Clinical and Vaccine Immunology, Apr. 2010, p. 691–694 Vol. 17, No. 4
1556-6811/10/$12.00 doi:10.1128/CVI.00356-09

Prevalence of Protective Measles Virus Antibody Levels in Umbilical Cord Blood Samples in Catalonia, Spain▽

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Received 4 September 2009/Returned for modification 20 October 2009/Accepted 4 February 2010

The prevalence of protective antibody levels (>160 mIU/ml) in neonates was 98.5%. The mean measles virus antibody level was 3,406 mIU/ml and increased with maternal age. Measles vaccination was reported by 42% of pregnant women and decreased with age.

Catalonia, a region in the northeast of Spain, began administration of one dose of the measles, mumps, and rubella (MMR) vaccine at 12 months of age in the routine vaccination schedule in 1980 (5). In 1987, administration of the first dose was shifted to 15 months of age, and in 1988, a second dose of MMR vaccine was added at 11 years of age to replace the rubella vaccine administered to girls. In 1998, administration of the second dose was shifted to 4 years of age to ensure that more than 95% of children <10 years of age were immune to measles (5).

Immunization has reduced the incidence of measles in Catalonia and the rest of Spain. The incidence of measles in Spain has decreased from 427 per 100,000 persons in 1997 to 0.37 per 100,000 persons in 2000, and by the year 2000, indigenous measles virus transmission was interrupted in four Spanish regions (Asturias, Cantabria, Catalonia, and Navarra) (2, 17). In 2005, there were no reported cases of measles in 10 Spanish regions (3). Nevertheless, in 2006, a measles outbreak affecting 381 people occurred in Catalonia (7). Analysis of the epidemiological characteristics of the outbreak showed that that 76% of the cases occurred among individuals aged <25 years, 50% occurred among children aged ≤15 months, and 89% occurred among nonvaccinated individuals (7). The measles outbreak occurred possibly because children aged ≤15 years had low measles virus antibody levels and the prevalence of protection among individuals aged <25 years was lower than the herd immunity threshold (16).

In pregnant women, measles can be a serious disease if complications occur or the infection is transmitted to the fetus (18). In Catalonia, measles immunity and measles virus IgG antibody levels are not studied routinely in women of childbearing age, although this assessment may be necessary to immunize unprotected women. The objective of this study was to investigate measles virus antibody levels and the prevalence of protective levels in umbilical cord blood samples of neonates from a representative sample of pregnant women in Catalonia.

A representative sample of pregnant women in Catalonia was obtained from 27 hospitals between August and December 2003. The sample size, calculated taking into account a prevalence of protective antibody levels of 98% in women aged 25 to 34 years (6), an alpha error of 5%, and a precision of ±0.007, was 1,536. Informed consent to obtain umbilical cord blood samples and study variable data were obtained from all pregnant women. The sociodemographic variables assessed were age, place of birth, urban or rural habitat, and social class. An immigrant woman was defined as a woman not born in Catalonia or another Spanish region. Social class was determined by occupation using the English classification (I to III, IV and V, and VI) (14). Medical variables included history of vaccination and diseases. Measles virus immunoglobulin G (IgG) levels were measured in umbilical cord blood by enzyme-linked immunosorbent assay (Enzygnost; Behring) according to the manufacturer's instructions. Measles virus IgG antibody levels of >160 mIU/ml in umbilical cord samples were considered indicative of immune protection (Enzygnost; Behring).

Statistical analysis was carried out using the SPSS program (version 17; SPSS Inc.). Mean measles virus IgG antibody levels, prevalence of protective antibody levels, and their 95% confidence intervals (CIs) were determined in different sociodemographic groups. The *t* test was used to compare mean antibody levels, and the chi-square test was used to compare prevalences, considering a *P* value of <0.05 statistically significant. Correlation between mean antibody levels and study variables was assessed using Pearson's correlation coefficient (*r*), considering a *P* value of <0.05 statistically significant. A multiple linear regression equation to explain measles virus antibody levels was developed using the stepwise method to select variables. The possible association between sociodemographic variables and measles vaccination in pregnant woman was analyzed by calculating the crude and adjusted odds ratios (ORs). Multiple logistic regression analysis was used to adjust significant ORs.

The composition of the sample (n = 1,498) of pregnant women included in the study according to sociodemographic variables was similar to that of the population of Catalonia (10). The prevalence of protective measles virus antibody lev-

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▽ Published ahead of print on 17 February 2010.

TABLE 1. Measles virus IgG antibody levels and prevalence of protective (>160 mIU/ml) measles virus antibody levels in umbilical cord blood samples by maternal sociodemographic variables in Catalonia, Spain, 2003

Maternal variable	Measles virus antibody level (mIU/ml)		Prevalence of protective measles virus antibody level			*n*
	Mean	SD	No. positive	% Positive	95% CI	
Age (yr)						
15–24	2,461.9	2,043.9	280	97.2	95.1–99.3	288
25–29	3,217.4[a]	2,053.5	374	98.7	96.9–99.6	379
30–34	3,775.5[a,b]	2,262.4	522	98.7	97.6–99.7	529
35–49	3,898.8[a,b]	1,916.6	299	99.0	97.1–99.8	302
Total	3,406.6	2,165.0	1,475	98.5	97.8–99.1	1,498
Habitat						
Urban	3,365.4	2,134.2	1,216	98.5	97.7–99.2	1,235
Rural	3,599.9	2,298.5	259	98.5	96.1–99.6	263
Place of birth						
Spain	3,442.7	2,140.8	1,187	98.4	97.7–99.2	1,206
Other	3,135.6	2,182.0	288	98.6	96.5–99.6	292
Educational level						
<Primary	3,365.9	2,101.1	587	98.2	97.0–99.3	598
≥Primary	3,465.7	2,164.4	676	98.7	97.8–99.6	685
Social class						
I-III	3,604.4[c]	2,145.3	399	99.3	97.9–99.8	402
IV-V	3,369.9	2,133.7	553	98.6	97.5–99.6	561
VI	3,296.4	2,207.5	523	97.8	96.5–99.1	535
Measles vaccination						
Yes	2,906.0	2,073.4	670	97.9	96.8–99.1	633
No	3,772.9[d]	2,158.4	805	98.4	98.1–99.6	865

[a] $P < 0.001$ versus age of 15 to 24 years.
[b] $P < 0.001$ versus age of 25 to 29 years.
[c] $P < 0.05$ versus social class VI.
[d] $P < 0.001$.

els (>160 mIU/ml) in neonates was 98.5% (Table 1). The prevalence of protective measles virus antibody levels was >95% in all sociodemographic groups. The measles virus antibody levels were <1,000 mIU/ml in 172 (11.5%) samples, between 1,000 and 10,000 mIU/ml in 1,315 (87.8%) samples, and >10,000 mIU/ml in 11 (0.7%) samples.

The mean measles virus IgG antibody level was 3,406.6 mIU/ml (Table 1). Measles virus antibody levels increased with maternal age, from 2,461 mIU/ml in neonates of women aged 15 to 24 years to 3,898 mIU/ml in those of women aged 35 to 49 years, with a correlation coefficient (r) of 0.23 ($P < 0.001$) (Table 1). Measles virus antibody levels were higher in neonates of women of social classes I to III than in those of social class VI, although women of classes I to III had a higher mean age than those of social class VI: 31.9 years versus 29.8 years ($P < 0.001$).

The multiple linear regression equation to explain measles virus antibody levels in neonates was as follows: measles virus antibody level (mIU/ml) = 610.1 + (93.0 × maternal age). This model was associated with a multiple correlation coefficient of 0.22 ($P < 0.001$).

Table 2 compares measles virus antibody levels and the prevalence of protective levels in neonates of indigenous and immigrant women. Measles virus antibody levels were higher in neonates of indigenous women aged 30 to 49 years with a primary or higher education than in neonates of immigrant pregnant women of the same age and educational level.

Measles vaccination was reported by 42% of the pregnant women studied (Table 3). A history of measles was reported by 10% of the pregnant women studied. Measles virus antibody levels were lower in neonates of vaccinated women than in neonates of unvaccinated women ($P < 0.001$) (Table 1). The bivariate statistical analysis showed that vaccination rates were associated with place of birth, education level, and social class. Nevertheless, the multiple logistic regression analysis showed that only the variable age was independently associated with measles vaccination (Table 3).

This study has found that most neonates were protected against measles, as 98.5% of the samples had measles virus antibody levels of >160 mIU/ml, although 11.4% of them, with measles virus antibody levels of <1,000 mIU/ml, could become unprotected before completing measles vaccination.

Measles virus antibody levels were higher in neonates of older women, women of social classes I to III, and indigenous women with a lower educational level. These results could be explained by three factors: (i) the correlation between maternal age and measles virus antibody levels in neonates, (ii) the higher prevalence of measles vaccination in younger pregnant women, and (iii) a lower immunogenicity from measles vaccination than from natural infection.

TABLE 2. Measles virus IgG antibody levels and prevalence of protective (>160 mIU/ml) measles virus antibody levels in neonates of indigenous and immigrant women by maternal sociodemographic variables in Catalonia, Spain, 2003

Maternal variable	Neonates of indigenous pregnant women				Neonates of immigrant pregnant women			
	Measles virus antibody level (mIU/ml)		Prevalence of protective level (%)	*n*	Measles virus antibody level (mIU/ml)		Prevalence of protective level (%)	*n*
	Mean	SD			Mean	SD		
Age (yr)								
15–24	2,427.5	2,061.7	97.5	199	2,538.9	2,013.0	96.6	89
25–29	3,176.5[a]	1,984.7	98.7	301	3,374.9	2,307.3	98.7	78
30–49	3,892.7[a,d]	2,134.9	98.6	706	3,411.0[c]	2,150.2	100.0	125
Total	3,472.2	2,156.7	98.4	1,206	3,135.6	2,182.0	98.6	292
Habitat								
Urban	3,425.0	2,110.9	98.4	967	3,150.6	2,207.2	98.5	268
Rural	3,663.4	2,327.9	98.3	239	2,967.9	1,910.2	100.0	24
Educational level								
<Primary	3,448.7	2,078.2	98.3	598	3,036.0	2,167.5	97.5	120
≥Primary	3,559.7	2,134.4	98.6	685	3,075.6	2,231.6	99.2	133
Social class								
I-III	3,661.6[b]	2,135.2	99.2	360	3,114.2	2,175.5	100.0	42
IV-V	3,447.3	2,116.6	98.3	473	2,953.8	2,189.5	100.0	88
VI	3,321.0	2,219.1	97.9	373	3,239.8	2,186.4	97.5	162
Measles vaccination								
Yes	2,896.5	2,095.9	98.0	461	2,981.6	2,233.1	97.7	172
No	3,828.5[a]	2,210.1	98.7	745	3,223.3	2,153.4	100.0	120

[a] $P < 0.001$ versus age of 15 to 24 years and versus vaccinated women in neonates of indigenous women.
[b] $P < 0.05$ versus social class VI in neonates of indigenous women.
[c] $P < 0.005$ versus age of 15 to 24 years in neonates of immigrant women.
[d] $P < 0.05$ for neonates of indigenous women versus neonates of immigrant women.

The multiple logistic regression analysis showed that measles vaccination in pregnant women was significantly associated only with the variable age. Measles vaccination in pregnant women depends only on the variable age because universal measles vaccination at 12 months of age was introduced in Catalonia in 1980.

Neonates with measles virus antibody levels lower than 1,000 mIU/ml could be considered at risk of measles virus infection since measles virus antibody levels decrease by 70% between 0 and 6 months of age (4, 8, 13, 19). In the near future, the percentage of neonates at risk of measles virus infection can increase if measles virus antibody levels decrease in pregnant women.

Two immunization strategies can be developed to reduce the risk of measles virus infection in neonates: (i) vaccination of women of childbearing age and (ii) early vaccination of infants. Studies on early vaccination of preterm infants against polio or hepatitis show that infants can obtain an adequate immune response (1). Nevertheless, the presence of maternal antibodies and potential adverse effects are obstacles to early measles vaccination (11). Measles virus antibody levels can be increased in neonates by vaccinating women of childbearing age since antibodies are transferred from the mother to the fetus. The strategy of increasing the level of maternal antibodies for transplacental transfer has been used successfully to combat neonatal tetanus and polio (12, 20) and has been proposed to increase immune protection of infants against pertussis (9, 15).

In conclusion, the results of this study show that most of the pregnant women and neonates studied in Catalonia were ad-

TABLE 3. Prevalence of maternal measles vaccination by sociodemographic variables in Catalonia, Spain, 2003

Maternal variable	Prevalence (%) of maternal measles vaccination (95 % CI)	Crude OR (adjusted OR)[c]	*n*
Age (yr)			
15–24	100.0 (98.7–100)	0.69 (0.67–0.72)[a]	288
25–29	60.2 (55.1–65.2)	0.64 (0.61–0.67)[a]	379
30–34	13.2 (10.2–16.2)		529
35–49	15.6 (11.3–19.8)		302
Total	42.3 (39.7–44.8)		1,498
Place of birth			
Spain	38.2 (35.4–41.0)	2.32 (1.78–3.00)[a]	1,206
Other	58.9[a] (53.1–64.7)	1.26 (0.85–1.84)	292
Educational level			
<Primary	42.8[b] (38.8–46.9)	1.29 (1.03–1.62)[b]	598
≥Primary	36.6 (40.3–45.9)	0.94 (0.68–1.31)	685
Social class			
I–III	29.4 (24.8–33.9)	2.13 (1.67–2.73)[a]	402
IV–V	40.5[a] (36.3–44.6)	0.87 (0.61–1.24)	561
VI	53.8[a] (49.5–58.1)		535
Habitat			
Urban	43.1 (40.3–45.9)		1,235
Rural	38.4 (32.3–44.5)		263

[a] $P < 0.001$.
[b] $P < 0.05$.
[c] OR adjusted by multiple logistic regression analysis including age (continuous), immigration (place of birth other than Spain), low educational level, and social classes IV to VI.

equately protected against measles, although the risk of measles virus infection in neonates could increase in the future. To prevent measles in neonates, a measles vaccination program for women of childbearing age could be developed.

We thank the following collaborating hospitals: Centre Mèdic Delfos of Barcelona, Consorci Hospitalari of Mataró, Centre Mèdic Sant Jordi of Barcelona, Fundació Sant Hospital of la Seu d'Urgell, H. Maternitat of Barcelona, H. Clínic of Barcelona, H. Comarcal of Palamos, H. Comarcal of Mora d'Ebre, H. Comarcal of Sant Boi de Llobregat, H. Creu Roja of L'Hospitalet, H. Dr. Trueta of Girona, H. General of Granollers, H. General Fundació Althaia of Manresa, H. General of Igualada, H. Germans Trias i Pujol of Badalona, H. Joan XXIII of Tarragona, H. Nuestra Señora del Remei of Barcelona, H. Materno-Infantil of la Vall d'Hebrón of Barcelona, H. Sagrat Cor of Barcelona, H. Sant Bernabe of Berga, H. Sant Jaume of Calella, H. Sant Jaume of Olot, H. Sant Jaume of Blanes, H. Santa Creu i Sant Pau of Barcelona, H. Verge de Cinta of Tortosa, Pius Hospital of Valls, and Quinta de Salut L'Aliança of Lleida.

We have no commercial or other associations that might pose a conflict of interest.

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