

ARAŞTIRMA / RESEARCH

Comparison of Toxoplasma and Rubella seropositivity rates of Syrian and Turkish pregnant women

Suriyeli ve Türk gebelerin Toksoplazma ve Rubella seropozitifliğinin karşılaştırılması

Gülnur Kul¹, Gökçe Turan²

¹Kırıkhan State Hospital, Department of Infectious Diseases and Clinical Microbiology, Hatay, Turkey ²Gazi University, School of Medicine, Department of Obstetrics and Gynecology, Ankara, Turkey

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Abstract

Purpose: Toxoplasma gondii, rubella and cytomegalovirus (TORCH) infections are the leading causes of perinatal morbidity and mortality, especially in developing countries. This study aimed to compare the seroprevalence of Toxoplasma and Rubella in Turkish pregnant women and Syrian refugee pregnant women, whose number is increasing in our region.

Materials and Methods: Syrian and Turkish pregnant women between the ages of 18 and 49 who were admitted to a secondary care hospital for their first prenatal visit between March 2018 and November 2019 were included in this retrospective study. Age, gravida, parity, nationality and anti-T. gondii IgM, anti-T. gondii IgG, anti-Rubella IgM, and anti-Rubella IgG test results of the patients included in the study were retrospectively recorded from the hospital archive and compared.

Results: Out of 3,606 pregnant women included in the study, 2,768 (76.7%) were Turkish and 838 (23.3%) were Syrian. Anti-T. gondii IgM positivity rate (6.1%) of Syrian pregnant women was significantly higher than the rate (2.1%) of Turkish pregnant women. Although Anti-Rubella IgG positivity was not statistically significantly different it was higher in Turkish pregnant women (85.2% and 88.7% respectively).

Conclusion: Knowing the incidence and prevalence of toxoplasma and rubella infection in pregnant women plays a critical role in determining the burden of the disease, planning screening programs, and active use of primary healthcare services. Screening programs in antenatal care for toxoplasma and rubella should especially be planned in regions that provide healthcare by considering the increasing number of Syrian refugees.

Keywords: pregnancy, rubella, seroprevalence, Syrian refugees, Toxoplasma gondii

Öz

Amaç: Toxoplasma gondii, rubella ve sitomegalovirüs (TORCH) enfeksiyonları, özellikle gelişmekte olan ülkelerde perinatal morbidite ve mortalitenin önde gelen nedenleridir. Bu çalışmada bölgemizde artan Suriyeli mülteci gebeler ile Türk gebelerdeki Toxoplasma ve Rubella seroprevelansının karşılaştırılması amaçlanmıştır. Gereç ve Yöntem: Çalışmamıza Mart 2018-Kasım 2019 tarihleri arasında hastanemize ilk prenatal vizitte başvuran 18-49 yaş arası Suriyeli ve Türk gebeler dahil edildi. Dahil edilen hastaların yaş, gravida, parite, uyruğu ve ilk trimesterdaki anti- T. gondii IgM, anti- T. gondii IgG, anti-Rubella IgM, anti-Rubella IgG sonuçları hastane arşivinden retrospektif olarak kaydedildi ve karşılaştırıldı. Bulgular: Calismaya katılan 3606 gebenin 2768'i (%76,7) Türk, 838'si (%23,3) ise Suriyeli idi. Suriyeli gebelerin anti T. gondii IgM pozitifliği (%6,1), Türk gebelere göre (%2,1) anlamlı olarak daha yüksek bulundu. Anti Rubella IgM pozitifliği her iki grupta benzerdi. Anti rubella IgG ise istatistiksel olarak anlamlı olmamakla birlikte Türk gebelerde daha yüksekti (sırasıyla %85,2 ve %88,7).

Sonuç: Gebe kadınlarda toksoplazma ve rubella enfeksiyonu sıklığı ve yaygınlığı hakkında bilgi sahibi olmak, hastalık yükünün belirlenmesinde, tarama programlarının planlanmasında ve birinci basamak sağlık hizmetlerinin aktif kullanımında kritik bir rol oynamaktadır. Toksoplazma ve rubella gibi doğum öncesi bakımda tarama programları, Suriyeli mülteci sayısının artması dikkate alınarak sağlık hizmeti veren bölgelere özel olarak planlanmalıdır.

Anahtar kelimeler: gebelik, rubella, seroprevalans, Suriyeli mülteciler, toxoplasma gondii

Yazışma Adresi/Address for Correspondence: Dr. Gülnur Kul, Kırıkhan State Hospital, Department of Infectious Diseases and Clinical Microbiology, Hatay, Turkey E-mail: gkul2004@gmail.com

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INTRODUCTION

Infections are among the most important agents that increase perinatal morbidity and mortality. It was revealed in studies that infections available during pregnancy had a risk to infect the fetus by crossing the placenta and increase fetal mortality and morbidity¹. As a result of physiological changes during pregnancy, the immune system is suppressed and pregnant women become sensitive to infections. Although the prevalence of *Toxoplasma gondii* (*T. gondii*) and *Rubella* virus infections is high they are generally asymptomatic. However, they may cause congenital malformations in the fetus by crossing the placenta in case of exposure to them especially in the first trimester of pregnancy^{2,3}.

T. gondii may cause sensory losses such as visualhearing loss in the fetus, mental and psychomotor retardations, hepatosplenomegaly, or death of the fetus. Maternal rubella virus infections may cause serious congenital defects by resulting in spontaneous abortus or fetal infection4. Firstly, there may be antibodies developing in T. gondii infection and then, they become negative in most of the cases after a few months. The negative result of a sensitive test in immunocompetent individuals is a finding that will eliminate the acute infection. However, a positive result may not always be a sufficient criterion to decide on the acute infection^{5.} Toxoplasma IgM antibodies may be detected about a week after the infection and stay high for a few months or years. Therefore, only the detection of IgM antibodies is not sufficient for the diagnosis of acute infection. Although IgM positivity continues after 2-3 weeks during the follow-ups the possibility of false IgM positivity due to the factors such as rheumatoid factor and anti-nuclear antibody should be considered in case no IgG positivity was observed6.

It was seen in the literature review that previous studies on Toxoplasma and Rubella Seroprevelans during pregnancy were mostly conducted on Turkish pregnant women^{2,7-11}. Studies in which the antibody results during pregnancy in Turkish women and Syrian refugee pregnant women are compared are limited^{12,13}. However, the increasing immigrant population in our region and our country after the Syrian civil war has led to changes in our daily practice. The elevated *T.gondii* IgM seropositivity detected in the migrant population increased the importance of the screening tests and emphasized the necessity of early diagnosis and treatment once again.

The contribution of our study to the literature is that it emphasized that the immigrant population with different living habits must be focused on for pregnancy screening tests. In this way, diagnosis and treatment of congenital infections may be performed earlier.

Due to these serious complications they may cause, identification of *T. gondii*, *Rubella*, and *CMV* infections at an early period constitutes an important part of prenatal care. There are still different views on the issue of the necessity for screening of these agents in the TORCH group during pregnancy. Seropositivity rates in a region must primarily be known to decide whether routine screening for these agents will be performed in antenatal care or not.

Many Syrian people had to leave their country and migrate to different countries due to the civil war that started in 2011. About 3.7 million Syrian refugees live in our country. Of this population, 79% densely live in 10 cities, one of which is our city¹⁴. Refugees face housing, nutrition, access to healthcare, and language barriers in the countries to which they migrate. The Turkish government has provided free healthcare services for Syrian refugees and therefore, they have a high opportunity to access healthcare. The rates of pregnancy and birth are high among Syrian refugees and the fertility rate of Syrians is 5.3 children per woman^{14,15}. Turkish physicians mostly see the pregnant refugees during delivery for the first time as they do not regularly see their doctors for pregnancy follow-up and their vaccination status in their countries is not known. Sufficient measures against these agents cannot be taken due to the reasons such as differences in their diet and hygiene habits and deficiencies in their vaccination programs and therefore, both mother and fetus become at risk.

This study aimed to analyze *T. gondii* and *rubella* results of Turkish and Syrian refugee pregnant women in the first trimester admitted to the Gynecology and Obstetrics Outpatient Clinic of our hospital and compare the results.

MATERIALS AND METHODS

Procedure

In our study, the files of patients admitting to the gynecology and obstetrics clinic of a second-step hospital between March 2018 and November 2019 were examined retrospectively. Ethical approval for the study was obtained from the Ethics Committee

of Mustafa Kemal University (Ethics Committee Number: 2019/02). The pregnant women who were between the ages of 18 and 49, those with missing demographic data, those with missing pregnancy notification forms, and those who did not provide blood for requested Toxoplasma and Rubella antibody tests in the first trimester were excluded from the study. The total number of pregnant women admitting to the clinic during this time was 19.250. When it was found that 14.520 of these women were at the second and third trimester pregnancy weeks, 44 were below the age of 18, 400 women had missing demographic data in their files, and 680 pregnant women did not provide blood samples for Toxoplasma and Rubella antibody tests in the first visit, a total of 3.606 patients were included in the study. The age, gravida, parity, nationality, and anti-T. gondii IgM, anti- T. gondii IgG, anti-Rubella IgM, anti-Rubella IgG results of these patients were recorded and compared from the hospital archives.

Our hospital is a second-step state hospital, and Kırıkhan is the 6th largest District of Hatay in terms of population density. Since Hatay is neighboring the Syrian border, the number of refugees in our region is higher. The anti- *T. gondii* IgM, anti- *T. gondii* IgG, anti-Rubella IgM, anti-Rubella IgG are requested from pregnant women admitting to our hospital to screen TORCH infections. When the results of the requested tests are positive in terms of congenital infections, patients are redirected to an upper-level healthcare center for advanced examination and treatment for avidity tests.

Serological tests

Serological tests are carried out in our hospital's microbiology laboratory by following the instructions of the manufacturer on Cobas 601 (Roche) device with the Electrochemiluminescence Method. The blood samples taken from fasting patients in the morning are centrifuged after waiting for at least 20-30 minutes. The centrifugated serum antibody is then examined in the antibody device. The results of the centrifuged serum sample tests and the age, gravida, parity, and nationality data of the pregnant women were obtained from hospital operating system files in this study.

In the test results, if anti-toxo IgM and anti-Rubella IgM were ≥0.8 COI, it was deemed positive, if it was <0.8, negative; if anti-toxo Igg was ≥30 IU / mL, it was deemed positive, if it was <30 IU / mL, it was deemed negative; if anti-rubella IGG was ≥10 IU /

If ML, it was deemed positive, and if it was <10 IU / ML, it was deemed negative.

Statistical analysis

Continuous variables were expressed as median (minmax), and categorical data were expressed in the form of numbers and percentages. The normality analysis was performed with the Kolmogorov-Smirnov Goodness of Fit Test in the inter-group analysis of continuous variables. The Mann-Whitney U-Test was used in the analyzes between the two groups because the distribution of continuous variables was not normal. The Chi-Square Test was used in the comparisons of categorical data. The analyzes were made with the IBM SPSS package program version 24.0 (IBM Corporation, Armonk, NY, USA). The level of statistical significance was taken as p<0.05.

RESULTS

A total of 4,730 pregnant women in the first trimester were admitted to our outpatient clinic between March 2018 and November 2019. Of these pregnant women, 3,606 had anti-Toxoplasma IgM, anti-Toxoplasma IgG, anti-Rubella IgM, and anti-Rubella IgG test results and were included in the study. The mean age of all pregnant women included in the study was 27±6.25. Out of 3,606 pregnant women, 2,768 (76.7%) were Turkish and 838 (23.3%) were Syrian. The mean ages of Syrian and Turkish pregnant women were 26 and 27 respectively. Among demographic data of the patients, the mean gestational week was 17.48±11.50, mean gravida was 4.29±2.48 and mean parity was 3.00±2.42 in Syrian pregnant women and mean gestational week was 11.34±6.94, mean gravida was 3.53±1.97, and mean parity was 2.15±1.64 in Turkish pregnant women.

Comparison of *T. gondii* and *Rubella* IgG and IgM test results of Syrian and Turkish pregnant women was listed in Table 1. Anti-*T. gondii* IgM positivity (6.1%) of Syrian pregnant women was significantly higher than that (2.1%) of Turkish pregnant women (p:0.004). While anti-*T. gondii* IgG positivity was higher in Syrian pregnant women this difference was not statistically significant (45.7% and 41.9% respectively, p>0.05). Anti-*Rubella* IgM positivity was similar in both groups. Although Anti-*Rubella* IgG positivity was not statistically significantly different it was higher in Turkish pregnant women (85.2% and 88.7% respectively, p>0.05).

Antibody values of Syrian and Turkish pregnant women according to the age groups were listed in Table 2. When the antibody results of pregnant women were categorized according to the age groups and assessed it was observed that anti-*T. gondii* IgM

positivity increased by age in Syrian pregnant women. It was also observed that anti-*T. gondii* IgG positivity had the highest rates in the age group between 20-29 in both pregnant groups.

Table 1. Comparison of toxoplasma and rubella positivity rates in Syrian and Turkish pregnant women

	Syrian Pregnant Women	Turkish Pregnant Women	Total (n=3.606)	p	
	(n=838)	(n=2.768)	(= 3,333)		
Toxo IgM (n, %)	,	, ,		0.004*	
Positive	52 (6.1%)	59 (2.1%)	111 (3.0%)		
Negative	774 (92.4%)	2.673 (96.6%)	3.447 (95.6%)		
Suspected	12 (1.5%)	36 (1.3%)	48 (1.3%)		
Toxo IgG (n, %)				0.155*	
Positive	382 (45.7%)	1.160 (41.9%)	1.542 (42.8%)		
Negative	456 (%54.3)	1.580 (57.1%)	2.036 (56.4%)		
Suspected	0 (0.0%)	28 (1.0%)	28(0.8%)		
Toxo IgM and IgG		45 (%1.6)	97 (%2.6)		
Positive (n, %)	52 (6.1%)				
Rubella IgM (n, %)				0.978*	
Positive	6 (0.8%)	22 (0.8%)	28 (0.8%)		
Negative	828 (98.9%)	2.732 (98.7%)	3.560 (98.8%)		
Suspected	1 (0.4%)	14(0.5%)	15 (0.4%)		
Rubella IgG (n, %)				0.126*	
Positive	714 (85.2%)	2.455 (88.7%)	3.169 (87.9%)		
Negative	124 (14.8%)	313 (11.3%)	437 (12.1%)		
Total	838 (100.0%)	2.768 (100.0%)	3.606 (100.0%)		

Table 2. Comparison of toxoplasma and rubella positivity rates in Syrian and Turkish pregnant women according to age groups

	Ages <20		Ages between 20-29		Ages between 30-39		Ages ≥ 40			
	n=230	n=159	n=1535	n=433	n=919	n=203	n=84	n=43		
	Turkish	Syrian	Turkish	Syrian	Turkish	Syrian	Turkish	Syrian	р	
	Pregnant	Pregnant	Pregnant	Pregnant	Pregnant	Pregnant	Pregnant	Pregnant		
	Women	Women	Women	Women	Women	Women	Women	Women		
Toxo	5(0.2%)	13 (1.5%)	37	17	17	22	0 (0.0%)	0 (0.0%)	0.355*	0.450*
IgM (+)		, ,	(1.3%)	(1.9%)	(0.6%)	(2.6%)	, ,			
(n, %)			, ,	, ,		, ,				
Toxo	75	41 (4.9%)	600	196	445	110	40	35	0.076*	0.001*
IgG (+)	(2.7%)		(21.7%)	(23.4%)	(16.1%)	(13.2%)	(1.4%)	(4.1%)		
(n, %)										
Rubella	0 (0.0%)	0 (0.0%)	19(0.7%)	3 (0.4%)	0 (0.0%)	3 (0.4%)	3(0.1%)	0 (0.0%)	0.102*	0.921*
IgM (+)										
(n,%)										
Rubella	204	124	1374	380	805	168	72	42	0.740*	0.435*
IgG (+)	(7.4%)	(14.8%)	(49.6%)	(45.2%)	(29.1%)	(20.1%)	(2.6%)	(4.9%)		
(n, %)										

DISCUSSION

In our study, anti-*T.gondii* IgM positivity (6.1%) of Syrian pregnant women was found to be higher than Turkish pregnant women at a significant level (2.1%). *Toxoplasma* IgG seropositivity, on the other hand, was found to be 41.9% in Turkish pregnant women, and

anti *T.gondii* Igg seropositivity rate was 45.7% in Syrian pregnant women. Also, Rubella IgG seropositivity was found to be 88.7% in the Turkish population, and 85.2% in Syrian pregnant women. The results on Toxoplasma and Rubella IgG seropositivity are in line with the literature data.

In our study, when *Toxoplasma* IgM seropositivity rates were compared between Syrian and Turkish pregnant women positivity rates were observed to be statistically higher in Syrian pregnant women. In another similar study conducted by Coşkun et al., the *Toxoplasma* IgM seropositivity rates in Turkish and Syrian pregnant women were found to be 1.28% and 2.47%, respectively, and the difference was at a statistically significant level between the two groups (14). In this study, in line with our study results, anti-T.gondii IgM positivity was found to be high in Syrian refugees. These rates may be affected by the differences in lifestyle, hygiene habits, and diet of Syrian refugees.

In studies worldwide from different countries such as Brazil, Italy, France, Singapore, and Iran, the positivity rate ranges from 0.4% to 3.4% for T. gondii IgM and from 17.7% to 71% for T. gondii IgG 16-18. The rates were found higher in studies from countries with different nutritional habits, low socioeconomic status, and insufficient hygiene conditions such as India and Nepal^{19,20}. In studies with different numbers of patients from different regions of our country, the T. gondii IgM seropositivity rate was between 0.3-3% and T. gondii IgG seropositivity rate was between 18.3-60.4%2,8,21,22. In our study, the Toxoplasma IgG seropositivity rate in Turkish pregnant women was 41.9%, which is similar to the results of other studies. In a study performed in 2015 in Turkey, anti-T. gondii IgG results of 84 Syrian pregnant refugees were analyzed and the rate was 64.6% ¹². Anti-T. gondii IgG seropositivity rate in Syrian pregnant women in our study was 45.7% and the result was lower than the one in literature. However, it was observed that most of the Syrian pregnant women included in our study adopted a settled life in our city and adapted to the society's nutritional and hygiene habits. T. gondii IgG seropositivity rates in both groups were found higher in the age group between 20-29, which is consistent with the findings in the literature^{2,8,21}. The time of infection is not related to the age, but the first gestational age is generally in this range, which can be explained by assessing more patient data.

Congenital *rubella* syndrome may occur after vertical transmission of the *Rubella* virus during pregnancy. Cardiac and ocular anomalies, deafness, autism, and microcephaly can be seen in the fetus¹⁶. *Rubella* is considered to be responsible for about 2-3% of congenital anomalies caused by prenatal infections. The mortality rate in infants with severe congenital

rubella syndrome is about 35%17. The incidence rate of congenital rubella differs according to regions depending on the viral circulation in the community, sensitivity of individuals, and use of rubella vaccine4.

In *Rubella* IgG seroprevalence studies, the rates are 94% in Iran and 97% in Greece²³. While this rate is 89.3% in Brazil it is 99.3% in America²⁴. This rate decreases to 68.3% in India which is a far eastern country and 65.3% in Sudan. The reason for these low rates may be that the *Rubella* vaccine has not been included in their national vaccination program²⁵. It is reported that the risk for acute infection and congenital *rubella* syndrome will increase in women in their reproductive years in case *Rubella* immunity is under 90%.

According to the meta-analysis in which 26 studies on *rubella* seroprevalence in our country were analyzed, the *Rubella* IgG seropositivity rate was 93.4%. Different rates were observed due to sociocultural differences and geographical locations of the regions where the studies were performed. In our study, the *Rubella* seropositivity rate in the Turkish population was 88.7%, which is similar to the results of other studies in the literature. The high IgG antibody seropositivity rate in our country reveals that we have a successful vaccination policy compared with the other developing countries.

In the seropositivity study on Syrian pregnant women, while Rubella IgG positivity rate was 92.8% in Syrian pregnant women it was 95.6% in Turkish pregnant women¹³. This rate is significantly higher than the rate (85.2%) in Syrian pregnant women in our study. The 3-year data were included in this study that was conducted by Coşkun et al. on Syrian pregnant women. The number of patients was more than in our study. However, when it is considered that our region works with an intense refugee population, we believe that the data of our study will make significant contributions to the literature. The difference may be due to differences in access to healthcare and socioeconomic conditions of refugees living in the cities where these 2 studies were performed.

Limitations of our study include that avidity in *T. gondii* IgM and IgG positive patients could not be measured in our center and that the results of these patients referred to a tertiary healthcare center could not be obtained. However, the strength of our study is that it is a comprehensive study in terms of antenatal follow-up of Syrian refugees. Results of our

study will be guided in both training and information activities and regulation of *rubella* vaccination programs for Syrian women in their reproductive years.

In conclusion, it is necessary to focus on prenatal screening programs as there are a considerable amount of Syrian refugees in our city. Training for washing hands frequently, cleaning vegetables and fruits well, cooking meat well, and avoiding cat feces to protect against *Toxoplasma* infection should be designed especially for migrant people. *Rubella* vaccination status of migrants cannot be questioned due to the language barrier. Therefore, we recommend the regulation of vaccination campaigns following screening programs for migrant women in their reproductive years.

The number of Syrian refugees in their reproductive years is high in our region. As their lives and nutritional conditions are unsanitary, planning should be made on the management of *T. gondii* infection. Moreover, when the problems that will occur due to having primary infection during pregnancy are considered the implementation of effective vaccination programs for *rubella* infection will be an effective method. Vaccination programs for women in their reproductive years in primary healthcare institutions and migrant healthcare centers will provide a basis for protective medicine.

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