Seroepidemiological profile of pregnant women after inadvertent rubella vaccination in the state of Rio de Janeiro, Brazil, 2001–2002

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ABSTRACT

Objectives.   *To analyze postvaccination serological status in pregnant women inadvertently vaccinated against rubella in the state of Rio de Janeiro, Brazil.*

Methods.   *This was a cross-sectional study of pregnant women 15 to 29 years old, vaccinated against rubella and measles from November 2001 to March 2002, who were unaware of their pregnancy at the time of vaccination or who became pregnant within 30 days thereafter. They were tested for rubella-specific immunoglobulin M (IgM) and G (IgG) and classified as immune (IgM-negative, IgG-positive, tested within 30 days after vaccination), susceptible (IgM-positive after vaccination) or indeterminate (IgM-negative, IgG-positive, vaccination–serological testing interval greater than 30 days).*

Results.   *Of 2 292 women, 288 (12.6%) were susceptible, 316 (13.8%) immune, 1 576 (68.8%) indeterminate, 8 (0.3%) ineligible, and 104 (4.5%) lost to follow-up. IgM seropositivity by vaccination–serological testing interval was 16.1% (≤ 30 days), 15.4% (30–60 days), and 14.2% (61–90 days). Considering the campaign's target age, the 20-to-24-year age group had the largest proportion of individuals susceptible to rubella (14.8%) and represented 42.4% (122/288) of all susceptible women. In 75% of susceptible pregnant women, gestational age was 5 weeks or less at the time of vaccination.*

Conclusions.   *Mass immunization of childbearing-age women was justified on the basis of epidemiological and serological data. Follow-up of vaccinated pregnant women revealed no cases of congenital rubella syndrome due to rubella vaccination. However, the observed rate of congenital infection supports the recommendation to avoid vaccinating pregnant women, and to avoid conception for up to 1 month following rubella vaccination.*

Key words   Brazil, epidemiological surveillance, pregnancy, rubella, vaccination.

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Rubella is usually a mild disease in childhood. However, the clinical and public health relevance of this disease is due to congenital rubella syndrome (CRS), which affects fetuses and newborns of mothers infected during pregnancy, mainly in the first trimester. Congenital rubella syndrome is a serious disease with high psychosocial costs, and requires specialized medical

care due to its most frequent manifestations: congenital malformations (cataract, glaucoma, cardiopathies etc.), deafness, and mental retardation (1–3).

Since Brazil launched measles epidemiological surveillance in 1992, rubella detection has improved significantly (4). Notification of rubella cases has been compulsory in Brazil since 1996 (3). From 1997 to 2000, the rate of postnatal rubella incidence declined from 20.6 to 9.9 per 100 000, with most cases occurring in individuals under 15 years of age. However, during this period incidence in the 15-to-29-year age group increased from 7.0 to 13.0 per 100 000 (3, 4). During the same period the number of confirmed CRS cases nationwide increased from 17 to 101 (3). Analysis of surveillance data suggested a change in the epidemiological pattern of rubella in the country after the incremental introduction of the combined measles, mumps, and rubella vaccination (MMR) in the National Immunization Program (NIP), beginning in 1992. Immunization in mass campaigns and primary care are free of charge and have achieved high coverage in the 1-to-11-year age group. However, the wild virus has continued to circulate among susceptible young adults (3, 4), exposing childbearing-age women and probably increasing the number of CRS cases.

To eliminate CRS, high vaccine coverage must be sustained in children and childbearing-age women (1, 3, 5–7). In view of the incidence of rubella in the population over 12 years old, in November 2001 the Brazilian NIP launched a nationwide vaccination campaign against rubella in women aged 12 to 39 years, using combined attenuated live virus vaccine for measles and rubella (MR) (Edmonston-Zagreb and RA 27/3 strains, respectively) manufactured by the Serum Institute of India. In the State of Rio de Janeiro, 1 441 838 vaccine doses were used from 5 November 2001 through 8 March 2002, covering 82.2% of the target population 15 to 29 years of age (8). The age range was narrower than recommended by the NIP (12–39 years) based on data indicating a substantial rise in rubella incidence in the sub-group aged 15 to 29 years (9). The vaccination campaign for childbearing-age women included the widely publicized recommendation to avoid vaccination of pregnant women. Also, women vaccinated against rubella were advised to avoid becoming pregnant during the first 30 days after vaccination.

Data from previous studies failed to show any damage to the fetus from rubella vaccines used during pregnancy (10–15). Nevertheless, the Centers for Disease Control Advisory Committee on Immunization Practices reviewed available data and considered that a maximum "theoretical" risk of CRS of 1.3% (the upper bound of the 95% confidence interval of 0–293) could not be ruled out (10). The likelihood that mass immunization could eventually include women unaware of their pregnancy, and uncertainties regarding the safety of the rubella vaccination for pregnant women, led the Ministry of Health in Brazil to organize a special surveillance scheme to identify and follow up women vaccinated during pregnancy. The data generated from the follow-up of pregnant women lent themselves to the analysis of programmatic issues presented in this paper.

The vaccination strategy was based on indirect evidence (increased rubella incidence during childbearing age) that the substantial proportion of women susceptible to rubella justified a mass campaign. The assumption was that the potential for new CRS cases justified the necessary expenditure, and that it was worth the theoretical risk of fetal damage by the vaccine. We took advantage of available empirical data that could help assess the vaccination campaign's success beyond vaccination coverage. Despite the logical association with adverse events in newborns, an in-depth analysis of clinical and laboratory data from newborns was thought to constitute a distinct issue and to justify a separate report.

One assumption underlying the vaccination campaign was that a large contingent of women were susceptible to rubella, but no data were available on the susceptibility rate for childbearing-age women at the time of the campaign. This study analyzes the serological status of women vaccinated against rubella during the mass campaign, who were unaware of being pregnant or who became pregnant within 30 days after vaccination.

MATERIALS AND METHODS

This was a cross-sectional study of women 15 to 29 years old residing in the State of Rio de Janeiro, Brazil, vaccinated with combined MR vaccine during the campaign lasting from 5 November 2001 to 8 March 2002. The main inclusion criterion for the present analysis was pregnancy at the time of vaccination or within 30 days after vaccination. Women who had contact with rubella cases or who received vaccines other than MR were excluded. A small number (29) of pregnant women vaccinated after 8 March 2002 according to the same protocol as in the main vaccination campaign was included in the study.

Women included in the present study were notified and followed according to the Protocol for Health Care and Follow-Up of Newborn Children of Mothers Inadvertently Vaccinated Against Rubella (16, 17) issued by the Brazilian Ministry of Health (briefly described below). The protocol was implemented in seven Brazilian states (Rio de Janeiro, São Paulo, Pernambuco, Minas Gerais, Goiás, Bahia, and Rio Grande do Sul) after the national immunization campaign against rubella in 2001 and 2002. In the State of Rio de Janeiro, individual notification of pregnant women who had been vaccinated was sent to the advisory group on vaccine-preventable diseases at the Rio de Janeiro State Health Secretariat, following data collection by the various Municipal Health Secretariats in the state. Together with notification, a special form was completed and blood samples were drawn for serological investigation of rubella within the first 30 days after vaccination. Pregnant women first tested up to 15 days after vaccination and who tested negative for rubella IgM and IgG were retested

later to detect seroconversion. Susceptible women discovered to be pregnant at the time of vaccination were followed up to obtain data on the outcome of pregnancy. Newborns whose mothers were susceptible were also tested serologically and were followed up according to the protocol mentioned above (16–18).

Data from the notification forms were keyed in with Epi-Info version 6.04d software (19). The main study variables were the pregnant woman's age, city of residence, date of vaccination, date of serological testing, last menstrual period, gestational age at date of vaccination, and rubella IgM and IgG results. The study protocol was approved by the Research Ethics Committee of the Brazilian National School of Public Health, Fundação Oswaldo Cruz (Report no. 22/05).

Laboratory tests

For serological diagnosis, enzyme immunoassays for anti-rubella IgM and IgG were performed at the Virology Reference Laboratory, Fundação Oswaldo Cruz, with the commercial Enzygnost® anti-rubella virus/IgM and anti-rubella virus IgG kits (Dade Behring, Marburg, Germany).

A total of 2 665 pregnant women (0.2% of the 15-to-29-year-old population of vaccinated women) were reported. The study forms designed by the Ministry of Health for inadvertent vaccination were available for 2 292 women (86.0%). Susceptible pregnant women with a positive IgM result were followed during pregnancy, and their newborn babies were evaluated for clinical and laboratory findings. The mothers were advised to bring their newborns for follow-up appointments every 3 months.

In a significant number of pregnant women (1 576), blood for serological tests was collected more than 30 days after the date of vaccination for reasons apparently unrelated to the study objectives. In this subgroup, negative IgM and positive IgG results were not considered a reliable indicator of the pregnant woman's immune status at the

time of vaccination (16, 17). In the state of Rio de Janeiro, the recommendation was to monitor these pregnant women and their newborns with the same approach as for susceptible women (17).

Gestational age was calculated on the basis of reported last menstrual period or ultrasound findings. Estimates of gestational age at the time of vaccination were obtained with the formula: date of vaccination – date of last menstrual period + 7 days, based on Nägele's rule for calculating probable date of delivery, according to Araujo et al. (20).

Pregnant women were classified as *immune* if their sera were negative for IgM and positive for IgG and they were tested serologically within 30 days after vaccination. They were classified as *susceptible* if they were IgM-positive for rubella after vaccination, regardless of the interval between vaccination and testing. For purposes of assessing immune status before vaccination, women were classified as *indeterminate* if the interval between vaccination and serological testing was greater than 30 days and the serum sample was IgM-negative and IgG-positive.

Data analysis

The proportion of women with susceptible, immune, and indeterminate findings was estimated for subgroups according to the woman's age, gestational age, and city of residence. Time between vaccination and serological testing was stratified by intervals of 0–30, 31–60, 61–90 and >90 days. For susceptible pregnant women, the first 30-day interval was further divided into 0–15 and 16–30 day intervals to estimate the proportion of IgM-negative/IgG-negative, IgM-positive/IgG-negative, and IgM-positive/ IgG-positive subjects. To assess the immunization campaign's potential impact, the proportion of susceptible women in the entire population of pregnant women in the State of Rio de Janeiro was assumed to be the same as that observed in this study. This proportion was applied to the number of births reported in the State of Rio de Janeiro in

2002 (18), which was the best available approximation for total pregnancies in that year. This provided a rough estimate of the number of vulnerable pregnancies in which CRS was averted by the vaccination campaign.

The significance of the differences in proportions was assessed with the chi-squared test, with a .05 level of significance. Data were managed and analyzed with Epi-Info version 6.04d (19), Microsoft Excel 97 (Microsoft Corporation, Redmond, Washington, US) and the Statistical Package for Social Sciences version 9 (SPSS Inc., Chicago, Illinois, US).

RESULTS

Data on 2 292 pregnant women were available for analysis. A total of 288 pregnant women (12.6%) were susceptible to rubella (IgM-positive), 316 (13.8%) were immune (IgM-negative, IgG-positive) when tested within 30 days after vaccination, and 1 576 (68.8%) were IgM-negative and IgG-positive in serological tests done more than 30 days after vaccination. For the latter, the results did not allow us to classify the woman's immune status at vaccination, so the proportion of immune women was probably underestimated. Twenty-three women failed to seroconvert following vaccination, 16 of them in the 15-to-29-year age group. Data from 8 women (0.3%) were disregarded since they were not eligible, and 104 women (4.5%) were lost to follow-up.

Women tested within 30 days after vaccination showed the highest proportion of IgM positivity (16.1%), but the lowest proportion of IgG positivity (55.6% of 63 IgM-positive women) when we compared intervals between vaccination and serological testing (Table 1). Longer intervals between vaccination and serological testing were associated with lower proportions of IgM positivity (Table 1). Nearly all IgM-positive pregnant women were also positive for IgG when the interval between vaccination and serological testing was 31–90 days, in contrast to pregnant women tested within 30 days postvaccination ($P = 0.000019$) (Table 1).

TABLE 1. Rubella seropositivity in pregnant women inadvertently vaccinated against rubella and measles, according to interval between vaccination and serological testing. State of Rio de Janeiro, Brazil, 2001–2002

Interval between vaccination and testing (days)	Total	IgM-positive		IgG-positive/ IgM-positive	
		No.	%[a]	No.	%[b]
<30	392	63	16.1	35	55.6
31–60	557	86	15.4	83	96.5
61–90	444	63	14.2	60	95.2
>90	783	60	7.7	57	95.0
Unknown	116	16	13.8	13	81.3
Total	2 292	288	12.6	248	86.1

[a] Proportion of IgM-positive women among all women; $\chi^2 = 26.88$; $P = 0.000006$.
[b] Proportion of IgG-positive women among IgM-positive women; $\chi^2 = 24.62$; $P = 0.000019$.
Data for 116 women for whom the interval between vaccination and testing was unknown were excluded.

Of 21 susceptible women tested within 15 days after vaccination, only one was both IgM- and IgG-positive. Sixteen of the 20 nonreactive women were retested, with seroconversion (positivity for IgM and IgG) in nine (56.2%) between days 16 and 30, and in seven (43.8%) between days 31 and 50 after vaccination.

The age distribution of pregnant women inadvertently vaccinated was 30.1% (691/2292) in the 15-to-19-year group, 36% (824/2292) in the 20-to-24-year group, and 25.1% (575/2292) in the 25-to-29-year group. The distribution was similar for IgM-positive (susceptible) pregnant women: 29.5% (85/288) were 15 to 19 years old, 42.4% (122/288) were 20 to 24 years old, and 19.8% (57/288) were 25 to 29 years old. Among susceptible pregnant women,

4.2% (12/288) were ≥30 years old, 0.3% (1/288) were <15 years old, and age was unknown for 3.8% (11/288).

Considering only the age groups targeted by the immunization campaign, the highest proportion of susceptible pregnant women was in the 20-to-24-year group ($P = 0.038$) (Table 2). The proportion of immune pregnant women increased slightly with age ($P = 0.332$, linear trend). In the small subgroup of pregnant women ≥30 years of age who were vaccinated despite being ineligible, 16.7% (12/72) were susceptible. A substantial proportion of women were not tested in time, thus reducing the number of women who met the serological diagnostic criteria. The proportion of women with indeterminate serological results was similar across age groups (61%–75%, Table

2), with no statistically significant differences ($P = 0.242$). Gestational age at vaccination was known in 1 185 (51.7%) of the total sample, and in 57.9% (167) of the susceptible women. In this group, mean gestational age was 4.4 weeks (standard deviation = 4.85) and the median was 3 weeks. Gestational age was 5 weeks or less (highest risk of fetal infection) in 75% of the susceptible women (Figure 1).

The prevalence of infection by rubella vaccine during pregnancy, derived from the proportion of vaccinated IgM-positive pregnant women, provided an estimate of the potential occurrence of cases of CRS if the vaccination campaign had not taken place. The 20-to-24-year age group had the highest rate of susceptibility to rubella in childbearing-age women (diamonds in Figure 2). In 2002, there were 169 401 live births in the state of Rio de Janeiro in women 15 to 29 years of age (18). Assuming that 12.6% were susceptible to rubella before the immunization campaign and that 82.2% were vaccinated, approximately 17 500 pregnancies that would have been vulnerable to CRS were protected in 2002.

The proportion of susceptible women varied widely across regions in the state of Rio de Janeiro (8.7%–19.6%; $P = 0.1796$), as did the campaign's coverage (77%–104%). In Greater Metropolitan Rio de Janeiro, with more than 60% of the state's population, 12.9% of the women in the target age group were susceptible, and the campaign coverage was 78.8%. The northwestern region of the state, with a proportionately large non–urban population, had a high proportion of susceptible women (10/51) and relatively low vaccination coverage (81%), providing a scenario that could allow viral circulation.

Of the 288 susceptible women who were followed up, the outcome of pregnancy was known for 216 (75.0%): there were 10 spontaneous abortions (4.6%), 2 stillbirths (1.0%), and 204 live births (94.4 %). Of a total of 1 580 newborns followed up, 9 (0.6%) tested positive for rubella-specific IgM in the first serum sample. Of these 9 children, 5 were born to susceptible women. In one child the wild rubella virus was identi-

TABLE 2. Distribution of pregnant women according to serological status for rubella and age group. State of Rio de Janeiro, Brazil, 2001–2002
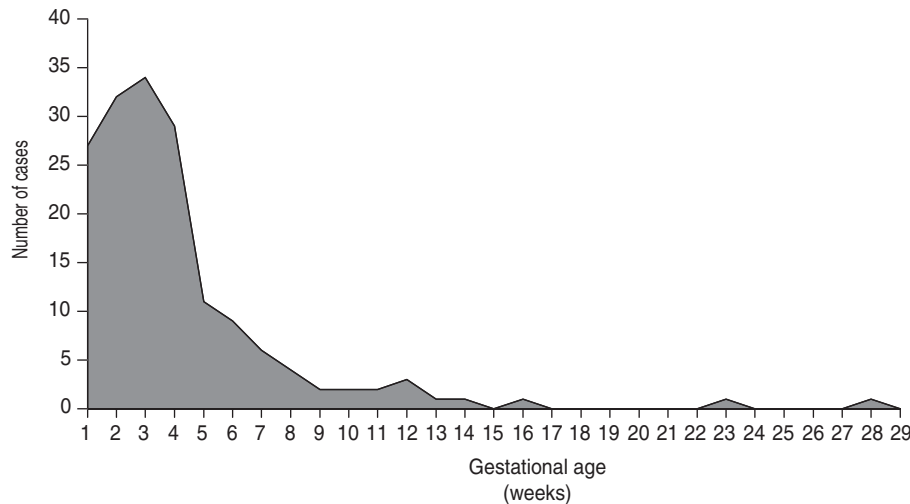
Age group (years)	Total	Susceptible[a]	%	Immune	%	Indeterminate[b]	%
<15	4	1	25.0	0	0	3	75.0
15–19	691	85	12.3	96	13.9	484	70.0
20–24	824	122	14.8	111	13.5	557	67.6
25–29	575	57	9.9	90	15.7	408	71.0
≥30	72	12	16.7	12	16.7	47	65.3
Unknown	126	11	9.0	7	5.6	77	61.1
Total	2 292	288	12.6	316	13.8	1 576	68.8

Note: Data for four women for whom age was <15 years and for 126 women for whom age was unknown were excluded.
[a] $\chi^2 = 8.40$; $P = 0.03844$.
[b] Women tested serologically more than 30 days after vaccination.

FIGURE 1. Distribution of susceptible pregnant women at the time of vaccination according to gestational age. State of Rio de Janeiro, Brazil, 2001–2002

histopathological examination showed no evidence of vaccine virus infection.

DISCUSSION

The mass immunization campaign against rubella targeted at childbearing-age women in the state of Rio de Janeiro posed several logistic challenges, and was further complicated by the difficulty of avoiding vaccinating pregnant women. The benefits to be obtained from immunizing 29 million women in Brazil were presumed on the basis of scarce surveillance data, and the present assessment of the campaign is limited to an analysis of vaccine coverage. Albeit limited, these data provide the few pieces of empirical evidence that mass immunization was justified.

fied through genotypical characterization, and the child's clinical condition was compatible with CRS. The 4 IgM-positive newborns of susceptible mothers had no clinical abnormality at 1-year follow-up. The rate of congenital infection by the rubella vaccine virus was 2.0% (4/204). The other 4 IgM-positive children were born to women

with indeterminate serological results (*n* = 2) or in whom no serum was available for testing (*n* = 2). These 4 newborns probably represented congenital infections, so that the resulting rate of CRS was 3.9% (95% CI: 1.7%–7.6%).

Of the few reported miscarriages (*n* = 52), those that provided material (embryonic remains, placenta) for

Follow-up data indicated that the state of Rio de Janeiro had a significant contingent of childbearing-age women susceptible to rubella during early pregnancy, the period of greatest risk for CRS. The susceptible women belonged to the cohort not previously targeted by immunization measures against rubella, which began in Rio de Janeiro in 1996. Because of the reduction in viral circulation, this cohort had not been exposed to natural infection (24). The proportion of susceptible study participants represents a crude but reasonable estimate of susceptibility in childbearing-age women. It is also possible that the proportion of susceptible individuals in the male population of the same age group is similar to that in women before the campaign, and that this may keep the virus circulating since men were not vaccinated. The proportion of IgM-positive women was similar to that found in blood donors in the city of Rio de Janeiro in 2000 (25), and corroborated the assumption that there was a contingent of rubella-susceptible women that would justify vaccination of all women in that age group. If one considers that mass vaccination protected only 12.6% of the women 15 to 29 years of age, this implies that it was necessary to vaccinate 8 childbearing-age women (1/0.126) to immunize (se-

FIGURE 2. Vaccination coverage against rubella and measles, and prevalence (per 10 000 inhabitants) of rubella vaccine infection in pregnant women by age group. State of Rio de Janeiro, Brazil, 2001–2002
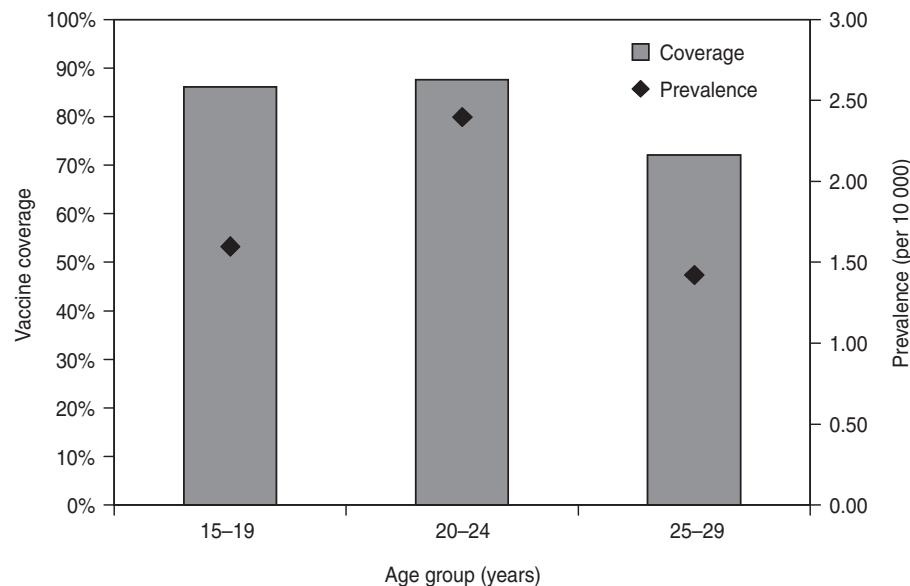
roconvert) one susceptible woman. For each pregnancy that may have been protected from rubella in the state of Rio de Janeiro in 2002, 82 women (1 754 071 vaccinees and 21 398 susceptible newborns in 2002) had to be immunized. This simplified estimate gives a rough idea of the effort per individual benefit expected from the vaccination campaign.

Overall vaccination coverage (82.2%) in the state of Rio de Janeiro (9) and the proportion of susceptible pregnant women (12.6%) for the entire state may hide disparities across regions. Women who remain susceptible after the campaign may be concentrated in local communities, as suggested by the proportion of susceptible women in the northwestern and southern-coastal regions of the State. These data may indicate the need for follow-up vaccination activities in order to achieve and maintain high, homogeneous coverage, or the need to switch immunization strategies.

The laboratory diagnostic procedures and criteria for serological classification of pregnant women were the same throughout the 4-month campaign. Our analysis assumed that classification errors arising from the diagnostic methods were negligible and that the proportion of false positives and false negatives would not substantially affect the results. This is a reasonable assumption, because the serological methods were highly sensitive and specific (21), and the results of early serological testing done within 15 days after vaccination were verified by later retesting. In the subgroup of women who were IgM-negative and IgG-positive more than 30 days after vaccination, immune status was classified as indeterminate. These pregnant women might have had detectable IgG levels prior to vaccination, indicating immunity, but this would have required laboratory confirmation in some cases with rubella avidity assays (22, 23). They might also have been susceptible without detectable IgM. However, not having done such tests did not affect follow-up of the pregnant women. Such testing was intended to gather clinical data for both treatment and research purposes. It is possible that unrecognized selective factors characterizing the subgroup who had serological testing within 30 days of vaccination may be related to rubella susceptibility, but the similarity in age distribution between pregnant women tested before and after the 30-day period suggests that the two groups did not differ substantially (Table 2).

Some limitations of this study should be acknowledged. Estimates of rubella susceptibility in women 15 to 29 years old were based on a sample of inadvertently vaccinated pregnant women comprising 0.2% of the total population of vaccinated childbearing-age women. Thus they did not constitute a probabilistic sample of pregnant women, who were strongly advised during the campaign to avoid vaccination. In addition, loss to follow-up may have added uncertainty to the estimates, because the protocol for obtaining information about pregnant women was not conceived for research purposes and may not have optimized follow-up. However, there appears to be no plausible association between returning late for serological testing (>30 days after vaccination) and susceptibility to rubella. Therefore, the proportion of susceptible women in the subgroup tested within 30 days of vaccination is likely to be similar to the proportion among those classified as indeterminate because of the interval between vaccination and serological testing. Several other studies (13, 15, 26–28) involving the inadvertent immunization of pregnant women against rubella reported similarly high proportions (>65%) of women with unknown immune status. This is not surprising, since inadvertent vaccination is more likely to occur in early stages of pregnancy, and it might take more than 30 days for women to confirm their pregnancy and to return to the health care unit for follow-up.

Pregnancy and inadvertent vaccination did not appear to be selection factors for rubella susceptibility, since the vaccination campaign targeted women regardless of history of disease or vaccination. In addition, the wide-spread efforts to identify and follow women exposed to the rubella vaccine during pregnancy, and the campaign's coverage against measles and rubella in the state of Rio de Janeiro, both support the hypothesis that women vaccinated during pregnancy were represented in the study sample. The survey's target population included women predominantly vaccinated in early pregnancy, who are of particular interest for investigating the potential teratogenicity of the rubella vaccine virus.

Although the strategy of vaccinating adult women was justified by epidemiological surveillance data, the contingent of susceptible women was unknown, as was the safety of vaccinating pregnant women, which was impossible to avoid completely. Follow-up of vaccinated pregnant women was an ethical requirement that added to the immunization program's cost. The data generated by this follow-up confirmed the absence of CRS cases associated with the rubella vaccine, although laboratory evidence of rubella vaccine infection in newborns was detected (see the Results section). Therefore, withdrawing the restrictions against vaccinating pregnant women was not warranted. Follow-up data on the susceptibility to rubella among pregnant women also provided information on the proportion of susceptible women in the entire age group. Considering the vaccination campaign's coverage and the maintenance of high MMR vaccination coverage in 12-month-old children with an additional dose at age 4 to 6 years as required by current policies, immunization of childbearing-age women may no longer be needed. Instead, routine vaccination of susceptible women in the early postpartum period should be emphasized. As in a previous study (15), we found susceptible women who had had previous pregnancies (6.6%), indicating that opportunities for postpartum vaccination had been missed. In addition, containment immunization with MMR or MR vaccine in response to suspected cases of exanthematous diseases is a surveillance strategy which allows appropriate control and may avoid the need for immunization campaigns in adolescent

and young adult men, as implemented in some countries (5).

If it had not been for the inadvertent vaccination of so many pregnant women, we would not have learned the extent of rubella susceptibility among childbearing-age women or the immunization campaign's potential impact. An alternative for analyzing the impact of vaccinating childbearing-age women would be serological studies using either blood donor plasma or stored serum from clinical tests, especially from women in antenatal care clinics, which would provide information about rubella immunity in population subgroups. Available secondary data should be gathered, and primary data should be generated for the specific purpose of supplying information to support decisions for immunization programs. It is hoped that our analysis will provide support for the Program on Rubella and CRS Control in Brazil, and for similar programs elsewhere, by showing how "incidental" data can be used to assess the impact of immunization measures and thus inform decisions concerning future activities such as immunization of adult males.

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RESUMEN

Perfil seroepidemiológico de embarazadas después de recibir inadvertidamente la vacuna antirrubeólica, estado de Rio de Janeiro, Brasil, 2001–2002

Objetivos.   Analizar el estado serológico de mujeres embarazadas tras haber recibido inadvertidamente la vacuna antirrubeólica, en el estado de Rio de Janeiro, Brasil.

Métodos.   Se realizó un estudio transversal de mujeres embarazadas de 15 a 29 años de edad que fueron vacunadas contra la rubéola y el sarampión entre noviembre de 2001 y marzo de 2002 y que no sabían que estaban embarazadas en ese momento o que concibieron en el transcurso de los siguientes 30 días. Se les aplicaron las pruebas detectoras de inmunoglobulina M (IgM) e inmunoglobulina G (IgG) contra el virus de la rubéola y se les clasificó de inmunes si se obtenían resultados negativos a IgM y positivos a IgG al aplicar las pruebas en un lapso no mayor de 30 días después de la vacunación; de susceptibles si se obtenía un resultado positivo a IgM después de la vacunación, o indefinido si se obtenían resultados negativos a IgM y positivos a IgG tras un intervalo mayor de 30 días entre la vacunación y la aplicación de las pruebas serológicas.

Resultados.   De 2 292 mujeres, 288 (12,6%) se mostraron susceptibles; 316 (13,8%) se mostraron inmunes; 1 576 (68,8%) tuvieron resultados indefinidos; 8 (0,3%) tuvieron resultados ilegibles y 104 (4,5%) no tuvieron seguimiento. La seropositividad a IgM, según el intervalo transcurrido entre la vacunación y la aplicación de las pruebas serológicas, fue de 16,1% (≤ 30 días), 15,4% (31–60 días), y 14,2% (61–90 días). En lo respectivo a la edad de las personas a las que se dirigió la campaña, se encontró que el grupo de 20 a 24 años tenía la mayor proporción de personas susceptibles a la rubéola (14,8%) y representaba a 42,4% (122/288) de todas las mujeres susceptibles. En 75% de las embarazadas susceptibles, la edad gestacional fue de 5 semanas o menos en el momento de la vacunación.

Conclusiones.   Se justificó la vacunación poblacional de todas las mujeres en edad fecunda sobre la base de datos epidemiológicos y serológicos. Durante el seguimiento de las embarazadas no se observó ningún caso de síndrome de rubéola congénita ocasionado por la vacuna antirrubeólica. No obstante, el porcentaje de infección congénita observado refuerza la recomendación de que se evite vacunar a mujeres embarazadas y de que estas procuren no concebir durante un mes como mínimo después de la vacunación antirrubeólica.

Palabras clave   Vigilancia inmunológica, embarazo, rubéola (sarampión alemán), síndrome de rubéola congénita, vacunación, Brasil.

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