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# Seroprevalence of *Toxoplasma, Rubella* and *Cytomegalovirus* in Women of Fertility Age in Our Region

## *Bölgemizde Doğurganlık Çağındaki Kadınlarda Toksoplazma, Rubella ve Sitomegalovirüs Seroprevalansı*

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## ABSTRACT

**Objective:** *Toxoplasma gondii* (*T. gondii*), *Rubella* and *Cytomegalovirus* (CMV) infections can cause severe morbidity in the fetus when transmissed during pregnancy. In our study, it was aimed to examine the seropositivity rates for *T. gondii*, *Rubella* and CMV infections in women of childbearing age who applied to our hospital.

**Methods:** Anti-*Toxoplasma* IgG, anti-*Toxoplasma* IgM, anti-*Rubella* IgG, anti-*Rubella* IgM, anti-CMV IgG and anti-CMV were studied in women of childbearing age (18-49 years old) who applied to our hospital's outpatient clinics between January 2018 and December 2020. The tests were performed in our microbiology laboratory using the ELISA method on Architect i2000 (Abbott, USA) and COBAS e601 (Roche, Germany) devices.

**Results:** As a result of the data obtained, the percentages of IgM and IgG positivity for anti-*Toxoplasma* were calculated as 1.4% and 30.9%, respectively. Anti-*Rubella* IgM positivity was 0.7%, anti-*Rubella* IgG positivity was 91%, anti-CMV IgG positivity was 98.8%, and anti-CMV IgM positivity was 2%.

**Conclusion:** Having its own seroprevalence for each region has is important in terms of planning pregnancy screenings. The seropositivity rates in our region are in line with other studies in the country. Since CMV seropositivity is very high in the population and there is no effective treatment or vaccine, screening may not be not necessary. *T. gondii* and *Rubella* screenings can be recommended due to the lower immunity rates and the availability of vaccine and treatment options.

**Keywords:** *Citomegalovirus*, childbearing age, pregnancy, *Rubella*, seroprevalence, *Toxoplasma gondii*

## ÖZ

**Amaç:** *Toxoplasma gondii* (*T. gondii*), *Rubella* ve *Cytomegalovirüs* (CMV) enfeksiyonları gebelikte geçirildiğinde fetüste ağır tablolara sebep olabilmektedir. Çalışmamızda, hastanemize başvuran doğurganlık çağındaki kadınların *T. gondii, Rubella* ve CMV enfeksiyonlarına yönelik seropozitiflik oranlarının incelenmesi amaçlanmıştır.

**Yöntemler:** Çalışmamıza hastanemiz polikliniklerine Ocak 2018-Aralık 2020 tarihleri arasında başvuran, doğurganlık çağındaki (18-49 yaş) kadınlarda çalışılması istenen anti-Toxo IgG, anti-Toxo IgM, anti-*Rubella* IgG, anti-*Rubella* IgM, anti-CMV IgG ve anti-CMV IgM tetkikleri dahil edilmiştir. Testler mikrobiyoloji laboratuvarımızda ELISA yöntemiyle Architect i2000 (Abbott, ABD) ve COBAS e601 (Roche, Almanya) cihazlarında çalışılmıştır.

**Bulgular:** Elde edilen veriler sonucunda anti-Toxo için IgM ve IgG pozitiflik yüzdeleri sırasıyla 1.4 ve 30.9 olarak hesaplandı. Anti-*Rubella* IgM pozitifliği %0.7, anti-*Rubella* IgG pozitifliği %91, anti-CMV IgM pozitifliği %2, anti-CMV IgG pozitifliğinin ise %98.8 olduğu tespit edildi.

**Sonuç:** Her bölgenin kendi seroprevalansına sahip olması gebelik taramalarının planlanması açısından önem taşımaktadır. Bölgemizdeki seropozitiflik oranları ülkedeki diğer çalışmalarla uyumludur. Toplumda CMV seropozitifliği çok yüksek olduğu ve etkili bir tedavisi ya da aşısı olmadığı için taranması gerekli olmayabilir. *T. gondii* ve *Rubella* taramaları ise hem bağışıklık oranlarının daha düşük olması hem de aşı ve tedavi seçeneklerinin var olması sebebiyle önerilebilir.

**Anahtar Kelimeler:** *Cytomegalovirüs*, doğurganlık çağı, gebe, *Rubella*, seroprevalans, *Toxoplasma gondii*

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Türkiye PARAZİTOLOJİ Dergisi

## INTRODUCTION

*Toxoplasma*, *Rubella*, and *Cytomegalovirus* (CMV) infections are a group of infections that are common in the community, mostly asymptomatic, but can cause severe symptoms and postpartum sequelae in the fetus if experienced during pregnancy (1). Since these infections are difficult to distinguish from each other clinically, their diagnosis is mostly based on serological detection of specific antibodies. IgM and IgG-type antibody levels determined as a result of these serological tests provide information about exposure to the agent and whether the infection is acute or past (2,3).

Although there is no consensus about routine *Toxoplasma, Rubella* and CMV screening in pregnant women in our country, the opinion that screening for CMV and *Toxoplasma* antibodies is not necessary in regions where the incidence is not high is more common (4,5). Unlike *Toxoplasma* and CMV, *Rubella* screening allows vaccination in case of detection of seronegativity. It is recommended more frequently (6). The low cost-effectiveness of the tests used for screening makes it difficult to reach consensus on the necessity of screening (7). Knowing the regional seropositivity rates is a guide for clinicians in making the screening decision (8).

In this study, we aimed to discuss the necessity of screening pregnant women by retrospectively examining the antibody levels against *Toxoplasma, Rubella* and CMV in women of childbearing age (15-49 years) who applied to our polyclinics from our region and constitute the risk group for intrauterine infections.

## METHODS

In our study, 3143 anti-*Toxoplasma* IgG, 4162 anti-*Toxoplasma* IgM, 3442 anti-*Rubella* IgG and 4142 anti-*Rubella* IgM, 4142 anti-*Rubella* IgM, 3108 anti-CMV IgG and 4139 anti-CMV IgM tests were requested from women aged 18-49 who applied to Recep Tayyip Erdoğan University Training and Research Hospital polyclinics between 01.01.2018 and 31.12.2020 with various complaints and retrospectively analyzed. Only the first examinations of patients with more than one request were included in the study.

Serum samples obtained from the blood of the patients after centrifugation at 4000 rpm for 10 minutes were analyzed by macro ELISA test. The ELISA tests, which were evaluated, were studied with the Architect i2000 (Abbott, USA) device between 01.01.2018 and 15.01.2020, and with the COBAS e601 (Roche, Germany) device between 16.01.2020-31.12.2020. The results were evaluated according to the reactive, non-reactive and borderline ranges accepted for each test, taking into account the kit contents and company recommendations (Table 1, 2).

### Statistical Analysis

SPSS (Statistical Package of Social Sciences, version 26.0, IBM Corp., Armonk, NY, USA) package program was used in the statistical analysis of the study.

For this study, 2022/71 approval was obtained from the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (date: 29.03.2022) and all steps of our study were carried out in accordance with the Declaration of Helsinki.

## RESULTS

The mean age of the women whose examinations were included in the study was found to be 32.04. Of the 4162 anti-*Toxoplasma* IgM tests examined, 58 (1.4%) were reactive and 4097 (98.4%) were non-reactive. Of the 3143 tests examined for anti-*Toxoplasma* IgG, 971 (30.9%) were observed as reactive and 2060 (65.5%) as non-reactive.

Of the 4142 tests whose anti-*Rubella* IgM levels were studied, 31 (0.7%) were reactive and 4074 (98.4%) were non-reactive. Of the 3442 tests examined for anti-*Rubella* IgG levels, 3131 (91%) were found to be reactive and 162 (4.7%) as non-reactive.

For anti-CMV IgM, 4139 samples were examined and 82 (2%) were reactive and 4016 (97%) were non-reactive. In anti-CMV

**Table 1.** Reference ranges of Roche ELISA COBAS E601 device

| Test name | Unit | Reactive | Borderline | Non-reactive |
|---|---|---|---|---|
| Anti-*Toxoplasma* IgM | COI | ≥1 | 1>-≥0.8 | <0.8 |
| Anti-*Toxoplasma* IgG | IU/mL | ≥3 | 3>-≥1 | <1 |
| Anti-*Rubella* IgM | COI | ≥1 | 1>-≥0.8 | <0.8 |
| Anti-*Rubella* IgG | IU/mL | ≥10 | - | <10 |
| Anti-CMV IgM | COI | ≥1 | 1>-≥0.7 | <0.7 |
| Anti-CMV IgG | IU/mL | ≥1 | 1>-≥0.5 | <0.5 |

CMV: *Cytomegalovirus*

**Table 2.** Reference ranges of the Architect i2000 SR (ABBOTT) device

| Test name | Unit | Reactive | Borderline | Non-reactive |
|---|---|---|---|---|
| Anti-*Toxoplasma* IgM | IU/mL | ≥0.6 | 0.6>-≥0.5 | <0.5 |
| Anti-*Toxoplasma* IgG | IU/mL | ≥3 | 3>-≥1.6 | <1.6 |
| Anti-*Rubella* IgM | IU/mL | ≥1.6 | 1.6>-≥1.2 | <1.2 |
| Anti-*Rubella* IgG | IU/mL | ≥10 | 10>-≥5 | <5 |
| Anti-CMV IgM | IU/mL | ≥1 | 1>-≥0.85 | <0.85 |
| Anti-CMV IgG | AU/mL | ≥6 | - | <6 |

CMV: *Cytomegalovirus*

IgG levels, the number of reactivity and non-reactivity in 3108 samples was 3070 (98.8%) and 38 (1.2%), respectively (Table 3).

## DISCUSSION

*Toxoplasma*, *Rubella* and CMV infections during pregnancy may not cause any problems in the fetus, and may cause severe clinical pictures that may result in intrauterine death (9). Especially infections in the first trimester increase fetal exposure and cause perinatal morbidity and mortality (10). Women of childbearing age constitute the risk group for these infections. The incidence of these infections may vary depending on many parameters such as nutrition and hygiene habits, contact with animals, socio-economic level, climate and environmental conditions (11). Although they are common all over the world and easy to diagnose, there are different opinions about the routine screening of these infections in pregnant women (12).

Diagnosis of *Toxoplasmosis*, *Rubella* and CMV infections is made by looking at the IgM and IgG type antibody levels detected by ELISA method at the first stage (4). Routine screening in pregnant women is not recommended in the Prenatal Care Guide of the Ministry of Health (13). Again, they are not among the infections recommended by the American Society of Gynecology and Obstetrics and the World Health Organization (WHO) to be routinely screened in the first trimester (4,14). However, there are countries that include these infections in the routine screening program in pregnant women (4). The reasons for the controversy over the necessity of these screenings may be the cost of the tests and the fact that antibody levels in the population differ between countries and even provinces.

In our study, anti-*Toxoplasma* IgM, anti-*Toxoplasma* IgG, anti-*Rubella* IgM, anti-*Rubella* IgG, anti-CMV IgG and anti-CMV IgM, requested from pregnant women of childbearing age who applied to our hospital, which is a tertiary center in Rize province, for three years (2018-2020). We found IgM and IgG positivity percentages for anti-*Toxoplasma* as 1.4 and 30.9, respectively. Anti-*Rubella* IgM positivity was 0.7%, anti-*Rubella* IgG positivity was 91%. We found anti-CMV IgG positivity as 98.8% and anti-CMV IgM positivity as 2%. These rates are consistent with the data in a similar study conducted in our institution in previous years (15). It also shows parallelism with the rates in similar studies in our country (15-19).

The causative agent of *Toxoplasmosis* is the parasite *T. gondii* (20). Congenital *Toxoplasmosis*, which may be caused when transmitted during pregnancy, is 90% asymptomatic at birth, but later on, symptoms appear and the patient presents with the triad of hydrocephalus, intracranial infection, and chorioretinitis (21). When detected in pregnant women, spiramycin, a macrolide antibiotic, can be used to prevent transplacental transmission to the fetus, and this treatment allows the fetus to be protected from the severe clinical manifestations of congenital toxoplasmosis (22).

The frequency of *Toxoplasma* infections varies in a wide range, such as 10% to 90% between different countries, depending on food habits, social habits (feeding cats, etc.) and hygiene rules (4). In a study that compiled the data of more than one billion pregnant women worldwide, it was reported that the *Toxoplasma* seropositivity was 33.8% (23). Data in our country vary between regions. Anti-*Toxoplasma* IgG seropositivity is higher in Southeastern Anatolia Region, where dishes such as raw meatballs are widely consumed, compared to western provinces (10). In our study, we found anti-*Toxoplasma* IgG positivity as 30.9% and anti-*Toxoplasma* IgM positivity as 1.4% in women of childbearing age in Rize province. A study conducted our country, it was reported that anti-*Toxoplasma* IgM was positive in 1.3% of 3607 patients and in another study, it was positive in 1.8% of 5013 patients which are compatible with our study (18,19).

*Toxoplasma* screening can be recommended due to the fact that there is preventive treatment during pregnancy, there are preventive measures and the seroprevalence of anti-*Toxoplasma* IgG type antibodies is not very high in our society. Pregnant women who are found to be seronegative as a result of screening should be advised to be informed about protective measures (9).

*Rubella* infection is primarily a childhood disease, but can also occur in adults (24). Adults without immunity are at risk for *Rubella* infection, and especially if pregnant women in the first trimester have this infection, congenital *Rubella* syndrome can be seen in which the fetus is severely affected (16). In this syndrome, severe conditions such as retardation in fetal development, cataract, deafness, congenital heart diseases and microcephaly may ocur (17). It is estimated that 110,000 cases of congenital rubella syndrome occur in the world each year (8).

Since *Rubella* can be transmitted very easily and spread very quickly among unvaccinated children, and it is included in the routine vaccination program, the level of immunity in our society is high (25). In a meta-analysis compiling 16-year data, the rate of *Rubella* seronegativity in women was reported as 9.5% in the world (26). In similar studies conducted in our country, the anti-*Rubella* IgG positivity rates in different time periods ranged from 86% to 97% (18). In our study, we found the anti-*Rubella* IgG positivity rate as 91% and the anti-*Rubella* IgM positivity rate as 0.7% in the Rize region.

There is not enough evidence that screening is unnecessary in countries with low *Rubella* seropositivity, and there are also resources recommending screening for *Rubella* antibodies, especially in countries with low incidence, as it provides postnatal

**Table 3.** Distribution of the results obtained from the three-year data

| Test | Non-reactive (n %) | Borderline (n %) | Reactive (n %) | Total (n %) |
|---|---|---|---|---|
| Anti-*Toxoplasma* IgM | 4097 (98.4) | 7 (0.2) | 58 (1.4) | 4162 |
| Anti-*Toxoplasma* IgG | 2060 (65.5) | 112 (3.6) | 971 (30.9) | 3143 |
| Anti-*Rubella* IgM | 4074 (98.4) | 37 (0.9) | 31 (0.7) | 4142 |
| Anti-*Rubella* IgG | 162 (4.7) | 149 (4.3) | 3131 (91) | 3442 |
| Anti-CMV IgM | 4016 (97.0) | 41 (1.0) | 82 (2.0) | 4139 |
| Anti-CMV IgG | 38 (1.2) | 0 (0) | 3070 (98.8) | 3108 |

CMV: *Cytomegalovirus*

vaccination if *Rubella* seronegativity is detected during screening (4). *Rubella* seropositivity rate is over 90% in our region, but these rates should not be interpreted as unnecessary screening. Because the WHO determined the safe seronegativity rate for *Rubella* as 95% and above (27). According to the European Centre for Disease Prevention and Control, 25 countries in EU/EEA involved in the surveillance system for congenital *Rubella* and five of them have separate system for *Rubella* in pregnancy. These countries are Denmark, France, Malta, Iceland and Italy (28).

CMV is the most common of the perinatal infectious agents (29). While it is mostly asymptomatic in non-pregnant individuals, it can cause perinatal infections in pregnant women and as a result, problems such as hearing loss, growth retardation, microcephaly, intracerebral calcifications, cognitive disorders, thrombocytopenia, anemia, jaundice, hepatosplenomegaly, chorioretinitis in newborns (29).

In a study in which global data were compiled, CMV seropositivity was determined as 83% worldwide, and our country was reported as the country with the highest seropositivity rate in the study with 97% (30). In the same study, the European average was determined as 66% and the Eastern Mediterranean average as 90% (30). The percentage of CMV seropositivity in our country varies between 90.4% and 99.8%, as stated in various studies (8). We also found the anti-CMV IgG positivity rate as 98.8% and the anti-CMV IgM seropositivity as 1.2% in our region. These rates are in parallel with the literature. In our study, anti-CMV IgG positivity was found to be high (98.8%) in line with the literature (4,18). All these reasons suggest that routine screening for CMV antibodies is not effective.

## CONCLUSION

There is no consensus on the screening of *Toxoplasma, Rubella* and CMV infections in pregnant women. Each physicians should make the screening decision by looking at the seropositivity rates in their own region. For this reason, it is important for each region to have it his own data for effective scanning.

Screening should not be seen as the only option in the fight against these infections. Awareness should be raised about prevention methods, transmission routes and vaccines.

The data we obtained are compatible with other studies conducted throughout country. Our study is important in that it is the first study to compile these data from the province of Rize.

### * Ethics

**Ethics Committee Approval:** For this study, 2022/71 approval was obtained from the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (date: 29.03.2022) and all steps of our study were carried out in accordance with the Declaration of Helsinki.

**Informed Consent:** Not required.

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### * Authorship Contributions

Concept: İ.B., E.K., D.A., U.B.K., Design: İ.B., Ö.F.D., Y.E.İ., U.B.K., Data Collection or Processing: E.K., Ö.F.D., D.A., U.B.K., Analysis or Interpretation: İ.B., E.K., D.A., Y.E.İ., Literature Search: Ö.F.D., D.A., Y.E.İ., Writing: İ.B., E.K., Ö.F.D.

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