Rubella Seroprevalence among Women of Childbearing Age Residing in a Rural Region: Is There a Need for Rubella Vaccination in Turkey?

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SUMMARY: It is essential to evaluate the susceptibility of women in the reproductive age group to rubella virus in order to set strategies for the prevention of congenital rubella syndrome (CRS). Turkey began implementing measles-mumps-rubella vaccination as part of the national vaccination schedule for children (12 months, 6 years) and adolescents (14 years) in July, 2006, and there is an ongoing discussion of the need for a policy of vaccinating women of child-bearing age against rubella. The aim of this study was to determine the rubella seroprevalence among women in the reproductive age group in a rural district in Ankara and to provide data about rubella susceptibility for policymakers. Four hundred ninety of the women in the 15- to 49-year-old age group in the region who were targeted were reached (68.2%), and 467 (65.0%) of them who had a convenient serology were included in the study. Rubella IgG antibodies were quantified by the enzyme-linked immunosorbent assay method. Seropositivity was 95.5% for the total group and 96.2% among pregnant women. The seropositivity of this rural group of women was found to be high, but in order to rule out the need for a rubella vaccination program for women of child-bearing age, large-scale studies in different settings and studies that describe the CRS burden in Turkey are required.

INTRODUCTION

Rubella is an acute exanthematous viral infection that predominantly affects children but is also seen in adults. Although life-long immunity and protection against rubella result from natural infection with the virus, when susceptible pregnant women are exposed to the virus in the first months of their pregnancies, the virus can cause congenital rubella syndrome (CRS) and can have disastrous effects on the fetus. Therefore, the susceptibility of women in the reproductive age group to rubella virus, especially before gestation, is closely related to the potential risk for congenital infection and sequelae (1,2).

Since many rash illnesses may mimic rubella infection, and up to 50% of the infections may be subclinical, immunity against the virus cannot be confidently predicted from a patient’s clinical history of disease, and can only be documented through the determination of rubella-specific antibodies (2). Clinical immunity is usually parallel to the serum rubella antibody titers (3).

Successful rubella vaccination policies have been implemented in most western developed countries (4-7), and high seropositivity rates have been obtained through vaccination, although some resurgences have also been reported (7).

In many developing countries, CRS is an under-recognized public health problem, and there is an urgent need for the collection of appropriate data (8).

In developing countries, the burden of CRS has been assessed by: (i) surveillance of CRS; (ii) surveillance of acquired rubella; (iii) age-stratified serosurveys; and (iv) serosurveys documenting the rubella susceptibility of women of childbearing age (9).

In Turkey, rubella and CRS were not notifiable diseases, and there was no national incidence figure until the new surveillance system for communicable diseases was put into practice in January, 2005 (10). Under this new system, the number of confirmed rubella cases was reported to be 2,245 with a morbidity rate of 3.1 per 100,000 people in 2005, whereas there was only one CRS case in the same year (11). The actual figures were likely to be higher than reported since the surveillance system is rather new, and it may take some time to encourage country-wide reporting.

It is necessary to determine the rubella susceptibility in a population in order to determine the feasibility of rubella vaccination as a national policy.

The susceptibility of women in the reproductive age group should be the first to be determined in order to set strategies for the prevention of CRS. Thus, the aim of the present study was to determine the rubella seroprevalence among women in the reproductive age group in the Karagedik region in Gölbaşı District, a rural area near Ankara, and to provide data for the rubella susceptibility profile of women of childbearing age in Turkey.

MATERIALS AND METHODS

The study population included all of the women in the 15- to 49-year-old age group (n = 718), residing in the Karagedik region, and sera were collected in April- May 1998. Four hundred ninety of the women were reached (68.2%), and 467 (65.0%) of them with a convenient serology were included in the study. None were vaccinated against rubella.

For each woman, a questionnaire consisting of questions about her age, marital status, education, occupation, rubella vaccination history, and coverage by social insurance was completed in a face-to-face interview. Since the disease could be confused with a number of exanthematous diseases and the memory factor could form a bias, disease history was
considered to be non-confidential and not asked about on the questionnaire.

In order to determine the rubella serology, 7 cc venous blood samples were collected, and the sera were kept at –70°C until IgG antibodies for rubella were quantified by enzyme-linked immunosorbent assay (ELISA) using the Trinity Biotech Rubella IgG ELISA kits (Trinity Biotech, Jamestown, N.Y., USA). All sera with antibody titers equal to or below 6.50 IU/ml were regarded as seronegative, titers between 6.51 - 8.10 IU/ml were regarded as equivocal, and titers 8.11 IU/ml and above were regarded as seropositive as indicated in the kit prospectus. Sera with titers in the equivocal range were retested once, and the sera that were still in the equivocal range were presented as equivocal.

Data obtained were analyzed by the SPSS for Windows statistics program using the chi-square test and One-Way ANOVA analysis of variance after logarithmic transformation of geometrical means. The Bonferroni test was used for post hoc analysis. Geometrical means and mean deviations were calculated using the Microsoft Excel program.

**RESULTS**

Table 1 shows some of the sociodemographical properties of the evaluated women. Most of the evaluated women were married (70.2%), elementary school graduates (59.5%), and housewives (91.4%). Median age was found to be 30 years. Among them, 75.4% were not socially insured. Twenty-six (5.6%) of the evaluated women were pregnant. None of the women were vaccinated against rubella.

The distribution of rubella IgG antibody titers according to the age group of the evaluated women is shown in Table 2. Fifty point seven percent of the women had antibody titers between 15.01 and 30.00 IU/ml. Table 3 shows the geometrical and arithmetical means of the rubella IgG antibody titers, and the seropositivity percentages by age group. Among all of the subjects, 446 (95.5%) of the women were seropositive, 8 (1.7%) were seronegative, and 13 (2.8%) had antibody titers in the equivocal range. The highest seropositivity of 98.6% was encountered in the 20- to 24-year-old age group. This was followed by the 15- to 19-year-old age group at 97.6% and the 25- to 29-year-old age group at 96.1%. The seropositivity then declined with age and fell to 93.0% in the 40-year-old and over age group. There was a statistically significant difference between age groups with respect to the arithmetical and geometrical means of rubella IgG antibody titers ($P < 0.05$). The mean titers were higher in the 15- to 19-year-old age group than in the other age groups. But when the serological evaluation as seropositive or seronegative was made, no statistically significant differences were observed between the age groups ($P > 0.05$). There was no difference between the seropositivity rates with respect to marital status, education, occupation or coverage by social insurance.

The seropositivity among pregnant women was found to be 96.2%.

**DISCUSSION**

Infection with rubella virus can be disastrous in early gestation. The virus may affect all organs and can cause a variety of congenital defects in the fetus if a susceptible pregnant woman is exposed to it, especially in the early gestational weeks. This condition is called congenital rubella infection or syndrome and has a very high estimated lifetime cost for both parents and governments (2). The following strategies for the prevention of CRS have been reported by the World Health Organization (WHO): (i) providing direct protection...
before the implementation of the rubella vaccination in 1969, the figures reported by the WHO collaborative study groups is lower than the figure found in this study (16). The above were patients at various clinics in a hospital, a figure that 87.2% seropositivity among women of child-bearing age who those of these previous studies. Nuhoglu et al. reported a Istanbul (15). The results of the present study are similar to the 20- to 41-year-old age group residing in the northwest of Seker et al. reported 100.0% seropositivity among women in the 15- to 19-year-old and 20- to 29-year-old age groups, respectively (14). seropositivity rates of 89.7% and 91.6% for the 15- to 19- al. conducted a community-based study, and they reported the last 10 years among women of child-bearing age. Aksit et conducted a community-based seroprevalence studies for rubella have been performed over the period 2005 -2010 includes several strategies to control rubella. The strategies in the plan related to rubella are: (i) achieve and sustain very high coverage (≥95%) with at least 1 dose of rubella vaccine through high-quality routine immunization services; (ii) provide rubella vaccination opportunities, including supplementary immunization activities, to all rubella-susceptible children, adolescents and women of child-bearing age; (iii) strengthen surveillance systems through rigorous case investigation and laboratory confirmation of suspected cases; and (iv) improve the availability of high-quality, valued information for health professionals and the public on the benefits and risks associated with immunization against measles and rubella (13). As indicated in the plan, the provision of rubella vaccination opportunities to all rubella-susceptible women as well as children and adolescents is crucial. There is no country-wide research which documents the susceptibility profile of Turkey; such studies are important to begin to elucidate the situation.

In the present study, rubella IgG antibody seropositivity was found to be over 95% for women in the 15- to 49-year-old age group in a rural region of Turkey. This finding shows that in the absence of a vaccination program, about 95% of girls have become seroimmune by the age of 15 in this setting. In Turkey, only a limited number of community-based seroprevalence studies for rubella have been performed over the last 10 years among women of child-bearing age. Aksit et al. conducted a community-based study, and they reported seropositivity rates of 89.7% and 91.6% for the 15- to 19-year-old and 20- to 29-year-old age groups, respectively (14). Seker et al. reported 100.0% seropositivity among women in the 20- to 41-year-old age group residing in the northwest of Istanbul (15). The results of the present study are similar to those of these previous studies. Nuhoglu et al. reported a 87.2% seropositivity among women of child-bearing age who were patients at various clinics in a hospital, a figure that is lower than the figure found in this study (16). The above studies have reported figures that are relatively higher than the figures reported by the WHO collaborative study groups before the implementation of the rubella vaccination in 1969, when the immunity gap was found to be 15-20% (17,18).

Rubella infection elimination efforts have been increased in Europe, and by the year 2002, over 80% of the European region countries used the measles-mumps-rubella (MMR) vaccine. It was then anticipated that most of the countries would be using the MMR vaccine within the next 5 years (19). Therefore, most if not all recent seroprevalence studies conducted in Europe were conducted among vaccinated groups. The seropositivity determined in the present study was similar to the seropositivity rates reported by different studies conducted in non-vaccinated groups in different countries. Seroposivities have been reported to be as 96.2% in Iran (20) and 91.1% in Saudia Arabia (21) among non-vaccinated women in the reproductive age group. Seropositivity has been reported to be as 92.2% for women in the same age group in Egypt (22).

The target group in which rubella infection is of greatest concern is pregnant women. In the present study, the seropositivity rate for pregnant women was found to be high (96.2%). Most of the studies in Turkey have been conducted among pregnant women who were seen at obstetric and gynecology clinics in hospitals and have been shown to have seropositivity rates between 88.1 and 100.0% (15,23-25) in different regions of Turkey. The present study found a seropositivity rate similar to the rates of 93.6% (24), and 92.5% (25) reported in several studies conducted in Ankara and Adana, respectively. Beginning in July, 2006, Turkey implemented a new vaccination schedule and introduced rubella vaccine as a triple MMR vaccine for children aged 12 months and 6 years, and as a rubella vaccine for children aged 14 years. No vaccination program has been implemented for women of child-bearing age, but discussions of the need for a vaccination policy for this age group are ongoing.

Rubella vaccination has been reported to be very efficient and cost-effective in preventing CRS (26). A key strategy for preventing rubella and CRS is ensuring sufficient population immunity through natural disease or through vaccination programs that achieve high coverage (27). But if the vaccination coverage cannot be kept high, there is a risk of the resurgence of CRS as was experienced in Greece after subsequent years of low coverage scores in infant immunization (28). The universal rubella immunization coverage provided for 12-month-old and 6-year-old children should therefore be kept high to minimize this risk. Also, a vaccination policy should be implemented for women at risk, which may be carried out either through the vaccination of whole cohorts of women of child-bearing age (e.g., 15 - 44 years) or cohorts of particular groups of women such as health care workers, schoolgirls, government workers, college students, postpartum women or premarital couples (2,13).

The other issue that needs to be discussed is the role of private immunization and its effect on the epidemiology of viral circulation. Although MMR was not included until recently in the national immunization schedule, it has been on the market for more than 10 years and has been administered by pediatricians. The use of the vaccination has been more common in big provinces, and directly reflects private immunization practices. A recent study conducted in Istanbul reported 13.3% coverage in the Umranie District. This study documented the increase in private immunization in urban areas among families at high socioeconomic levels (29). These cohorts should also be considered in the planning of rubella immunization practices in the future.

The goal in Turkey, as in European countries (13), is undoubtedly to stop the circulation of the disease. This should

| Table 3. Arithmetical and geometrical means of the rubella IgG antibody titers and the seropositivity percents by age group |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age group (year) | Arithmetical mean (±Standard deviation) | Geometrical mean (Mean deviation) | Seropositivity (%) |
| 15-19 | 14.00(±3.83) | 20.44 (0.65) | 97.6 |
| 20-24 | 17.45 (±5.67) | 15.65 (10.35) | 98.6 |
| 25-29 | 16.24 (±4.64) | 17.21 (4.75) | 96.1 |
| 30-34 | 15.92 (±4.90) | 18.53 (2.85) | 94.6 |
| 35-39 | 16.10 (±6.02) | 18.26 (11.48) | 93.1 |
| ≥40 | 15.18 (±5.62) | 10.34 (1.10) | 93.0 |

P<0.05
P<0.01
P<0.005

1: One-Way ANOVA.
2: Chi-square.
be done through rigorous efforts to keep rubella immunization coverage high among infants and children, and through implementing immunization policies for women of child-bearing age in the light of the evidence on rubella susceptibility and CRS burden.

In this study, the susceptibility among women in the 15- to 49-year-old age group was found to be low, and rubella vaccination was not found to be needed in this group of women. However, further studies among women in different age groups in urban and rural settings, preferably large-scale screening exercises, are required in order to determine the need for a national rubella vaccination program among women of child-bearing age in different settings. If such a need exists, it must be determined which age group of women should be vaccinated in Turkey. Determining whether CRS is a substantial problem will also help in the future planning of appropriate interventions.

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REFERENCES


