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Comparing the rubella seronegativity in pregnant women who received one dose of rubella vaccine at different ages in Taiwan

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ABSTRACT

Introduction: Vaccination is the best strategy to prevent rubella and congenital rubella. The aim of our study was to assess the immunity to rubella and determine rubella virus antibody titers in pregnant women who were offered a single dose of rubella vaccine at different ages of their lives.
Methods: A total 15,067 rubella IgG antibody test results for Taiwanese pregnant women who received routine prenatal checkup at Fooyin University Hospital from 1999 to 2014 were analyzed in this study. The women were divided into five birth cohorts in order to compare their rubella seronegativities and antibody titers according to the different period of rubella vaccination policy in Taiwan.
Results: The total rubella seronegativity rate was 11.2% (95% CI: 10.7–11.7%) and the mean rubella antibody titers was 51.0 IU/mL (SD = 54.7 IU/mL). The junior school cohort has the lowest rubella seronegativity of 7.6% (95% CI: 6.9–8.2%). The seronegativities were significantly high in the preschool cohort and in the 15-month-old cohort, 14.9% (95% CI: 13.2–16.6%) and 14.8% (95% CI: 11.5–18.1%), respectively. The OR values were 2.1 (95% CI: 1.8–2.5, $p < 0.001$) in the preschool cohort and 2.2 (95% CI: 1.6–2.8, $p < 0.001$) in the 15-month-old cohort, respectively, against the junior school cohort. Women in the 15-month-old cohort have lowest average rubella IgG titer, 25.4 IU/mL.
Conclusion: The total rubella seronegativity rate was 11.2% in all native pregnant women. Women who received one dose rubella vaccine at preschool and 15-month-old have highest seronegativities. The 15-month-old cohort has the lowest average rubella IgG titer. We recommend a revised catch-up immunization policy to women who received one dose rubella vaccine at a younger age.

1. Introduction

Rubella virus is a single-strain virus which usually causes an acute mild disease. However, it can cause severe birth defects known as congenital rubella syndrome (CRS) when the pregnant women are infected during the first trimester of pregnancy [1]. Vaccination is the best strategy to prevent rubella and CRS. Taiwan's rubella and Measles-Mumps-Rubella (MMR) vaccination program started in 1986 (Table 1). During 1986–1991, schoolgirls in third grade junior high schools were the target population. Between 1992 and 1994, the MMR vaccine was given to all junior high school, elementary school and preschool children. From January 1992 to August 2001, this MMR vaccination policy was expanded to include 15-month-old children. Therefore, the indigenous Taiwanese women born between September 1971 and August 1994 received only one dose of rubella vaccine. Thereafter, residents born after September 1994 received two doses of rubella vaccine. The rubella vaccination programs among junior high school girls had a high coverage rate (about 98%) [2]. The rubella and congenital rubella are reportable diseases in Taiwan. Any suspected case must be reported to Taiwan's Center for Disease Control (CDC). From 1998 to 2014, the confirmed rubella cases fluctuated from 2 cases in 2003 (0.09/million) to 60 cases in 2011 (2.60/million). Furthermore, only 3 cases of CRS were reported in 2001, one case in 2007 and another in 2008 [3]. International travel has become increasing popular over the years. In 2014 alone, about 11.8 million Taiwan nationals travelled abroad. Among them, 25.1% visited Japan, 48.8% visited China (including Hong Kong and Macau), 13.8% went to Southeast Asian countries and 12.3% travelled to the rest of the world. During that same year

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Table 1
Rubella and MMR vaccination program in Taiwan.

Time	Type of vaccine (dose given)	Population	Birthdate (yy/mm) of affected cohort
1986–1991	Rubella (1)	Girls in the third year of junior school (15 years old)	1971/9–1976/8
1992–1994	MMR (1)	All junior high school students (15 years old) All elementary school students (7–12 years old) Preschool children	1976/9–1979/8 1979/9–1985/8 1985/9–1990/8
1992–2001/8	MMR (1)	15 months old children	1990/9–1994/8
2001/9–2005/12	MMR (2)	First dose: 15 months years old Booster dose: first year of elementary school	Born after 1994/9
2006/1–2009/4	MMR (2)	First dose: 12–15 months years old Booster dose: first year of elementary school	
2009/4–2012/4	MMR (2)	First dose: 12 months years old Booster dose: first year of elementary school	
2012/4-current	MMR (2)	First dose: 12 months years old Booster dose: 5 years old	
1987–2001/6	Rubella (1)	Women of childbearing age with seronegative rubella IgG	Childbearing age
2001/7-current	MMR (1)	Women of childbearing age with seronegative rubella IgG	Childbearing age

Adapted from the report of the Centers for Disease Control, Taiwan.
MMR: Measles, Mumps, and Rubella.

in 2014, a total 9.9 million foreign people came to Taiwan. Among these visitors, 54.1% came from China (including Hong Kong and Macau), 16.5% from Japan, and 14.0% from Southeast Asian countries [4]. Therefore, close contacts between the inhabitants of these countries and Taiwan occur very frequently. A large scale rubella epidemic appeared in Asia from 2012 to 2014. There were 17,032 rubella cases along with 45 CRS cases in Japan, a total 69,529 rubella cases in China and more than 11,000 rubella cases among Southeast Asian countries [5–8]. The increase in travel to and from Asian countries with circulating rubella may increase the chance of rubella outbreak in Taiwan. At the same time, the women born before September 1994 who received only one dose of rubella vaccine are reaching their fertility age. The knowledge of rubella virus antibodies in these childbearing age women is an important issue in the prevention of CRS. The aim of our study was to assess the immunity to rubella and determine rubella virus antibody titers in pregnant women who were offered a single dose of rubella vaccine at different ages of their lives.

2. Materials and methods

2.1. Subject

A total 15,067 rubella IgG antibody test results for Taiwanese pregnant women who received routine prenatal checkup at Fooyin University Hospital from 1999 to 2014 were analyzed in this study. The rubella IgG antibody was a compulsory test of pregnant women. Therefore, all test results were included into present study except for non-native Taiwanese women who accounted for 16.7% of total. Fooyin University Hospital is a teaching hospital located in Pingtung County, southern Taiwan. It has a large catchment area, providing care to approximately 800–1200 pregnant women each year.

The women were divided into five birth cohorts according to the different period of rubella vaccination policy in Taiwan. Women in cohort 1 (no vaccination cohort) were born before September 1971: no rubella vaccination program was provided. Women in cohort 2 to cohort 5 received one dose of rubella vaccine at different ages. Women in cohort 2 (junior school cohort) were born from September 1971 to August 1979, and received vaccine when they were junior high school students. Women in cohort 3 (primary school cohort) were born from September 1979 to August 1985, and received vaccination when they were elementary students. Women in cohort 4 (preschool school cohort) were born from September 1985 to August 1990, and received vaccination during the preschool period. Women in cohort 5 (15-month-old cohort) were born from September 1990 to August 1994, and received vaccination at 15 months old. This study was approved by the Ethics Review Board of Fooyin University Hospital (IRB No. FYH-IRB-970003 and FYH-IRB-104-03-01-A).

2.2. Serological test

Serologic testing for rubella IgG antibodies were performed through a microparticle enzyme immunoassay (MEIA) on an AsXYM analyzer (Abbott Laboratories, Chicago, IL, USA) before May 2010. Thereafter, the Chemiluminescent Microparticle Immunoassay (CMIA) was used on an ARCHITECT i2000 SR analyzer (Abbott Laboratories, Chicago, IL, USA). The lower and upper detection limits of both methods were 0.1 and 500 IU/mL, respectively. As the rubella antibodies levels >500 or <0.1 IU/ML, the levels were assigned of 500 and 0.1 IU/mL for calculation antibodies titers, respectively. Serum IgG levels of 10 IU/mL or above were considered to be seropositive or immune; those below 10 IU/mL were considered to be seronegative, susceptible, or nonimmune.

2.3. Statistics analysis

The subjects were analyzed annually from 1999 to 2014 and categorized into 5 different birth cohorts according to the birth year of the pregnant women. We expressed continuous data, like age and titers, as mean ± 1SD, as well as the seronegativities and 95% confidence intervals for subjects who were rubella seronegative. Differences in the five birth cohorts were compared using a chi-square test. Logistic regression was performed to estimate the risk (measured in odds ratio, OR) of rubella seronegative status. A $p < 0.05$ was regarded as statistically significant. Data were analyzed using the software SPSS 18.0 for Windows.

3. Results

From 1999 to 2014, 15,067 native pregnant women who received prenatal checkup were included in this study. The total rubella seronegativity rate was 11.2% (95% CI: 10.7–11.7%) and the mean rubella antibody titers was 51.0 ± 54.7 IU/mL. The lowest seronegativity, 8.5%, occurred in 2007, and the highest seronegativity, 14.7%, appeared in 2014. Meanwhile, the highest and lowest