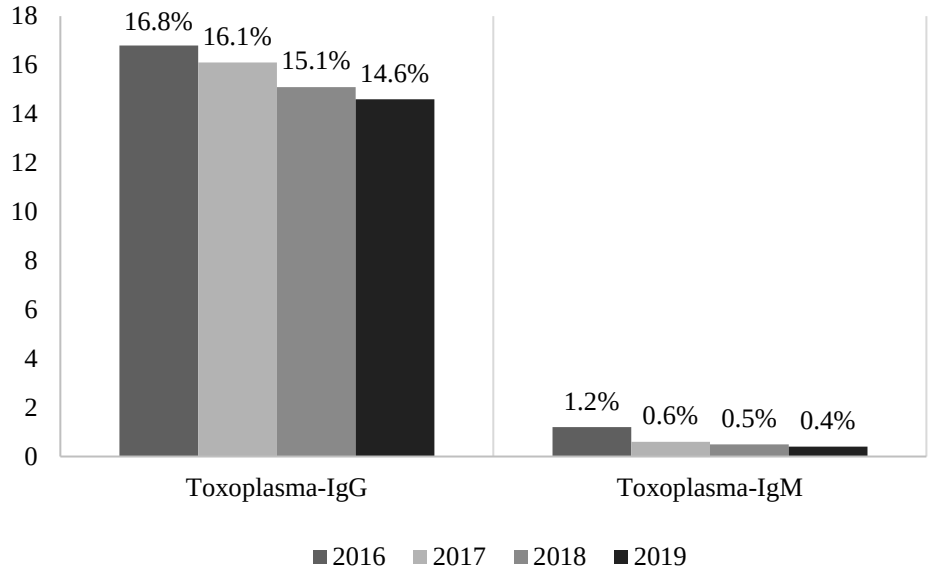

Figure 1. Toxoplasma-IgM and Toxoplasma-IgG seropositivity according to years

DISCUSSION

Toxoplasmosis is a common zoonotic disease all over the world. Congenital toxoplasmosis is the major complication of this infection. Having the infection during pregnancy exposes the patient to the possibility of congenital toxoplasmosis, which might include microcephaly, hydrocephalus, psychomotor, and mental retardation [8]. Thus clinicians investigate Toxoplasma infection in women who pregnant or planning pregnancy. In the present study, 92.8% of studied samples were sent from the Gynecology and Obstetrics clinic. In most studies, it has been observed that the clinic that most requires the Toxoplasma analysis is Gynecology and Obstetrics [9-11]. In a study from Istanbul, 91% of the samples were sent from the Gynecology and Obstetrics Clinic. The researcher thought that although not required by law, doctors preferred screening the patient and they recommended considering the prevalence values of the country in evaluating the cost and necessity of Toxoplasma screening [11].

Toxoplasma gondii seropositivity has been reported to vary according to age, climate and environmental conditions, occupational groups, socioeconomic situation, etc. Toxoplasma IgG positivity reported that as 12.3% in China, 13.2% in USA, 35.1% in Qatar, 58.5% in Brazil and 67.5% in Egypt [12-16]. In Turkey the highest T. gondii IgG seropositivity rate reported in Urfa with 68.9% and 63% in pregnant and childbearing -age women, respectively [17]. In our study Toxoplasma-IgG seropositivity was detected as 15.7% among childbearing age women. Similarly, Eroglu et al. was reported to Toxoplasma IgG seropositivity rate as 14.5 % among pregnant women in our province [18]. The Toxoplasma gondii seroprevalence has highly variable worldwide, so it can be different between countries and even regions within the same country. The Toxoplasma IgM seropositivity is acceptable as a parameter that active infection. It was observed that Toxoplasma-IgM seropositivity ranged from 0.1-4% in recent studies conducted in our region in childbearing age women

[9,10,19]. In present study we have found as 0.7% Toxoplasma IgM seropositivity in this group. The T. gondii infections are related to climate, environmental conditions, socioeconomic situation, etc. and, our results are concordance with the studies conducted in our region.

In recent studies, Toxoplasma seropositivity has shown a statistically significant increase at middle age [9,20,21]. In our study, it is also increased by age, similar to the literature, especially in that the 31-35 years of age group is the most affected group (28.2%). This is an expected result of increased exposure with age.

The positive Toxoplasma-IgM test result can be explained as an acute infection, passed prior infection, or false positivity. Therefore, Toxoplasma-IgG antibody should be investigated in Toxoplasma-IgM positive samples, and if Toxoplasma IgG is positive, IgG avidity test should be performed [5,22]. The Toxoplasma IgG avidity test aims to detect the increase in functional affinity between Toxoplasma-specific IgG and Toxoplasma antigen. It has been reported that the low avidity of the antigen-antibody complexes indicates that this is closer to the recent infection. Acute primary maternal toxoplasmosis if acquired during the first trimester of pregnancy can cause significant morbidity and mortality in developing fetus [23]. In present study, Toxoplasma-IgM and IgG positive samples were examined for additionalToxoplasma IgG avidity test. Confirmatory tests showed high avidity in 43 patients. So, 69.4% of the Toxoplasma-IgM positive women had high avidity antibodies suggesting that the infection was acquired before so with the detection of high avidity antibodies Toxoplasma infection up to 3-5 months ago has been excluded. Especially in pregnant women, the diagnosis of primary infection of T. gondii in the first trimester pregnancy by Toxoplasma-IgG avidity test is crucial in order to offer them early therapy or other interventions to prevent congenital infection of fetuses [24]

A study from Portugal has investigated the seroprevalence in women of childbearing age over the past three decades (1979 to 2013). As a result of the study it was reported that Toxoplasma-IgG seropositivity decreased from 47% to 22% in the past three decades [25]. Although the prevalence differs according to several characteristics of the population and region, it is obvious that the frequency has decreased the last two decades worldwide [26]. Similarly, in the present study T. gondi seropositivity rate was decreased from 2016 to 2020. We thought that it is probably a result of increasing awareness of the disease among individuals.

Limitations

This study has some limitations. It is a retrospective, single-center study based on laboratory data. Also, we did not include the patients' clinical features, risk factors, diagnosis, and treatment protocols.

Conclusions

As a result, Toxoplasma-IgG seropositivity rate was found to be 15.7% in Karabuk and it was observed that the Toxoplasma-IgG seropositivity rate increased with age. In the diagnosis of Toxoplasmosis, it is crucial to determine Toxoplasma IgM and IgG antibodies simultaneously, and if both are positive, distinguish between acute infection and previous infection with the Toxoplasma IgG avidity test. The T. gondii seropositivity rate was decreased from 2016 to 2020; it is probably a result of increasing awareness of the disease among women. We think our results will contribute to the epidemiological data in our province and country and raise awareness.

Conflict of Interest: The authors have stated that they have no conflict of interest.

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