

# Seroprevalence of *Toxoplasma Gondii*, Rubella, and Cytomegalovirus Among Pregnant Refugees and Turkish Women: A Retrospective Comparative Study

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## ABSTRACT

**Objective:** To evaluate the prevalence of *Toxoplasma gondii*, rubella, and cytomegalovirus (CMV) among pregnant Turkish women as well as Syrian refugees in Istanbul.

**Methods:** Among pregnant women who were admitted to the Esenler Maternity and Children Hospital in Istanbul between January 2014 and January 2015, antibodies against *T. gondii*, rubella, and CMV were measured using the micro-ELISA method. The test results were evaluated retrospectively.

**Results:** Out of a total of 1066 pregnant women screened in the present study, 963 (90.3%) were Turkish, and 103 (9.7%) were Syrian refugees. IgM positivity rates of *T. gondii*, rubella, and CMV were determined as 0.2%, 0%, and 0.2% in Turkish women and 0.1%, 0%, and 0% in Syrian refugees, whereas IgG positivity rates were determined as 26.3%, 93.8%, and 99.5% in Turkish women and 58.3%, 87.4%, and 100% in Syrian refugees. The seroprevalence of *T. gondii* was lower, and rubella was higher among pregnant Turkish women and among pregnant Syrian refugees and statistically significant ( $p < 0.05$ ).

**Conclusion:** Since immunity against *T. gondii* in pregnant Turkish women is lower than that in Syrian refugees who are in the reproductive age group, routine screening should be conducted. Immunization against rubella should be considered for Syrian refugees who are in the reproductive age group.

## INTRODUCTION

The microorganisms that cause perinatal mortality and morbidity have similar manifestations in pregnancy and are called TORCH complex (*Toxoplasma gondii*, Other (syphilis), rubella, cytomegalovirus (CMV), Herpes simplex virus).<sup>[1]</sup> While the course of toxoplasmosis will be asymptomatic in immunocompetent individuals, especially if it is transmitted in the first trimester of pregnancy, it may cause hydrocephalus, chorioretinitis, cerebral calcifications, or death of the fetus.<sup>[2]</sup> Rubella causes a congenital syndrome with sensorineural hearing loss, cataract, cardiac malformations, and neurological and endocrinological sequelae in the fetus. Congenital CMV infection is associated with clinical findings, such as chorioretinitis, cerebral calcifications, and mental retardation in the fe-

tus, and the prevalence of infection is 0.6% in developing countries.<sup>[3]</sup>

Positive IgM levels indicate the presence of acute infection, positive IgG levels indicate the previous infection, and negative IgG levels indicate no immunity.

The prevalence of TORCH infection varies between countries, regions, and ethnic groups. In pregnancy, TORCH immunity screening provides early diagnosis of subclinical infection, and thus it is helpful to avoid fetal damages and to protect against the disease. It is recommended to be performed according to the seropositivity rates of the region. In Istanbul, refugee influx and warfare affect not only the general society but also the special groups, such as pregnant women. The aim of the present study was to evaluate the seropositivity rates of a particular population

changing with migration due to the geographical location of our region.

## MATERIAL AND METHODS

This retrospective study evaluated the immunity rates of *T. gondii*, rubella, and CMV IgM and IgG among 1066 pregnant women who were admitted to the Esenler Maternity and Children Hospital between January 2014 and January 2015 for routine examination. Serum analyses were performed using the micro-ELISA method according to the manufacturer's instructions (VIRCELL, Granada, Spain). Samples with indexes >11 IU/mL were considered as positive for IgM and IgG. Samples with indexes <9 IU/mL were considered as negative IgM and IgG. Samples with indexes between 9 and 11 IU/mL were considered as equivocal, and a new sample was obtained and tested. Statistical analyses were performed using Number Cruncher Statistical System 2007 (Kaysville, UT, USA). Student's t-test was

used for comparison of quantitative data. Pearson's chi-square test, Fisher's exact test, Fisher-Freeman-Halton test, and Yates' continuity correction test (chi-square test with Yates correction) were used for comparison of qualitative data. A p value <0.05 was considered as statistically significant.

## RESULTS

Out of a total of 1066 pregnant women, 963 (90.3%) were Turkish, and 103 (9.7%) were Syrian. The average age of the pregnant women was  $27.51 \pm 5.3$  years (Table 1). IgM positivity rates of *T. gondii*, rubella, and CMV were determined as 0.2%, 0%, and 0.2% among pregnant Turkish women and 0.1%, 0%, and 0% among pregnant Syrian refugees. In addition, IgG positivity rates of *T. gondii*, rubella, and CMV were determined as 26.3%, 93.8%, and 99.5% among pregnant Turkish women and 58.3%, 87.4%, and 100% among pregnant Syrian refugees (Table 2).

**Table 1.** Examination of the age distributions according to nationalities

Age (year)	Total pregnant women (n=1066)	Turkish citizens (n=963)	Syrian refugees (n=103)	*p
≤20	121 (11.4)	87 (9.0)	34 (33.0)	
21–30	627 (58.8)	577 (59.9)	50 (48.5)	
31–40	286 (26.8)	271 (28.1)	15 (14.6)	
>40	32 (3.0)	28 (2.9)	4 (3.9)	
Avg±SD	27.50±5.93	27.80±5.79	24.80±6.54	0.001

\*Student's t-test; p<0.05. SD: Standard deviation.

**Table 2.** The seroprevalence of *T. gondii*, cytomegalovirus, and rubella

	Total of pregnant women (n=1066)		Turkish citizens (n=963)		Syrian refugees (n=103)		p
	n	%	n	%	n	%	
<i>T. gondii</i> IgM							
Negative	1063	99.7	961	99.8	102	99.0	<sup>b</sup> 0.263
Positive	3	0.3	2	0.2	1	0.1	
<i>T. gondii</i> IgG							
Negative	753	70.6	710	73.7	43	41.7	<sup>c</sup> 0.001
Positive	313	29.4	253	26.3	60	58.3	
Rubella IgM							
Negative	1066	100.0	963	100.0	103	100.0	–
Positive	0	0.0	0	0.0	0	0.0	
Rubella IgG							
Negative	73	6.8	60	6.2	13	12.6	<sup>d</sup> 0.025
Positive	993	93.2	903	93.8	90	87.4	
CMV IgM							
Negative	1064	99.8	961	99.8	103	100.0	<sup>b</sup> 1.000
Positive	2	0.2	2	0.2	0	(0.0)	
CMV IgG							
Negative	5	0.5	5	0.5	0	(0.0)	<sup>b</sup> 1.000
Positive	1061	99.5	958	99.5	103	(100.0)	

<sup>a</sup>Fisher's exact test. <sup>b</sup>Pearson's chi-square test. <sup>c</sup>Yates' continuity correction test.

## DISCUSSION

Perinatal infections constitute 2% to 3% of all congenital anomalies. The TORCH agents cause only asymptomatic or mild infection in the mother but may provide irreversible damage to the fetus depending on the onset time of the infection during pregnancy. Screening pregnant women for these pathogens provides early diagnosis of infection and prevents fetal infection to avoid fetal damages.<sup>[4]</sup>

*T. gondii* is a ubiquitous protozoon infecting animals and humans. Transmission occurs through exposure to oocysts on cats and cysts via consuming raw or undercooked meat. *T. gondii* infection is typically asymptomatic in immunocompetent hosts. The acute toxoplasmosis can be subclinical and diagnosed by routine serological examinations in pregnancy. The risk of transmission increases with increasing gestational weeks, from <15% at 13 weeks of gestation to >70% at 36 weeks of gestation. Spontaneous abortion, stillbirth, chorioretinitis, blindness, encephalitis, microcephalia, intracranial calcifications, and hepatosplenomegaly may be seen if fetal infection occurs. The incidence of congenital toxoplasmosis is reduced by early diagnosis and maternal treatment.<sup>[5]</sup> In the present study, the positivity rate of *T. gondii* IgM was found to be 0.2% in pregnant Turkish women and 0.1% in pregnant Syrian refugees. In addition, the positivity rate of *T. gondii* IgG was found to be 26.3% in pregnant Turkish women and 58.3% in pregnant Syrian refugees. The seropositivity of *T. gondii* was determined to be significantly lower in pregnant Turkish women than in pregnant Syrian refugees ( $p=0.001$ ). In the study conducted by Keskin et al.<sup>[6]</sup> in our region in 2013, the positivity rate of *T. gondii* IgG was found to be 31.2%, which is higher than the results of our study for pregnant Turkish women. The seropositivity rates of *T. gondii* (36.9%, 33.9%, and 28.8%) in other studies performed in different geographical regions of our country were found to be higher than those in our results.<sup>[7-9]</sup> The results were similar in every study conducted in Turkey. When we checked other countries, the seropositivity rates of *T. gondii* were 7% in Norway, 10% in the United Kingdom, 19% in Italy, 29.9 in Sri Lanka,<sup>[10]</sup> 31.7% in Thailand–Myanmar,<sup>[11]</sup> 32% in Spain, 33% in Austria, 34% in Slovenia, 44% in France,<sup>[12]</sup> 46.2% in Yemen,<sup>[13]</sup> and 82.6% in Lebanon.<sup>[14]</sup> Our results were similar to Mediterranean countries.

Different seropositivity rates of *T. gondii* in pregnant women are due to climate variability and life standards of the people in the defined areas. Culture of the society and different eating habits are also some factors involved in the variation of seroprevalence of anti-*T. gondii* antibodies in pregnant women across the globe. Routine measurement or determination of antibodies may be suggested to pregnant Turkish women due to their high seronegativity rates for *T. gondii*.

Rubella, which is a single-stranded positive-sense RNA virus, is a childhood disease. Infection and transmission of the mother occur through inhalation of aerosolized

particles from an infected individual. Maternal infection can result in miscarriage, stillbirth, or congenital rubella syndrome (CRS). Clinical manifestations of CRS are sensorineural deafness, cardiac malformations, cataracts, and neurological and endocrinological sequelae. Prevention of congenital rubella is achieved by providing all children and adolescents with rubella vaccination. Rubella vaccination is included in the routine triple pediatric vaccination (i.e., MMR for measles, mumps, and rubella) in Turkey. The rubella immunity rate for pregnant Turkish women in our study (93.8%) was found to be similar to the results of many other studies (95.1%, 96.1%, and 94.3%) performed in different geographical regions of Turkey.<sup>[15-17]</sup> When other seroprevalence studies performed worldwide are taken into consideration, the seropositivity rates for rubella virus were reported as 88.7% in Northern Ireland,<sup>[18]</sup> 87.6% in Canada,<sup>[19]</sup> and 61.8% in India.<sup>[20]</sup>

In view of the present study, the seroprevalence of rubella was determined to be significantly higher in pregnant Turkish women than in pregnant Syrian refugees. Routine immunization for rubella should be mandatory to Syrian refugees who are in the reproductive age group.

CMV is found universally throughout all geographical locations and in areas of low socioeconomic conditions. Maternal CMV infection during pregnancy most often results from close contact with young children's saliva, direct contact with infected urine, or through sexual intercourse.<sup>[21]</sup> If fetal infection occurs, clinical manifestations include petechiae, hepatosplenomegaly, microcephaly, intracranial calcifications, sensorineural hearing loss, and chorioretinitis. In our study, there was no significant difference between the CMV seropositivity rates of Turkish and Syrian pregnant women. The CMV seropositivity rate (98.2%, 99.4%, and 99.3%) in studies performed in different regions of our country was found to be similar with the results of our study.<sup>[22-24]</sup> The seroprevalence of anti-CMV IgG was 94.70% in 2887 pregnant women in China.<sup>[25]</sup> Out of 200 pregnant women, 88.5% were CMV IgG positive in Ethiopia,<sup>[26]</sup> 46.8% in France,<sup>[27]</sup> 56.3% in Finland,<sup>[28]</sup> and 60% in the United States.<sup>[29]</sup> It seems that the prevalence of CMV infection observed in the present study was similar to that reported in other developing communities but higher than in the developed one. This may be attributed to low socioeconomic status and poor hygienic practices, which might play significant roles in the rate of CMV infection.

Our study has a limitation. There are potential risk factors not assessed for CMV, *T. gondii*, and rubella.

In conclusion, owing to the high *T. gondii* seronegativity rates among pregnant Turkish women, routine screening of antibodies and informing women in the reproductive age group about the routes of transmission and measures of prevention will be helpful to avoid primary infections and congenital toxoplasmosis. Clear benefits obtained by wide coverage of routine immunization for rubella outweigh the routine screening for women in the reproductive age group in both Turkish and Syrian populations.

Moreover, routine CMV screening for pregnant women does not seem to be necessary anymore considering the 100% seropositivity rates in both populations.

#### Ethics Committee Approval

This was a retrospective study, there for no ethics comita approval was taken.

#### Informed Consent

Retrospective study.

#### Peer-review

Internally peer-reviewed.

#### Authorship Contributions

Concept: L.N.A.; Design: L.N.A., K.K.Y.; Data collection: L.N.A., A.B.E.; Analysis: L.N.A., K.K.Y.; Literature search: L.N.A., G.K.; Writing: L.N.A., G.K., A.B.E.

#### Conflict of Interest

None declared.

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## Türk ve Mülteci Gebeler Arasındaki *Toxoplasma Gondii*, Rubella ve Sitomegalovirus Seroprevalansı: Geriye Dönük Karşılaştırmalı Bir Çalışma

**Amaç:** İstanbul'daki Suriyeli mülteciler ve Türk gebeler arasındaki *Toxoplasma gondii*, rubella ve sitomegalovirus (CMV) prevalansını değerlendirmek.

**Gereç ve Yöntem:** Ocak 2014–Ocak 2015 tarihleri arasında Esenler Kadın Doğum ve Çocuk Hastalıkları Hastanesi'ne başvuran gebeler arasında *Toxoplasma gondii*, kızamıkçık ve CMV'ye karşı antikorlar mikro-elisa yöntemi ile ölçüldü. Test sonuçları geriye dönük olarak değerlendirildi.

**Bulgular:** Bu çalışmada taranan toplam 1066 gebeden 963'ü (%90.3) Türk, 103'ü (%9.7) Suriyeli mülteci idi. *T. gondii*, rubella and CMV Ig M pozitiflik oranları Türk gebelerde sırasıyla %0.2, %0, %0.2, Suriyeli mültecilerde ise %0.1, %0, %0, IgG pozitiflik oranları ise Türk gebelerde %26.3, %93.8, %99.5, Suriyeli gebelerde %58.3, %87.4, %100 saptandı. Türk gebelerde *T. gondii* seroprevalansı Suriyeli sığınmacı gebelerden anlamlı olarak düşük, rubella seroprevalansı ise anlamlı olarak yüksek bulunmuştur.

**Sonuç:** Bölgemizde, göç ve savaşlar nedeniyle toplumsal profil yanında gebeler gibi özel gruplarda da değişimler yaşanmaktadır. Türk gebelerde *T. gondii*'ye karşı bağışıklık oranının düşük olması nedeniyle Türk gebelerde bu hastalık için rutin tarama, doğurganlık çağındaki Suriyeli sığınmacılara ise rubella için bağışıklama yapılması düşünülebilir.

**Anahtar Sözcükler:** Gebe; rubella; sitomegalovirus; *Toxoplasma gondii*.