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Research Article

A public health problem in pregnant women: acute toxoplasma infection - a retrospective study of 12 years of data from a training and research hospital in Izmir

Gebelerde bir halk sağlığı sorunu: akut toksoplazma enfeksiyonu-İzmir'deki bir eğitim ve araştırma hastanesinin 12 yıllık verilerinin retrospektif çalışması

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Abstract

Introduction: The aim of this study is to identify the prevalence of acute toxoplasmosis in pregnant patients who are monitored in our hospital and to provide insight into screening and management options by assessing maternal and fetal outcomes.

Methods: Pregnants between the ages of 18-49, who were followed up in the Gynecology and Obstetrics Polyclinic/Clinic and Infectious Diseases Polyclinic/Clinic of a Training and Research Hospital between January 1, 2010 and December 31, 2021, were included in this study. *T. gondii* IgM, IgG and avidity tests which were performed for pregnant women were evaluated retrospectively.

Results: The study consisted of 7480 pregnants. Three hundred eighty-six (%5.16) of the pregnant women tested positive. Anti-*T. gondii* IgM seropositivity was found to be most common in the 18-28 age group (7.82%), and this frequency gradually decreased as age progressed. Two of the 122 patients whose polymerase chain reaction for *T. gondii* was examined from amniotic fluid at the outer center had congenital toxoplasmosis, and these pregnancies were terminated.

Conclusions: Pregnant women continue to have a considerable risk of developing acute toxoplasmosis. For this infestation, which still remains on the agenda as a public health problem, every individual who is planning a pregnancy and has not had a serological test before should be screened before pregnancy. Pregnant women should continue to be informed and educated about this parasite, in our opinion.

Keywords: Avidity, Infestation, Pregnancy, Toxoplasma

Öz

Giriş: Bu çalışmanın amacı hastanemizde takip edilen gebe hastalarda akut toksoplazmoz prevalansını belirlemek, anne ve fetus sonuçlarını değerlendirerek tarama ve yönetim seçeneklerine ışık tutmaktır.

Yöntem: Bu çalışmaya 1 Ocak 2010 ile 31 Aralık 2021 tarihleri arasında bir Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Polikliniği/Kliniği ve Enfeksiyon Hastalıkları Polikliniği/Kliniğinde takip edilen 18-49 yaş arası gebeler dahil edildi. Gebelere yapılan *T. gondii* IgM, IgG ve avidite testleri geriye dönük olarak değerlendirildi.

Bulgular: Çalışma 7480 gebe içermektedir. Gebelerin 386'sının (%5,16) testi pozitif çıktı. Anti-*T. gondii* IgM seropozitifliğinin en sık 18-28 yaş grubunda (%7,82) görüldüğü ve yaş ilerledikçe bu sıklığın giderek azaldığı görüldü. Amniyotik sıvıdan, dış merkezde *T. gondii* için polimeraz zincir reaksiyonu bakılan 122 hastanın ikisinde konjenital toksoplazmoz tanısı konuldu ve bu gebelikler sonlandırıldı.

Sonuç: Gebe kadınlarda akut toksoplazmoz gelişme riski önemli ölçüde devam etmektedir. Halen bir halk sağlığı sorunu olarak gündemde olan bu infestasyon için gebelik planlayan ve daha önce serolojik test yaptırmamış her bireyin gebelik öncesinde tarama yaptırması gerekmektedir. Bizce gebe kadınların bu parazit hakkında bilgilendirilmesi ve eğitilmesi devam etmelidir.

Anahtar kelimeler: Avidite, İnfestasyon, Gebelik, Toksoplazma

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Key Points

1. Pregnant women continue to have a considerable risk of developing acute toxoplasmosis.
2. Anti-*T. gondii* IgM seropositivity was found to be most common in the 18-28 age group, and this frequency gradually decreased as age progressed.
3. Prior to becoming pregnant, any person who is contemplating motherhood and has never undergone a serological test should be examined.

Introduction

Most warm-blooded animal species are susceptible to infection by the single-celled parasite *Toxoplasma gondii* (*T. gondii*). Humans and other animals are regarded as intermediate hosts, despite the fact that cats are the parasite's sole host throughout its entire life cycle. Consuming contaminated raw or undercooked meat from intermediate hosts like poultry, cattle, sheep, and goats as well as consuming contaminated seafood can all result in the spread of the disease to humans. Other risk factors include failing to wash hands after coming into contact with contaminated soil or cat litter. Additionally, contaminated blood or tissue transfusions and placental transmission from the mother to the fetus are ways in which it can spread from person to person. Toxoplasmosis affects 30% of individuals worldwide, but only a tiny percentage of those affected experience symptoms, making it a serious public health concern [1-3]. In the past 20 years, seroprevalence has declined in Europe and the United States, while many other nations continue to have high prevalence levels. This is assumed to be a result of advancements in food safety and purity (the use of contemporary farming practices, new industrial processes, and improvements in food storage and preservation) [4,5]. The nervous system and reticuloendothelial system are the principal organs affected by toxoplasmosis. The majority of infected people show no symptoms, however in a small number of cases it can result in fever, exhaustion, headaches, anemia, or lymphadenopathy. In people with compromised immune systems, it could have major life-threatening effects. The fetus may experience severe issues from acute toxoplasmosis that develops during pregnancy, including cerebral calcifications, hydrocephalus, and even death. Because of this, some medical professionals advise serological testing during pregnant [6,7]. About 40% of pregnant women who have *T. gondii* for the first time also have transplacental transmission of the disease. Congenital toxoplasmosis may sporadically manifest in women with compromised immune systems as a result of the reactivation of an earlier infection [8,9].

As gestational age rises, the chance of an infection being transmitted transplacentally during pregnancy increases dramatically. The probability is 15% at week 13, 44% at week 26, 71% at week 36, and this rate is over 90% in the final weeks of pregnancy. Of all fetuses, 25–30% are susceptible to congenital infection [10,11]. There is disagreement on whether or not pregnant women should be routinely checked for *T. gondii* Immunoglobulin (Ig) G and IgM antibodies [12]. Pre-pregnancy screening actually makes it possible to identify anti-toxoplasma IgG seronegative women who are likely to be infected, and positive antibodies found during pregnancy are the most reliable sign of infection in the pregnant woman [9,13,14]. If the antibody test is performed for the first time in the last trimester and a negative IgM result is found, this cannot rule out an infection acquired in early pregnancy because IgM can disappear from the blood in a short period of time. Positive IgG and negative IgM values detected for the first time in the first two trimesters suggest that the infection was acquired before pregnancy. Contrarily, while positive IgM can occasionally stay in the blood for years, it does not always imply an acute infection. As a result, the presence of anti-toxoplasma IgM antibodies alone cannot confirm the existence of acute infection because they emerge positive about a week after infection and can continue to be high for months or years [9,15,16]. An avidity test is carried out to determine whether the pregnant woman is actually infected when both antibodies are found to be positive. This technique, known as the IgG avidity test, assesses the immunogenic binding potency of the antibody. Infection in the past four months, which is typically thought of as an acute infection, is excluded by high avidity. A result with a low or grey zone avidity suggests an acute infection. In this particular case, the diagnosis is verified through the use of PCR and amniocentesis [10,17-19]. Once the mother's primary toxoplasma infection has been identified, monthly ultrasounds should be done to check for fetal malformations until term. The primary ultrasonography results include ventriculomegaly and intracranial calcifications. Even if the fetus is infected, the pregnancy shouldn't be terminated if there are no serious complications, but it is essential that the family and medical professionals interact in order to treat such a pregnancy [20,21]. Spiramycin, a macrolide that decreases transplacental transmission by reaching significant placental concentrations and has no effect in the presence of fetal infection, is favored in cases of acute infection discovered within the first 18 weeks [22]. The combination of pyrimethamine, sulfonamide, and folinic acid is the gold standard treatment when a transmitted infection is discovered after the 18th week. The teratogenic consequences of this treatment make it inappropriate before the 14th week [21].

To highlight the significance of toxoplasma infection in pregnant women, which continues to be a major public health issue in underdeveloped countries, we organized this study to show the data of pregnant women whom we followed for a long time.

Methods

This study comprised pregnant patients who were monitored between January 1, 2012, and December 31, 2012, at the Gynecology and Obstetrics Polyclinic/Clinic and Infectious Diseases Polyclinic/Clinic of a Training and Research Hospital. *T. gondii* IgM, IgG and avidity tests which were performed for pregnant women were evaluated retrospectively. According to the manufacturer's recommendations, the macro ELISA method was used to examine anti-*T. gondii* IgM and IgG using the commercial kit Immulite® 2000 XPiTM Immunoassay System (Siemens, Germany). Index values based on commercial kit Anti-*T. gondii* IgM, cases with index 1.1 were regarded as positive, those with index values between 0.9 and 1.1 were regarded as intermediate, and those with index 0.9 were regarded as negative. Anti-*T. gondii* IgG cases with indices of 8 or higher were regarded as positive, those with indices of 6.5-8 as intermediate, and those with indices 6.5 as negative. Patients with anti-*T. gondii* IgM and IgG positivity were tested using an ELISA technique and an anti-*T. gondii* IgG avidity kit (DIA. PRO, Milan, Italy). Low avidity is characterized by an avidity index below 20, intermediate avidity is characterized by an avidity index between 21 and 29 (the "gray zone"), and high avidity is characterized by an avidity index above 30. Two weeks later, gray zone findings were frequently reassessed. Results with a low repetition rate were considered to have a low avidity. Anti-*T. gondii* IgG avidity and anti-*T. gondii* IgM positivity findings are categorized by age groups, and anti-*T. gondii* IgM positivity is also categorized by years.

Ethical approval

The research was approved by the Izmir Katip Celebi University (İKCU) Ethics Committee (İKCU Non-Invasive Clinical Research Ethics Committee Decision Form: 0024/20.01.2022).

Results

In the research, it came to light that 7480 pregnant women applied to our hospital and underwent anti-*T gondii* IgM and IgG testing during the course of a 12-year period between 2010 and 2021. Anti-*T. gondii* IgM was discovered to be positive in 386 of the pregnant women. The rate of overall *T. gondii* IgM seropositivity was found to be 5.16%. The patients were found to be 32.76 years old on average. The 18-28 age group was shown to have the highest prevalence of anti-*T. gondii* IgM seropositivity (7.82%), and as people aged, this frequency gradually dropped (Table 1). According to the analysis done by year, the anti-*T. gondii* IgM seropositivity percentage was determined to be greater in 2016, 2012, and 2019 (Table 2).

Table 1. Distribution of anti-*T.gondii* IgM positive cases by age groups

Age groups	Number of patients (n)	Anti-*T gondii* IgM (+) (n)	%
18-28	2326	182	7.82
29-38	4648	191	4.11
39-49	506	13	2.56
Total	**7480**	**386**	**5.16**

Table 2. Distribution of Anti-*T gondii* IgM positivity by years

Years	Number of patients (n)	Anti-*T gondii* IgM (+) (n)	%
2010	585	32	5.47
2011	612	28	4.57
2012	626	37	5.91
2013	594	25	4.21
2014	635	34	5.35
2015	532	21	3.94
2016	702	44	6.26
2017	681	39	5.72
2018	674	33	4.89
2019	713	42	5.89
2020	504	19	3.76
2021	622	32	5.14
Total	**7480**	**386**	**5.16**

Both Anti-*T. gondii* IgM and Anti-*T. gondii* IgG positive results were subsequently tested for IgG avidity test in 373 patients. In 167 of these patients, the IgG avidity test revealed low levels. High risk for congenital toxoplasmosis was identified in 180 patients with low avidity as a result of IgG avidity and those with anti-*T. gondii* IgM positive/anti-*T. gondii* IgG negative antibodies (Table 3).

Table 3. Distribution of Anti-*T gondii* IgM, Anti-T IgG positive and low avidity patient results by age groups

Age	Anti-*T gondii* IgM (+) (n)	Anti-*T gondii* IgM and IgG (+) (n)	Low avidity	
			(n)	%
18-28	182	173	85	49,13
29-38	191	187	79	42,24
39-49	13	13	3	23,07
Total	386	373	167	44,77

Such individuals were referred to the Infectious Diseases Clinic for collaborative monitoring. High-risk cases were initiated on spiramycin 3x1 g/day after being informed about congenital toxoplasmosis, and amniocentesis was recommended after the 18th week of pregnancy. Independently of amniocentesis, all pregnant women underwent ultrasound screening for abnormalities between 18 and 22 weeks' gestation. None of the ultrasonographic findings, such as intrahepatic calcifications, hydrocephalus, intracranial calcifications, echogenic bowel, hepatosplenomegaly, pleural-pericardial effusions, ascites placental thickening/ calcifications, hydrops fetalis and intrauterine growth restriction, that may be linked to congenital *T. gondii* infection were observed in our cases.

Patients were informed of the potential hazards associated with the invasive technique of amniocentesis and why it was essential. 122 of these individuals (n=180) who agreed to the procedure had amniocentesis with their informed permission. Amniocentesis-related problems didn't arise in any of the patients. For a *T. gondii* PCR analysis, the obtained materials were transferred to the outer reference laboratory. Two of the patients had *T. gondii* PCR results that were positive. Both of these patients opted termination after receiving thorough information on the toxoplasmosis process, therapy, follow-up choices, and termination itself. In 120 individuals who had amniocentesis and were found to have negative *T. gondii* PCR results, spiramycin medication was continued until the end of pregnancy, whereas it was refused by 58 patients.

Discussion

The seroprevalence of *T. gondii* antibodies increases with age in humans. This condition; it varies greatly based on socioeconomic class, geographic location, degree of education, personal hygiene, food preferences, host sensitivity, soil moisture status, and climatic circumstances. Seroprevalence has decreased recently as a result of rising frozen meat consumption, improved sanitary conditions, and rising urbanization rates [23,24]. Many studies have been conducted in our country investigating *T. gondii* seropositivity. According to current statistics, anti-*T. gondii* IgG positive rates range from 17.5% to 69.5%, while anti-*T. gondii* IgM positivity rates range from 0% to 5.4% [25]. There are geographical variations, but the global frequency of acute infection in pregnant women is 1.1% [23].

In a Turkish facility, over a three-year period between 2012 and 2014, 37% of 1296 suspected toxoplasmosis patients had anti-*T. gondii* IgG positivity detected in their blood samples. Anti-*T. gondii* IgG and IgM antibodies were both found to be positive in 1.9% of the study's subjects. Separate anti-*T. gondii* IgG seropositivity was discovered in pregnant women to be 24.2%; concurrent anti-*T. gondii* IgM and IgG seropositivity was found to be 0.7%. No case had isolated IgM positivity. Thirteen pregnant women and 25 patients with probable toxoplasmosis underwent anti-*T. gondii* IgG and IgM co-positivity tests, and only one from each group had low avidity found [26].

In our study, where a 12-year screening was performed, *T. gondii* IgM was found positive in 386 (5.16%) of a total of 7480 pregnant women. The age range between 18 and 28 is the one where anti-*T. gondii* IgM seropositivity is most prevalent, and it has been seen that this frequency steadily declines as people become older.

Numerous studies have demonstrated the value of initiating therapy as soon as possible (preferably within 3 weeks of seroconversion) to stop the spread of infection and the emergence of congenital disease [27-30]. In all patients with suspected acute toxoplasma, we immediately began spiramycin therapy. 180 of 373 individuals with both anti-*T. gondii* IgM and anti-*T. gondii* IgG results were determined to be high risk. Of the 122 expecting mothers who consented to do amniocentesis, two had PCR results that were positive, and it was found that these expecting mothers desired abortion. 120 pregnant women who tested PCR negative and 58 pregnant women who did not have an amniocentesis continued to receive therapy until delivery.

The traditional trio of congenital toxoplasma infection includes hydrocephalus, cranial calcifications, and chorioretinitis. However, 90% of these infants are asymptomatic at delivery. In two-thirds of congenital toxoplasmosis cases, it has been observed that ultrasonography cannot identify any abnormalities [31]. The incidence of ventricular dilatation and cerebral calcification was found to be 6% in a research done in Europe. Poor prognosis ultrasonography findings include severe ventricular dilatation, brain necrosis, rotational abnormalities, and microcephaly. Pregnant women with the condition in the first trimester who did not receive therapy experienced more difficulties in their unborn children [32]. About 4% of children with symptoms of congenital toxoplasmosis have hydrocephalus, which is by far the most severe sign [33].

Congenital infection prevalence and illness severity have considerably decreased in France and Austria as a consequence of advancements in detection and treatment in recent years. In a retrospective analysis of 88 congenital toxoplasmosis cases, 51.1% of the patients had one or more brain lesions, with cerebral nodular foci being the most prevalent kind of lesion In the course of our research, no followed fetus had any aberrant ultrasonographic results [34].

Strengths and limitations

One of the study's advantages is the substantial number of expectant mothers included in it. Nonetheless, the results of the study could have been slightly impacted by Syrian pregnant women because ethnicity was not taken into consideration. This represents a shortcoming in our study. In Turkey, getting an avidity test might be challenging, particularly if you live outside of the big cities. In that regard, it might be seen as a helpful study that provides insight into the topic. Because patient income levels are not taken into consideration, biases may arise when maternal and perinatal data are generalized to the overall community. A longer-term surveillance of the offspring of spiramycin-treated expectant mothers would have enhanced the strength of our research.

Conclusion

T. gondii is one of the most significant zoonotic agents due to the fact that it is widespread in both animals and humans, making its management essential for maintaining public health. It still poses a hazard, despite the fact that its frequency has declined recently. Unfortunately, there is yet no medicine that will completely eliminate the agent. The incomprehensible complexity of the infection process and immunopathogenesis still remains. Therefore, it is crucial to develop new methods and medications, particularly for the detection and treatment of obstetrical and congenital infections, in order to improve quality of life. Additionally, according to the results of our study, it was observed that acute toxoplasmosis is still diagnosed at a considerable rate and the practice of educating expectant mothers on the matter should continue in order to enlighten and safeguard them. The infestation of acute toxoplasmosis in pregnancy, which is still a public health issue, should not be disregarded. Prior to becoming pregnant, any person who is contemplating motherhood and has never undergone a serological test should be examined.

Conflict of Interest: The authors declared no conflict of interest regarding this article.

	Author Contributions	**Author Initials**
SCD	Study Conception and Design	KK, MS
AD	Acquisition of Data	KK, MS
AID	Analysis and Interpretation of Data	KK, MS
DM	Drafting of Manuscript	KK
CR	Critical Revision	KK, MS

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References

1. WHO Estimates of the Global Burden of Foodborne Diseases (2015). *Available from URL: www.euro.who.int/_data/assets/pdf_file/0011 Accessed: February 18, 2022.*
2. Centers for Disease Control and Prevention. Toxoplasmosis (Toxoplasma gondii) (2022). *Available from URL: http://www.cdc.gov/dpdx/toxoplasmosis/ index.html Accessed: June 24, 2022*
3. Li K, Wang M, Zhang H, Lei Z, Zhang L, Luo H, et al. Epidemiology of Toxoplasma gondii infection in native Tibetans in Tibet, China. Acta Parasitol. 2017;26;62(3):529-32. https://doi.org/10.1515/ap-2017-0063
4. Pinto B, Mattei R, Moscato GA, Cristofano M, Giraldi M, Scarpato R, et al. Toxoplasma infection in individuals in central Italy: does a gender-linked risk exist? Eur J Clin Microbiol Infect Dis. 2017;36(4):739-46. https://doi.org/10.1007/s10096-016-2857-8
5. McLeod R, Cohen W, Dovgin S, Finkelstein L, Boyer KM. Human Toxoplasma infection. In Weiss LM and Kim K (eds), (2020). Toxoplasma gondii: The Model Apicomplexan – Perspectives and Methods, 3rd Edn. London: Academic Press, pp. 117–227.
6. Xia J, Yolken RH. Strain hypothesis of Toxoplasma gondii infection on the outcome of human diseases. Acta Physiol (Oxf). 2015;213(4):828-45. https://doi.org/10.1111/apha.12458
7. Paquet C, Yudin MH, Society of Obstetricians and Gynaecologists of Canada. Toxoplasmosis in pregnancy: prevention, screening, and treatment. J Obstet Gynaecol Can. 2013;35(1):78-81. https://doi.org/10.1016/s1701-2163(15)31053-7
8. Kaye A. Toxoplasmosis: diagnosis, treatment, and prevention in congenitally exposed infants. J Pediatr Health Care. 2011;25(6):355-64. https://doi.org/10.1016/j.pedhc.2010.04.008
9. Peyron F, Wallon M, Kieffer F and Garweg J. Toxoplasmosis. InWilson CB, Nizet V, Maldonado YA, Remington JS and Klein JO (eds), (2016). Infectious Diseases of the Fetus and the Newborn Infant, 8th Edn. Philadelphia, PA, USA: Elsevier. pp. 949–1042.
10. Bollani L, Auriti C, Achille C, Garofoli F, De Rose DU, Meroni V, et al. Congenital Toxoplasmosis: The State of the Art. Front Pediatr. 2022;6;10:894573. https://doi.org/10.3389/fped.2022.894573
11. Bollani L, Strocchio L, Stronati M. Congenital toxoplasmosis. Early Human Development. 2013;89:70-2. https://doi.org/10.1016/S0378-3782(13)70107-5
12. Wallon M, Peyron F. Congenital toxoplasmosis: a plea for a neglected disease. Pathogens. 2018;23;7(1):25. https://doi.org/10.3390/pathogens7010025
13. Picone O, Fuchs F, Benoist G, Binquet C, Kieffer F, Wallon M, et al. Toxoplasmosis screening during pregnancy in France: opinion of an expert panel for the CNGOF. J Gynecol Obstet Hum Reprod. 2020;49(7):101814. https://doi.org/10.1016/j.jogoh.2020.101814
14. Binquet C, Lejeune C, Seror V, Peyron F, Bertaux AC, Scemama O, et al. The cost effectiveness of neonatal versus prenatal screening for congenital toxoplasmosis. PLoS One. 2019;18;14(9):e0221709. https://doi.org/10.1371/journal.pone.0221709
15. Saso A, Bamford A, Grewal K, Noori M, Hatcher J, D'Arco F, et al. Fifteen-minute consultation: management of the infant born to a mother with toxoplasmosis in pregnancy. Arch Dis Child Educ Pract Ed. 2020;105(5):262-9. https://doi.org/10.1136/archdischild-2018-316603
16. Liu Q, Wang ZD, Huang SY, Zhu XQ. Diagnosis of toxoplasmosis and typing of Toxoplasma gondii. Parasit vectors. 2015; 28;8:292. https://doi.org/10.1186/s13071-015-0902-6
17. Remington JS, Thulliez P, Montoya JG. Recent developments for diagnosis of toxoplasmosis. J Clin Microbiol. 2004;42(3):941-5. https://doi.org/10.1128/jcm.42.3.941-945.2004
18. Beder D, Taşbent FE. General Features and Laboratory Diagnosis of Toxoplasma gondii Infection. Turkiye Parazitol Derg. 2020;44(2):94-101. https://doi.org/10.4274/tpd.galenos.2020.6634
19. Sepúlveda-Arias JC, Gómez-Marin JE, Bobić B, Naranjo-Galvis CA, Djurković-Djaković O. Toxoplasmosis as a travel risk. Travel medicine and infectious disease. 2014;12(6 Pt A):592-601. https://doi.org/10.1016/j.tmaid.2014.05.007
20. Dhombres F, Friszer S, Maurice P, Gonzales M, Kieffer F, Garel C, et al. Prognosis of fetal parenchymal cerebral lesions without ventriculomegaly in congenital toxoplasmosis infection. Fetal Diagn Ther. 2017;41(1):8-14. https://doi.org/10.1159/000445113
21. Peyron F, L'ollivier C, Mandelbrot L, Wallon M, Piarroux R, Kieffer F, et al. Maternal and congenital toxoplasmosis: diagnosis and treatment recommendations of a French multidisciplinary working group. Pathogens. 2019; 18;8(1):24. https://doi.org/10.3390/pathogens8010024
22. Dunay IR, Gajurel K, Dhakal R, Liesenfeld O, Montoya JG. Treatment of toxoplasmosis: historical perspective, animal models, and current clinical practice. Clin Microbiol Rev. 2018; 12;31(4):e00057-17. https://doi.org/10.1128/cmr.00057-17
23. Rostami A, Riahi SM, Contopoulos-Ioannidis DG, Gamble HR, Fakhri Y, Shiadeh MN, et al. Acute Toxoplasma infection in pregnant women worldwide: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2019;14;13(10):e0007807. https://doi.org/10.1371/journal.pntd.0007807
24. Borkakoty B, Biswas D, Jakharia A, Mahanta J. Seroprevalence of Toxoplasma gondii among pregnant women in Northeast India. J Assoc Physicians India. 2016;64(10):24-8. PMID: 27766799
25. Malatyalı E, Yıldız İ, Tilekliođlu E, Ertabaklar H, Ertuğ S. Retrospective Analysis of T.gondii Serology Results from Adnan Menderes University Faculty of Medicine Parasitology Laboratory from 2007 to 2017. Turkiye Parazitol Derg. 2019;28;43(1):1-4. https://doi.org/10.4274/tpd.galenos.2018.6098

26. Selek MB, Bektöre B, Baylan O, Özyurt M. Serological Investigation of Toxoplasma gondii on Pregnant Women and Toxoplasmosis Suspected Patients Between 2012-2014 Years on a Tertiary Training Hospital. Turkiye Parazitol Derg. 2015;39(3):200-4. https://doi.org/10.5152/tpd.2015.3961
27. Prusa AR, Kasper DC, Pollak A, Gleiss A, Waldhoer T, Hayde M. The Austrian toxoplasmosis register, 1992-2008. Clin Infect Dis. 2015;15;60(2):e4-e10. https://doi.org/10.1093/cid/ciu724
28. SYROCOT (Systematic Review on Congenital Toxoplasmosis) study group, Thiébaut R, Leproust S, Chêne G, Gilbert R. Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients' data. Lancet. 2007;13;369(9556):115-22. https://doi.org/10.1016/s0140-6736(07)60072-5
29. Olariu TR, Press C, Talucod J, Olson K, Montoya JG. Congenital toxoplasmosis in the United States: clinical and serologic findings in infants born to mothers treated during pregnancy. Parasite. 2019;26:13. https://doi.org/10.1051/parasite/2019013
30. Hotop A, Hlobil H, Gross U. Efficacy of rapid treatment initiation following primary Toxoplasma gondii infection during pregnancy. Clin Infect Dis. 2012;54(11):1545-52. https://doi.org/10.1093/cid/cis234
31. İnceboz T, Korkmaz M, Dirim Erdoğan D, İnceboz Ü. Acute Toxoplasmosis During Pregnancy: A Hard Call. Turkiye Parazitol Derg. 2021;45(3):223-6. https://doi.org/10.4274/tpd.galenos.2021.43043
32. Cortina-Borja M, Tan HK, Wallon M, Paul M, Prusa A, Buffolano W, et al. Prenatal treatment for serious neurological sequelae of congenital toxoplasmosis: an observational prospective cohort study. PLoS Med. 2010;12;7(10):e1000351. https://doi.org/10.1371/journal.pmed.1000351
33. Hutson SL, Wheeler KM, McLone D, Frim D, Penn R, Swisher CN, et al. Patterns of hydrocephalus caused by congenital Toxoplasma gondii infection associate with parasite genetics. Clinical Infectious Diseases. 2015;61, 1831-4. https://doi.org/10.1093/cid/civ720
34. Codaccioni C, Picone O, Lambert V, Maurice P, Pomar L, Winer N, et al. Ultrasound features of fetal toxoplasmosis: a contemporary multicenter survey in 88 fetuses. Prenatal Diagnosis. 2020;40(13):1741-52. https://doi.org/10.1002/pd.5756