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Seroprevalence of rubella in Colombia: a birth-year cohort analysis

ABSTRACT

OBJECTIVE: To estimate the seroprevalence of rubella and associated factors.

METHODS: Population-based seroprevalence study in a random sample of 2,124 individuals, aged six to 64 years, representative by age, sex and area in Medellín, Colombia, 2009. Biological and socioeconomic variables were analyzed for their association with serum protection against rubella, according to birth-year cohort; those born before (1954-1990) and after (1991-2003) the introduction of universal immunization. Titer of IgG antibodies against the rubella virus was detected using a high sensitivity (AxSYM® Rubella IgG – Abbott Laboratories) and a high specificity test (VIDAS RUB IgG II® – BioMerieux Laboratories). Proportions and weighted averages derived from a complex sample, including a correction factor for differences in gender participation, were estimated. Association with protection for groups of biological and social variables according to birth cohort was analyzed using a logistic regression model.

RESULTS: Titers of IgG antibodies were higher in those born before (mean 110 UI/ml, 95%CI 100.5;120.2) compared to those born after (mean 64 UI/ml; 95%CI 54.4;72.8; p = 0.000) the introduction of mass immunization. The proportion of protection increased from 88.9% in those born 1990-1994, to 89.2% in those born 1995-1999 and to 92.1% in those born between 2000 and 2003, possibly due to boosters being administered from 1998 onwards. In those born before the introduction of the immunization, seroprotection was associated with previous contact with cases (OR 2.6; 95%CI 1.1;5.9), self- perceived health status (OR 2.5; 95%CI 1.05;6.0), educational level (OR 0.2; 95%CI 0.08;0.8) and years of residence in the neighborhood (RD 0,96; 95%CI 0.98;1.0) after adjusting for all variables. In those born after, serum protection was associated with effective sleep time (OR 1,4; 95%CI 1.09;1.8) and self-perceived health status (OR 5.5; 95%CI 1.2;23.8).

CONCLUSIONS: The seroprevalence profile changed with the mass immunization plan, with higher titers of IgG antibodies in those born before the start of the immunization. It is recommended that the level of long-term protection be monitored and concerted action taken to improve potentially associated socioeconomic conditions.

DESCRIPTORS: Rubella Vaccine, supply & distribution. Rubella, prevention & control. Cohort Effect. Socioeconomic Factors. Seroepidemiologic Studies.

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INTRODUCTION

The Americas proposed to eliminate rubella and congenital rubella syndrome by 2010.[20] Confirmed cases decreased by 98.0% between 1998 and 2006, but there was an outbreak between 2006 and 2009, primarily affecting young men who had not been included in the vaccination campaign, which was aimed at women of childbearing age. There were 18,230 confirmed cases of rubella and 27 of congenital rubella syndrome, especially in Brazil, Chile and Argentina.[6,7]

In Colombia, there were 928 confirmed cases between 1995 and 2005, falling to 18 cases between 2006 and 2009. Immunization coverage increased from 82.0% in 1995 to 93.0% in 2002.[25] Coverage had been less than 90.0% in several years in the last decade, in addition there are some areas with less than 80.0% coverage,[a] and there are gaps in immunization coverage among localities.[1] The immunization campaign began with children aged under five in 1995. In 1998, a booster at age ten was included. From 2002, this booster started to be given at age five. There have been a variety of immunization campaigns aimed at children, teenagers and adults, from ten to 12 years old in 1996, from 14 to 15 in 1997 and from 14 to 39 in 2005. The current immunization scheme includes a Measles-Mumps and Rubella (MMR) dose at one year of age.

In Medellín, the second biggest city in Colombia, with 2.4 million inhabitants,[b] a reduction in incidence has also been observed, although MMR coverage was above 100.0% between 2005 and 2009 (2005 = 127.6%; 2006 = 114.7%; 2007 = 107.5%; 2008 = 109.6%; 2009 = 111.4%), suggesting limitations of the available data.[a]

Knowledge of the socioeconomic factors associated with seroprevalence may help guide the design of comprehensive health care and immunization programs. Immunization coverage depends on access to health care services, which differs according to health insurance and socioeconomic condition.[24] Rubella transmission could be favored by close and prolonged contact,[3] relating to crowding and social mixing at home, school and neighborhood.

The above mentioned factors are important in this region, the country and the city, where considerable poverty and social inequalities exist.[5] The experience of coordinating health promoting activities with immunization and elimination efforts is also promising.[18]

The aim of this study was to estimate the seroprevalence of rubella and associated factors in Medellin. We seek to evaluate the impact of immunization and to document the disease elimination, given the limitations of the immunization data and because about 20.0% and 50.0% of rubella infections are asymptomatic.[8]

METHODS

In 2009 a population-based seroprevalence survey in urban and rural areas in Medellín was conducted. The sample size of 2,400 individuals (200 in each age group, sex and area), was calculated to detect a seropositive proportion of 75.0% based on a previous study.[22]

A random cluster survey design was used. Each sector, neighborhood and home constituting a stage and one individual in each home was selected by simple random sampling. Inclusion criteria were: being male or female aged between six and 64 years old, residing in the selected household whose home was included in official cartography data. Individuals with potentially hazardous phlebotomy were excluded.

A structured questionnaire was applied to investigate the three groups of variables:[26] (a) proximal variables of natural or artificial exposure to rubella virus (immunization status according to immunization record, length of residence in the neighborhood and history of contact with diagnosed cases, or reporting travel to places in Colombia where cases had been notified between 2003 and 2009, or to countries where outbreaks had occurred between 2006 and 2008[7]); (b) Intermediate variables or potential mediators of the immune response (self-perceived health status, nutritional status – body mass index, availability of protein-rich foods – and effective sleep time, namely the hours between going to bed and getting up, subtracting the time not spent sleeping); (c) socioeconomic variables (socioeconomic status according to the official classification, self-perceived household problems in the preceding year, household crowding – persons per room, satisfaction with household income, home ownership, education level education and health insurance affiliation according to accreditation card).

Weight and height were measured and a blood sample taken. The data were collected by experienced nursing staff.

The blood samples were centrifuged at 10,000 rpm for ten minutes before testing. The sera were stored at -70ºC in the serum bank at the Regional Public Health Laboratory, until tested.

IgG titers were determined using the AxSYM® Rubella IgG (Abbott Laboratory) test, with 98.8% sensitivity

[a] Ministerio de Salud y Protección Social de Colombia. Coberturas de vacunación en Colombia. Bogotá; 2011 [cited 2012 Sep 28]. Available from: http://www.minsalud.gov.co/salud/Paginas/ProgramaAmpliadodeInmunizaciones(PAI).aspx
[b] Departamento Administrativo Nacional de Estadística de Colombia. Proyecciones de población 2012. [cited 2012 Sep 12]. Available from: http://www.dane.gov.co/index.php?option=com_content&view=article&id=75&Itemid=72

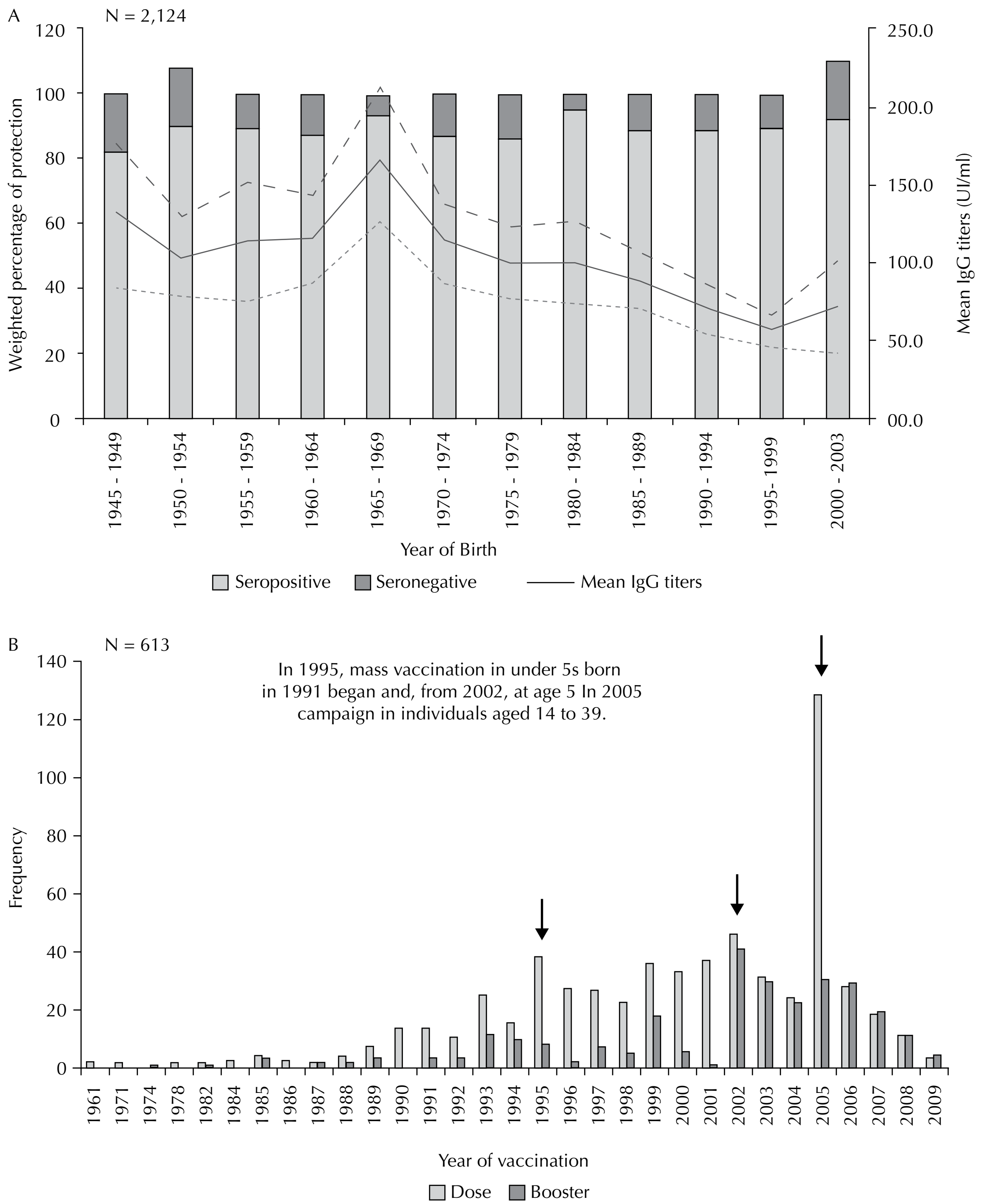

Figure. (A) Distribution of mean IgG titers for rubella by birth year, *versus* proportion of seroprevalence; (B) Frequency of immunized individuals *versus* year in which anti-rubella immunization was administered. Medellín, Colombia, 2009.

and 87.3% specificity.[10] Samples with results between 5 UI/ml and 20 UI/ml were tested using the VIDAS RUB IgG II® test (BioMerieux Laboratory) with a specificity of 95.8%.[10] Individuals with titers ≥ 15 UI/m were considered to indicate seropositivity, whereas those seronegative had titers < 15 UI/ml.[10]

All estimates were weighted to represent the total city population and non-response to the household interview. No significant difference were found between participants and non-participants for age group (p = 0.087) nor for area (p = 0.160). Differences for sex (p = 0.010) were adjusted using a correction factor.[23]

Variables demonstrating a p value of less than 0.25 were included in the multivariate analysis. The logistic regression model estimated, separately, the association between rubella seroprevalence in those born between

Table 1. Weighted proportion of seroprevalence and mean IgG antibodies for rubella for variables of exposure to the virus, immune response and socioeconomic variables, according to year of birth – before and after immunization began – and seroprevalence against rubella. Medellín, Colombia, 2009.

Variable	Overall				Born before (1954-1990)				Born after (1991-2003)			
	Seropositive		Seronegative		Seropositive		Seronegative		Seropositive		Seronegative	
	Categorical variables											
	WP	95%CI	WP	95%CI	WP	95%CI	WP	95%CI	WP	95%CI	WP	95%CI
Natural or artificial exposure												
Contact with cases[a]												
Yes	93.3	89.5;94.3	7.7	5.7;10.5	**93.2**	**90.0;95.5**	**6.8**	**4.5;10.0**	90.5	84.6;94.3	9.5	5.7;15.4
No	85.6	80.6;89.5	14.4	10.5;19.4	**84.8**	**78.7;89.5**	**15.2**	**10.5;21.3**	87.0	77.9;92.8	13.0	7.2;22.1
Rubella immunization[a]												
Yes	92.8	89.5;95.2	**7.2**	**4.8;10.5**	94.2	88.9;97.1	**5.8**	**2.9;11.1**	91.8	86.5;95.1	8.2	4.9;13.5
No	84.4	78.3;89.0	**15.6**	**11.0;21.7**	83.5	76.8;88.6	**16.5**	**11.4;23.2**	90.6	74.3;97.0	9.4	3.0;25.7
Immune response												
Health status[a]												
Regular/Bad/Very bad	93.4	88.3;96.3	6.6	3.7;11.7	91.7	85.2;95.5	8.3	4.5;14.8	98.7	94.0;99.7	**1.3**	**0.6;6.0**
Good/ very good	88.7	85.7;91.2	11.3	8.8;14.3	89.1	85.3;;92.0	10.9	8.0;14.7	88.1	82.6;91.9	**11.9**	**8.1;17.4**
Availability of protein-rich foods[b]												
Yes	90.9	87.3;93.5	9.1	6.5;12.7	91.6	87.2;94.6	8.4	5.4;12.8	89.5	82.6;93.9	10.5	6.1;17.4
No	87.6	83.4;90.8	12.4	9.2;13.9	87.0	81.8;90.9	13.0	9.1;18.2	88.5	80.9;93.4	11.5	6.6;19.1
Socioeconomic												
Education level												
Primary to Postgraduate	90.5	87.6;92.8	9.5	7.2;12.4	**91.5**	**88.5;93.8**	**8.5**	**6.2;11.5**	88.0	81.2;92.5	12.0	7.5;18.8
None	85.3	77.5;90.7	14.7	7.3;26.4	**77.7**	**62.7;87.8**	**22.3**	**12.2;37.3**	90.5	82.1;95.1	9.5	4.9;17.9
Self- perceived household problems[a]												
Yes	87.1	81.6;91.2	12.9	8.8;18.4	90.7	85.3;94.8	9.3	5.2;16.1	80.7	68.7;88.9	19.3	11.1;31.3
No	90.1	87.2;92.4	9.9	7.6;12.8	89.2	85.3;92.1	10.8	7.9;14.7	91.9	86.4;95.2	8.1	4.8;13.6

Continue

Continuation

Satisfied with income[a]												
More than the minimum	95.2	82.9;98.8	4.8	1.2;17.1	95.0	73.7;99.2	5.0	0.8;26.3	95.5	83.2;98.9	4.5	1.1;16.8
No less than the minimum	89.1	86.3;91.3	10.9	8.7;13.7	89.3	85.9;91.9	10.7	8.1;14.1	88.0	83.5;92.5	11.2	7.5;16.5
Persons per room[b]												
Up to one	89.9	87.4;91.9	10.1	8.1;12.6	89.5	86.3;92.0	10.5	8.0;13.7	90.7	86.1;93.9	9.3	6.1;13.9
More than one	85.6	73.6;92.7	14.4	7.3;26.4	89.6	72.1;96.7	10.4	3.3;27.9	77.5	55.8;90.4	22.5	9.6;44.2
Socioeconomic status[b]												
High (4.5.6)	90.8	84.1;94.8	9.2	5.2;15.9	89.0	80.5;94.0	11.0	6.0;19.5	95.8	83.3;99.0	4.2	1.0;16.7
Low (1.2.3)	89.4	86.5;91.8	10.6	8.2;13.5	89.6	86.2;92.4	10.4	7.6;14.0	89.1	83.8;92.8	10.9	7.2;16.2
Home ownership[b]												
Yes	95.2	82.9;98.8	4.8	1.2;17.1	95.0	73.7;99.2	5.0	0.8;26.3	95.5	83.2;98.9	4.5	1.1;16.8
No	89.1	86.3;91.3	10.9	8.7;13.7	89.3	85.9;91.9	10.7	8.1;14.1	88.0	83.5;92.5	11.2	7.5;16.5
Health insurance[b]												
Insured	89.9	87.4;91.9	10.1	8.1;12.6	89.5	86.3;92.0	10.5	8.0;13.7	90.7	86.1;93.9	9.3	6.1;13.9
Not insured	85.6	73.6;92.7	14.4	7.3;26.4	89.6	72.1;96.7	10.4	3.3;27.9	77.5	55.8;90.4	22.5	9.6;44.2

	Quantitative variables											
	Mean	95%CI	Mean	95%CI	Mean	95%CI	Mean	95%CI	Mean	95%CI	Mean	95%CI
Length of residence (years)a	14.9	13.8;15.9	16.0	12.3;19.7	17.0	15.6;18.2	21.6	16.6;26.5	**11.1**	**9.8;12.3**	**6.1**	**4.0;8.1**
Body Mass Index (kg/m^2)[a]	23.0	22.6;23.4	24.4	22.9;25.9	25.1	24.7;25.5	26.7	25.1;28.3	19.2	18.7;19.7	20.3	17.6;22.9
Effective sleep time (hours)[a]	8.2	8.0;8.3	7.7	7.3;8.1	7.8	7.6;7.9	7.6	7.0;8.1	9.0	8.7;9.2	8.0	7.5;8.5

WP: Weighted proportion

Variables with significant differences (p obtained with non-weighted data in the simple logistic regression): [a] p value below 0.05; [b] p value between 0.05 and 0.25.

Variables with significant p value in bold.

1954 and 1990 (before mass immunization began – i.e., born before) and those born between 1991 and 2003 (born after), adjusting the variables in five models: model 1, univariate analysis; model 2, natural and artificial exposure variables; model 3, exposure to the virus and variables mediating the immune response; model 4, exposure to the virus and socioeconomic variables; model 5; all variables. Variables with a p value of less than 5% were considered significant.

The analyses were conducted using the SPSS program, version 15 (IBM SPSS Statistics).

The study was approved by the Ethics Committee of the National Public Health School, *Universidad de Antioquia* (Record 17, 2007). All national ethical regulations for human research (Resolution 8430 of 1993 Colombian Ministry of Health) and the principles of the Declaration of Helsinki were adhered to.[27] In the case of children, consent was obtained from parents or guardians.

After visiting 2,390 homes, 2,124 individuals agreed to participate. Percentages of participation were as follows: overall 88,5%, urban 83,8% and rural 93.2%. Twenty-two individuals did not meet the inclusion criteria and 244 individuals refused to participate due to declining to provide a blood sample (14.9%), lack of time (9.7%), change of address (7.9%) and lack of parental consent for children (7.5%).

RESULTS

The overall weighted proportion of seropositivy was 89.4% (95%CI 86.8;91.6) and seronegativity was 10.6% (95%CI 8.4;13.2)

No difference was observed in seropositive for age in the groups aged six to 17 years old (88.9%; 95%CI 83.8;92.5), 18 to 40 years old (90.8%; 95%CI 86.2;94.1) and 41 to 64 years old (87.9%; 95%CI 83.2;91.4). There were not differences in seropositivity in males (88.5%; 95%CI 83.8;91.9) and females (90.3%; 95%CI 87.3;92.6), nor in inhabitants in urban (87.4%; 95%CI 85.2;87.8) and rural areas (90.2%; 95%CI 84.2;95.0).

Mean IgG titers were significantly different between those born before (mean 110 UI/ml; 95%CI 100.5;120.2) and after mass vaccination began (mean 64 UI/ml; 95%CI 54.4;72.8), p = 0.000 (Figure, A).

No differences were recorded in the weighted proportion of seropositive (born before: 89.6; 95%CI 86.3;92.1; born after: 89.1; 95%CI 84.1;92.7) and seronegative (born before: 10.4; 95%CI 7.9;13.7; born after: 10.9; 95%CI 84.1;92.7). An increasing proportion of seropositive was found according to the dates of birth of the individuals born after: from 88.9% in those born between 1990 and 1994, 89.2% in those born between 1995 and 1999 and 92.1% in those born between 2000 and 2003 (Figure, A).

Of the sample, 33.7% of individuals presented their immunization record (95%CI 30; 37.5), particularly those born after mass immunization began (59.9%; 95%CI: 53.5;66.1). Of 613 individuals, a single vaccination dose was administered to 32.0% and 22.8% of those born before and after, respectively. In those born before, the mean age of receiving the first dose was 21 years old (median = 20; CV = 58.7%), in a mass immunization campaign in 2005 (17.9%), and in those born after the mean age was one year old (median = 3, CV = 128.7%) (Figure, B). The booster was received by 8.6% of those born before and 36.5% of those born after, especially from 2002 onwards, with a median age of five years in both groups (Figure, B).

In those born before, significant differences were observed in seroprevalence by previous immunization and contacts with cases (Table 1).

The mean length of residence in the neighborhood was high in those born before. The seroprevalence was significantly different in those born after, with longer mean residence in seropositive (Table 1).

The difference in self-reported health status in seronegative was significant in individuals born after, with a higher proportion of seropositivity in those who reported their health to be good or very good (Table 1).

No association was observed between self-perceived health status and rubella immunization either overall (OR 1.6; 95%CI 0.93;2.8) nor disaggregated by birth-year cohort (born before: OR 1.12; 95%CI 0.61;2.5; born after: OR 3.6; 95%CI 0.68;19.2).

Significant differences were found in education level, with a higher seropositivity in those who had attained a higher level, compared with those who had not (Table 1). An potential association was observed between education levels and immunization status in those born before (OR 0.14; 95%CI 0.06;0.34) but not in those born after nor overall (born after: OR 1.8; 95%CI 0.4;8.2; overall: OR 1.2; 95%CI 0.8;2.0).

A potential association was observed in individuals born before, adjusting for all variables (model 5), according to: previous contact with cases, length of residence in the neighborhood, self-perceived health status and education level (Table 2).

The odds of seropositivity were two times greater among those who had had contact with cases, than those who had not and in those who did not perceive their health to be good, compared with those who did. Individuals with education levels between primary and postgraduate had higher odds of seropositvity than those who had no schooling. Adjusted ORs for length of residence in the neighborhood and body mass index were significant, although the upper limit of the confidence interval was equal to one (Table 2).

Table 2. Potential factors associated with rubella seroprevalence in those born between 1954 and 1990, before mass vaccination began. Medellín, Colombia, 2009.

Variable	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Natural or artificial exposure										
Contact with cases (Yes/No)	**2.4**	**1.3;4.4**[a]	1.9	0.9;4.3	1.9	0.82;4.9	**2.6**	**1.2;5.8**[b]	**2.6**	**1.1;5.9**[b]
Rubella immunization (Yes/No)	**3.2**	**1.4;7.3**[b]	**2.4**	**1.06;5.6**[b]	**2.2**	**1.0;5.2**[c]	2.0	0.8;4.4	1.9	0.8;4.3
Length of residence (years)	**0.98**	**0.9;1**[b]	**0.98**	**0.95;1**[b]	0.98	0.95;1.0	**0.98**	**0.96;1**[b]	**0.96**	**0.98;1.0**[b]
Immune response										
Health status (Regular, bad, very bad/Good, very good)	1.34	0.6;2.8			2.01	0.8;4.9			**2.5**	**1.05;6.0**[b]
Body mass index (kg/m2)	**0.9**	**0.8;0.9**[b]			**0.94**	**0.8;1.0**[c]			0.95	0.9;1.0
Effective sleep time (hours)	1.05	0.9;1.2			1.03	0.8;1.2			1.0	0.85;1.1
Availability of protein-rich foods (Yes/No)	0.6	0.3;1.1			0.6	0.2;1.5			0.6	0.2;1.4
Socioeconomic										
Education level (None/Primary to postgraduate)	**0.3**	**0.1;0.7**[b]					**0.2**	**0.09;0.6**[b]	**0.2**	**0.08;0.8**[b]
Self- perceived household problems (Yes/No)	1.18	0.5;2.4					2.3	0.8;6.5	2	0.7;5.7
Satisfaction with income (more than the minimum/Less than the minimum)	**0.4**	**0.2;0.9**[b]					0.5	0.1;1.8	0.6	0.1;2.2
Persons per room (More than one/up to one)	0.9	0.64;1.5					0.7	0.3;1.5	0.7	0.3;1.5
Socioeconomic status (Low/High)	1.07	0.5;2.2					2.2	0.8;6.1	2.2	0.8;5.9
Home ownership (Yes/No)	2.2	0.3;15.9					1.5	0.1;13.1	1.4	0.1;12.3
Health insurance (Not insured/ Insured)	1.02	0.3;3.5					0.9	0.2;3.5	0.7	0.1;2.6

Model 1: Simple Model; unadjusted OR (95%CI);
Model 2: Independent variables of natural or artificial exposure: previous contact with cases of rubella, immunization history, length of residence in the neighborhood; adjusted OR (95%CI);
Model 3: Independent variables of natural or artificial exposure and potential mediators in immune response (self-perceived health status, body mass index, effective sleep time in hours, availability of protein-rich foods); adjusted OR (95%CI);
Model 4: Independent variables of natural or artificial exposure and socioeconomic variables (education level, Self-perceived household problems, satisfaction with household income, number of persons per room, home ownership, health insurance); adjusted OR (95%CI);
Model 5: Complete model. Independent variables of natural or artificial exposure, potential mediators in immune response and socioeconomic variables; adjusted OR (95%CI).
Variables with significant p value in bold.
[a] p value 0.003 to 0.005
[b] p value 0.01 to 0.04
[c] p value = 0.05

Previous contact with cases was significant in model 1 and when adjusted for socioeconomic variables (models 4 and 5). Previous immunization was significant when adjusted for variables of exposure and mediating immune response (models 1, 2 and 3), but not for socioeconomic variables (Table 2).

The OR was significant in individuals born after in model 5, according to self-perceived health status and effective sleep time (Table 3).

The odds of seropositivity were greater among individuals who perceived their health status to be worse than those who felt it to be good. No association was observed in seroprevalence for previous immunization or contact with cases, in individuals born after mass immunization began (Table 3).

DISCUSSION

This study estimated an overall proportion of seropositivity of 89.4% (95%CI 86.8;91.6), below the minimum proportion of 90.0% required to achieve herd immunity (95%CI 88.6;95.2).[15] In the six to 17 year old age group, the proportion was 88.9% (95%CI 83.8;92.5). In a previous study from 1997,[22] 74.8% of seropositive was found in 912 children, aged between one and 14. Despite limitations of this comparison, an increase in prevalence was observed in this group, although protection needs to be increased in order to sustain rubella elimination in the Region.[14,15]

The lack of differences in seroprevalence for sex and area may be due to immunization programs being aimed equally at these groups.[12]

Table 3. Potential factors associated with rubella seroprevalence in those born between 1991 and 2003, after mass vaccination began. Medellín, Colombia, 2009.

Variable	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Natural or artificial exposure										
Contact with cases (Yes/No)	1.4	0.6;3.2	0.7	0.2;2	0.9	0.2;2.9	0.5	0.2;1.7	0.7	0.1;2.7
Rubella immunization (Yes/No)	1.1	0.3;4.3	1.2	0.3;4.3	2.4	0.6;9.2	0.7	0.2;2.9	1.3	0.3;4.9
Length of residence (years)	1.1	1.02;1.1	1.06	0.9;1.1	1.06	0.9;1.1	1.06	0.9;1.1	1.0	0.9;1.1
Immune response										
Health status (Regular, bad, very bad/Good, very good)	**10.2**	**2;52**[b]			**6.1**	**1.1;33.9**[a]			**5.5**	**1.2;23.8**[a]
Body mass index (kg/m2)	0.9	0.8;1			1.01	0.8;1.1			1.0	0.9;1.2
Effective sleep time (hours)	1.2	1.0;1.5			**1.4**	**1.1;1.9**[a]			**1.4**	**1.09;1.8**[a]
Availability of protein-rich foods (Yes/No)	0.9	0.4;2			1.1	0.3;3.5			0.9	0.3;2.9
Socioeconomic										
Education level (None/Primary to postgraduate)	1.3	0.5;3.1					2.7	0.8;9.1	2.5	0.5;11.0
Self- perceived household problems (Yes/No)	**0.3**	**0.1;0.8**[a]					**0.3**	**0.1;0.96**[a]	0.3	0.1;1.02
Satisfaction with income (more than the minimum/Less than the minimum)	1.7	0.4;5.9					4.0	0.6;26.3	4.4	0.7;26.7
Persons per room (More than one/up to one)	2.3	0.9;5.7					4.1	0.4;34.4	6.3	0.5;80
Socioeconomic status (Low/High)	0.3	0.07;1.7					0.4	0.07;3.5	0.5	0.05;5.7
Home ownership (Yes/No)	2.7	0.5;12.5					1.5	0.2;8.6	1.3	0.2;8.7
Health insurance (Not insured/ Insured)	0.3	0.1;1.04					0.3	0.1;1.5	0.3	0.08;1.5

Model 1: Simple Model; unadjusted OR (95%CI);
Model 2: Independent variables of natural or artificial exposure: previous contact with cases of rubella, immunization history, length of residence in the neighborhood; adjusted OR (95%CI);
Model 3: Independent variables of natural or artificial exposure and potential mediators in immune response (self-perceived health status, body mass index, effective sleep time in hours, availability of protein-rich foods); adjusted OR (95%CI);
Model 4: Independent variables of natural or artificial exposure and socioeconomic variables (education level, Self-perceived household problems, satisfaction with household income, number of persons per room, home ownership, health insurance); adjusted OR (95%CI);
Model 5: Complete model. Independent variables of natural or artificial exposure, potential mediators in immune response and socioeconomic variables; adjusted OR (95%CI).
Variables with significant p value in bold.
[a] p value 0.003 to 0.005
[b] p value 0.01 to 0.04
[c] p value = 0.05

In individuals born before 1991, a potential association was found among seroprevalence for previous contact with cases, length of residence in the neighborhood, self- perceived health status and education level.

The higher mean levels of antibody titers in individuals born before, corresponds to findings by other authors.[3] The association for previous contact with cases and length of residence in the neighborhood may be due to greater time and opportunities to be exposed to the virus and to higher incidence of the disease before 1995. Mandatory reporting of rubella was initiated in 1978[c] and, therefore, data on exposition before this date is limited. Those born before 1991 had probably been repeatedly exposed to the virus, due to the frequent epidemics which occurred in these years, including the pandemic in the 1960s, which are not found in local records.

Although those born before 1991 had not received free immunization, a higher proportion of seropositive was observed in individuals between 17 and 39 years old. This may be related to access to mass immunization aimed at adults in 2005.[25]

An association was observed between seroprevalence and immunization status of those born before 1991, when the exposure and mediating immune response

[c] Dirección Seccional de Salud de Antioquia. Series cronológicas de salud. Medellín: Oficina de Epidemiología; 1994.

variables were analyzed. Although no association was found between immunization in those born after, the increasing proportion of seropositivity, according to date of birth, is possibly related to the administration of the booster from 1998 onwards and the reduction to five years of age from 2002 onwards.

The positive impact of immunization onto increasing the protection of the groups to whom immunization strategies are directed has also been observed in population – based studies in the United States between 1988 and 1994 (The National Health and Nutrition Examination Survey – NHANES III) and 1999 to 2004 (NHANES IV).[11,16]

A limitation of this study was the quality of immunization data. Fewer than 40.0% of the individuals had immunization records, which limited the ability to differentiate between natural and artificial exposure. A potential association was observed between previous immunization and seroprevalence, without disaggregating by date of birth (OR 2.39; 95%CI 1.3;4.2). Likewise, consistency was observed between immunization and seroprevalence: the proportion of seropositive was higher among those who had been immunized and the proportion of seronegative was higher among those who had not been immunized (Table 1).

Although the data on vaccine doses received were limited, it may indicate the need for timely compliance with the scheme. Administration of the first dose varies in those born after 1991, with median age of one year old, and an average of three years old, which may be due to missed immunization opportunities, as has been seen in other studies.[19] Seroprevalence data were reliable given the high sensitivity and specificity of the tests used.[10]

Education level was a protector factor in those born before 1991, with higher odds for seropositivity in those who had achieved some schooling.[2] This may be related to access to immunization. In these individuals, schooling could influence the opportunity of exposure in schools and colleges, where viral dissemination was usually facilitated.

A potential association was found with self-perceived health status and effective sleep time in individuals born after 1991.

Self-perceived health status has been studied as a predictive indicator of mortality, access to health care services and is a proxy of health status,[9] and it has been studied in other studies of seroprevalence.[11,16] Reliability has been observed between self-reported health status according to age, sex and cultural conditions.[13] Understanding the potential mediating role of perceived health status, related to immunization and access to health care services requires further studies. The higher seropositivity found in those who reported having better health status may be associated with immunization, and this in turn may be related to access to health care services. No association was found between rubella immunization and self-reported health. The proxy variable of access to health care services was health insurance affiliation, which was not associated with either immunization or seropositivity.

Over the last years, researchers have accumulated evidence about sleep and immune response. Additional studies are needed to support the association between the production of specific antigens and the quality and quantity of sleep, as well as the association between sleep and long-term anti-body response as has been studied in other diseases, such as hepatitis A and B and influenza AH1N1.[4,17,21] To our knowledge this is the first report of a potential association between effective sleep time and rubella seroprevalence, however, it is a cross-sectional study, which limits the temporal analysis of exposure history to this factor and immune response.

The potential association of seropositivity with socioeconomic variables studied highlights the need for concerted actions to be taken to improve living conditions. New approaches to improve the timeliness of the immunization schedule are required, to increase and sustain herd immunity and monitor the level of long-term protective antibody titers.

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The authors declare that there are no conflicts of interest.