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Toxoplasma, Rubella and Cytomegalovirus Seroprevalence and Distribution by Age in Pregnant Women in Diyarbakir: Eight Years Experience

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Abstract

Objective: Toxoplasma, rubella and cytomegalovirus (CMV) infections can cause malformations in the fetus, usually in the first three months of pregnancy. In this study, we aimed to examine the distribution of Immunoglobulin M (IgM) type and immunoglobulin G (IgG) type antibodies against toxoplasma, rubella and CMV in pregnant women in XXX over an 8-year period according to age groups.

Methods: Pregnant women aged 15-49 years who applied to our hospital between 2015-2022 were included in this study. IgM and IgG antibodies for toxoplasma, rubella and CMV were studied with the Triturus automatic ELISA (Grifols SA, Barcelona, Spain) system and the Dia. ProDiagnostic Bioprobes (Milan, Italy) brand kit. Relationships between age groups and antibody seropositivity were investigated with the chi-square method at the $p<0.05$ significance level.

Results: IgM and IgG positivity values were 170 (0.8%) and 4455 (35.2%) for toxoplasma, 12 (0.1%) and 8711 (91.2%) for rubella, and 133 (1.5%) for CMV and 5012 (98.7%). While there was a statistically significant difference ($\chi2 = 233.250$, $p = 0.00$) in the distribution of toxoplasma IgG seropositivity according to age groups, there was no significant difference in the distribution of other antibodies.

Conclusion: There was a high rate of CMV and rubella seropositivity in pregnant women in our region. Toxoplasma IgG seropositivity was found to increase with age. However, seronegativity rates were still high. For this reason, pregnant women should continue to be screened, parasite vaccinations of pets should not be neglected, and seronegative pregnant women should stay away from undercooked meat and vegetables.

Keywords: Pregnancy, Seroprevalence, Toxoplasma, Rubella, Cytomegalovirus

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Diyarbakır Şehrindeki Gebe Kadınlarda Toksoplazma, Rubella ve Sitomegalovirüs Seroprevalansı ve Yaşa Göre Dağılımı: 8 Yıllık Deneyim

Öz

Giriş: Toksoplazma, rubella ve sitomegalovirüs (CMV) enfeksiyonları genellikle hamileliğin ilk üç ayında fetüste malformasyonlara neden olabilirler. Bu çalışmada XXX şehrinde 8 yıllık süreçte gebelerde toksoplazma, rubella ve CMV'ye karşı immünglobulin M (IgM) tipi ve immünglobulin G (IgG) tipi antikorların yaş gruplarına göre dağılımını incelemeyi amaçladık.

Yöntemler: Bu çalışmaya 2015-2022 yılları arasında hastanemize başvuran 15-49 yaş arası gebeler dahil edildi. Toksoplazma, rubella ve CMV için IgM ve IgG antikorları, Triturus otomatik ELISA (Grifols SA, Barselona, İspanya) sistemi ve Dia. ProDiagnostic Bioprobes (Milan, İtalya) marka kit ile çalışıldı. Yaş grupları ve antikor seropozitiflikleri arasındaki ilişkiler ki-kare yöntemiyle $p<0,05$ anlamlılık düzeyinde araştırıldı.

Bulgular: IgM ve IgG pozitiflikleri toksoplazma için 170 (%0,8) ve 4455 (%35,2), rubella için 12 (%0,1) ve 8711 (%91,2), CMV için ise 133 (%1,5) ve 5012 (%98,7) idi. Yaş gruplarına göre toksoplazma IgG seropozitifliğinin dağılımında istatistiksel olarak anlamlı ($\chi 2$ = 233,250, p = 0,00) farklılık bulunurken, diğer antikorların dağılımında anlamlı bir farklılık yoktu.

Sonuç: Bölgemizdeki gebelerde yüksek oranda CMV ve rubella seropozitifliği mevcuttu. Toksoplazma IgG seropozitifliğinin yaşla birlikte arttığı bulundu. Ancak seronegatiflik oranları hala yüksekti. Bu sebeple gebelerde tarama yapılmaya devam edilmeli, evcil hayvanların parazit aşıları ihmal edilmemeli, seronegatif gebeler az pişmiş et ve sebzelerden uzak durmalıdır.

Anahtar kelimeler: Gebelik, Seroprevalans, Toxoplasma, Rubella, Sitomegalovirüs.

INTRODUCTION

Toxoplasma, rubella, and cytomegalovirus (CMV) infections can occur in individuals of all ages and are typically without symptoms in the general population. However, when these infections occur in the first trimester of pregnancy, they cause fetal malformations. IgM-type antibodies against toxoplasma, rubella and CMV indicate primary or recurrent infection, while IgG-type antibodies indicate previous infection. After the formation of IgG-type antibodies, IgM-type antibodies may become negative or remain positive for a long time[1].

Toxoplasmosis is an infection caused by Toxoplasma gondii. Ninety percent of infants with congenital toxoplasmosis are asymptomatic in the neonatal period. In the later period, severe clinical situations such as hydrocephalus, intracranial calcifications, chorioretinitis, and mental retardation may develop. To prevent these life-threatening situations, screening and monitoring pregnant women for toxoplasmosis is very important. Although it has a mild course in the mother and in childhood, the rubella virus infection can cause serious fetal problems. CMV infection may cause chorioretinitis, mental retardation, and cerebral calcification in the fetus[2]. Screening pregnant women for toxoplasma, rubella and CMV infections is still a controversial issue. In order to decide whether routine screening for these agents should be performed in the antenatal follow-up of pregnant women in a region, it is very important to know the seropositivity rates in that region.

The aim of our study was to determine the distribution of seropositivity rates of IgM and IgG antibodies of toxoplasma, rubella, and CMV in pregnant women during 8-year period in XXX and its surroundings. There is no study in the literature with such comprehensive data in our region.

METHODS

This study is a retrospective cross-sectional study. The IgM and IgG antibody of toxoplasma (n = 35,049), rubella (n = 21,943), and CMV (n = 13,935) were evaluated by the Triturus automatic ELISA (Grifols SA, Barcelona, Spain) method and the Dia.ProDiagnostic Bioprobes (Milan, Italy) brand commercial test kit in

pregnant women who applied to the obstetrics and gynecology outpatient clinics in our hospital between January 2015 and December 2022. The study population were divided into three groups by age (15–25, 26–35, and 36–49 years).

Statistical Analysis

In this study, categorical variables were shown as numbers and percentages. Comparisons were made between age groups and antibody seropositivity with the chi-square test for statistical significance at the $p < 0.05$ level.

Ethical Approval

The study received ethical authorization from Non-Interventional Clinical Research Ethics Committee of XXX Training and Research Hospital on July 14, 2023, with approval number 463.

RESULTS

Toxoplasma IgM and IgG positivity were detected in 170 (0.8%) and 4455 (35.2%) (Table I); Rubella IgM and IgG positivity were 12 (0.1%) and 8711 (91.2%) (Table II); CMV IgM and IgG positivity were 133 (1.5%) and 5012 (98.7%) (Table III), respectively. Statistically significant differences in the distribution of toxoplasma IgG seropositivity by age group ($\chi2 = 233.250$, $p = 0.00$) have been detected. Toxoplasma IgG seropositivity also increases with age. No significant difference was found in the distribution of other antibodies according to age groups.

The mean age of the pregnant women included in our study was 28.3 years. Table I, Table II, and Table III show the seropositivity rates and statistical evaluation for toxoplasma (n = 35.049), rubella (n = 21.966), and CMV (n = 13.935) in each age group of pregnant women. The number and percentage of seropositivity of IgG antibodies for toxoplasma, rubella, and CMV in the studied serum samples were 4455 (35.2%), 8711 (91.2%), and 5012 (98.7%), respectively. The number and percentage of seropositivity for IgM antibodies were 170 (0.8%), 12 (0.1%), and 133 (1.5%), respectively.

Table I: Distribution of anti-Toxoplasma positivity according to age groups

Age Groups (Year)	Anti-Toxoplasma IgG			Anti-Toxoplasma IgM			Toxoplasma IgG Avidite	
	(-)	(+)	p	(-)	(+)	p	Number of Low Avidity Patients	Number of High Avidity Patients
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)
15-25	3510 (72,0)	1364 (28,0)	0.00 χ^2=233.250	8937 (99,2)	71 (0,8)	0.84 χ^2=0.332	0 (0,0)	71 (100)
26-35	3854 (62,4)	2324 (37,6)		10499 (99,2)	80 (0,8)		28 (35,0)	52 (65,0)
36-49	850 (52,6)	767 (47,4)		2774 (99,3)	19 (0,7)		7 (36,8)	12 (63,2)
Total	**8214 (64,8)**	**4455 (35,2)**		**22210 (99,2)**	**170 (0,8)**		**35 (20,6)**	**135 (79,4)**

According to Table I, a statistically significant ($\chi2 = 233.250$, $p = 0.00$) difference was found in the distribution of toxoplasma IgG seropositivity according to age groups. Toxoplasma IgG seropositivity increased with increasing age. There was no significant difference between age groups in terms of IgM antibodies ($\chi2 = 0.33$, $p = 0.84$).

Table II: Distribution of anti-Rubella positivity according to age groups

Age Groups (Year)	Anti-Rubella IgG			Anti-Rubella IgM		
	(-)	(+)	p	(-)	(+)	p
	n (%)	n (%)		n (%)	n (%)	
15-25	304 (8,4)	3319 (91,6)	0.09 χ^2=4.658	4837 (99,98)	1 (0,02)	0.09 χ^2=4.815
26-35	403 (8,6)	4274 (91,4)		5981 (99,85)	9 (0,15)	
36-49	129 (10,4)	1118 (89,6)		1589 (99,87)	2 (0,13)	
Total	**836 (8,8)**	**8711 (91,2)**		**12407 (99,90)**	**12 (0,10)**	

According to Table II, no significant difference was found between the age groups for both IgG seropositivity ($\chi 2$ =4.658, p = 0.09) and IgM seropositivity ($\chi 2$ =4.815, p = 0.09) for rubella antibodies. Rubella IgG/IgM positivity rate was determined as 5/12 (41.7%).

Table III: Distribution of anti-CMV positivity according to age groups

Age Groups (Year)	Anti-CMV IgG			Anti-CMV IgM		
	(-)	(+)	p	(-)	(+)	p
	n (%)	n (%)		n (%)	n (%)	
15-25	23 (1,3)	1782 (98,7)	0.64 χ^2=0.887	3080 (98,3)	54 (1,7)	0.44 χ^2=1.629
26-35	35 (1,4)	2564 (98,6)		4467 (98,6)	63 (1,4)	
36-49	6 (0,9)	666 (99,1)		1179 (98,7)	16 (1,3)	
Total	**64 (1,3)**	**5012 (98,7)**		**8726 (98,5)**	**133 (1,5)**	

According to Table III, there was no significant difference between the age groups for both IgG seropositivity ($\chi 2$ =0.887, p = 0.64) and IgM seropositivity ($\chi 2$ =1.629, p = 0.44) for CMV antibodies. CMV IgG/IgM positivity rate was determined as 49/133 (36.8%).

Table IV: Antibody seroprevalence in the 15-17 age group

Antibodies	Age Group (15-17 Years)		Toplam (n)
	Positive (%n)	Negative (%n)	
Anti-Toxoplasma IgM	2 (0,72)	418 (38,38)	624 (45,68)
Anti-Toxoplasma IgG	43 (15,52)	161 (14,78)	
Anti-Rubella IgM	0 (0,00)	398 (36,54)	604 (44,22)
Anti-Rubella IgG	183(66,06)	23 (2,11)	
Anti-CMV IgM	1 (0,36)	89 (8,17)	138 (10,10)
Anti-CMV IgG	48 (17,32)	0 (0,00)	
Toplam	**277 (100)**	**1089 (100)**	**1366**

According to Table IV, IgM and IgG antibody positivity was detected in 277 (20,28%) of 1366 patients in the 15-17 age group.

DISCUSSION

Toxoplasma, rubella, and CMV infections transmitted during pregnancy cause serious malformations in the fetus. Therefore, researchers believe that screening should be conducted, especially in endemic areas[3,4]. In order to decide whether to conduct routine screening for congenital infection agents in pregnant women in a region, it is very important to first know the seropositivity rates of that region[5].

Iraz et al.[6] investigated toxoplasma and rubella seroprevalence in pregnant women in Istanbul. In this study conducted in 2015, rubella IgG positivity was 95.8%, while toxoplasma IgG positivity was found to be 35.5%. The rates we found in our study are almost the same as the results of this study.

In 2019, Obut et al.[7] conducted a study to determine the seroprevalence of toxoplasma, rubella, and cytomegalovirus infections in pregnant women in XXX. The study prolonged

approximately two years. IgG antibodies were found to be 34.9%, 94.1%, and 99.2%, respectively. The data from our study were found to be compatible with these data.

Selek et al.[8] conducted a study on the prevalence of toxoplasma infection in pregnant women who were admitted to a tertiary training and research hospital in Istanbul, similar to our hospital. During this two-year study, a 37% prevalence of toxoplasma IgG positivity was observed. The obtained value is compatible with the findings of our study.

Numan et al.[9] conducted a seroprevalence study of toxoplasma, rubella, and CMV in pregnant women admitted to a hospital in Istanbul within two years in 2015. Toxoplasma IgG was found at 31%, Rubella IgG at 94.2%, and CMV IgG at 99.5%. These results are compatible with the data from our study.

In seroprevalence studies conducted in pregnant women in different provinces of Turkey[5,10-12, 14-17], toxoplasma IgG seropositivity rates were found to be 36%, 31.2%, 33.9%, 28.9%, 17.5%, 18.8%, 23.7%, and 31.9%. According to the results of these studies conducted between 2009 and 2019, toxoplasma IgG positivity was found between 17% and 36%. The rate we found (35.2%) is within this range and is consistent with the results of these studies.

When we examined the studies conducted in recent years, in 2020, Avcıoğlu et al.[18] found rubella and CMV IgG seropositivity in pregnant women to be over 90%, similar to other studies, while toxoplasma IgG positivity was 22%. In another study conducted by Tüfekçi et al.[19] in 2022, the toxoplasma IgG rate (20.3%) was similar to the result of this study. In another study conducted in the same year, Taşbent et al.[20] found toxoplasma IgG positivity in pregnant women to be 42.4%.

In another study conducted in 2023 by Bahçeci et al.[21], rubella and CMV IgG seropositivity were found to be above 90%, while toxoplasma IgG positivity was found to be 30.9%, similar to our study.

While seroprevalence studies conducted in various provinces of Turkey were mostly conducted with one or two years of data, our study was conducted with data from a long period of eight years. According to our literature search, there is no seroprevalence study for such a long period in recent years.

Upon reviewing recent global literature, Wang et al.[22] conducted a study in China in 2019 and discovered that the rates of rubella and CMV IgG were once again higher than 90%, while the levels of toxoplasma IgG were found to be 4.3%.

That is the lowest rate in all studies. In 2020, Al-Hakami et al.[23] in Saudi Arabia found the toxoplasma IgG rate to be 27.4%, and in 2022, Nabizadeh et al.[24] in Iran found it to be 26.5%. In 2021, Mocanu et al.[25] in Romania conducted a seroprevalence study in two different groups of pregnant women from 2008–2010 and 2015–2018. It was found that toxoplasma, rubella, and CMV seropositivity rates decreased and sensitivity increased in the second group compared to the first group. Hicks et al.[26] conducted a study in 2023 on pregnant women in and around Guatemala. The prevalence of toxoplasma IgG positivity was 69.7%, while the seropositivity rates for rubella and CMV were 80.8% and 99.5%, respectively. It is noteworthy that this rate is the highest among the other study results.

CONCLUSION

In conclusion, we do not recommend screening, as we found high rates of CMV and Rubella seropositivity in pregnant women in our region. Pre-pregnancy exposure to toxoplasmosis in Diyarbakır is 35.2%. Although we found that toxoplasma IgG seropositivity increases with age, we found that the Toxoplasma gondii seronegativity rate (64.8%) is still high in pregnant women, and we believe that it would

be more appropriate to screen pregnant women against toxoplasma. In addition, we believe that multicenter screening studies representing the whole of Turkey should be conducted.

In addition, it is of great importance that caution be exercised, especially considering that the habit of keeping pets at home has increased in recent years and the Toxoplasma gondii parasite is transmitted from cats. It would be appropriate to emphasize that parasite vaccinations of pets should not be neglected before pregnancy, and seronegative pregnant women should avoid undercooked meat and vegetables.

This study was presented as an electronic poster at the seventh national clinical microbiology congress held on 1-5 November 2023.

Ethics Committee Approval: The study received ethical authorization from Non-Interventional Clinical Research Ethics Committee of Health Sciences University Gazi Yaşargil Training and Research Hospital on July 14, 2023, with approval number 463. Since the study was retrospective, it was not necessary to obtain informed consent from the patients.

Conflict of Interest: No conflicts of interest were disclosed by the authors.

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