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Seroprevalence of Toxoplasma Gondii, Rubella and Cytomegalovirus Among Pregnant Women in Our Clinic

Kliniğimizde Takipli Gebelerin Toksoplazma Gondi, Rubella ve Sitomegalovirus Seroprevelansının İncelenmesi

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Öz

Gebelik döneminde toksoplazma, rubella ve sitomegalovirüs enfeksiyonlarında seropozitiflik oranını belirlemek. Muğla Sıtkı Koçman Üniversitesi Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Polikliniği'ne gebeliğin ilk 10 haftası içinde gebelik muayenesi için başvuran 4488 gebe çalışmaya alındı. Anti-Toksoplazma IgM ve IgG, Anti-Rubella IgM ve IgG, Anti-CMV IgM ve IgG sonuçları değerlendirildi. Çalışma grubunda Anti-Toksoplazma, Anti-Rubella, Anti-CMV IgG ve IgM seropozitiflik oranı sırası ile %21.6, %1.6; %92.8, %1; %98.5, %1.1 olarak tespit edildi. Günlük pratiğimizde sıklıkla değerlendirilen Toksoplazma, Rubella ve CMV seroprevalansını prekonsepsiyonel veya antenatal tarama döneminde bölgesel şartlara göre değerlendirilmesi maliyet ve etkinlik açısından daha uygun bir yaklaşım olacaktır. Anti-Rubella IgG taramasının prekonsepsiyonel dönemde taranması ve seronegatif hastalara aşılama yapılması uygun bir yaklaşım gibi görünmektedir.

Anahtar Kelimeler: CMV, Gebelik, Rubella, Seropozitivite, Seroprevelans, Toksoplazma

Abstract

To determine the rate of seropositivity in toxoplasma, rubella and cytomegalovirus infections during pregnancy. 4488 pregnants who applied to outpatient polyclinics of Gynecology and Obstetrics in Muğla Sıtkı Koçman University Training and Research Hospital for pregnancy examination in the first 10 weeks of pregnancy were included in the study. Results of anti-Toxoplasma IgM and IgG, anti-Rubella IgM and IgG, anti-CMV IgM and IgG were evaluated. Seropositivity rates of anti-Toxoplasma, anti-Rubella, anti-CMV IgG and IgM were determined respectively 21.6%, 1.6%, 92.8%, 1%; 98.5%, 1.1% in the study group. Toxoplasma, Rubella and CMV seroprevalence should be evaluated during preconceptional or antenatal screening according to regional conditions.

Keywords: CMV, Pregnancy, Rubella, Seropositivity, Seroprevalence, Toxoplasma

Introduction

Toxoplasma gondii, Rubella and Cytomegalovirus (CMV) viruses are among the infectious factors classified as the TORCH group (1). In recent years Zika virus and coronavirus family have also been added to this group. The reason why it is more common especially in the third world and developing countries is the high level of infection through fecal-oral and the crowded life due to poor sanitation conditions (2). They are generally asymptomatic or infections which come in sight with symptoms similar to upper respiratory tract infection. For this reason; the "suspicion" step, which is an important step in the diagnosis stage, is skipped (3). Discussions about routine screening before pregnancy or during the first trimester of pregnancy are still keep up-to-date due to the difficulty in reaching the serological situation of the patients before pregnancy, diagnostic difficulties and patient non-adherence (4).

Infection during pregnancy has a wide range of spectrum from asymptomatic infection to congenital malformation, recurrent abortion, premature birth and stillbirth (2). The infectious agent causing the transmission, the week of transmission, and the state of maternal and fetal immune system affect this spectrum (2). In this retrospective cross-sectional study after we have determined the seroprevalence of T. gondii, Rubella and CMV among pregnants living in Muğla province we aim at comparing our findings with studies conducted in the world in last 5 years.

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Material and Method

Our study, which was designed as a retrospective descriptive study, was included the pregnants between the ages of 16-45, applying to Muğla Sıtkı Koçman University Training and Research Hospital for routine pregnancy control for the first time between 2012-2020, with a pregnancy less than 10 weeks, and not being tested serologically for CMV, Rubella virus and T.gondii before pregnancy. The study was approved by the Clinical Research Ethics Committee of the Muğla Sıtkı Koçman University

(06.11.2020, 22). IgG and IgM antibody test results of pregnants against Rubella virus, CMV and T.gondii were retrospectively recorded by analyzing. Anti-Toxoplasma, anti-Rubella, anti-CMV IgG and IgM antibodies were studied with electro chemiluminescence immunoassay "ECLIA" method by being used Elecsys kits (Roche Diagnostics, GmbH) in the direction of the manufacturer's suggestions. The results were evaluated conveniently according to the manufacturer's instructions: <0.8 COI negative, (0.8-1.0 COI) intermediate value, ≥1.0 COI positive for anti-Toxoplasma and anti-Rubella IgM tests; <0.7 COI negative, (0.7-1.0 COI) intermediate value, ≥1.0 COI positive for anti-CMV IgM test; <1 IU / Ml negative, (1-3 IU / mL) intermediate value, ≥3 IU / mL positive for anti-Toxoplasma IgG antibodies; <10 IU / mL negative, ≥10 IU / mL positive for anti-Rubella IgG antibodies; <0.5 U / mL negative, (0.5-1.0 U / mL) intermediate value, ≥1.0 U / mL positive for anti-CMV IgG antibodies. After the patient test results obtained from the laboratory information management system were transferred to the Microsoft Excel program, the seroprevalences of the last 5 years were calculated.

That study also summarizes the results of the electronic research performed in PubMed, Scopus, and Google Scholar. All databases were assessed between 2015 and 2020 (printing year). The databases were searched for keywords "TORCH and pregnancy". The studies in which the number of pregnants was more than 400 were included in the evaluation.

Results

The prevalence of CMV IgG seropositivity was determined 98.5% (n: 4471) when 4539 pregnant women were evaluated, and the prevalence of CMV IgM seropositivity was determined 1.1% (n: 53) when 4709 pregnant women were evaluated. Rubella IgG seroprevalence was 95.4% (n: 2141) when 4978 women were evaluated, and Rubella IgM seroprevalence was 0.5% (n: 8) when 6306 pregnant women were evaluated. Toxoplasma IgG seroprevalence was determined to be 18% (n: 348) when 5158 pregnant women were evaluated, and Toxoplasma IgM seroprevalence was determined to be 0.46% (n: 9) when 5728 pregnant women were evaluated. (Table-1).

Table 1. Number and rates of CMV, Rubella Virus and Toxoplasma IgG and IgM seropositive patients.

Variable		Negative		Gray		Posivite	
	N	N	%	N	%	N	%
CMV IgG	4539	68	1.5%	0	0%	4471	98.5%
CMV IgM	4709	4603	97.7%	53	1.1%	53	1.1%
Rubella IgG	4978	357	7.2%	0	0%	4621	92.8%
Rubella IgM	6306	6187	98.1%	56	.9%	63	1%
Toxoplasma IgG	5158	4013	77.8%	29	.6%	1116	21.6%
Toxoplasma IgM	5728	5597	97.7%	37	.6%	94	1.6%

When the association of CMV Ig seroprevalence was evaluated, it was observed that 42 (1.08%) of 3886 patients were simultaneously CMV IgM and CMV IgG positive. In the same population, 64 (1.64%) patients were determined to be seronegative in terms of CMV IgM and CMV IgG at the same time. While CMV IgG was negative, any patient with a positive CMV IgM value was not observed at all (Table 2).

Table 2. Evaluation of IgG and IgM results together for CMV, Rubella Virus and Toxoplasma.

Variable	**IgM (+)**	IgM (-)	**Total number of patients who were examined**
Anti-CMV			
IgG (+)	42	3780	3886
IgG (-)	0	64	
Anti-Rubella			
IgG (+)	27	4087	4430
IgG (-)	4	312	
Anti-Toxoplazma			
IgG (+)	41	896	4488
IgG (-)	12	3539	

27 (0.6%) patients were determined to be simultaneously Rubella IgM and Rubella IgG positive among the 4430 patients in which the association of Rubella Ig seroprevalence was evaluated while 312 (7.04%) patients were simultaneously Rubella IgM and Rubella IgG negative. The number of patients with positive Rubella IgM value was determined to be 4 (0.09%) while Rubella IgG was negative (Table 2). 41 (0.91%) patients were found simultaneously Toxoplasma IgM and Toxoplasma IgG positive, 12 (0.26%) patients were found to be Toxoplasma IgM positive while Toxoplasma IgG was negative among the 4488 patients in whom the association of Toxoplasma Ig seroprevalence was evaluated. In the same population 1586 (76.85%) patients were found to be Toxoplasma IgM and Toxoplasma IgG negative at the same time. (Table 2).

Discussion

T. gondii, CMV and Rubella virus infections only cause an asymptomatic or mild infection in the mother, they can cause severe congenital malformations in the fetus (5). These malformations could generally meet us as the cause of congenital anomalies, intrauterine growth retardation and fetal

death, which cause problems both economically and socially (6). Diagnosis of congenital infection involves some difficulties due to the both limited technical possibilities and low patient consistence. Screening of these infectious agents both before and during pregnancy has always been a matter of debate. We evaluated the seropositivity prevalence of Toxoplasma, Rubella virus and CMV infections in pregnant examined regularly in our hospital in our study.

The positivity rate for anti-Toxoplasma IgM in the evaluation of T.gondii seroprevalence was found to be 1.6% (94/5728) in our study. Anti-Toxoplasma IgM seroprevalence positivity ranges from 0% to 2.5% as seen in Table 3, where studies being published in the literature since 2015 have been evaluated (7). The highest rate has been seen as 2.5% in the study that Zeb MA. et al conducted. We attribute the reason of this high rate to the negative sanitation conditions in Pakistan where the study was conducted (8). In our study Toxoplasma IgM positivity rate shows similarity with the study which Obaid HM. et al. conducted in Iraq (9). Seroprevalence positivity rate was found to be 21.6% (1116/5158) in the evaluation carried out for anti-Toxoplasma IgG. As seen in Table 3 seroprevalence positivity of anti-Toxoplasma IgG varies between 0.36% and 31% in different studies (7, 10). This rate was found to be 31% in the study Numan O. et al. carried out in our country (7). This study was conducted in Istanbul, and also the rate is higher than our study because of more crowded and heterogeneous socio-economic situation of Istanbul when we compare the studies. In addition, As seen in Table 3 anti-Toxoplasma IgG positivity rate is different in studies conducted in the same country by Wang LC et al. and Zhang N. et al. (4.34%, 0.36%) (10, 11). It may also be suggested that each region or city should evaluate its own results since we have different results with the study Numan O. et al. have carried out recently in our country.

The presence of IgM antibodies does not always indicate an acute infection since it can persist in the serum for years. Negativity of IgM also does not exclude infection. Because it may not be detected at the beginning of the infection, or it may be negative later on if it has been investigated in the late period of pregnancy although there is an infection during pregnancy. Besides, high avidity results have been determined to be a reliable method indicating that the infection was had at least 3-4 months ago especially in the first trimester of pregnancy, in cases with IgM negative and IgG positive results by ELISA. However; it should be kept in mind that evaluating low or suspicious avidity results with a single result may cause misinterpretation (12). In addition, the risk of having congenital toxoplasmosis in the fetus for a person who had primary toxoplasmosis infection during pregnancy, varies between 0-9% for the first trimester and 35-59% for the 3rd trimester.

Anti-Rubella IgM was found as 1% (63/6306) in the evaluation of Rubella seroprevalence in our study. Anti-Rubella IgM seroprevalence positivity ranges between 0.2% and 2.25% as seen in Table-3 and Table 4 (8, 13). When Cetinkaya et al. evaluated the data of 90988 patients in 26 studies conducted in our country, this rate was reported as 0.78% (17). Seroprevalence positivity rate in the evaluation made for anti-Rubella IgG was found to be 92.8% (4621/4978). Anti-Rubella IgG seroprevalence positivity varies between 16.8% and 96.4% as seen in Table-3 and Table 4. That rate was determined to be 93.47% in compilation that Cetinkaya et al. arranged (17).

Unlike toxoplasmosis while the possibility of Congenital Rubella Syndrome (CRS) of the fetus that encounters the virus in the 1st trimester is between 38-100%, it varies between 0-18% in the 3rd trimester. In addition, CRS at the beginning of pregnancy is more severe. The frequency of CRS has decreased significantly after MMR vaccine (18). 4.6% of patients were anti-Rubella IgG negative in our study. If these patients are detected in the preconceptional period, protection from infections that may occur during pregnancy by vaccination can be provided. Therefore, patients planning pregnancy should be provided to be checked for anti-Rubella IgG and vaccinated at least 1 month before pregnancy. So, we think that it would be more meaningful to be examined Rubella antibodies in the preconceptional period rather than the beginning of pregnancy.

CMV is the most common cause of intrauterine infection in developed countries. Pregnancy affects approximately 1% of it. It commonly causes hearing loss and learning difficulties the most. Besides, congenital infection occurs in 30-40% of those who have primary infection. Anti-CMV IgM was determined as 1.1% (53/4709) in the evaluation of CMV seroprevalence in our study. As seen in Table-3 anti-CMV IgM seroprevalence positivity varies between 0.2% and 3.7% (16). The results of our study show similarity with the study of Chen et al. (1.24%) (14). Seroprevalence positivity rate was determined to be 98.5% (4471/4539) in the evaluation made for anti-CMV IgG. As seen in Table-5 anti-CMV IgG seroprevalence positivity ranges from 19% to 99.5% (7, 9). The results of our study are similar to the study Ozdemir et al. conducted in 7 different cities in our country (Table-3) (16). It was recommended to screen for CMV infection in England in the study which Abdel-Fattah et al. carried out (4). We think that it would be more appropriate to inform about CMV infection and prevention methods and symptoms of acute infection rather than general screening in our country.

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Table 3. Comparison of toxoplasma, rubella and CMV seroprevalences of studies published since 2015.

Writer	Country	Year	The number of patients who participated in the study	The rate (%) of patient with Anti-Toxo IgM (+)	The rate (%) of patient with Anti-Toxo IgG (+)	The rate (%) of patient with Anti-Rubella IgM (+)	The rate (%) of patient with Anti-Rubella IgG (+)	The rate (%) of patient with Anti-CMV IgM (+)	The rate (%) of patient with Anti-CMV IgG (+)
Wang LC et al. (11)	**China**	**2015–2017**	18104	0.35	4.34	0.63	90	0.97	96.79
Sahu SK et al. (13)	**India**	**December 2016 to November 2017**	402	0.7	38.3	0.5	68.4	1.7	57.2
Zhang N. et al. (10)	**China**	**Aug. 2013 to Jan. 2016**	14852	0.48	0.36	1.64	84.82	0.43	95.04
Obaid HM. et al. (9)	**Iraq**	**2013-2014**	500	1.8	5.4	0.2	16.8	1.8	19
Chen L. et al. (14)	**China**	**August 2016 to July 2017**	10669	0.67	2.53	2.55	89.74	1.24	92.05
Wang Y. Et. al (15)	**China**	**January 2017 to August 2018**	1683	0.54	-	1.13	-	3.15	-
Numan O. et al. (7)	**Turkey (Istanbul)**	**September 2013 to January 2015**	1101	0	31	0.2	94.2	0.5	99.5
Zeb MA. Et al. (8)	**Pakistan**	**2013 to 2015**	800	2.5	-	1.5	-	1.8	-
Özdemir OM. et al. (16)	**Turkey (7 different cities)**	**Different dates between 2009-2013**	7523	-	-	0.6-1.6	76-96.4	0.2-3.7	87.8-100

Table 3. Comparison of Rubella seroprevalences of studies published since 2015.

Writer	Country (City)	Year	The number of patient participated in the study	The rate (%) of patient with Anti-Rubella IgM (+)	The rate (%) of patient with Anti-Rubella IgG (+)
Gülcen BS. et al. (19)	Turkey (Konya)	January 2013- 31 December 2015	2151	-	93.9
Aynalı A. et al. (20)	Turkey (Isparta)	January 2013- December 2013	781	1.9	96.2
Senturk S. et al. (21)	Turkey (Van)	31 July 2009- 01 August 2014	1037	1.9	93.9

In conclusion, there are many factors affecting the seroprevalence of Toxoplasma gondii, Rubella and CMV viruses such as communal life, sanitation conditions, age, migration. As screening of these factors before and during pregnancy continues as a matter of debate for obstetricians, it presents a dynamic situation with changing country conditions (war, migration, economic crisis, etc.). One of the most important parameters in screening is cost-effectiveness analysis.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of the Muğla Sıtkı Koçman University (06.11.2020, 22).

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