

# Evaluation of Toxoplasma, Rubella, and Cytomegalovirus serological results in women of childbearing age

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## SUMMARY

**OBJECTIVE:** This study aimed to determine the rates of IgG and IgM antibodies against cytomegalovirus, rubella, and *Toxoplasma gondii* (all of which may cause congenital infections) in women of childbearing age who were admitted to Bolu Abant İzzet Baysal University Training and Research Hospital.

**METHODS:** Between January 2015 and December 2017, *Toxoplasma gondii*, rubella, and cytomegalovirus IgM and IgG antibody levels were studied using the ELISA method (Architect i2000SR, Abbott, Germany) in patients aged 15 to 45 who attended the obstetrics and gynecology outpatient clinics. *Toxoplasma gondii* and cytomegalovirus IgG avidity levels were analyzed retrospectively.

**RESULTS:** A total of 13.470 tests were conducted in the laboratory. Seropositivity percentages of IgM antibodies were found to be 1.3%, 0.5%, and 1.6% for *Toxoplasma* (n = 3607), rubella (n = 3931), and cytomegalovirus (n = 3795), respectively. The seropositivity percentages of IgG antibodies were 22%, 94.2%, and 98.2% for *Toxoplasma* (n = 702), rubella (n = 693), and cytomegalovirus (n = 679), respectively. Primary infection (acute, recently acquired) was found in 7 (35%) patients with low *Toxoplasma* IgG avidity. One (3%) patient with low cytomegalovirus IgG avidity had a primary infection.

**CONCLUSION:** *Toxoplasma gondii* seronegativity was found to be high in the region. Therefore, screening women of childbearing age may be important for the prevention of congenital infections caused by *Toxoplasma gondii*.

**KEYWORDS:** *Toxoplasma*. Rubella. Cytomegalovirus. Immunoglobulin G. Immunoglobulin M.

## INTRODUCTION

*Toxoplasma gondii*, rubella, and cytomegalovirus (CMV) are microorganisms that can cause intrauterine infections and congenital anomalies in the fetus if they are transmitted during pregnancy<sup>1</sup>. In developing countries, infections that cause congenital anomalies are one of the most predominant causes of perinatal morbidity and mortality<sup>2</sup>. *Toxoplasma gondii* is a parasite that can cause hydrocephalus, intracranial

calcifications, and chorioretinitis in fetus<sup>3</sup>. It is known as congenital toxoplasmosis if it is passed from mother to fetus during pregnancy<sup>3</sup>. Rubella is a virus that can cause congenital rubella infection, which can lead to low birth weight, deafness, myopia, cataracts, glaucoma, congenital heart disease, and intellectual disability in the fetus<sup>4</sup>. Finally, CMV is one of the largest viruses of the herpesviridae family, a common

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double-stranded DNA genome<sup>5</sup>. Mothers who have a CMV infection during pregnancy may experience sequelae such as mental retardation, chorioretinitis, and cerebral calcification in their fetuses<sup>6</sup>.

The only way to prevent the risks of such infections during pregnancy is by serological screening of women of childbearing age. Informing prospective mothers in the risk group as a result of serological screening will help prevent congenital infections during pregnancy. Serological methods are used in the diagnosis of these infections, which can cause similar clinical manifestations. The IgG and IgM antibodies detected in the TORCH (*Toxoplasma gondii*, rubella, CMV, and HSV) group of microorganisms in human serum can assist in the diagnosis of acute, past, or recurrent infection<sup>7,8</sup>. This study aimed to determine the seroprevalence of *T. gondii*, rubella, and CMV infections through antenatal screening in the Bolu region, Turkey.

## METHODS

The study was approved by the Bolu Abant İzzet Baysal University Medical Faculty Human Ethics Committee (2018/278). *Toxoplasma*, rubella, and CMV antibodies were investigated in the serum samples of patients between the ages of 15 to 45 from January 2015 to December 2017. Positive serum samples were examined retrospectively.

*Toxoplasma gondii*, rubella, and CMV IgM and IgG antibody tests were performed using the ELISA method (Architect i2000SR, Abbott, Germany). Only the first result of each patient was considered; other repetitive results of the same patient were not included in the study. All positive or borderline IgM test results were checked twice. Specific IgM and IgG test results were interpreted as negative, borderline, or positive. *Toxoplasma* and CMV IgG avidity test results were evaluated as low (<30%), borderline (30% to 40%), or high (>40%) on the avidity index according to the manufacturer's instructions. IgG avidity tests are methods

used to determine whether the infection is primary (acute, recently acquired) or secondary (previously passed and immunized). In primary infections, the agent-specific IgG avidity is low, but in secondary infections it is high.

## RESULTS

A total of 13.470 tests were conducted in the laboratory. Anti-*Toxoplasma* IgM was positive in 50 of the 3607 serum samples (1.3%) in which *Toxoplasma* IgM was examined. Anti-rubella IgM was found to be positive in 22 of 2231 serum samples (0.5%). Anti-CMV IgM was positive in 64 of 3795 serum samples (1.6%) of CMV IgM. Anti-CMV IgG was positive in 669 of 679 serum samples (98.2%) of CMV IgG. (Table 1).

Low avidity was detected in seven patients (35%) according to the avidity test performed on 20 patients with positive *Toxoplasma* IgM. High avidity was detected in eight patients (40%) according to the avidity test performed for *Toxoplasma*. One (3%) of the 33 patients with positive CMV IgM had low avidity. High avidity was detected in 32 patients (97%) according to the avidity test performed for CMV. Seropositivity rates for *Toxoplasma* (n = 702), rubella (n = 693), and CMV (n = 679) based on age group are shown in Table 2.

## DISCUSSION

TORCH group infections can affect all age groups, but the transmission of these infections to the fetus during pregnancy is of growing concern, as these infections cause congenital anomalies in the fetus<sup>9</sup>. Conducting these screening tests during pregnancy or early pregnancy contributes to the early diagnosis of congenital anomalies that may occur in the fetus and also determines the regional seroprevalence<sup>10</sup>.

The seroprevalence of *Toxoplasma gondii* in the world may vary depending on a variety of factors, including dietary habits, lifestyle, socioeconomic

**TABLE 1.** THE RATES OF IGM AND IGG FOR RUBELLA, TOXOPLASMA GONDII, AND CYTOMEGALOVIRUS (CMV) INFECTIONS.

Test	Negative (n %)	Borderline (n %)	Positive (n %)	Total
<i>Toxoplasma</i> IgM	3544 (98.3)	13 (0.4)	50 (1.3)	3607
Rubella IgM	3893 (99)	16(0.4)	22(0.5)	3931
CMV IgM	3697(97.5)	34(0.9)	64 (1.6)	3795
<i>Toxoplasma</i> IgG	538 (76.6)	9 (1.3)	155 (22.1)	702
Rubella IgG	17(2.4)	23(3.3)	653(94.2)	693
CMV IgG	12 (1.8)	0	667 (98.2)	679

status, and geographical conditions<sup>11</sup>. Some serological studies of *Toxoplasma gondii* in Turkey and other countries are shown in Table 3<sup>12-18</sup>. Indian studies have shown varied results, with seroprevalence ranging from 11% to 55%<sup>19</sup>. In the present study, *Toxoplasma* IgM was 1.3%, and *Toxoplasma* IgG was 22%; these levels were lower than those found by the studies conducted abroad (especially in India and Saudi Arabia). In Turkey, *Toxoplasma* IgM and IgG levels were similar, except for those found by the study in Kilis. The high seropositivity in the Kilis study may have been due to the consumption of undercooked meat and raw vegetables.

Rubella is a common viral infection that is frequently seen in children and young adults. In women of childbearing age, this infection is critical; it causes congenital rubella syndrome. In countries using the rubella vaccine (MMR) in their national vaccination programs, congenital rubella infections are less common<sup>20</sup>. For example, in the routine vaccination program organized by the Ministry of Health in Turkey,

rubella vaccination is performed in the first month of childhood and in the first grade of primary school. In studies conducted in different regions of Turkey, rubella seropositivity has been reported as ranging between 86.5% and 96.2%<sup>11,19,21-23</sup>. In the present study, the rate of rubella IgG was 94.2%. According to this ratio, and considering the fact that no vaccination information was obtained from the women of childbearing age, seronegativity has been found for women in Turkey. Therefore, vaccination will be beneficial, as these women are at risk for congenital rubella syndrome.

CMV can be transmitted via vertical and horizontal contact, blood transfusion, and organ transplants. Seroprevalence increases with age and differs according to geographical regions and socioeconomic level<sup>5</sup>. While seropositivity rates in developed countries range from 50% to 60%, rates in developing countries are between 90% and 100%<sup>21</sup>. The results of serological studies of CMV in Turkey and other countries are shown in Table 4<sup>4,6,11,23</sup>. In the present study, the rate

**TABLE 2.** DISTRIBUTION OF TOXOPLASMOSIS, CYTOMEGALOVIRUS (CMV), AND RUBELLA SEROPOSITIVITY ACCORDING TO AGE GROUPS

Age (years)	Toxo IgG (n = 702)			CMV IgG (n = 679)			Rubella IgG (n = 693)		
	Positive	Negative	Borderline	Positive	Negative	Borderline	Positive	Negative	Borderline
<20	4(%28.6)	10(%71.4)	-	8(%72.7)	3(%27.3)	-	8(%88.9)	-	1(%11.1)
20-30	71(%19.2)	292(%78.9)	7(%1.9)	346(%99.9)	3(%0.1)	-	348(%94.5)	8(%2.2)	12(%3.3)
31-40	75(%24.4)	230(%74.9)	2(%0.7)	290(%97.9)	6(%2.1)	-	280(%92.7)	16(%5.3)	6(%2)
>40	4(%40)	6(%60)	-	23(%100)	-	-	17(%70.8)	3(%12.5)	4
Total	155(22.1)	538(76.6)	9(1.3)	667(98.2)	12(1.8)	-	653(94.2)	17(2.4)	23(3.3)

**TABLE 3.** COMPARISON OF STUDIES EVALUATING TOXOPLASMA SEROPREVALENCES FROM DIFFERENT REGIONS OF TURKEY AND OTHER COUNTRIES.

Study	Location, setting of the study	Test	Result(%)
Sen et al. <sup>12</sup>	India	<i>Toxoplasma</i> IgM	19.4%
Yasodhara et al. <sup>13</sup>	India	<i>Toxoplasma</i> IgM	13.1%
Khurana et al. <sup>14</sup>	India	<i>Toxoplasma</i> IgG, IgM	15.3% IgG, 3% IgM
Ghazi et al. <sup>15</sup>	Saudi Arabia	<i>Toxoplasma</i> IgG	35.6%
Demiroğlu et al. <sup>16</sup>	Kilis/Turkey	<i>Toxoplasma</i> IgG, IgM	63.4% IgG, 4% IgM
Aşci et al. <sup>17</sup>	Afyon/Turkey	<i>Toxoplasma</i> IgG, IgM	23, 6% IgG, 1.9% IgM
Sirin et al. <sup>18</sup>	Izmir/Turkey	<i>Toxoplasma</i> IgG, IgM	32.3% IgG, 1.9% IgM

**TABLE 4.** COMPARISON OF STUDIES EVALUATING CMV SEROPREVALENCES FROM DIFFERENT REGIONS OF TURKEY

Study	Location, setting of the study	Test	Result(%)
Efe et al. <sup>4</sup>	Van/Turkey	CMV IgG, IgM	99.5% IgG, 1.7% IgM
Tamer et al. <sup>23</sup>	Kocaeli/Turkey	CMV IgG, IgM	96.4% IgG, 0.7% IgM
Ocak et al. <sup>11</sup>	Hatay/Turkey	CMV IgG, IgM	94.9% IgG, 0.4% IgM
Bakacak et al. <sup>6</sup>	Kahramanmaras/Turkey	CMV IgG, IgM	99.3% IgG, 3.2% IgM

of CMV IgG was 98.2% and IgM was 1.6%. The highest CMV IgG results of studies conducted in Turkey was found by Efe et al<sup>4</sup>. The high seropositivity in this study indicates that the risk of primary infection due to crowded living conditions in our region may be high. Therefore, screening CMV IgG and IgM antibodies in women of child bearing age will prevent the risk of CMV congenital infection in the future.

Avidity tests are used to differentiate whether an infection is a primary infection, re-infection, or secondary (pre-established and immunocompromised) infection. In primary infections, the specific IgG avidity (antigen-binding force) is low, while it is high in secondary infections<sup>24</sup>. In this study, the number of positive patients with *Toxoplasma* IgM/G was 50, and the number of positive patients with CMV IgM/G was 64. However, the avidity test counts were 20 for *Toxoplasma* IgG avidity and 33 for CMV IgG avidity. In this study, *Toxoplasma* IgG was found to have a low avidity of 35%, and CMV IgG had a low avidity of 3%. In this study, low avidity detection in CMV IgG and *Toxoplasma* IgG avidity tests shows that there may still be acute CMV infections in our region. Therefore, it is important to evaluate avidity tests in women of childbearing age to differentiate between acute, past, and recurrent infections. Previous avidity studies in this country have been limited. Şimşek et al.<sup>10</sup> found that *Toxoplasma* IgG avidity was 27% (low) and CMV IgG was 27% (low). In the present study, CMV IgG avidity values were lower, and *Toxoplasma* IgG avidity values were similar.

This study faced a few limitations. *Toxoplasma*, rubella, and CMV IgG and IgM test numbers were not studied equally. For example, the avidity IgG test was not studied in all patients with *Toxoplasma* and CMV IgG/M positivity. Another important limitation was that the vaccination history of the patients was unknown. In addition, the patients' antibody levels were tested only at two years. The number of seropositive patients would have been higher if the study had been conducted over a longer period of time.

## CONCLUSION

In conclusion, this screening could be an effective approach for women of childbearing age due to the high rate of *Toxoplasma gondii* seronegativity among women in Turkey. Finally, the high seroprevalence of these agents, in our society, calls for preventive strategies such as reproductive hygiene and immunization to circumvent the otherwise inevitable fetal outcomes. This study showed that the seropositivity of rubella and CMV are similar to the results found by other studies conducted in this country.

## Author contributions

FA, MB collected the data; MB, MGK reviewed the literature; FA designed the study; FA wrote the manuscript; FA, MB, MGK approved the final version of the manuscript.

## RESUMO

**OBJETIVO:** O objetivo deste estudo foi determinar as taxas de anticorpos IgG e IgM contra citomegalovírus, rubéola e *Toxoplasma gondii* (todos os quais podem causar infecções congênicas) em mulheres em idade fértil que foram admitidas no Hospital de Pesquisa e Treinamento da Universidade Bolu Abant İzzet Baysal.

**MÉTODOS:** Entre janeiro de 2015 e dezembro de 2017, os níveis de anticorpos IgG e IgM para *Toxoplasma gondii*, rubéola e citomegalovírus foram estudados usando o método Elisa (Architect i2000SR, Abbott, Alemanha) em pacientes de 15 a 45 anos que compareceram a ambulatórios de obstetrícia e ginecologia. Os níveis de avididade de IgG para *Toxoplasma gondii* e citomegalovírus foram analisados retrospectivamente.

**RESULTADOS:** Um total de 13.470 testes foram realizados em laboratório. As porcentagens de soropositividade dos anticorpos IgM foram de 1,3%, 0,5% e 1,6% para *Toxoplasma* (n=3.607), rubéola (n=3.931) e citomegalovírus (n=3.795), respectivamente. As porcentagens de soropositividade dos anticorpos IgG foram 22%, 94,2% e 98,2% para *Toxoplasma* (n=702), rubéola (n=693) e citomegalovírus (n=679), respectivamente. Infecção primária (aguda, adquirida recentemente) foi encontrada em sete (35%) pacientes com baixa avididade para *Toxoplasma* IgG. Um (3%) paciente com baixa avididade para citomegalovírus IgG teve uma infecção primária.

**CONCLUSÃO:** A soronegatividade do *Toxoplasma gondii* foi alta na região. Portanto, testar mulheres em idade fértil pode ser importante para a prevenção de infecções congênicas causadas pelo *Toxoplasma gondii*.

**PALAVRAS-CHAVE:** *Toxoplasma*. Rubéola. Citomegalovírus. Imunoglobulina G. Imunoglobulina M.

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