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Investigation of Pregnancies with Toxoplasmosis Infection

Toksoplazmoz Enfeksiyonlu Gebeliklerin Araştırılması

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Abstract

Background: This study sought to retrospectively assess the perinatal outcomes, serological features, and efficacy of the prenatal care algorithm of pregnant women with toxoplasma gondii infection who were monitored at a tertiary-level hospital in Şanlıurfa.

Materials and Methods: A retrospective review was made of the medical records of 64 pregnant women who tested positive for toxoplasma IgG/IgM and gave birth between January 2020 and January 2025. The normal prenatal follow-up and treatment procedure was followed in the management of the patients. Prenatal treatment methods, ultrasound findings, amniocentesis and PCR results, clinical and laboratory data of the infants, demographic information, and serological test results were also examined. Descriptive statistics were used in the statistical analysis.

Results: The 64 pregnant women included in the study had an average age of 26.70 ± 4.56 years. In 58 cases, 90.6% had high IgG avidity. Low avidity led to the initiation of spiramycin treatment in six cases. Three patients underwent amniocentesis, and PCR results were positive in all three cases. Two cases resulted in pregnancy termination. Hepatosplenomegaly and hypotonia were observed in one infant with congenital toxoplasmosis. Most of the infants showed no symptoms of congenital infection and were toxoplasma IgM/IgG negative.

Conclusions: The high frequency of IgG avidity indicates that the infection was typically contracted before pregnancy. Congenital transmission was found to be effectively prevented by the present prenatal diagnosis and treatment protocol. Early treatment and careful monitoring are associated with positive perinatal outcomes, even in the small percentage of low avidity patients.

Keywords: *Toxoplasma gondii,* Congenital toxoplasmosis, Pregnancy, Prenatal diagnosis, Spiramycin

Öz

Amaç: Bu çalışmada Şanlıurfa'da üçüncü basamak bir hastanede takip edilen toksoplazma gondii enfeksiyonu olan gebelerin perinatal sonuçları, serolojik özellikleri ve doğum öncesi bakım algoritmasının etkinliğinin retrospektif olarak değerlendirilmesi amaçlanmıştır.

Materyal ve metod: Ocak 2020 ile Ocak 2025 tarihleri arasında toksoplazma IgG/IgM testi pozitif çıkan ve doğum yapan 64 gebenin tıbbi kayıtları retrospektif olarak incelendi. Hastaların yönetiminde normal doğum öncesi takip ve tedavi prosedürü izlendi. Doğum öncesi tedavi yöntemleri, ultrason bulguları, amniyosentez ve PCR sonuçları, bebeklerin klinik ve laboratuvar verileri, demografik bilgiler ve serolojik test sonuçları da incelendi. İstatistiksel analizde tanımlayıcı istatistikler kullanıldı.

Bulgular: Çalışmaya dahil edilen 64 gebe kadının ortalama yaşı 26,70 ± 4,56 yıldı. 58 olgunun %90,6'sında yüksek IgG aviditesi vardı. Düşük avidite nedeniyle altı olguda spiramisin tedavisine başlandı. Üç hastaya amniyosentez yapıldı ve her üç hastanın PCR sonucu pozitifti. İki olguda gebelik sonlandırıldı. Konjenital toksoplazmozlu bir bebekte hepatosplenomegali ve hipotoni gözlendi. Bebeklerin çoğunda konjenital enfeksiyon belirtisi yoktu ve toksoplazma IgM/IgG negatifti.

Sonuç: IgG aviditesinin yüksek sıklığı, enfeksiyonun genellikle gebelikten önce kapıldığını göstermektedir. Mevcut doğum öncesi tanı ve tedavi protokolü ile konjenital bulaşmanın etkili bir şekilde önlendiği bulunmuştur. Erken tedavi ve dikkatli takibin, düşük aviditeli hastaların küçük bir yüzdesinde bile olumlu perinatal sonuçlarla ilişkilidir.

Anahtar Kelimeler: *Toxoplasma gondii*, Konjenital toksoplazmoz, Gebelik, Prenatal tani, Spiramisin

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Introduction

All mammals and birds are susceptible to infection by the intracellular parasite Toxoplasma gondii. It is spread by consuming food and drinks tainted with cat excrement, eating raw or cooked foods harboring bradyzoites, receiving blood or organ transplants, or transplacental transmission (1, 2). In healthy people, toxoplasmosis manifests as minor or asymptomatic symptoms, but in immunocompromised individuals it can cause more severe health issues. There is less chance of vertical transmission to the fetus (10–15%) during the first trimester because the placental barrier is less porous. However, infection at this time might impact the process of fetal organogenesis, increasing the chance of serious abnormalities such as hydrocephalus, microphthalmia, and neurological impairment (2, 3). There is a greater probability of transmission (70–80%) in the third trimester due to the increased permeability of the placenta as it matures. However, the infection may be asymptomatic or show only mild signs (hepatosplenomegaly, jaundice, thrombocytopenia, etc.) because the fetal immune system and organ development are largely complete (4). As illnesses that occur two to three months before pregnancy have also been shown to affect the fetus, it is essential to detect infections occurring either before or during pregnancy (5).

In early infections, pregnancy may be terminated due to fetal loss or severe anomalies, while in late infections, subclinical infection may occur in the newborn and neurological sequelae such as vision loss and learning difficulties may occur in the long term (6). Spiramycin and sulfadiazine-pyrimethamine therapy for mothers may lessen the severity of infection and cut the risk of fetal transmission by 50–60% (4). Therefore, diagnosis and treatment of toxoplasmosis infection during pregnancy is very important.

More than 30% of people worldwide are thought to be infected with *T. gondii.* This can vary from 10% to 80% depending on the area and is caused by variations in climate, nutrition, and hygiene practices (7). The reported rates in recent studies in Türkiye range from 28.3% to 69.6%. Congenital toxoplasmosis is asymptomatic, so screening and diagnostic methods are recommended to be able to prevent the condition in expectant mothers (8). However, the lack of a diagnostic algorithm results in erroneous examination interpretation and occasionally unnecessary repeat testing. Costs increase, pregnant women experience unwarranted concern, acute infections are ignored, and there can be worse outcomes such as unnecessary curettage.

Toxoplasma gondii infection during pregnancy has varying prevalence rates across different geographic regions. Şanlıurfa is one of the cities with the highest incidence of congenital Toxoplasma infection in Türkiye. The primary reasons for this include sociocultural characteristics, dietary habits and widespread contact with animals. Therefore, a retrospective analysis of pregnancies at risk for congenital toxoplasmosis in Şanlıurfa is of great importance. The aim of this study was to contribute to the literature by evaluating the perinatal outcomes of toxoplasma-seropositive pregnant women who underwent a standard prenatal diagnosis and treatment algorithm at a tertiary-level referral centre in the region of Şanlıurfa, south-east Türkiye.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at the Department of Obstetrics and Gynecology of Harran University Hospital, a tertiary referral center in Şanlıurfa, Southeastern Turkey. Ethical approval for this study was obtained from the Harran University Clinical Research Ethics Committee (approval no: HRU/25.13.48, date: July 14, 2025). The medical records of all pregnant women who gave birth between January 1, 2020, and January 31, 2025, and who were tested for Toxoplasma gondii infection during prenatal care were screened for eligibility.

Study Population and Selection Criteria

The initial screening identified 6498 pregnant women with any Toxoplasma gondii serology testing in the defined period. From this pool, the final study cohort was selected according to the following criteria:

Inclusion Criteria:

1. Singleton pregnancy.
2. Seropositivity for Toxoplasma gondii, defined as anti-Toxoplasma IgG >4 IU/mL and/or IgM >0.8 COI Index.
3. Availability of complete medical records, including maternal demographic data, serial serology results (IgG, IgM, avidity), detailed prenatal follow-up notes, ultrasound reports, and comprehensive neonatal outcome data (birth weight, APGAR scores, clinical examination, and laboratory findings).

Exclusion Criteria:

1. Multiple pregnancies (twins, triplets, etc.).
2. Incomplete medical records (e.g., missing key serology results, absence of neonatal follow-up data).
3. Seronegativity for Toxoplasma gondii (IgG ≤4 IU/mL and IgM ≤0.8 COI Index).

After applying these criteria, 6434 cases were excluded (137 for incomplete records, 6215 for seronegativity, 82 for multiple pregnancies). Consequently, a total of 64 toxoplasma-seropositive pregnant women with complete data were included in the final analysis.

Data Collection and Variables

Retrospective analyses were performed on the following: APGAR scores, congenital infection findings, laboratory results, prenatal follow-up data, serological test results (toxoplasma IgM, IgG, and IgG avidity using the ELISA method), and the maternal demographic data (age, parity, and socioeconomic status).

Statistical Analysis

Data were analyzed using SPSS statistical software. Descriptive statistics (mean, standard deviation, percentage, min-max) were used. The level of statistical significance was accepted as $p<0.05$.

Logistic regression analysis was planned to identify independent risk factors associated with congenital toxoplasmosis. However, due to the very low number of congenital infection cases (n=1) in our cohort, multivariate modeling could not be performed reliably, as it would lead to overfitting and statistically unstable results. Therefore, we present only descriptive statistics for the congenital infection case.

Results

The information of the pregnant women and toxoplasmosis is given in Table 1.

Descriptive and toxoplasmosis-related data of the pregnant women are shown in Table 2.

Table 1. Distribution of demographic data and toxoplasma-related information of the pregnant women (N=64)

Demographic data and information about toxoplasma		**N**	**%**
Pre-pregnancy infection screening	No	64	100.0
Animal contact*	Yes	64	100.0
Seroconversion date	6^{th} week	6	9.4
	7^{th} week	15	23.4
	8^{th} week	17	26.6
	9^{th} week	9	14.1
	10^{th} week	7	10.9
	11^{th} week	6	9.4
	12^{th} week	3	4.7
	13^{th} week	1	1.6
Avidity status	Positive	58	90.6
	Negative	6	9.4
Spiramycin treatment	Yes	6	9.4
	No	58	90.6

Table 1. Continued			
Amniocentesis	Not applied	61	95.3
	Applied	3	4.7
PCR test result (in amniotic fluid)	Negative	61	95.3
	Positive	3	4.7
USG findings suggesting congenital infection	No	61	95.3
	Yes	3	4.7
Termination of pregnancy	No	62	96.9
	Yes	2	3.1
Sulfadiazine + Pyrimethamine treatment	Not initiated	64	100.0
USG findings	Normal	61	95.3
	Hepatosplenomegaly	2	3.1
	Ventriculomegaly	1	1.6
Newborn congenital Infection finding	No	61	95.3
	Yes	1	1.6
	Not specified	2	3.1
Neonatal TOXO IgM/IgG positivity Results	Negative	61	95.3
	Positive	1	1.6
	Not specified	2	3.1
Congenital toxoplasmosis diagnosis	No	61	95.3
	Hepatosplenomegaly	1	1.6
	Not specified	2	3.1
Neonatal clinical course	Normal	61	95.3
	Hypotonia	1	1.6
	Not specified	2	3.1
PCR: Polymerase chain reaction, USG: Ultrasound, TOXO IgM/IgG: Toxoplasma immunoglobulin M/immunoglobulin G * Direct contact with cats or consumption of food and drinks contaminated with cat faeces, or consumption of raw or cooked foods containing bradyzoites			

Table 2. Distribution of descriptive and toxoplasma-related information of the pregnant women (n=64)

Descriptive data and information about toxoplasma		**N**	**%**	
Long term results	Normal	61	95.3	
	Developmental delay	1	1.6	
	Not specified	2	3.1	
Postnatal follow-up Period	5 age	62	96.9	
	Not specified	2	3.1	
Developmental delay in the infant (Bayley Test)	No	61	95.3	
	Bayley positive	1	1.6	
	Not specified	2	3.1	
	Minimum	**Maximum**	**Mean**	**SD**
Age (years)	19	35	26.70	4.56
Number of pregnancies	1	7	2.95	1.58
Gestational week on first presentation	6	13	8.48	1.73
Seroconversion history week (gestational week when IgG/IgM was positive)	6	13	8.48	1.73
IgG Avidity test (%)	9.00	92.00	73.81	20.58
Newborn birth weight (grams)	2600	3300	3014.44	134.73
1st minute APGAR Score	7	8	7.23	0.42
5th minute APGAR Score	8	8	8.00	0.00
SD: Standard deviation, IgM/IgG: Immunoglobulin M/immunoglobulin G				

The pregnant women had a mean age of 26.70±4.56 years, the mean number of pregnancies was 2.95±1.58, the mean gestational week on first presentation was 8.48±1.73, mean week of seroconversion was 8.48±1.73, and the mean IgG avidity test was 73.81±20.58%. The birth weight of the newborns was mean 3014.44±134.73 g, and the APGAR scores were mean 7.23±0.42 at 1 minute and 8.00±0.00 at 5 minutes. Not all the pregnant women underwent pre-pregnancy infection screening and all had contact with animals. Positive avidity was determined in 90.6% of the pregnant women, 9.4% were given spiramycin treatment and 4.7% underwent amniocentesis. Of the 64 pregnant women, 61 (95.3%) had negative PCR results, while three (4.7%) had positive PCR results. There were no USG findings of congenital infection in 95.3%, 96.9% of these pregnancies were not terminated, and none started sulfadiazine + pyrimethamine treatment. USG findings were normal in 95.3% of pregnant women, there were no signs of congenital infection in the newborn, negative TOXO IgM/IgG positivity in the newborn, no diagnosis of congenital toxoplasmosis, the clinical course of the newborn was normal, the neurological evaluation

of the newborn was normal, and long-term outcomes were normal. Postnatal follow-up was 5 years in 96.9% of the babies, and 95.3% of the babies had no developmental delay.

The antibody test results are given in Table 3.

Table 3. Antibody test results (n=64)

	Minimum	Maximum	Mean	SD	Normal range
Anti-Toxoplasma IgG (IU/mL)	3.10	8.90	5.47	1.33	0-2
Anti-Toxoplasma IgM (COI Index)	0.80	3.10	1.80	0.56	0.51-0.60
Rubella IgG (IU/mL)	0.10	3.10	0.84	0.71	0-5
Rubella IgM (COI Index)	0.10	0.20	0.11	0.04	0.00-0.80

SD: Standard deviation, IgM: Immunoglobulin M, IgG: Immunoglobulin G, COI Index: Cut-off Value Index

The anti-toxoplasma IgG level was determined to be mean 5.47±1.33 IU/mL, which was above the normal range. The anti-toxoplasma IgM (COI index) level was mean 1.80±0.56 and was above the normal range. The rubella IgG level was mean 0.84±0.71 IU/mL and was below the normal range, and the rubella IgM (COI index) level was found to be mean 0.11±0.04, which was below the normal range.

Discussion

The aim of this retrospective study was to examine the clinical features, prenatal care, and perinatal results of pregnant patients with toxoplasma infection who were monitored at a tertiary-level hospital in Şanlıurfa. The results obtained offer crucial details about the treatment and results of pregnant women in this region who tested positive for toxoplasma.

Given the retrospective design of the study, the sample size (n=64) can be considered a sufficient number to evaluate a relatively rare clinical entity such as congenital toxoplasmosis. Previous important retrospective cohort studies, such as the study by Cortina-Borja et al. (9), have also made valuable contributions to the literature with similar or smaller sample sizes. By their nature, retrospective studies aim to evaluate all cases within a specific time period. By including all pregnant women diagnosed at a tertiary-level hospital between 2020 and 2025 who were followed up using a standard protocol, this study had sufficient power in terms of reliability and internal validity of the findings. The results can be considered to provide guidance for clinical practice in regions with similar patient profiles.

The results of this study have several important implications for clinical practice. First, the fact that high IgG avidity was determined in the vast majority of cases (90.6%) suggests that the infection in these pregnant women was most likely acquired before pregnancy and the risk of fetal impaction is low (10, 11). In a study by Schneider et al. (3), it was stated that high avidity scores suggest that the infection was contracted at least three to four months ago, in which case there is little chance of congenital transmission. This provides important guidance for clinicians to avoid unnecessary treatment interventions and unnecessary anxiety in pregnant women. Secondly, even in the limited number of cases with low avidity, the congenital transmission rate remained extremely low (1.6%) due to the early initiation of spiramycin therapy and close prenatal follow-up, thereby demonstrating the effectiveness of the adopted management algorithm. In conclusion, the results of this study demonstrate that in regions with high toxoplasma seroprevalence, serological screening during pregnancy and the implementation of a rigorous follow-up protocol play a vital role in preventing congenital toxoplasmosis and minimizing adverse perinatal outcomes.

Of the total participants in this study, six (9.4%) were diagnosed with low avidity and started on spiramycin medication as acute infection was suspected. After undergoing amniocentesis, PCR testing was positive in all three cases. The literature highlights the significance of PCR testing and amniocentesis for prenatal

diagnosis in cases of suspected acute infection (12, 13). However, the early response to treatment, low suspicion of infection, or the patient's wish to avoid intrusive treatments could all account for the low occurrence of amniocentesis in this study. According to the SYROCOT trial, patients undergoing prenatal therapy had a significantly lower risk of congenital infection (14). The low congenital transmission rate among spiramycin-treated patients in the current study is consistent with previous research.

Two of the three cases in the congenital toxoplasmosis at-risk group had hepatosplenomegaly, and one had ventriculomegaly. The characteristic ultrasonographic findings of congenital toxoplasmosis are in line with these results (15, 16). Nonetheless, the congenital infection diagnosis rate of 1.6% was quite low in the current study, suggesting that fetal transmission may be avoided by starting therapy as soon as possible in cases when an acute infection is suspected (17). In a prospective cohort analysis by Garweg et al. (18), it was seen that prenatal therapy dramatically decreased the chance of severe neurological sequelae.

In the current study, no fetal infection symptoms were seen, and the majority of infants (95.3%) tested negative for toxoplasma IgM/IgG. This outcome can be a reflection of how well the prenatal care and follow-up plan worked. However, the identification of hypotonia and developmental delay in one case is a reminder that the characteristics of congenital toxoplasmosis can be asymptomatic but eventually lead to neurological consequences (19). Although 80–90% of congenital toxoplasmosis patients may be asymptomatic at birth, neurological and ophthalmological problems may develop later in life, according to Maldonado and Read (20). Therefore, it is crucial to monitor patients in respect of probable congenital toxoplasmosis over an extended period of time.

Our study was conducted in Şanlıurfa, a region hosting a large refugee population. It is important to consider seroprevalence differences between indigenous and refugee communities when developing public health strategies for congenital toxoplasmosis prevention. A study conducted in Turkey reported a significantly higher Toxoplasma gondii seropositivity among Syrian refugee pregnant women compared to the local population, highlighting specific risk factors and vulnerabilities in this group (21). Therefore, future screening and prevention programs in similar demographic settings should include targeted approaches for refugee populations, encompassing education, accessible screening, and appropriate follow-up to mitigate the risk of congenital transmission.

This study provides an original contribution to the literature as it is one of the first studies to demonstrate the effectiveness of the current management protocol with concrete data in the Southeastern Anatolia region, where high seroprevalence is observed. Strong aspects of the study include being among the first to examine the perinatal outcomes of pregnancies in this region that tested positive for toxoplasma and thereby gauge how well the prenatal follow-up approach is working.

Study Limitations

This study has several limitations that should be considered when interpreting the results. First, the retrospective design inherently carries the risk of selection bias and incomplete data retrieval, despite our efforts to include only cases with complete records. Data on potential confounding factors, such as precise gestational timing of infection or detailed treatment adherence, could not be consistently obtained. Second, the relatively small sample size (n=64), particularly the very low number of cases with adverse outcomes (e.g., only one confirmed congenital infection), limits the statistical power of the study. This precluded meaningful multivariate regression analyses to identify independent risk factors for congenital transmission, as any model would be statistically unstable and prone to overfitting. Finally, the single-center nature of the study, conducted in a tertiary hospital in a specific geographical region, may limit the generalizability of the findings to other populations with different demographic or seroprevalence characteristics. Despite these limitations, our study provides valuable real-world data on the outcomes of a standardized management protocol in a high-prevalence area.

Conclusion

In conclusion, the prevention of congenital transmission and fetal problems during pregnancy requires early detection and treatment of toxoplasmosis infection. Pregnancy termination rates and unnecessary therapy can be decreased by using amniocentesis and PCR testing for prenatal diagnosis in low-avidity pregnant women. Furthermore, in areas where toxoplasmosis seroprevalence is high, extensive preconception screening programs can be recommended. For the early identification and treatment of any potential after-effects, patients with congenital toxoplasmosis must have ongoing neurological and developmental monitoring.

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Author Contributions:
Concept: E.U., Ö.T.
Design: E.U., Ö.T.
Data Collection or Processing: A.A., Ö.T.
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