Seroprevalence of Antibodies for Rubella and Cytomegalovirus among Pregnant and Antenatal Females in Western Turkey

Serdar GÜNGÖR¹ & Berrin UZUN²

Abstract

Primary infections caused by rubella and cytomegalovirus (CMV) can lead to serious complications due to their potentially teratogenic effects during pregnancy. Rubella and CMV screening of pregnant females is not routinely carried out in Turkey. The purpose of this study was to determine the prevalence of rubella and cytomegalovirus in Izmir among pregnant and antenatal females, and to review seroprevalences reported from different regions of Turkey.

Between January 2011 and December 2015, we retrospectively evaluated anti-rubella antibodies and anti-CMV antibodies of pregnant and antenatal females. Females aged 18-45 years were included in the study. Rubella and CMV IgM and G antibodies were tested using the IMMULITE® 2000XPi Immunoassay System. Rubella IgG and rubella IgM seropositivity were detected in 16,255 (96.5%) of 16,845 and in 206 (1.1%) of the 18,720 pregnant and antenatal females, respectively. Positivity for the anti-CMV IgG and anti-CMV IgM antibody were found in 11,950 (98.7%) and 40 (0.3%) of 13,412 females. In conclusion, this study showed that in our province, a high percentage of pregnant and antenatal females had been exposed to rubella and CMV prior to reaching a child-bearing age. Rubella and CMV seroprevalences show a relatively homogeneous distribution throughout Turkey.

1. Introduction

Prenatal infections are thought to be responsible for 2%-3% of all congenital anomalies (Surpam et al., 2006). Rubella infection is a common cause of exanthematous disease, predominantly affecting children, and is an important public health issue because of the potential for teratogenic effects in pregnant females. When the primary infection occurs in the first trimester of pregnancy, the virus may elicit congenital rubella syndrome, which is associated with multiple developmental anomalies such as congenital cataracts, deafness, mental retardation, and cardiac defects. The risk of congenital malformations in affected fetuses is approximately 90% (Pehlivan, 2007; URL1, 2011).

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It is difficult to determine rubella seropositivity solely by examining a patient’s history because many illnesses with rashes may simulate rubella and up to 50% of rubella infections may pass without any symptoms. Therefore, serologic testing is necessary for detection of susceptible patients (URL1, 2011; Özdemir et al., 2011). The American College of Obstetricians and Gynecologists currently recommends screening pregnant females only for immunity to rubella (American Academy of Pediatrics, 2007). Further, there is great variation in the age specific seroprevalence of rubella among populations hailing from different countries.

CMV is the most common cause of congenital infections worldwide and is endemic throughout the world (Aljumaili et al., 2014). Seroprevalence of CMV varies across different populations and countries. CMV infection is usually asymptomatic in adults, but its significance is many times increased when it occurs during pregnancy. CMV is the most frequent cause of congenital viral infections and frequently causes sensorineural hearing loss and mental retardation (Cannon, 2010). Intrauterine transmission of CMV occurs as a result of maternal infection. But unlike rubella and toxoplasmosis, fetal infection can occur following both primary and recurrent infection (reactivation of endogenous virus or re-infection with a new strain) (Kenneson and Cannon, 2007; Kim, 2010). The time of infection during pregnancy is another important facture; it is lowest at the time of conception, stable through the second and first trimester, and highest in the third trimester. It has been reported that primary infection occurs in 0.15% to 2.0% of all pregnancies and may be transmitted to the fetus in up to 40% of cases (Uyar et al., 2008).

The aim of this study was to assess the seroprevalence of rubella and CMV infections in antenatal and pregnant females in Izmir province, Western Turkey and compare our findings with those of other studies. We think that the results of this study provide further information to estimate the susceptibility of antenatal and pregnant females to congenital infections, thereby enforcing appropriate preventive measures.

2. Materials and Methods

Between January 2011 and December 2015, pregnant females undergoing routine obstetrical evaluation and females who presented for their antenatal visit to Katip Celebi University Atatürk Training and Research Hospital in Izmir province, Turkey were included. Laboratory results were retrospectively evaluated in this study.

We collected a 5 ml blood sample from each participant, which was then stored at -20 °C until testing. Sera were analyzed for anti-rubella IgM, anti-rubella IgG, anti-CMV IgM, and anti-CMV IgG antibodies by a chemiluminescent enzyme immunoassay method using the IMMULITE® 2000XPi Immunoassay System (Siemens Germany). The assays were performed according to the manufacturer’s instructions. Anti-CMV IgM antibody titers and anti-CMV IgG antibody titers greater than 1,1 IU/ml were regarded as positive. Anti-rubella IgG antibody titers above a 10,0 ratio and anti-rubella IgM titers above a 1,1 ratio were considered positive. All positive results were double-checked. Additionally, we reviewed the relevant literature reporting seroprevalences from different regions of Turkey.
3. Results

A total of 18,720 females with a mean age of 27.19 years (range, 18-45 years) were tested for rubella IgM and 16,845 females with a mean age of 27.72 years (range, 18-45 years) were screened for rubella IgG seroprevalence. A total of 13,412 females with a mean age of 27.18 years (range, 18-45 years) were screened for CMV IgM and 12,108 females with a mean age of 27.09 years (range, 18-45 years) were tested for CMV IgG seroprevalence.

Rubella IgG seropositivity was detected in 16,255 (96.5%) of 16,845 subjects. Seropositivity for rubella IgM was found in 206 (1.1%) of the 18,720 pregnant and antenatal females. Among the serum samples, 179 were found to be positive for both Rubella IgM and IgG. Anti-CMV IgG antibodies were found in 11,950 (98.7%) and anti-CMV IgM antibodies in 40 (0.3%) of 13,412 pregnant and antenatal individuals. Among the serum samples, 43 were found to be positive for both CMV IgM and IgG. The rates of seropositivity for rubella and CMV antibodies are shown in Table 1. The review of the pertinent literature reported from Turkey showed a range 94.3%-99.5% seroprevalence rate for rubella, and 96.4%-99.5% seropositivity for CMV (Table 2).

Table 1: The rates of seropositivity for rubella and cytomegalovirus (CMV) infections.

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Negative (n)</th>
<th>%</th>
<th>Positive (n)</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Rubella IgM</td>
<td>18514</td>
<td>98.9</td>
<td>206</td>
<td>1.1</td>
<td>18720</td>
</tr>
<tr>
<td>Anti-Rubella IgG</td>
<td>590</td>
<td>3.5</td>
<td>16255</td>
<td>96.5</td>
<td>16845</td>
</tr>
<tr>
<td>Anti-CMV IgM</td>
<td>13372</td>
<td>99.7</td>
<td>40</td>
<td>0.3</td>
<td>13412</td>
</tr>
<tr>
<td>Anti-CMV IgG</td>
<td>158</td>
<td>1.3</td>
<td>11950</td>
<td>98.7</td>
<td>12108</td>
</tr>
</tbody>
</table>

Table 2: Comparison of studies evaluating rubella and CMV seroprevalences from different regions of Turkey.

<table>
<thead>
<tr>
<th>Study</th>
<th>District</th>
<th>Rubella seropositivity (%)</th>
<th>CMV seropositivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karabulut et al. [6]</td>
<td>Denizli</td>
<td>95.1%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Ozdemir et al. [7]</td>
<td>Konya</td>
<td>95.9%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Uyar et al. [13]</td>
<td>Samsun</td>
<td>94.3%</td>
<td>97.3%</td>
</tr>
<tr>
<td>Tamer et al. [14]</td>
<td>Kocaeli</td>
<td>96.1%</td>
<td>96.4%</td>
</tr>
<tr>
<td>Ocak et al. [15]</td>
<td>Hatay</td>
<td>95.5%</td>
<td>97.3%</td>
</tr>
<tr>
<td>Efe et al. [16]</td>
<td>Van</td>
<td>99.5%</td>
<td>99.5%</td>
</tr>
<tr>
<td>Agca et al. [17]</td>
<td>Kutahya</td>
<td>94.6%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Akinci et al. [18]</td>
<td>Izmir</td>
<td>95.9%</td>
<td>98.2%</td>
</tr>
<tr>
<td>Present Study</td>
<td>Izmir</td>
<td>96.5%</td>
<td>98.7%</td>
</tr>
</tbody>
</table>

4. Discussion

Cytomegalovirus and rubella can cause prenatal and perinatal infections and exert potentially teratogenic effects in pregnant females. These infections often lead to mild or asymptomatic maternal infections and may result in serious congenital abnormalities, intrauterine growth retardation, and even death of the fetus (Surpam et al., 2006; Kenneson and Cannon, 2007; Uyar et al., 2008). In this cross-sectional study, we assessed the immune status against rubella and cytomegalovirus infection in pregnant and antenatal females in Izmir province, and showed that a high percentage of females (96.5% for rubella and 98.7% for CMV) were previously exposed to the viruses. The seropositivity for rubella IgM and CMV IgM were 1.1% and 0.3%, respectively.
Rubella is a systemic disease that can be prevented by vaccination. Rubella vaccine use varies by stage of economic development: 100% for industrialized countries, 71% for countries with economies in transition, and 48% for developing countries (De Santis et al., 2006). In Turkey, the rubella vaccine was incorporated into the national immunization program in 2006. This study revealed seropositivity against rubella infections in pregnant and antenatal females in 96.5% of those examined. Rubella IgG positivity was 95.9% in a different study conducted in pregnant patients in Izmir (Akınç et al., 2007). The seroprevalence rate of 96.5% in our study indicates a small elevation, possible attributable to the rubella vaccination program that commenced in 2006 for under 18 years of age. However, because we did not obtain data with respect to rubella vaccination status in our study, we cannot definitively determine the degree of influence of the vaccination program.

In our study, few pregnant females were susceptible to rubella infections. There is continued controversy in Turkey as to the necessity of rubella vaccination among childbearing females due to outbreaks occurring abroad. These conditions warrant repeat consideration.

Previous studies from different regions of Turkey reported very high rubella seropositivity, ranging between 94.3% and 99.5% among pregnant females (Table 2). The high rate of seropositivity detected in this study was also similar to previously-reported rates out of Turkey. Similar seropositivity findings from Western, Central, and Eastern parts of Turkey suggest a wide incidence of rubella infection throughout the countries. A number of studies reveal a rubella seroprevalence of 98% in pregnant females and females of child-bearing age in Spain (Pedranti et al., 2007), 95.3% in antenatal females from Mozambic (Barreto et al., 2006), and 94.5% in pregnant females from Pakistan (Ali, 2014). Likewise, the rubella seropositivity in females of reproductive age has been reported as 70-99% in conducted studies from different countries (Montoya and Kovacs, 2005).

For CMV infections, communal living and poor hygiene conditions facilitate early spread. In a high seroprevalence population a pregnant female has a higher likelihood of being exposed to someone who is infected with CMV. Thus, seropositive pregnant females have a higher risk of reinfection and the relatively few seronegative pregnant females have a higher risk of primary infection (Kenneson and Cannon, 2007). In our country, the seroprevalence of CMV is reportedly between 96.4% and 99.5% among pregnant females (Table 2). In our study, the seropositivity rates of pregnant and antenatal females for anti-CMV IgM and anti-CMV IgG antibodies were 0.3% and 98.7%, respectively. If pregnant females are seronegative for CMV, contact precautions must be taken. Whether the CMV testing should be offered all pregnant females, or restricted to high risk populations is still a topic of debate.

CMV is found throughout all geographic locations and socioeconomic groups, but is more widespread in developing countries and in communities with lower socioeconomic status (Kim, 2010; Kenneson and Cannon, 2007). Global prevalence of CMV infection is reported to be approximately 40%-80%, but it has been estimated to vary from about 45% in developed countries and to 100% in developing countries (Cannon et al., 2010; Kim, 2010; Kenneson and Cannon, 2007). CMV seropositivity was 46.8% in France (Picone et al., 2009), 56.3% in
Finland (Alanen et al., 2005), and 84% in Spain (Estripeaut et al., 2007). CMV infections are highly associated with poor hygienic conditions, communal lifestyles, and close contact with day care units. Therefore, hygiene information has a positive impact and could significantly reduce the incidence of maternal CMV infection during pregnancy for seronegative patients (Picone et al., 2009).

Our study has a few limitations. First, we did not obtain information about the rubella vaccination status of pregnant and antenatal females. Since July 2006, all females under the age of 18 are vaccinated; therefore, we can assume that females under the age of 21 have probably been vaccinated previously. Second, we also did not collect information about the living conditions or socioeconomic and educational status, which could have improved our understanding of CMV seropositivity rates.

5. Conclusion

Results for rubella and CMV seropositivity in Izmir district were similar to those of other regions of Turkey. In our province, most females were previously exposed to rubella and CMV before child-bearing age. The necessity of a rubella vaccination program in adults is a subject of debate in this country due to the high rate of rubella seropositivity. The education of pregnant and antenatal females about transmission routes and measures seems an effective strategy for protecting seronegative females from CMV infections. CMV and rubella infections during pregnancy can cause congenital fetal anomalies. Education should be given to the females of childbearing age, especially regarding the transmission routes of CMV and rubella, in order to prevent the spread of infectious diseases. This education should be further expanded by adding it to primary care services. Furthermore, when problems arising from primary infection in pregnant females, it is important to inform the mother about rubella vaccination. This can help determine the mother’s pre-pregnancy immunity status for CMV help prevent CMV transmission during pregnancy. Screening high-risk pregnant females will be more appropriate when considering the financial costs of screening programs. The potential benefits of such programs include early detection of perinatal infections and protection of fetuses.

Acknowledgments

No financial support

Author Contributions

Serdar Güngör conceived the paper, oversaw data collection, conducted data analysis, wrote the manuscript and approved the final version, participated in study design, data analysis and interpretation, critically revised manuscript and approved final version. Berrin Uzun provided oversight to the study, participated in data interpretation and revision of the manuscript, and approved the final version. The authors declare that they have no conflicts of interest.
References


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