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Seroprevalance of Rubella Antibodies Among Pregnant Women in a Regional Maternity Hospital in Eastern Turkey

Türkiye'nin Doğusunda Bir Bölge Hastanesinde Gebelerde Rubella Seroprevalansı

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Abstract

Introduction: Rubella infection in pregnancy may cause severe complications, including still birth, miscarriage, preterm labor, growth deficiency, congenital malformation, blindness, cardiac defects, central nervous system abnormalities, and congenital cataract and hearing loss. The purpose of this study was to investigate the seroprevalence of rubella in pregnant women presenting to our hospital for routine antenatal examination, to compare our results with those from other countries, and to contribute to the literature by discussing opinions concerning rubella screening in pregnancy with data from 27.465 patients.
Material and Methods: This retrospective study involved anti-rubella IgM and IgG screening results of pregnants in the first trimester, aged 17-45 and presented to our hospital for antenatal examination between 2013 and 2016. Data were collected from the hospital's electronic records system and patient files. Rubella antibody levels were determined using commercially available ELISA kits (ALISEI SEAC, Italy) in the medical microbiology laboratory. Anti-rubella IgM-positive cases were also evaluated using the avidity test. The results were analyzed using the SPSS v.15.0 (SPSS Inc., Chicago, Illinois, USA) data analysis system.
Results: Rubella IgM antibody positivity was determined in 205 (0.8%) of 27.465 pregnants whose anti-rubella IgM status was investigated, and positive values were observed in 16.526 (9.2%) of 17.186 cases subjected to anti-rubella IgG antibody analysis. Anti-rubella avidity tests revealed high avidity in 92.7% of patients, low avidity in 3.4%, and intermediate avidity in 3.9%.
Conclusion: We think that rubella screening during pregnancy is essential, and that the best means of reducing the adverse effects of rubella virus would be to provide full immunization before pregnancy for females of child-bearing age.
Keywords: Pregnancy, rubella, prevalence, screening, seroprevalence

Öz

Giriş: Rubella, gebelerde düşük, ölü doğum, erken doğum, gelişme geriliği, konjenital malformasyon, körlük, kalp anomalileri, santral sinir sistemi anomalileri, konjenital katarakt ve işitme kaybı gibi ağır komplikasyonlara yol açabilmektedir. Bu çalışmada, rutin antenatal takip amacıyla hastanemize başvuran gebelerde rubella seroprevalansını araştırmayı, verilerimizi diğer ülke verileri ile karşılaştırmayı ve 27465 hasta verisiyle literatüre katkı sağlamayı, gebelerde rubella taraması konusundaki görüşleri literatürler eşliğinde tartışmayı amaçladık.
Gereç ve Yöntem: Bu çalışmada 2013-2016 yılları arasında antenatal takip için hastanemize başvuran, 17-45 yaş arası, ilk trimester gebelerde anti-rubella IgM ve IgG tarama sonuçları retrospektif olarak değerlendirildi. Veriler hastane otomasyon sistemi ve hasta dosyalarından elde edildi. Kan örnekleri hastanemiz mikrobiyoloji laboratuvarında mikro-ELISA (ALISEI SEAC, İtalya) yöntemi ile çalışıldı. Anti-rubella IgM olumlu olgular ayrıca anti-rubella IgG avidite testi ile de değerlendirildi. Sonuçlar SPSS.15.0 (SPSS Inc, Chicago, Illionis, USA) programında analiz edildi.
Bulgular: Anti-rubella IgM çalışılan 27465 gebenin 205 tanesinde (%0,8) rubella IgM antikor olumluluğu saptanırken, anti-rubella IgG antikor bakılan 17186 olgudan 16526 tanesinde (%96,2) olumlu değer saptandı. Anti-rubella IgG avidite çalışılan hastaların %92,7'sinde yüksek avidite, %3,4'ünde düşük avidite, %3,9'unda ara değer saptandı.
Sonuç: Rubellanın gebelikte taranmasının önemli olduğu ancak, doğurganlık çağındaki kız çocuklarında rubella bağışıklığının tamamlanması ve immünizasyonun sağlanmasının bu konudaki en güvenilir yaklaşım olacağı kanaatindeyiz.
Anahtar Kelimeler: Gebelik, kızamıkçık, prevalans, tarama, seroprevalans

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Introduction

Infections occurring during pregnancy may lead to prenatal morbidity and mortality. Congenital malformations may develop when the agent of infection is transmitted to the fetus through the placenta. These infections may be asymptomatic or may also manifest in the form of intrauterine death, abortus, congenital defects, severe intrauterine growth retardation, hepatosplenomegaly, cataract, deafness, and other abnormalities[1].

Rubella infection during pregnancy may cause teratogenicity and represents a major community health problem. In early pregnancy, and especially in the first trimester, almost the entire fetus becomes infected as a result of maternal infection eight weeks after menstruation. Congenital malformation develops in most of the infected fetuses. There is a 90% risk of congenital malformation as a result of primary rubella infection in the first trimester. The disease, known as congenital rubella syndrome, may also cause congenital cataract, deafness, mental retardation, and cardiac defects[2].

Rubella seropositivity rates in different countries range between 54.1% and 95.2%[3].

Rubella-IgG seropositivity indicates past infection or immunization. However, rubella-IgM seropositivity is usually a sign of active infection or recent vaccination. Negative results indicate that no antibody is detected. Acute infection and nonspecific bonding reaction may give rise to uncertain results. As a result of studies on the subject of (Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex virus) TORCH, pregnant women with a poor obstetric history are now advised to receive routine TORCH check-ups, meaning that complications can be managed easily[4].

The American College of Obstetricians and Gynecologists recommends routine screening in early pregnancy for detecting rubella infections. Check-ups will make it possible to identify a history of rubella infection or immunization. Rubella is a systemic disease, and vaccination can provide protection against it. Vaccination is recommended for women of childbearing age. The purpose of this descriptive study was to determine the rubella seroprevalence in our secondary-care hospital in Turkey and to compare our findings with other national data.

Materials and Methods

Blood samples were collected from the 1st trimester pregnants presenting to the Erzurum Nene Hatun Maternity Hospital for antenatal check-ups between January, 2013 and January 2017. The samples were analyzed in the microbiology laboratory using the Micro-ELISA method (ALISEI SEAC, Italy). Anti-rubella IgM and anti-rubella IgG values were obtained retrospectively from the hospital electronic records system and patient files. Avidity of anti-rubella IgG in anti-rubella IgM-positive cases were also evaluated. Patients with multiple serology results were excluded from the study. The results were analyzed using SPSS v.15.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 27.465 pregnants aged between 17 and 45, were tested with anti-rubella IgM and 17.186 with anti-rubella IgG. The average age of the patients was 27±5.9 years. Two hundred five of the 27.465 tested with IgM exhibited seropositivity, while positive results were obtained from 16.526 (96%) of the 17.186 subjects tested for anti-rubella IgG. Of the patients tested for anti-rubella IgG avidity, 92.7% exhibited high avidity (>60%), 3.4% low avidity (<30%), and 3.9% moderate avidity (30-60%). Anti-rubella results are shown in Table 1, seropositivity rates according to age groups in Table 2 and avidity values in Table 3.

Discussion

Congenital rubella syndrome was first defined by Gregg in 1941. While the first symptoms were determined as cardiovascular

Table 1. Anti-rubella results of the study sample

Year	Anti-rubella IgM (+) N (%)	Anti-rubella IgG (+) N (%)
2013	63/7891 **(0.8%)**	4624/4649 **(99.5%)**
2014	46/6375 **(0.7%)**	2439/2507 **(97.3%)**
2015	52/6574 **(0.8%)**	4831/5214 **(92.7%)**
2016	44/6625 **(0.7%)**	4632/4816 **(96.2%)**
Total	205/27465 **(0.8%)**	16526/17186 **(96.2%)**

Table 2. Seropositivity rates according to age groups

Year	Anti-rubella IgG (+)				Anti-rubella IgM (+)			
	<20 age	20-29 age	30-39 age	>40 age	<20 age	20-29 age	30-39 age	>40 age
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
2013	369 (7.94)	2501 (53.82)	1597 (34.36)	157 (3.38)	6 (0.08)	24 (0.3)	30 (0.38)	3 (0.04)
2014	213 (8.5)	1364 (54.41)	788 (31.44)	74 (2.95)	10 (0.15)	24 (0.37)	10 (0.15)	2 (0.03)
2015	382 (7.72)	2747 (55.5)	1544 (31.19)	138 (2.79)	13 (0.2)	19 (0.29)	15 (0.23)	5 (0.08)
2016	340 (7.06)	2544 (52.84)	1507 (31.3)	142 (2.95)	3 (0.05)	26 (0.41)	10 (0.16)	5 (0.08)

Table 3. Avidity values

Year	Low avidity N (%)	High avidity N (%)	Intermediate avidity N (%)
2013	3 (4.7)	55 (87.3)	5 (7.9)
2014	2 (4.3)	42 (91.3)	2 (4.3)
2015	1 (2)	50 (96)	1(1.9)
2016	1 (2.3)	43 (97.7)	0
Total	7 (3.4)	190 (92.7)	8 (3.9)

Table 4. Studies investigating the prevalence of rubella during pregnancy in Turkey

	Anti-rubella IgM (+)	Anti-rubella IgG (+)
	N (%)	N (%)
Ocak et al.[16]*	9 (0.5)	1570 (95)
Akıncı et al.[17]*	-	468 (95.9)
Uyar et al.[3]*v	10 (1.7)	566 (94.3)
Efe et al.[18]*	2 (3.3)	610 (99.5)
Dündar et al.[19]*	4 (0.3)	1230 (95.2)
Karabulut et al.[20]*	0	1206 (95.1)
Aşık et al.[21]*	10 (1.8)	465 (92.5)
İnci et al.[22]*	4 (0.3)	1230 (95.2)
Akpınar and Akpınar[23]*	91 (4.9)	785 (97.5)
Kasap et al.[24]*	1 (0.8)	170 (89.5)
The present study	205 (0.8)	16526 (96.2)

*Reference no.

diseases, cataract and deafness, subsequent studies revealed new symptoms and risks associated with the month in which the infection occurred. Rates of congenital defects and clinical manifestations in congenital rubella syndrome vary depending on the time of maternal infection. Congenital defect rates range between 38-100% in the first trimester, and desreases gradually to 4-60% in the second trimester and 0-18% in the third trimester[5]. This study was a retrospective study and the clinical follow-up of congenital rubella syndrome (congenital defects and clinical manifestations) was not performed.

The rubella prevalence varies among different countries: 53% in Nigeria[6], 76% in Sri Lanka[7], 77.5% in Russia[8], 94.1% in Spain[9], 93.4% in Haiti[10], 93% in Australia[11], 89.1% in Taiwan[12], 87% in Germany[13], 72% in Sudan[14], and 96% in Iran[15]. Studies investigating the prevalence of rubella in Turkey are listed in Table 4.

Rubella vaccine is an attenuated vaccine used as a trivalent vaccination against measles, mumps and rubella (MMR) or as a monovalent vaccine for rubella alone. It is not recommended during pregnancy. Rubella vaccination has been included in the national immunization program in Turkey since 2006. MMR vaccine is administered to children in two doses; the first dose is for children in their 12th month, while the second is for children aged seven. The rubella IgG level in this study was 99.4%, indicating probably the success of this vaccination program.

Screening pregnant women for rubella is a controversial subject. In the United States of America (USA), rubella serology screening is recommended at the first prenatal visit, while in the United Kingdom, routine monitoring for rubella is not recommended. The USA introduced and has achieved the goal of eliminating endemic rubella transmission and congenital rubella syndrome. Elimination of endemic rubella was documented and verified in the USA in 2004. However, there is still a strong likelihood of imported cases of rubella because of international travel and countries lacking routine rubella vaccination. In order to maintain elimination, the USA should continue to achieve high vaccination rates among children, to ensure that women of childbearing age, particularly women born outside the country, are vaccinated, and to maintain sensitive surveillance in order to detect both rubella and congenital rubella syndrome. Particular care should be taken when rubella IgM is detected in a pregnant woman with no history of illness or contact with a rubella-like illness. Although this is not recommended, many pregnant women with no known exposure to rubella are nevertheless tested for rubella IgM as part of their prenatal care regimen. Additional laboratory evaluation should be performed if rubella test results are IgM-positive for individuals with no or low risk of exposure to rubella[23,25].

A recent short report from the United Kingdom discussed a failure to protect women against rubella infection by the MMR vaccination program. The number of pregnant women susceptible to rubella in the West Midlands in England rose from 1.4% to 6.9 in 2011. The investigators concluded that screening for rubella in pregnancy offers no advantages in terms of the current pregnancy and that it may be time to review the universal MMR vaccination program, which would in turn would eliminate the need for maintaining this practice[26].

The aim of screening is to prevent rubella virus infecting others by identifying rubella unimmunized individuals and to prevent congenital rubella syndrome, with the help of postnatal vaccination. A further aim is to detect active infection with the help of check-ups and to provide necessary management of rubella infection.

The presented study has several limitations. First, only the results of patients in the hospital electronic records system were analyzed. Second, clinical conditions, such as vaccine history and rash, in IgM seropositive patients could not be evaluated. In addition, information concerning curettage, amniotic biopsy or malformation in patients with IgM seropositivity and moderate and low avidity was not available.

Conclusion

In conclusion, our findings for rubella are similar to those reported from other countries. We think that since ours is a reference hospital for nearby towns, our findings concerning rubella are an accurate reflection of our region, Eastern Anatolia.

Although we believe that investigation of rubella during pregnancy is essential, the best approach in terms of reducing the adverse effects of rubella virus would be to provide full immunization before pregnancy for young women of child-bearing age.

Ethics

Ethics Committee Approval: Since this was a retrospective study, there was no need for ethical committee approval.

Informed Consent: Since this was a retrospective chart review study, there was no informed consent.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.Ç.T., L.D., Concept: E.Ç.T., Z.Ö., Design: B.G.K., H.A., Data Collection or Processing: E.Ç.T., B.G.K., H.A., Analysis or Interpretation: E.Ç.T., Z.Ö., Literature Search: E.Ç.T., L.D., Writing: E.Ç.T., L.D., H.A.

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References

1. Cutts FT, Robertson SE, Diaz-Ortega JL, Samuel R. Control of rubella and congenital rubella syndrome (CRS) in developing countries, Part 1: Burden of disease from CRS. Bull World Health Organ. 1997;75:55-68.
2. Best JM, Banatvala JE. Principles and practise of Clinical Virology. In: Zuckerman AJ, Banatvala JE, Pattison JR, Griffiths PD, Schoub BD, editors. 5th ed. John Wiley and Sons, Ltd, West Sussex, England;2004:427-57.
3. Uyar Y, Balci A, Akcali A, Cabar C. Prevalence of rubella and cytomegalovirus antibodies among pregnant women in northern Turkey. New Microbiol. 2008;31:451-5.
4. Pokhrel T, Sharma S, Bhat SR. TORCH Profile: A Convenient Method for Screening Infection in Pregnancy by ELISA: A Review. Research & Reviews: A Journal of Microbiology & Virology. 2014;4:16-21.
5. De Santis M, Cavaliere AF, Straface G, Caruso A. Rubella infection in pregnancy. Reprod Toxicol. 2006;21:390-8.
6. Bukbuk DN, el Nafaty AU, Obed JY. Prevalence of rubella-specific IgG antibody in non-immunized pregnant women in Maiduguri, north eastern Nigeria. Cent Eur J Public Health. 2002;10:21-3.
7. Palihawadana P, Wickremasinghe AR, Perera J. Seroprevalence of rubella antibodies among pregnant females in Sri Lanka. Southeast Asian J Trop Med Public Health. 2003;34:398-404.
8. Odland JØ, Sergejeva IV, Ivaneev MD, Jensen IP, Stray-Pedersen B. Seropositivity of cytomegalovirus, parvovirus and rubella in pregnant women and recurrent aborters in Leningrad County, Russia. Acta obstet Gynecol Scand. 2001;80:1025-9.
9. Vilajeliu A, García-Basteiro AL, Valencia S, Barreales S, Oliveras L, Calvente V, Bayas JM. Rubella susceptibility in pregnant women and results of a postpartum immunization strategy in Catalonia, Spain. Vaccine. 2015;33:1767-72.
10. Fitter DL, Anselme R, Paluku G, Rey G, Flannery B, Tohme RA, Vertefeuille JF. Seroprevalence of measles and rubella antibodies in pregnant women Haiti, 2012. Vaccine. 2013;32:69-73.
11. Sathanandan D, Gupta L, Liu B, Rutherford A, Lane J. Factors associated with low immunity to rubella infection on antenatal screening. Aust NZJ Obstet Gynaecol. 2005;45:435-8.
12. Lin CC, Yang CY, Shih YL, Hsu HW, Yang TH, Cheng YW, Huang YL. Rubella seroepidemiology and estimations of the catch-up immunisation rate and persistence of antibody titers in pregnant women in Taiwan. BJOG. 2011;118:706-12.
13. Sauerbrei A, Prager J, Bischoff A, Wutzler P. Antibodies against vaccine-preventable diseases in pregnant women and their offspring. Measles, mumps, rubella, poliomyelitis, and varicella]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2004;47:10-5.
14. Hamdan HZ, Abdelbagi IE, Nasser NM, Adam I. Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virol J. 2011;8:217.
15. Honarvar B, Moghadami M, Moattari A, Emami A, Odoomi N, Bagheri Lankarani K. Seroprevalence of anti-rubella and anti-measles IgG antibodies in pregnant women in Shiraz, Southern Iran: outcomes of a nationwide measles-rubella mass vaccination campaign. PloS One. 2013;8:55043.
16. Ocak S, Zeteroglu S, Ozer C, Dolapcioglu K, Gungoren A. Seroprevalence of *Toxoplasma gondii*, rubella and cytomegalovirus among pregnant women in southern Turkey. Scand J Infect Dis. 2007;39:231-4.
17. Akıncı P, Altuğlu İ, Sertöz R, Zeytinoğlu A. Rubella and cytomegalovirus infection in pregnants in İzmir, Turkey. İnfeksiyon Dergisi. 2007;21:183-6.
18. Efe Ş, Kurdoğlu Z, Korkmaz G. Seroprevalance of cytomegalovirus, rubella and toxoplasma antibodies in pregnant women of Van region. Van Tıp Dergisi. 2009;16:6-9.
19. Dündar Ö, Çelik S, Tütüncü L, Ergür AR, Atay V, Müngen E. Toxoplasmosis and rubella among pregmant women delivered in our clinic between 2000 and 2005. Zeynep Kamil Tıp Bülteni. 2009;40:1-9.
20. Karabulut A, Polat Y, Türk M, Işık Balcı Y. Evaluation of rubella, *Toxoplasma gondii*, and cytomegalovirus seroprevalences among pregnant women in Denizli province. Turk J Med Sci. 2011;41:159-64.
21. Aşık G, Ünlü BS, Er H, Yoldaş Ö, Köken G, Çufalı D, Yılmazer M. Seroprevalence of toxoplasma and rubella in pregnant women in Afyon region. Pam Tıp Derg. 2013;6:128-32.
22. İnci A, Yener C, Güven D. The investigation of toxoplasma, rubella and cytomegalovirus seroprevalances in pregnant women in a state hospital. Pam Tıp Derg. 2014;7:143-6.
23. Akpınar O, Akpınar H. Investigation of the rubella and cytomegalovirus seroprevalences by elisa method in pregnant women. Balikesir Saglik Bil Derg. 2017;6:11-5.
24. Kasap B, Öner G, Küçük M, Turhan NÖ, Akın MN, Arıkan S, Çaylak SD. Evaluation of toxoplasmosis, rubella, cytomegalovirus and hepatitis prevalence of pregnant women in Muğla. Tepecik Eğit ve Araşt Hast Dergisi. 2017;27:31-6.
25. CDC. Surveillance Manual, 5th edition. Rubella Chapter, 2012;14-1.
26. Skidmore S, Boxall E, Lord S. Is the MMR vaccination programme failing to protect women against rubella infection? Epidemiol Infect. 2014;142:1114-7.