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ORIGINAL ARTICLE

Seroprevalence of Toxoplasma Gondii Antibodies in Pregnant Women in Thrace Region of Turkey - A Tertiary Center Experience

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Abstract

Introduction: The objective of the study is to investigate Toxoplasma gondii antibody seroprevalence in pregnancies who applied for prenatal care to the tertiary center in Trakya (Thrace) Region of Turkey between January 01, 2014, and December 31, 2018, retrospectively.

Methods: This study retrospectively analyzes seroprevalence of T. gondii IgM and IgG antibodies of 2.317 pregnant patients in their first trimester attended to the Obstetrics and Gynecology Antenatal Care Unit in Trakya University, Faculty of Medicine between January 01, 2014, and December 31, 2018. For this purpose, IgM, IgG and if necessary, IgG avidity results were evaluated.

Results: In our study period 2.317 pregnant women were analyzed. 1.630 pregnant women (70.3%) were IgG and IgM seronegative, 607 (26.1%) were IgG seropositive, 61 (2.6%) were both IgG and IgM seropositive and 19 (0.9%) were only IgM positive. 30 of 61 patients with both IgG and IgM seropositivity showed low avidity. After 2 weeks for seroconversion control, in 16 of the patients with just IgM positivity, only 3 18.7%) showed seroconversion. We excluded patients who did not participate our routine follow-ups.

Discussion and Conclusion: Even toxoplasma exposure rate in the pregnant women from the Trakya Region of Turkey is high (26.1%) before pregnancy, about 70% of first-trimester pregnant patients were found seronegative. Screening during the first trimester would be appropriate and prenatal education should be given to the patients.

Keywords: Congenital toxoplasmosis; pregnancy; prenatal diagnosis.

Toxoplasma gondii, the causative agent of toxoplasmosis, is widely seen all over the world. It is an intracellular parasite that can infect all mammals and birds including humans. Transmission occurs by consumption of foods and beverages contaminated with cat feces, cooked or raw consumption of food containing bradyzoites, blood transfusion, organ transplantation, and transplacental way.[1] Toxoplasmosis is seen asymptomatic or mild findings in healthy patients but in immunosuppressive patients can lead to more serious conditions. In pregnancy, this infection causes negative effects on the fetus. The risk of transmission is low in the early period of pregnancy (10–15% in the first trimester) but the risk of congenital toxoplasmosis syndrome higher. Infection in late pregnancy the risk

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of transmission to the fetus is high (70–80% in the third trimester) but in the fetus the findings may be mild or even asymptomatic. It is also reported that infections 2–3 months before pregnancy may have an effect on the fetus. Therefore, detection of infections prior to or during pregnancy is very important.[2]

It is estimated that more than 30% of the world's population is infected with T. gondii. This is due to differences in climate, nutrition, and hygiene habits and can change between 10% and 80% by region.[3] In recent years in our country, the studies reported rates vary between 28.3% and 69.6%. Screening and diagnostic algorithm are recommended for pregnant women for prevention of congenital toxoplasmosis due to its asymptomatic course.[4] However, deficiency of diagnostic algorithm leads to the interpretation of examinations not properly and sometimes unnecessary repetition of tests. This results in increased costs, unnecessary anxiety in pregnant women, missed acute infection, and even more serious consequences such as unnecessary curettage. In this study we aim to determine the seropositivity of toxoplasmosis in the early period of pregnancy who applied to our hospital and the evaluation of Trakya Region comparing with other regions of Turkey and also sharing our clinic diagnostic algorithm protocol in the evaluation of toxoplasmosis.

Materials and Methods

A retrospective surveillance study was conducted on the basis of hospital records of 2.317 pregnant women who admitted to Trakya University School of Medicine, Department of Gynecology and Obstetrics during a period between 1 January 2014 and 31 December 2018. The patient information was collected from the medical records and clinical database with the approval of the Trakya University Human Ethics Committee (2019/46) in accordance with the Declaration of Helsinki. Patient age, gravida and parity evaluated. All the samples analyzed by Cobas Core (Roche, Germany) quantitative kits. Analysis of all blood was performed by the Macro ELISA method and Cobas e 601 device (Roche Diagnostics, Germany) which uses a patented electrochemiluminescence technology for immunoassay analysis employed at the Microbiology Laboratory of the Faculty of Medicine of Trakya University. During the study period same device used.

In the evaluation of the results anti-Toxoplasma IgG >4 IU/ml positive, <4 IU/ml negative and anti-Toxoplasma IgM >0.8 COI index positive, <0.8 COI index was considered negative. For the IgG avidity test, <70% low avidity, 70–80% border avidity and ≥80% high avidity was accepted with Cobas device. Patients with IgG and IgM positivity, avidity test requested. With low avidity, oral spiramycin treatment started and also, we followed up patients by ultrasonography. Test repetition was requested after 2 weeks from the patients with only IgM test (+) positive. We excluded patients who didn't participate our routine follow-ups. Patients were managed according to our protocol. In our algorithm, we applied all pregnant patients Toxoplasma IgG and Toxoplasma IgM tests. When both tests were negative we educated patients about not eating or handling raw or insufficiently-cooked meat, not handling contaminated soil or water, or contact with cats' feces. When both tests were positive we acquired IgG avidity tests. When avidity was lower we offered amniocentesis to patients for applying PCR test. We began to spiramycin treatment to these patients until delivery. Even though none of the patients accepted to amniocentesis, in our algorithm when we detect positive PCR test or ultrasound findings we offer termination of pregnancy or starting on sulfadiazine plus pyrimethamine treatment to these patients.

Statistical analysis was performed using the SPSS Statistics Version 22. Descriptive statics was used. Serological test results were examined according to the positivity rates of the tests for the determination of seroprevalence; expressed as number (n), percentage (%), and standard deviation.

Results

Mean age of the patients was 26.4 ± 6. 1780 (76.8%) of them were housewives and 537 (23.2%) were working. Mean age, gravida, parity, and worker numbers are shown in Table 1.

Patients were managed according to our algorithm protocol illustrated in Figures 1 and 2. 1630 (70.3%) patient were IgG and IgM seronegative, 607 (26.1%) were IgG seropositive, 61 (2.6%) were both IgG and IgM seropositive, 19

Table 1. Demographic characteristics of the cases and serological results of toxoplasma

	IgG (+) IgM (+) (n=61)	IgG (–) IgM (+) (n=19)	IgG (+) IgM (–) (n=607)	IgG (–) IgM (–) (n=1630)	Total (n=2317)
Age	26.5±6.1	25.8±5.6	26.2±6.1	26.3±6.2	26.4±6
Worker	14 (22.9%)	5 (26.93%)	151 (24.8%)	367 (22.5%)	537 (23.2%)
Gravida	3±1.6	2.2±1.1	2±0.6	1.6±0.8	2.2±1.1
Parity	1.6±1.3	1±1.1	1±0.6	1±0.7	1.1±1

Data are expressed as mean±standart deviation. n: Number, IgM: Immunglobin M, IgG: Immunglobin G.

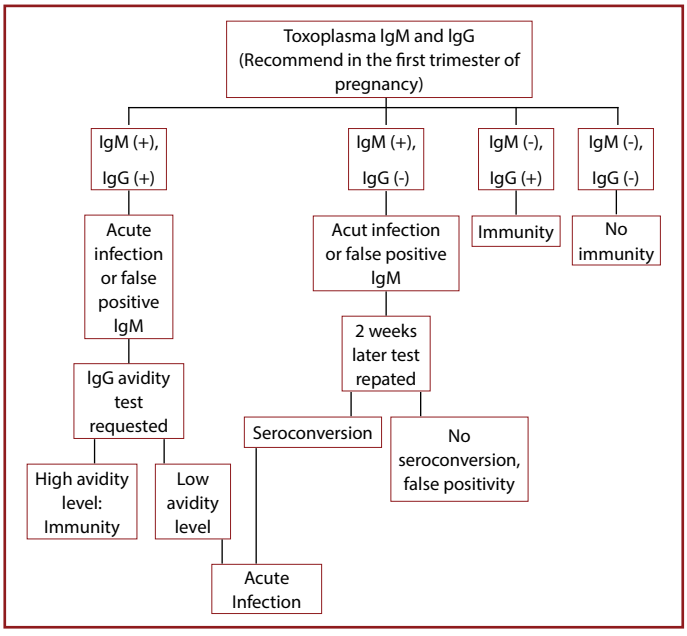

Figure 1. Pretanal serological screening for toxoplasmosis.

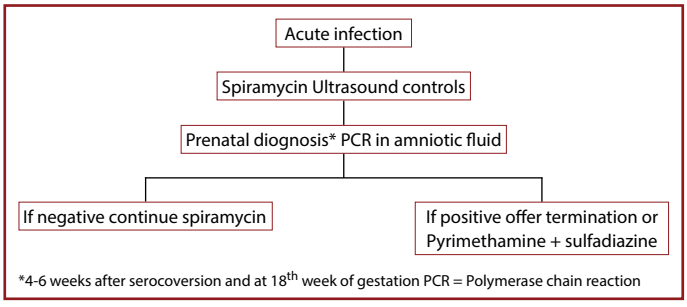

Figure 2. Diagnostic flow-chart for Toxoplasma gondii acute infection in pregnancy.

(0.9%) were IgM positive. IgG avidity was low in 30 of 61 (49.1%) patients with IgG and IgM positivity. In 5 (8.1%) patient borderline avidity detected (Fig. 3). After 2 weeks tests were repeated. No low avidity was encountered among these patients. We began to spiramycin 1 gr 3 times in a day orally to the patients with low avidity. We offered amniocentesis to all the patients in order to make PCR test. None of the patients accepted invasive method. Hence, we began to follow-up patients with ultrasound to detect ultrasonographic signs in fetus such as ventriculomegaly, hepatosplenomegaly, calcification in the brain and abdomen. In no fetus, we found abnormal signs.

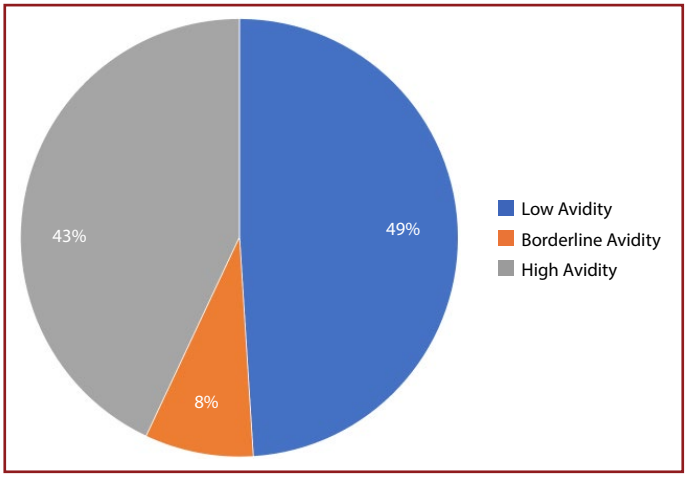

Figure 3. Avidity percentages of patients.

In 19 of the patients, we detected just IgM positivity. If the IgM antibody is positive 2–3 weeks later, but the IgG antibody remains negative, the initial IgM may be a false-positive. Therefore, after 2 weeks we repeated the tests. In 16 (84.3%) of the patients, IgG was still negative so we concluded these results with false-positivity. 3 (15.7%) of them had active infection and we started to spiramycin and offered amniocentesis at least 4 weeks after the detection but none of the patients accepted it. In ultrasonography, we did not detect any abnormality correlating with congenital toxoplasmosis. No infected newborn was observed during our study period.

Discussion

T. gondii is one of the few protozoan parasites that cross the placenta and infect the fetus. Consequences of congenital infection range from spontaneous abortion or prematurity to asymptomatic or overt congenital toxoplasmosis.[5]

Fetuses are at risk during primary infection or even after reactivation of chronic ones.[6] Antenatal screening for toxoplasma infection is now as important as VDRL, HIV, and HBV, and HCV screenings due to congenital toxoplasmosis can be prevented. When primary infection develops during pregnancy, early diagnosis and treatment can diminish the frequency and severity of the disease in the neonates.[7]

The seroprevalence of toxoplasmosis in the world ranges from 12% to 90% depending on the factors such as age, education, hygiene, collective life, tradition, and eating habits. For this reason, seropositivity rates in our country vary according to regions, lifestyle differences, dietary habits, socioeconomic conditions, age groups, and study groups.[8] Among different studies made in Turkey Toxoplasma IgG positivity in ranges between 17.2% and 69.5% and Toxoplasma IgM positivity ranges from 0.1% to 9.9%. The highest seroprevalence rates were seen in Urfa 69.5%, Diyarbakır 61.3%, Sivas 52.2%, Hatay 52.1%, Adıyaman 48.4%, Kocaeli 48.3% and Denizli 37%.[9-11] In general, higher seropositivity rates are observed in our Southeastern provinces.[12] It is noteworthy that these rates are similar to those of France,[13] Austria[14] and Italy[15] where toxoplasma screening is a

legally mandatory. In our study IgG positivity was lower than the Southeastern part of Turkey (26.1%). Varol et al.[16] studied seropositivity in pregnant women between years 2000 and 2009 in the Trakya Region of Turkey and the result was higher than our study (31.9%) (Figs. 4 and 5). This may be due to the improvement in the social hygiene habits of our region and the increase in the knowledge level of the patients and also prenatal education. In our clinic, we educate patients who desire pregnancy or pregnant woman with seronegativity about not eating or handling raw or insufficiently-cooked meat, not handling contaminated soil or water, or contact with cats' feces. In Cochrane review one study from Canada involved 432 women. In this study they were randomly allocated to a 10-min presentation during a prenatal class about toxoplasmosis prevention or to a usual prenatal class. Even though losses to follow-up were high and just 285 finished the post-test questionnaire in the third trimester, the authors finalized that prenatal education can efficiently alter pregnant women's behavior because it increased knowledge and awareness about pet, personal, and food hygiene.[17]

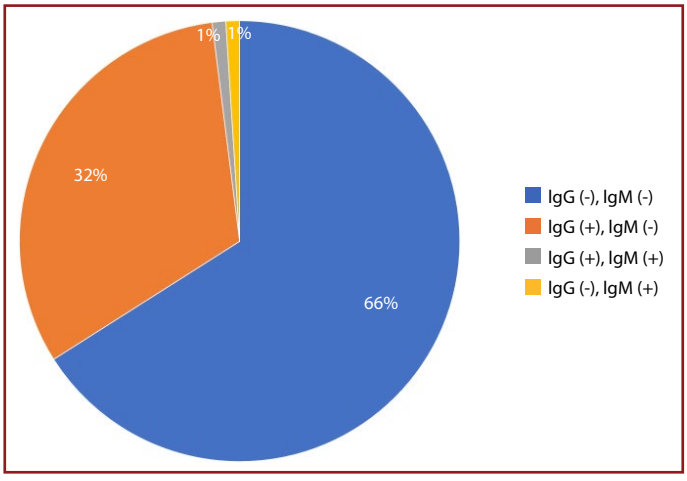

Figure 4. Toxoplasma antibody seroplavance between years 2000 and 2009 in Trakya Region of Turkey.

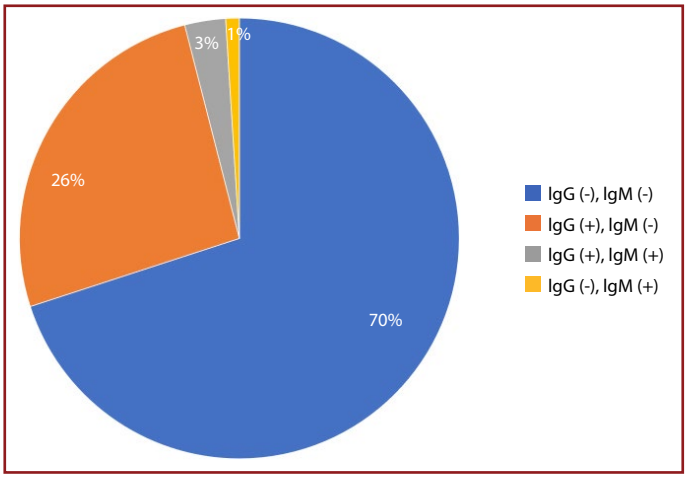

Figure 5. Toxoplasma antibody seroplavance between years 2014 and 2018 in Trakya Region of Turkey.

When acute toxoplasmosis is detected in mother, amniocentesis should be performed for PCR test after 18 weeks of pregnancy and at least for 4 weeks after acute infection. Prusa et al.[18] studied 707 pregnant patients with acute toxoplasmosis between the years 1992 and 2008 and with amniocentesis 39 infected fetuses diagnosed. In our study we recommended amniocentesis but no patient accepted it. We informed patients about amniocentesis procedure. We talked about the risk of fetal loss about 0.5–1% after procedure.[19] Patients declined the procedure and declared that in all circumstances they wanted to continue their pregnancies.

Ultrasound findings in congenital toxoplasmosis are hydrocephalus, microcephaly, thickened placenta with hyperechoic areas, liver echogenicity (due to T. gondii hepatitis), hepatomegaly, ascites, pericardial-pleural effusions, and congenital cataract.[20] In our follow-ups no ultrasonographic signs detected.

We started on spiramycin, a macrolide that is concentrated in the placenta, to women diagnosed during pregnancy with acute toxoplasma infection. Spiramycin is a safe drug and it can be used in pregnancy. It is a macrolide antibiotic similar to erythromycin (Category B).[21] Spiramycin is given for the first 21 weeks of gestation or until the term in fetuses that do not show signs of congenital infection. The recommended dosage of spiramycin is 3 g/day or 1.5 g twice a daily.[22] In our study, we gave spiramycin when we detected acute infection in mother and continued it until delivery. Meroni and Genco[23] offers also similar algorithm. But there is no data available on which to base recommendations for the drug choice and optimal duration of treatment. Mandelbrot et al.[24] in their randomized trial compared pyrimethamine plus sulfadiazine treatment to spiramycin for reducing placental transmission of toxoplasmosis. In their trial comprising 143 patients they found out transmission rate in pyrimethamine plus sulfadiazine group was 18.5% and in spiramycin group, it was 30%. They concluded that there was a trend toward lower transmission with pyrimethamine plus sulfadiazine, but it did not reach statistical significance. When PCR and sonography are negative, the approach to treatment is less clear. Some authors do not continue treatment in the setting of a negative PCR and sonography since the congenital infection has been excluded.[25] However, we continued treatment because our patients declined amnio-

centesis while some others continue because of concerns about false-negative test results.

Spiramycin likely diminishes the risk of transmission by nearly 60% but it is not sufficient to heal an infected fetus or infant.[26] Therefore, if fetal infection is diagnosed after 18 weeks of gestation more strong antibiotic regimens are advised than spiramycin. Pyrimethamine and sulfadiazine therapy has been associated with reducing of the signs of active congenital toxoplasmosis, mostly within the 1st week after treatment is started.[27] These 2 drugs act together toward T. gondii with a combined activity 8 times greater than expected if their effects were only additive.[28] Thus, the concurrent use of both drugs is indicated if there is suspicion of congenital fetal or infant infection. Regimen dose contains pyrimethamine 50 mg/day, and sulfadiazine, 1 g orally 3 times a day. Pyrimethamine is a folic acid antagonist and can lead to suppression of the bone marrow therefore 10–20 mg Leucovorin (folinic acid) is given per day to diminish the adverse effects of pyrimethamine.

Screening and diagnostic algorithm are recommended for pregnant women for prevention of congenital toxoplasmosis due to its asymptomatic course.[29] In countries such as Italy, Austria, and France, where the rate of congenital toxoplasmosis is high, screening is mandatory by law and diagnostic algorithms to be used are determined. In France, screening is done in every trimester in case when seronegativity is detected in the first trimester.[30] In North America, the United Kingdom, and some parts of Europe, the consensus opinion is against screening because the prevalence of the disease and incidence of maternal infection are very low.[31,32] There is no national screening program in Turkey but our study and other studies showed that the prevalence of toxoplasma is high like the countries where the screening program is mandatory (France, Italy, Austria).[33-35] In our opinion, toxoplasmosis screenings should be started in the first 3 months of pregnancy. So, in our clinic, we screen all pregnant women in the first trimester and after the first trimester, we request tests again if we detect IUGR (in utero growth retardation) or findings correlating with infection; calcifications, ventriculomegaly, microcephaly etc. During the study period, 182 patients with IUGR observed and no positivity of toxoplasmosis detected in these patients.

Conclusion

Considering the rates in our region and in our country, it is important to evaluate pregnant women in terms of acute toxoplasmosis. In the first trimester, screening should be done and prenatal education should be given. Tests should be repeated when there are suspicious signs in ultrasonography in the second or late trimester. In particular, a systematic serological screening of pregnant women should be created and performed in a national program to minimize the problems encountered in diagnosis and follow-up.

Ethics Committee Approval: Trakya University Human Ethics Committee (2019/46).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: C.Y.; Design: F.V.; Data Collection or Processing: I.U., H.S.; Analysis or Interpretation: B.Y., B.B., S.A.; Literature Search: C.S.; Writing: C.Y.

Conflict of Interest: None declared.

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