

## Prevalence of congenital toxoplasmosis among a series of Turkish women

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### ABSTRACT

**Background:** *Toxoplasma gondii* infection during pregnancy causes congenital malformations. Pregnant women should be screened for this infection since it is preventable and treatable. **Aim:** To study the seroprevalence of *Toxoplasma gondii* infection among pregnant women living in Izmir, Turkey. **Material and Methods:** A blood sample was obtained from 4651 women aged between 15 and 45 years, during their first trimester of pregnancy. IgM and IgG antibodies against *Toxoplasma gondii* were measured using an ELISA assay. Among women with both IgG and IgM antibodies positive, an IgG avidity test was performed, using a VIDAS kit. **Results:** IgG antibodies were positive in 1871 (39.9%) participants. Of these, 48 (2.5%) also had positive IgM antibodies. In 41 of these 48 women, the IgG avidity test was performed and only one woman had a low avidity. This woman was treated with Spiramycin. Her offspring had an intrauterine growth retardation and oligohydramnios. A chorioretinitis was diagnosed in the offspring of other woman with both antibodies positive. **Conclusions:** In this series, the prevalence of congenital toxoplasmosis was low. However, women with positive antibodies against *Toxoplasma Gondii* should be further studied and followed during their pregnancy.

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**Key words:** Pregnancy; Toxoplasmosis, congenital; *Toxoplasma gondii*.

## Prevalencia de toxoplasmosis congénita en una serie de mujeres en Turquía

**Antecedentes:** La infección por *Toxoplasma gondii* durante el embarazo causa malformaciones congénitas. Se debe efectuar serología para esta infección en mujeres embarazadas ya que es prevenible y tratable. **Objetivo:** Estudiar la seroprevalencia de infección por *Toxoplasma gondii* en mujeres embarazadas que viven en Esmirna, Turquía. **Material y Métodos:** Se obtuvo una muestra de sangre en 4.651 mujeres cuyas edades fluctuaban entre 15 y 45, años, durante su primer trimestre de embarazo. Los anticuerpos IgM e IgG en contra de *Toxoplasma gondii* se midieron por ELISA. En mujeres que tenían anticuerpos IgG e IgM positivos, un ensayo de avidéz de IgG se efectuó utilizando el kit VIDAS. **Resultados:** Los anticuerpos IgG fueron positivos en 1.871 participantes (39,9%). De estas, 48 (2,5%) también tenían anticuerpos IgM positivos. En 41 de estas 48 mujeres, se efectuó el test de avidéz y sólo una tenía una baja avidéz. Esta mujer se trató con espiramicina y su producto de concepción tuvo un retardo de crecimiento intrauterino y un oligohidroamnios. Una corioretinitis se diagnosticó en el producto de concepción de otra mujer con ambos anticuerpos positivos. **Conclusiones:** La seroprevalencia de toxoplasmosis congénita en esta serie de pacientes fue baja, sin embargo, las mujeres con anticuerpos positivos deben ser tratadas y seguidas.

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**T**oxoplasmosis is a parasitic infection disease which is caused by *Toxoplasma gondii* and courses with various clinical findings. While the primary infection during pregnancy is generally asymptomatic, it can be characterized with fever, malaise, sore throat, headache, maculopapular rash and lymphadenopathy<sup>1</sup>. The exposure of people to parasites occurs by eating undercooked meat, drinking water or eating vegetables contaminated with cat feces<sup>2</sup>. During the primary infection acquired during pregnancy, the effective parasite transmits to fetus through placenta, causes congenital infection and various sequels.

Development of fetal infection and the severity of sequels that may develop are related to the gestational week<sup>3-4</sup>. The incidence of congenital infection is 10-25% in the first trimester, 30-54% in the second trimester and 60-65% in the last trimester<sup>5-9</sup>. While the transplacental transmission appears to be less frequent in early pregnancy, the sequels occurring are more severe. The transmission rate is higher in latent period but the severity of the infection developing in fetus is mild. Mild symptoms may develop in fetus or they are asymptomatic in delivery<sup>10-11,12</sup>.

The clinical picture is notably variable in congenital toxoplasmosis. While sometimes no symptoms or findings are seen, spontaneous abortions and stillbirth may occur. The most frequent findings are chorioretinitis, intracranial calcifications and hydrocephalus. In the babies born as asymptomatic, hearing and visual impairment, neurologic findings and mental retardation may develop after long years. The serologic tests to be performed during pregnancy allow the early diagnosis of primary infection. Thus treatment is started and intrauterine infection development and progress of the infection developed in babies can be prevented. It also decreases the costs of long term care for the babies in which disability develops<sup>5-9</sup>. Seronegative women in pre-pregnancy and early pregnancy can be diagnosed do to studies on toxoplasmosis. Also, training is provided for protection in our country and in several places in the world. Infection should be detected in pregnant women and early diagnosis should allow treatment in seropositive women.

The aim of this study is to determine toxoplasmosis prevalence in asymptomatic pregnant women attending to an outpatient clinic of pregnancy during the first trimester of pregnancy and

to follow the clinical course in the cases in which congenital infection is diagnosed.

## Method

In this study, toxoplasmosis seroprevalence was searched in asymptomatic pregnant women attending the outpatient clinic of MH Tepecik Hospital of Gynaecology and Obstetrics between 2003 and 2008. Antibodies related with toxoplasma were studied serologically through Enzyme-Linked Immunosorbent Assay (ELISA) method by scanning IgM and IgG. On the cases in which both of IgM and IgG antibodies were identified positive, IgG avidity test was performed. (VIDAS, bioMérieux, France). Information about the patients was obtained by scanning their outpatient clinic records retrospectively. Statistical analyses were made by using SPSS 10.0 for Windows, SPSS Inc, Chicago IL. Computer program.

## Result

4,691 pregnant women who were between 15 and 45 years of age and in the first trimester of pregnancy were included in the study. IgG and IgM antibodies were identified as negative (seronegative) in 2,820 (60%). IgG antibody was identified as positive (seropositive) in 1,871 (39.9%) of the pregnant women of which anti toxoplasma antibody results were evaluated. While IgM antibody was identified as negative in 1,823 of 1,871 pregnant women of which IgG was identified as positive, in 48 (2.5%) of them IgM and IgG antibodies were both identified as positive. On 41 of 48 pregnant women IgG avidity test was performed and low avidity in 14th gestational week was measured in only one of them. In the follow-up of this pregnant woman in which low avidity was measured, treatment of 3g/day of spiramycin (Rovamycine, Eczacıba 1-Istanbul) was administered. Intrauterine growth retardation and oligohydramnios developed in fetus in USG follow-up. The gestational age of fetus that was evaluated biometrically was found 31 week rather than 35 weeks and AFI (amniotic fluid index) was measured as 40 in four quadrant measurement. Postpartum associated anomaly was not found. High avidity was measured in other 40 pregnant women.

**Table-1. Toxoplasma antibody seroprevalence according to age**

Age (year)	IgM and IgG (-)	IgM (+), IgG (-)	IgM (-), IgG (+)	IgM and IgG (+)	Total
15-24	775 (59%)	0	534 (40,6%)	4 (0,3%)	1313
25-34	1680 (62,3%)	0	986 (36,5%)	29 (1%)	2695
35-44	365 (53,4%)	0	303 (44,3%)	15 (2,2%)	683

Regular follow-up of the seven of pregnant women of which IgM and IgG antibodies were identified as positive could not be made during pregnancy. Chorioretinitis was diagnosed in one of the seven babies after birth. No anomaly was found in the other six babies. When pregnant women were evaluated according to age group, it was found that the incidence of toxoplasma IgM antibody increased with age but there was not a significant difference between the incidence of IgG antibody and age. Anti toxoplasma antibodies identified according to age groups are given in Table 1.

## Discussion

Toxoplasmosis is an infectious disease which is generally asymptomatic in persons with fully functioning immune system. The infections occurred during pregnancy are generally asymptomatic but it may cause abortion, stillbirth, intrauterine growth retardation and various congenital malformations in fetus. Therefore it is recommended for the pregnant women to be screened serologically from the first trimester and tests of the seronegative cases to be repeated every three months<sup>13-14</sup>. Congenital infection incidence and severity may vary according to the trimester in which the mother is infected with the disease. The lowest incidence is seen in the first trimester and the highest incidence is seen in the third trimester. The severity of the congenital infection is inversely proportional with the trimester in which the mother is infected with the disease. Infection causes more severe congenital malformations in case it develops in the early period of the pregnancy. So screenings should be made in the first trimester. *Toxoplasma gondii* infection is diagnosed through clinical findings and ultrasonographic monitoring together with serological tests, polymerase chain reaction (PCR), histopathological methods or the isolation of the factor<sup>15</sup>. Serological tests are the

most commonly used among them. It is significant in congenital toxoplasmosis diagnosis if the toxoplasma antibodies that are negative before pregnancy become positive during pregnancy. It will indicate an acute infection in case only the IgM antibody is identified as positive from the serological tests. However IgM antibodies may be identified as positive in blood for as long as a year<sup>16</sup>. Thus it may indicate a previously infected disease or false-positive. In 1997, a report of the Food and Drug Administration showed that only 40% of the IgM test results that were studied with commercial methods and identified as positive indicated a recent infection<sup>17,18</sup>. IgG antibodies generally develop in the 7-14<sup>th</sup> days of the infection, with a peak in the 30-60<sup>th</sup> days, generally stay positive lifelong and indicate a previous infection<sup>19</sup>. In this case congenital infection risk is very low<sup>5</sup>. Screening for IgG antibodies in the early period of pregnancy is significant. If it is found in the latent gestational period, the primary toxoplasma infection gone through in the early period of the pregnancy cannot be excluded, because the patient may have been infected with the parasite in the early gestation period and her anti-toxoplasma IgG antibodies may have become positive in the progressive periods. In this case anti-toxoplasma IgM antibody may be positive or negative<sup>20-21</sup>. Performing IgM and IgG tests together in the early gestation period is the most appropriate screening method. In the cases when both tests are positive IgG avidity test should be applied. Avidity means the bonding intensity of an antibody molecule with a multivalent antigen. During the primary infection in which parasite encounters with an antigen, IgG antibodies that develop against this factor show low avidity in the first weeks, then gradually grow and have high avidity<sup>22</sup>. IgG avidity test is a very useful test in the diagnosis of toxoplasma infection during pregnancy. It has been developed to distinguish the present or recent infection from a previous infection<sup>23</sup>.

While low avidity indicates a current infection, high avidity is assessed for previous infection. Other tests that are used in the diagnosis of congenital toxoplasmosis are not used routinely in diagnosis. Diagnostic methods that could be helpful in the diagnosis of the disease include: histopathologic examination of the infected tissue, examination of body fluids such as cerebrospinal fluid through PCR and parasite culture. PCR test for the determination of parasite DNA should be made in the amniotic fluid in the prenatal diagnosis<sup>19</sup>.

Toxoplasma prevalence differentiates according to geographical location, socioeconomic conditions and nutritional habits. In studies made on pregnant women and/or women in productive age in the different regions of our country, show IgG seropositivity of *T. gondii* in 44.4% in Izmir, 39.6% in Malatya, 35.8% in Istanbul, 30.7% in Ankara, 30.1% in Aydın and 19.2% in Samsun; it was measured as 42.3% in East of Black Sea Region, 31-37.1% in Eastern Anatolia and 69.5% in Southeastern Anatolia<sup>16</sup>.

Our study composes the widest series of cases among in literature. In our study, totally 4691 pregnant women were serologically examined through ELISA method for toxoplasmosis and IgG seroprevalence was measured as 39.9%. The high number of pregnant women examined is significant for reflecting the toxoplasmosis seroprevalence in Izmir and close provinces. The results obtained from our study is similar to the results in the different regions of our country, it is only different from the results obtained in Southeastern Anatolia. This situation has been correlated with the better sanitation operations and diet difference in our region. Prevalence rates varying between 20 and 43% in the various places of the world have been reported<sup>24-25</sup>. Studies made in the Middle East and Arabian Peninsula show results similar to ours. IgG positivity prevalence is low in European countries. This situation is thought to be related to the differences in climate, culture and diet habits.

While in 1,871 (39.9%) of pregnant women, IgG antibody was identified as positive and IgM antibody was identified as negative, IgG and IgM antibody was identified as positive in 48 (2.5%) pregnant women. IgG avidity test was performed on 41 of 48 pregnant women, low avidity was measured only in one (2.4%) of them and acute toxoplasma infection was diagnosed. In a study

reported by Yazar et al, in Kayseri, high avidity was measured in 70.8%, low avidity in 4.7% and avidity levels within suspicious limits in 24.5% of 695 pregnant women of which *T. gondii* antibodies were identified as positive<sup>26</sup>. In a study made by Bahar I.H. et al. in Izmir Dokuz Eylül University, IgG, IgM and IgA antibodies developing against *T. gondii* was investigated; IgG avidity test was performed on cases that had IgM or IgA positivity besides IgG positivity. Low avidity in nine (29%), liminal avidity in eight (25.8%) and high avidity in 14 (25.8%) of 31 pregnant women on which anti *T. gondii* IgG avidity test was performed<sup>27</sup>. IgG avidity was measured as high as in 78.2% of 92 patients with positive anti *T. gondii* IgM antibody in a study made by Jennum PA et al. in Norway<sup>28</sup>. Generally high avidity levels were found in our study, similar to the other studies made in our country and abroad. However the frequency of low avidity presence is similar with a study made in Kayseri but relatively less than the other studies. This low rate of low avidity levels found in pregnant women indicates that the congenital toxoplasmosis incidence in pregnant women in Izmir is lower than thought.

Intrauterine growth retardation was diagnosed in the fetus of a pregnant woman in which low avidity was found in our study. Postpartum chorioretinitis was diagnosed in the baby of a pregnant woman who had IgG and IgM positive association. Fetal chorioretinitis does not develop only due to congenital toxoplasmosis. It is known that viral infections during pregnancy such as mumps, CMV also cause fetal chorioretinitis<sup>29-30</sup>. IgG avidity test and other possible etiological agents could not be performed on this pregnant woman.

It is required for pregnant women that are diagnosed toxoplasmosis to start spiramycin and the treatment should be continued until the end of the pregnancy. As spiramycin may not cross the placenta, if the infection is diagnosed in fetus, pyrimethamine sulfadiazine and folinic acid combination should be preferred. However, the use of this combination should be avoided before the 12-14th week of pregnancy as it is teratogenic<sup>31</sup>. In our study, spiramycin was administered to the pregnant woman in whom low avidity was found until the end of the pregnancy. No anomaly was observed in the newborn. There are some inadequacies of our study. Simultaneous PCR in amniotic fluid and parasitological culture could not

be performed besides avidity test on the pregnant women which had IgM and IgG positivity. More accurate results can be obtained with the addition of PCR and culture methods of toxoplasma infections develop during pregnancy.

## Conclusion

Toxoplasmosis is a parasitic infection disease that may cause congenital infections during pregnancy. The possible sequels can be avoided with early diagnosis and treatment. Therefore examinations for the toxoplasma diagnosis should be performed in the first trimester and in the pregnancy follow-up. The analysis of IgM and IgG antibodies for diagnosis are the most common tests that may be used routinely. Avidity tests should be applied on patients in whom both antibodies are identified as positive. Toxoplasma frequency in pregnant women in Izmir is similar to the results in other areas of our country, avidity levels were found generally high in comparison to other studies. Congenital toxoplasmosis frequency is low. The high number of patients in our study can give light on toxoplasmosis sero prevalence in our region. All pregnant women should be screened for toxoplasmosis as it is a preventable and treatable disease.

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