

Rubella Immune Status in Pregnant Women in a Northern Mexican City

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Abstract

Background: The seroepidemiology of rubella virus infection in pregnant women in northern Mexico is largely unknown. We sought to determine the seroprevalence of rubella virus infection in pregnant women in the northern Mexican city of Durango, Mexico. Seroprevalence association with the socio-demographic, clinical and behavioral characteristics of the pregnant women was also investigated.

Methods: Through a cross-sectional study, we determined the seroprevalence of IgG and IgM anti-rubella virus in 279 pregnant women (mean age 29.17 ± 5.96 years; range 15 - 43 years) attending in a clinic of family medicine using enzyme-linked fluorescent assays. A questionnaire was used to obtain the socio-demographic, clinical and behavioral characteristics of the pregnant women. The association of rubella seropositivity and characteristics of the women was assessed by bivariate and multivariate analyses.

Results: Anti-rubella IgG antibodies (≥ 15 IU/mL) were found in 271 (97.1%) of the 279 pregnant women examined. None of the 279 pregnant women were positive for anti-rubella IgM antibodies. Multivariate analysis of socio-demographic, clinical and behavioral variables showed that seroreactivity to rubella virus was positively associated with national trips (OR = 7.39; 95% CI: 1.41 - 38.78; P = 0.01), and negatively associated with age (OR = 0.26; 95% CI: 0.06 - 0.99; P = 0.04).

Conclusions: Rate of rubella immunity in pregnant women in the northern Mexican city of Durango is high. However, nearly 3% of pregnant women are susceptible to rubella in our setting. Risk fac-

tors associated with rubella seropositivity found in this study may be useful for optimal design of preventive measures against rubella and its sequelae.

Keywords: Rubella; Pregnant women; Epidemiology; Seroprevalence; Cross-sectional study; Mexico

Introduction

Rubella virus is a single-stranded ribonucleic acid virus of the Togaviridae family [1, 2], and is a sole member of the genus Rubivirus [3]. Infection with rubella virus occurs by inhalation of contaminated droplets [1], and can be vertically transmitted to fetuses during maternal infection leading to congenital infection [4]. Rubella virus is an important pathogen worldwide [5]. Infection with rubella virus causes a febrile rash illness in children and adults [6]. In addition, infection with rubella virus in adults may cause severe inflammation and pain in the joints [1]. However, infection with rubella virus during the first trimester of pregnancy can lead to prematurity, low birth weight [7], miscarriage, stillbirth [6], and congenital rubella syndrome [6, 8]. This syndrome is characterized by fetal anomalies including mental retardation [9], heart defects, cataracts [8], blindness, deafness [9], and hepatomegaly and jaundice [10]. There is not currently antiviral treatment for rubella [1]. An effective and sure vaccine against rubella is available [1, 5]. However, rubella outbreaks in Japan and other countries have been reported recently [2, 5, 11].

The seroepidemiology of rubella virus infection in Mexican populations has been scantily studied. An 87% seroprevalence of anti-rubella antibodies in puerperal women from Delicias City in the northern Mexican city of Chihuahua was reported [12], whereas a 92.6% seroprevalence of rubella virus infection in pregnant women in two zones of the valley of Mexico was found [13]. In a study in Leon, Guanajuato, Mexico, researchers found a 71% seroprevalence of rubella in 176 women at reproductive age [14]. To the best of our knowledge, there is not any study on the seroepidemiology of rubella virus infection in pregnant women in northern Mexico. Therefore, this study was aimed to determine the seroprevalence of rubella virus infection in pregnant women in the northern Mexican city of Durango, Mexico. Furthermore, rubella seroprevalence

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association with the socio-demographic, clinical and behavioral characteristics of the pregnant women was also assessed.

Materials and Methods

Study design and population

We performed a cross-sectional study using stored serum samples from a previous survey of cytomegalovirus infection in pregnant women in Durango City, Mexico [15]. Samples were originally obtained to determine the seroprevalence of anti-cytomegalovirus antibodies in pregnant women attending a public primary health care center (Clinic of Family Medicine, Institute of Security and Social Services of State Workers) in Durango City, Mexico. Serum samples were obtained from April to November 2013. Inclusion criteria for enrollment of the participants were: 1) pregnant women attending prenatal care; 2) aged 15 years and older; 3) residence in Durango City; and 4) who voluntarily accepted to participate in the survey.

Socio-demographic, clinical and behavioral characteristics of participants

We obtained the socio-demographic, clinical and behavioral characteristics from the participants with the aid of a questionnaire. Socio-demographic items included age, birthplace, residence, educational level, occupation and socio-economic status. Clinical items included health status, history of lymphadenopathy, frequent headaches; impairments of memory, vision and hearing; and history of blood transfusions. In addition, the obstetric history (month of pregnancy, number of pregnancies, deliveries, cesarean sections and miscarriages) from each participant was recorded. Behavioral items included foreign traveling, alcohol consumption, tobacco use, and washing hands before eating.

Laboratory tests

Sera of the participants were kept frozen until analyzed. Sera were examined for anti-rubella IgG antibodies by a commercially available enzyme-linked fluorescent assay (ELFA) "VIDAS RUB IgG II" kit (bioMerieux SA, Marcy-l'Etoile, France) and for anti-rubella IgM antibodies by a commercially ELFA "VIDAS RUB IgM" kit (bioMerieux SA, Marcy-l'Etoile, France). Anti-rubella IgG antibody levels of ≥ 15 IU/mL were considered as a cut-off for seropositivity. This titer suggests protection against rubella [16, 17]. All tests were performed according to the manufacturer's instructions.

Ethical aspects

This study was performed using stored serum samples from a previous survey. In such previous study, the purpose and procedures of the study were explained to all participants, and a

written informed consent was obtained from all of them and from the next of kin of minor participants. The ethical committee of the Institute of Security and Social Services of State Workers in Durango City, Mexico approved this study.

Statistical analysis

Results were analyzed with the aid of the Epi Info version 7 and SPSS version 15.0 software. For calculation of the sample size, we used a value of 15,000 as a population size from which the sample was selected, a reference seroprevalence of 87.0% [12] as expected frequency of the factor under study, 5.0% of confidence limits, a design effect of 1.0, one cluster, and a confidence level of 95%. The result of the calculation was 172 subjects. We evaluated the association between the characteristics of the women and rubella seropositivity by using bivariate and multivariate analyses. For comparison of the frequencies among groups, the Pearson's Chi-square and the Fisher exact test (when values were less than 5) were used. As a strategy to include variables in the multivariate analysis, we selected only variables with a P value equal to or less than 0.05 obtained in the bivariate analysis. We calculated the odds ratios (ORs) and 95% confidence intervals (CIs) by multivariate analysis using the Enter method. Statistical significance was set at a P value < 0.05 .

Results

We enrolled a total of 279 pregnant women. Their mean age was 29.17 ± 5.96 years (range 15 - 43 years). Table 1 shows the general socio-demographic characteristics of the pregnant women studied. Anti-rubella IgG antibodies were found in 271 (97.1%) of the 279 pregnant women examined. None of the 279 pregnant women were positive for anti-rubella IgM antibodies. Of the socio-demographic characteristics of the pregnant women, the variables including age group and socioeconomic status were associated with anti-rubella IgG antibodies by bivariate analysis, whereas the variables including birthplace, residence, educational level, and occupation did not associate with anti-rubella IgG antibodies.

With respect to clinical characteristics, rubella seroprevalence was similar in ill and healthy pregnant women. Table 2 shows a correlation of rubella seroprevalence and clinical characteristics of pregnant women. Rubella seroprevalence was significantly ($P = 0.02$) higher in pregnant women with frequent headaches, whereas women with history of deliveries had a higher (borderline significance: $P = 0.05$) rubella seroprevalence than women without this history. Other clinical characteristics of women including history of lymphadenopathy, impairments of memory, vision and hearing; history of blood transfusions, month of pregnancy, number of pregnancies, deliveries, cesarean sections and miscarriages did not show an association with rubella seroprevalence by bivariate analysis.

Concerning behavioral characteristics of women, the variable "national trips" showed a borderline ($P = 0.05$) association with rubella seroprevalence. Other behavioral characteristics

Table 1. Socio-Demographic Characteristics of Pregnant Women and Seroprevalence of Rubella IgG Antibodies (≥ 15 IU/mL)

Characteristic	No. of women tested ^a	Rubella seroprevalence		P value
		No.	%	
Age groups (years)				
15 - 24	61	60	98.4	0.01
25 - 34	159	157	98.7	
35 - 43	59	54	91.5	
Birth place				
Durango State	259	252	97.3	1.00
Other Mexican State	16	16	100.0	
Residence place				
Durango State	278	270	97.1	1.00
Other Mexican State	1	1	100.0	
Residence area				
Urban	264	257	97.3	0.42
Suburban	4	4	100.0	
Rural	11	10	90.9	
Educational level				
Up to 6 years	1	1	100.0	0.30
7 - 12 years	102	97	95.1	
13 or more years	176	173	98.3	
Occupation				
Unemployed ^b	81	78	96.3	0.69
Employed ^c	198	193	97.5	
Socioeconomic level				
Low	15	13	86.7	0.02
Medium	257	252	98.1	
High	3	3	100.0	

^aSums may not add up to 279 because of some missing values. ^bUnemployed: none occupation, student or housewife. ^cEmployed: employee, professional, business, or other.

including traveling abroad, alcohol consumption, tobacco use, and washing hands before eating did not show an association with rubella seroprevalence.

Multivariate analysis of socio-demographic, clinical and behavioral variables with P values ≤ 0.05 by bivariate analysis including age, socioeconomic status, frequent headache, number of deliveries, and national trips showed that seroreactivity to rubella was positively associated only with national trips (OR = 7.39; 95% CI: 1.41 - 38.78; P = 0.01), and negatively associated only with age (OR = 0.26; 95% CI: 0.06 - 0.99; P = 0.04).

Discussion

Very little is known about the serological status against rubella virus in pregnant women in Mexico. Therefore, this study aimed to determine the seroprevalence of IgG and IgM anti-

bodies against rubella virus in pregnant women in the northern Mexican city of Durango. Results indicate that 97.1% of the pregnant women studied had protective (≥ 15 IU/mL) antibodies against rubella virus infection. In Mexico, vaccination against rubella started in 1998 [18]. Although the majority of pregnant women tested had protective antibodies, nearly 3% of women were susceptible to rubella. This figure seems low but considering that there are nearly 40,000 births a year in Durango State (<http://cuentame.inegi.org.mx/monografias/informacion/dur/poblacion/dinamica.aspx?tema=me&e=10>), thus there are about 1,200 pregnant women susceptible to rubella virus just in this Mexican state. Concerning studies in Mexico, the seroprevalence of rubella found in the present study is higher than the 87% seroprevalence of rubella in early puerperium women in the northern Mexican city of Delicias, Chihuahua [12], the 92.6% seroprevalence of rubella in pregnant women from Iztapalapa and Nezahualcoyotl areas in the valley of Mexico [13], and the 71% seroprevalence in women

Table 2. Bivariate Analysis of Clinical Data and Seropositivity to Rubella Virus in Pregnant Women in Durango City, Mexico

Characteristic	No. of women tested ^a	Rubella prevalence		P value
		No.	%	
Clinical status				
Healthy	267	260	97.4	0.27
Ill	11	10	90.9	
Lymphadenopathy ever				
Yes	42	41	97.6	1.00
No	237	230	97.0	
Headache frequently				
Yes	112	112	100.0	0.02
No	167	159	95.2	
Memory impairment				
Yes	63	63	100.0	0.20
No	216	208	96.3	
Hearing impairment				
Yes	20	20	100.0	1.00
No	259	251	96.9	
Visual impairment				
Yes	79	76	96.2	0.69
No	199	194	97.5	
Blood transfusion				
Yes	13	12	92.3	0.32
No	265	258	97.4	
Pregnancies				
One	89	89	100.0	0.11
Two	97	93	95.9	
Three	50	49	98.0	
Four	31	28	90.3	
Five	9	9	100.0	
More than 5	2	2	100.0	
Deliveries				
Zero	157	153	97.5	0.05
One	65	63	96.9	
Two	41	41	100.0	
Three	11	9	81.8	
Four	3	3	100.0	
More than 4	1	1	100.0	
Cesarean sections				
Zero	195	189	96.9	0.72
One	62	61	98.4	
Two	21	20	95.2	
Miscarriages				
Zero	223	217	97.3	0.88
One	46	44	95.7	
Two	8	8	100.0	
Three	1	1	100.0	
Month of pregnancy				
1 - 3	100.0	98	98.0	0.1
4 - 6	118	116	98.3	
7 - 9	56	52	92.9	

^aSums may not add up to 279 because of some missing values.

of reproductive age in Leon, Guanajuato [14]. However, this comparison should be taken with care since these studies were performed in different years and laboratory tests used were different from the tests we used. Previous seroprevalence studies in Mexico were performed from 1993 to 2004. In those years, the coverage of rubella vaccination was lower than the one in the recent years. We used ELFA to detect IgG antibodies against rubella virus, whereas in the previous studies, the hemagglutination inhibition method [13, 14] was used. In addition, we studied pregnant women in the urban city of Durango, whereas rural and urban women were enrolled in the study in Delicias, Chihuahua [12]. In an international context, the seroprevalence of rubella in pregnant women in Durango is higher than the 93.1% seroprevalence of rubella found in pregnant women seen in a tertiary hospital in Zaria, Nigeria [19], and 87.5% seroprevalence in pregnant women in Osogbo, Nigeria [20] using enzyme-linked immunosorbent assays. Similarly, our prevalence is higher than the 85.8% seroprevalence reported in pregnant women in southern Italy using a microparticle enzyme immunoassay [21]. The rubella seroprevalence found in our study is comparable with the 95.1% seroprevalence of rubella reported in pregnant women in Sudan [22], the 93.3% seroprevalence in pregnant women in Portugal [23], the 94.4% seroprevalence in pregnant women in Oslo, Norway [24], and 95.4% seroprevalence in women of childbearing age in Venezuelan Yupka indigenous communities [25].

We searched for factors associated with rubella seroprevalence. We found that seroreactivity to rubella was positively associated with national trips and negatively associated with age. International travel has been linked to rubella importation in the USA [26]. We did not find an association of international travel with rubella seropositivity. However, it is possible that rubella exposure occurs also by national trips as results of the present study suggests. Therefore, traveling to high endemic rubella regions should be avoided by pregnant women. In the present study, seroprevalence decreases with age. This fact might reflect the higher coverage of rubella vaccination in young women.

This study has limitations including a small sample size, and enrollment of women in only one clinic of family medicine. Further studies with larger sample sizes and in several clinics to determine the seroprevalence of rubella in Mexican communities should be conducted.

Conclusions

Rate of rubella immunity in pregnant women in the northern Mexican city of Durango is high. However, nearly 3% of pregnant women are susceptible to rubella in our setting. Risk factors associated with rubella seropositivity found in this study may be useful for optimal design of preventive measures against rubella and its sequelae.

Conflicts of Interest

The authors declare that no conflicts of interest exist.

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