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Rubella susceptibility in pregnant women and results of a postpartum immunization strategy in Catalonia, Spain

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ABSTRACT

Background: Elimination of congenital rubella syndrome depends not only on effective childhood immunization but also on the identification and immunization of rubella susceptible women. We assessed rubella susceptibility among pregnant women and evaluated the adherence and response to postpartum immunization with measles, mumps and rubella (MMR) vaccine.
Methods: Cross-sectional study of women who gave birth at the Hospital Clinic de Barcelona (Spain) between January 2008 and December 2013. Antenatal serological screening for rubella was performed in all women during pregnancy. In rubella-susceptible women, two doses of MMR vaccine were recommended following birth. We evaluated rubella serological response to MMR vaccination in mothers who complied with the recommendations.
Results: A total of 22,681 pregnant women were included in the study. The mean age was 32.3 years (SD 5.6), and 73.6% were primipara. The proportion of immigrants ranged from 43.4% in 2010 to 38.5% in 2012. The proportion of women susceptible to rubella was 5.9% (1328). Susceptibility to rubella declined with increasing maternal age. Immigrant pregnant women were more susceptible to rubella (7.6%) than women born in Spain (4.6%). Multivariate analyses showed that younger age (≤19 years) aOR 1.7 (95% CI 1.1–2.5), primiparas aOR 1.3 (95% CI 1.1–1.5) and immigrant women aOR 1.6 (95% CI 1.4–1.8) were more likely to be susceptible. The second dose of MMR vaccine was received by 57.2% (718/1256) of rubella-susceptible women, with the highest proportion being immigrant women compared with women born in Spain. After vaccination, all women showed rubella immunity.
Conclusions: The higher rubella susceptibility found in the three youngest age groups and in immigrant women highlights the relevance of antenatal screening, in order to ensure identification and postpartum immunization. The postpartum immunization strategy is an opportunity to protect women of childbearing age and consequently prevent occurrence of CRS, and to increase vaccination coverage against rubella and other vaccine-preventable diseases.

1. Introduction

Rubella infection occurring just before conception and during early pregnancy may result in miscarriage, fetal death, or congenital defects known as congenital rubella syndrome (CRS) [1–4]. The extent of the involvement depends on the time of pregnancy at which infection occurs. The highest risk of CRS is found in countries with high rates of rubella susceptibility among women of childbearing age [2].

In 1998, the World Health Organization (WHO) European Region approved the aims of eliminating indigenous measles and rubella,

Abbreviations: AVC, Adult Vaccination Centre; CI, confidence interval; CRS, congenital rubella syndrome (CRS); HCB, Hospital Clinic of Barcelona; IgG, immunoglobulin G; IU, international units; MMR, measles, mumps and rubella vaccine; OR, odds ratio; SD, standard deviation; WHO, World Health Organization.

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and controlling congenital rubella [2,5,6]. The most important strategy for preventing rubella is immunization of susceptible individuals. However, individuals may be immunized by past vaccination or natural infection [2]. The effectiveness of the rubella vaccine has been demonstrated by the elimination of rubella and CRS from the Region of the Americas [2,7]. The aim of interrupting the endemic transmission of measles and rubella in Europe in 2015 will only be achieved with a high coverage of vaccination (>95% with two doses of measles, mumps and rubella (MMR) vaccine) in all geographical areas and all population groups, together with a high-quality surveillance system [8].

Post-delivery vaccination strategies should include MMR vaccination in women susceptible to these diseases. In susceptible pregnant women, immunization with this live attenuated vaccine should be administrated during the postpartum period [2,9,10].

In Spain, rubella is a notifiable disease and is monitored through the Spanish Surveillance System [11]. Reported cases of rubella in 2012 were the highest since 2008 (64 confirmed cases: 0.14 cases per 100,000 inhabitants) and most cases occurred in unvaccinated adolescents and young adults. In the 2008–2012 period, 4 rubella outbreaks and 3 cases of CRS have been recorded in immigrants from countries where the rubella vaccine is not routinely administered in childhood [8]. Although the viral circulation of rubella in Spain is supposedly low, it is important to monitor rubella susceptibility, especially in immigrant women, given the observed increase in the immigrant population in recent years, with Spain being one of the main receptor countries in the European Union [12]. In Catalonia, the region where this study was conducted, all pregnant women are screened for rubella antibodies in the first antenatal blood test [11,13].

The objectives of this study were to assess rubella susceptibility in the antenatal rubella serology screening; to identify factors associated with susceptible women and to evaluate the adherence and the immunological response to postpartum immunization strategy with MMR vaccine in rubella susceptible women.

2. Materials and methods

2.1. Study characteristics

We made a cross-sectional study of women who gave birth at the Hospital Clinic of Barcelona (HCB) between January 2008 and December 2013.

2.2. Rubella immunization practices

In Catalonia, an autonomous region in the northeast of Spain with nearly 7.5 million inhabitants, rubella-containing vaccine was introduced into the routine immunization schedule in 1978 for all girls aged 11 years (women born after 1967) [14]. In 1980, in order to improve measles control, the MMR vaccine was introduced in children aged 15 months. In 1987, the MMR replaced the rubella vaccine at 11 years of age. In 1998, the age of administration of the second MMR dose was advanced from 11 to 4 years. Finally, in 2008, it was recommended that the age of administration of the first dose of MMR should be changed from 15 to 12 months [15]. Similar schedules for rubella-containing vaccine have been introduced in other Spanish regions [8].

2.3. Laboratory methods

Following the recommendations of the Department of Health of Catalonia, serological screening for rubella was made in all pregnant women during their first blood test, which is usually made during the first trimester of pregnancy [13]. Levels of rubella IgG antibodies were determined using the ADVIA® Centaur G™ Rubella Assay (Siemens Healthcare Diagnostics Inc.). The immune status was determined using the following cut-off values: <15.0 IU/ml (susceptible), ≥15 IU/ml (immune). According to the manufacturer, the sensitivity and specificity of the method are 97.2% and 99.5%, respectively. The intra-assay and inter-assay coefficients are less than 5% and 6.1%, respectively. All samples were analyzed at the HCB microbiology laboratory.

In women susceptible to rubella, two doses of MMR vaccine were recommended in the postpartum period. The vaccine used was Priorix (GlaxoSmithKline, S.A.) which contains live attenuated measles, mumps and rubella viruses [16]. The first dose was administered in the immediate postpartum period, before discharge. After a minimum of one month, a visit was scheduled at the Adult Vaccination Centre (AVC) of the HCB for the administration of the second dose of MMR vaccine. A postvaccination sample was obtained approximately one month later in the AVC to assess rubella antibody titers. Only mothers who returned to the AVC to determine the postvaccination immunological response were included in the immunogenicity assessment.

2.4. Collection of variables

Variables were limited to information recorded in the medical records, including maternal date of birth, country of birth, parity, delivery date, date of administration of first and second dose of MMR vaccine, and date of post-vaccination blood sample. All women not born in Spain were considered immigrants. Rubella antibody levels during pregnancy were established as the main endpoint and adherence to the second MMR dose and post-vaccination rubella response as the secondary endpoints. We merged data extracts from medical information systems from Maternal-Fetal Medicine Department and the AVC.

2.5. Statistical analysis

In the univariate analysis, absolute frequencies and percentages were used to describe categorical variables and means and standard deviation (SD) or 95% confidence intervals (CI) to describe quantitative variables with a normal distribution, and medians and interquartile range otherwise. We calculated the proportion of women susceptible to rubella with the odds ratios (OR) and 95% CI. To determine variables independently associated with rubella susceptibility and adherence to MMR immunization, the crude odds ratios were calculated for different variables. For each variable studied, we took the group with the lowest rubella susceptibility as the reference group. Odds ratios were adjusted using multiple logistic regression analysis. The statistical analysis was performed using the STATA® statistical package v12.1. Statistical significance was established as <0.05.

2.6. Ethical considerations

The study investigators followed the principles of the Declaration of Helsinki. Since this study is based on routinely collected medical records, individual informed consent was not obtained. Patient records/information were anonymized and de-identified prior to analysis. The study was approved by the HCB Clinical Research Ethics Committee (HCB/2014/0619).