Serological statuses of pregnant women in an urban Brazilian population before and after the 2008 rubella immunization campaign

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ARTICLE INFO

ABSTRACT

Background: Vaccinating populations against rubella aims to mitigate viral circulation and to ensure that women of childbearing age are immunized to reduce the incidence of congenital rubella syndrome. This study determined the serological statuses of pregnant women in an urban Brazilian population before and after the national rubella immunization campaign that was undertaken in 2008, and it assessed the socio-demographic factors associated with seronegativity.
Methods: Pregnant women living in Maceió, Alagoas, Brazil, who participated in a municipal prenatal screening program that involved blood tests for rubella, were assessed between June 2007 and May 2012. Socio-demographic factors associated with seronegativity were assessed, including the year of the blood test, categorized as before or after the 2008 immunization campaign, and the women's birth cohorts, the women's ethnicities, the gestational ages at the first prenatal visit, and the women's districts of residence.
Results: A total of 54,717 capillary blood samples were tested for rubella. The prevalence of pregnant women who were seronegative for rubella declined from 9.4% before the national immunization campaign to 2.8% after the national immunization campaign. Women were more likely to be seronegative for rubella before and after the immunization campaign if they were born between 1990 and 2000 or delayed starting prenatal care.
Conclusions: The decline in the prevalence of pregnant women who were seronegative for rubella to <5% indicates that the 2008 Brazilian rubella immunization campaign was successful in Maceió.

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1. Introduction

When acquired outside of the gestational period, rubella is a benign and self-limiting disease that rarely leads to adverse events. However, when women are infected with rubella before the twelfth week of pregnancy, the conceptus may become infected and develop congenital rubella syndrome (CRS), leading to possible fetal death, or hearing, neurological, heart, or eye problems, among others [1,2]. Therefore, vaccinating populations against rubella aims to mitigate viral circulation and to ensure that women of childbearing age are immunized [2,3].

In 2003, the Pan American Health Organization established a goal to eliminate rubella in the Americas by 2010, and population immunization and case surveillance underpinned the achievement of this goal [4]. In 1992, the National Immunization Program (NIP) led by Brazil's Ministry of Health introduced a single-dose combination vaccine for measles, mumps, and rubella (MMR) to be administered at 15 months of age [5], and this was gradually implemented within the Brazilian states until 2000 [6]. In 2003, the initial MMR vaccine dose was administered at 12 months of age, followed by a second dose at 4–6 years of age [7], but since 2013, the second dose has been administered at 15 months of age, along with the varicella vaccine [8]. The NIP only recommends the vaccination of adolescents when the childhood vaccine doses were not administered [9]. Campaigns to vaccinate women of childbearing age began in 2001 [5]. However, despite a reduced incidence of rubella among women, an increased frequency of rubella cases among men maintained the circulation of the virus within the population, and a new national campaign that was initiated in 2008 broadened the target

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population to all individuals aged between 20 years and 39 years, regardless of their gender, or immunization and disease histories [6,10]. At the time, this was considered the largest vaccination campaign ever undertaken in the world, and it involved a high level of national mobilization that included vaccination activities in soccer stadiums, condominiums, and shopping malls, and its coverage reached 97% nationwide, with 47% homogeneity among the municipalities [11]. In Maceió, 326,928 people, who included 174,993 women, were vaccinated during the rubella vaccination campaign between August 9, 2008 and September 12, 2008, and 100% coverage of the target population was reported by DATASUS, the Ministry of Health's information system [12].

This study determined the prevalence of rubella seronegativity among pregnant women in an urban Brazilian population before and after the national rubella immunization campaign that took place in 2008, and it assessed whether there were any socio-demographic factors associated with seronegativity in this population.

2. Methods

This cross-sectional, observational, descriptive study that involved a large number of subjects, assessed secondary data from the prenatal disease screening program held by Maceió's Municipal Health Office (MHO).

2.1. Population, prenatal testing, data collection, and processing

Maceió is the capital of the State of Alagoas, which is located in northeastern Brazil. It had a population of 932,748 people in 2010 [13] and 76,862 babies were born between June 2007 and May 2012 [14]. Based on the mean miscarriage rate of 16% in northeastern Brazil [15], there were an estimated 89,159 pregnancies in Maceió during this time, and 25.3% of the women had access to private insurance or healthcare [16].

From June 2007 to May 2012, 54,813 pregnant women sought treatment from Maceió's Universal Healthcare System (Sistema Único de Saúde), and they were screened for infections that are transmissible to the fetus, including rubella, during their first prenatal visits. Thus, the MHO prenatal disease screening program accessed 61.4% of the pregnant women in the municipality during the study period and 81.2% of the pregnant women who regularly used the Universal Healthcare System. Women who sought treatment from private clinics were not assessed.

The screening involved obtaining capillary blood samples on S&S #903 filter paper (Schleicher & Schuell BioScience, Inc., Keene, NH) that were tested at the laboratory of the Instituto de Pesquisa e Diagnóstico Laboratorial of the Association of Parents and Friends of Handicapped Children of Maceió (Associação de Pais e Amigos dos Excepcionais, Maceió).

The Q-Preven IgG-DBS kit (Symbiosis Diagnóstica Ltda, São Paulo, Brazil) was used to test the blood samples for rubella immunoglobulin (Ig)G. According to the manufacturer's specifications, serum samples are reactive to enzyme immunoassay (EIA) IgG levels of $\geq$15 IU/mL, are non-reactive to EIA IgG levels of <10 IU/mL, and are indeterminate (or equivocal) for the intermediate IgG levels. Since this study evaluated blood obtained from pregnant women, participants with EIA IgG levels of $\geq$15 IU/mL were considered immune to rubella and those with EIA IgG levels of <15 IU/mL were considered seronegative for rubella to prevent false-positive results [7,17,18].

The pregnant women's identification forms contained information relating to their birth dates, their self-reported ethnicities, the gestational ages at their first prenatal visits, and their districts of residence according to the municipality's health districts. The

health districts are defined using common geographic characteristics, but they have significant intra-urban social inequalities [19].

2.2. Data analysis

We analyzed the data from two blood sampling periods, namely, the pre-campaign period that comprised samples that were taken from June 2007 to August 2008, and the post-campaign period that comprised samples that were taken from September 2008 to May 2012.

The statistical analyses were performed using Stata software version 12.1 (StataCorp LP, College Station, TX, USA). The prevalence of rubella IgG antibodies at concentrations of <15 IU/mL was calculated according to the test years, namely, 2007–2012, and the samples were categorized into "pre-campaign" and "post-campaign" samples based on the 2008 national rubella immunization campaign. We also categorized the samples according to the birth cohort, which involved pooling the samples into 15 groups of 2 years, namely, "1966–1967", "1968–1969", "1970–1971", "1972–1973", "1974–1975", "1976–1977", "1978–1979", "1980–1981", "1982–1983", "1984–1985", "1986–1987", "1988–1989", "1990–1991", "1992–1993", and "1994–1995", and the samples were pooled into two birth cohort groups, specifically, women "born before 1990" and those "born after 1990", based on the previous immunization strategies to which they were exposed, namely, the national campaigns implemented in 2001 and 2008. The samples were also categorized according to the self-reported ethnicity, which included "mixed", "white", "black", or "Asian", according to the gestational age at the first prenatal visit, namely, "less than 12 weeks of gestation" and "12 or more weeks of gestation", and according to the woman's district of residence, which were numbered from 1 to 7.

The differences between proportions were compared using the chi-square test. A binary regression logistic analysis was performed to identify factors associated with IgG levels of <15 IU/mL after the national immunization campaign. Variables with p values $\leq$0.20 in the univariate analyses were included in the multivariate analysis. A p value <0.05 was considered statistically significant for all of the analysis.

2.3. Ethical approval

This study was approved by Maceió's MHO in July 2012 and by the Local Ethics Committee of the Instituto de Medicina Integral Professor Fernando Figueira (CAAE: 06733812.2.0000.5201).

3. Results

Of the 54,813 women from whom capillary blood samples were taken, 54,717 (99.8%) samples were tested for rubella IgG antibodies, and 39,880 (72.9%) women began prenatal care after the national rubella immunization campaign. Birth dates were reported for 99.2%, ethnicities were reported for 92.6%, gestational ages at the first prenatal visit were reported for 85.1%, and the districts of residence were reported for 96.3% of the participants. Table 1 presents the proportions of the variables before and after the national rubella immunization campaign.

The average prevalence of women who were seronegative for rubella during the pre-campaign period was 9.4% (95% confidence interval [CI]: 8.95–9.89), and this declined to 2.8% (95% CI: 2.63–2.96) during the post-campaign period (chi-square correction: 1081.02; p < 0.001). Fig. 1 shows the proportions of the pregnant women who were seronegative for rubella before and after the immunization campaign.

The prevalence of pregnant women who were seronegative for rubella declined to <5% after the national immunization campaign,