

Are healthcare workers immune to rubella?

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Abbreviations: CI, confidence interval; CRS, congenital rubella syndrome; HCW, healthcare worker; IgG, immunoglobulin G; MMR, measles mumps rubella; OR, odds ratio; WHO, World Health Organization

Healthcare workers (HCW) have high exposure to infectious diseases, some of which, such as rubella, are vaccine-preventable. The aim of this study was to determine the immunity of HCW against rubella. We performed a seroprevalence study using a self-administered survey and obtained blood samples to determine rubella Immunoglobulin G (IgG) antibody levels in HCW during preventive examinations by five Primary Care Basic Prevention Units and six tertiary hospitals in Catalonia. Informed consent was obtained. IgG was determined using an antibody capture microparticle direct chemiluminometric technique. The odds ratio (OR) and 95% confidence intervals (CI) were calculated. Logistic regression was made to calculate adjusted OR.

Of 642 HCW who participated (29.9% physician, 38.8% nurses, 13.3% other health workers and 18% non-health workers), 46.6% were primary care workers and 53.4% hospital workers. Of total, 97.2% had rubella antibodies. HCW aged 30–44 years had a higher prevalence of antibodies (98.4%) compared with HCW aged <30 years (adjusted OR 3.92; 95% CI 1.04–14.85). The prevalence was higher in nurses than in other HCW (adjusted OR: 5.57, 95% CI 1.21–25.59).

Antibody prevalence did not differ between females and males (97.4% vs. 97.1%, *P* 0.89), type of center (97.7% vs. 96.8%, *P* 0.51) or according to history of vaccination (97.3% vs. 96.8%, *P* 0.82). Seroprevalence of rubella antibodies is high in HCW, but workers aged <30 years have a higher susceptibility (5.5%). Vaccination should be reinforced in HCW in this age group, due to the risk of nosocomial transmission and congenital rubella.

Introduction

Rubella is an exanthematic disease caused by the rubella virus of the genus *Rubivirus*. Although 20–50% of infected people are asymptomatic, newborns are the group with the most serious complications (malformations). Congenital rubella syndrome (CRS) can affect all fetal organs causing birth defects, still-birth, spontaneous abortion or premature birth, with deafness being one of the most common manifestations.¹ The extent of involvement depends on the time of pregnancy at which infection occurs, but in a susceptible woman infected during the first trimester, the fetus is affected in between 80% and 100% of cases.^{2,3} More than 20% of maternal infections occur within the first 8 wk of gestation, causing miscarriage.¹ Because rubella, as measles, is a vaccine-preventable disease with an exclusively human reservoir, the virus cannot survive in the environment and there are specific and sensitive techniques to diagnose cases, in 1998 the WHO European Region approved the aims of eliminating indigenous measles and rubella and controlling congenital rubella.⁴ In 2003, a plan focused on achieving these objectives by 2010 was approved and in 2005, a strategic plan for 2005–2010 was approved with the aims of eliminating endemic rubella and

preventing CRS (<1 case per 100 000 live births). Finally, in September 2010, the aims of the WHO European Region were postponed to 2015.^{5,6} However, the incidence of rubella remains substantial: 121 378 cases of rubella and 162 cases of CRS were reported worldwide in 2009, and 94 030 and 300, respectively, in 2012.⁷

Rubella vaccination of all girls aged 11 y was introduced into the routine immunization schedule in Catalonia in 1978. In 1980, the MMR vaccine (measles and mumps rubella) was introduced in children aged 12 mo. In 1987, the MMR was changed from 12 to 15 mo, and in 1988 the MMR replaced the rubella vaccine at 11 y. In 1999, the age of administration of the second MMR dose was advanced from 11 to 4 y. Finally, in 2008, the age of administration of the first dose of MMR was advanced from 15 to 12 mo. The global prevalence of rubella antibodies in a seroprevalence study performed in 2002 in a representative sample of the population aged ≥15 y in Catalonia^{8,9} was 95.7% and the distribution of rubella antibodies according to age groups showed no statistical differences. However, there are no prevalence data in health care workers (HCW).

Recent outbreaks in Spain^{10–12} and Europe¹³ have affected pregnant women.^{12–14} There are also reports of rubella outbreaks

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Table 1. Sociodemographic and epidemiological characteristics of study subjects (n = 642)

Characteristics	n	%
<i>Age group</i>		
<30 y	128	19.9
30 - 44 y	254	39.6
45 - 54 y	169	26.3
≥55 y	91	14.2
<i>Sex</i>		
Male	151	23.5
Female	491	76.5
<i>Professional category</i>		
Physicians	191	29.9
Nurses	248	38.8
Other clinical workers	85	13.3
Non-clinical workers	115	18.0
<i>Type of center</i>		
Primary health	299	46.6
Hospital	343	53.4
<i>History of vaccination</i>		
Yes	95	14.8
No	547	85.2

that affected between 15 and 47 hospital HCW.¹⁵⁻¹⁷ In 1980, in the United States, a hospital with 2983 workers reported a nosocomial outbreak that affected 47 people, one of whom was a pregnant woman,¹⁵ and 5 y later, another hospital with 3900 HCW reported an outbreak that affected 19 HCW, whose contacts included five pregnant women.¹⁶ In Japan, in 2003, a local outbreak affected 15 HCW.¹⁷

The aim of this study was to determine the immune status of HCW against rubella and factors associated to this status.

Results

A total of 642 HCW participated in the study (46.6% primary care and 53.4% hospital). The sociodemographic and epidemiological characteristics of the participants are shown in Table 1.

Of the 642 participants, 97.2% (95% CI 95.6–98.3) had titers of IgG antibodies ≥ 10 IU/mL, which according to Skendel¹⁸ is indicative of seroprotection. There was a higher percentage of immune HCW in the ≥ 55 y age group with respect to the <30 y age group (the reference group), although the differences were not statistically significant. In both the bivariate and multivariate analyses, significant differences were found in the prevalence of immunity in HCW aged 30–44 y compared with those aged <30 y (adjusted OR 3.92; 95% CI 1.04–14.85). No significant differences were found between males and females (97.4%, 95% CI 93.4–99.3 vs. 97.1%, 95% CI 95.3–98.4) (Table 2).

Physicians and nurses had the highest prevalence of immunity. Both the bivariate and multivariate analyses showed that nurses had significantly higher levels of immunity than other HCW (adjusted OR 5.57, 95% CI 1.21–25.59) (Table 2). Primary care HCW had a slightly higher, not-significant prevalence of immunity than hospital workers (97.7% [95% CI 95.2–99.1] vs. 96.8% [95% CI 94.3–98.4]). The prevalence of immunity in HCW who reported being vaccinated showed no significant differences (97.3% [95% CI 95.5–98.5] vs. 96.8% [95% CI 91.0–99.3]). The prevalence of rubella antibodies did not differ significantly in HCW with and without a recorded history of vaccination by age group or according to the other study variables (Table 3).

Discussion

The prevalence of HCW with protective rubella antibodies in Catalonian health centers included in this study (97.2%) is higher than that found in other studies,¹⁹⁻²³ probably due to the vaccination programs performed in Catalonia since 1978. A Saudi Arabian study¹⁹ found a prevalence of antibodies of 90%. In Madurai (India), 84.85% of HCW in a university hospital had antibodies.²⁴ A study in a Brazilian university hospital found that the prevalence of one dose of MMR or a history of disease confirmed by serology was 62.5% in residents in the final year of pediatrics.²⁰ In Japan, in a study performed in 2001,²¹ 95.9% of physicians and nurses had rubella antibodies, but in a more recent study²⁵ the prevalence was 89.5%. In Australia, antibodies to measles, mumps, and rubella were found in 89–94% of participating HCW.²⁶ Campagna et al.²² found a wide range of seroprevalence (47%–96.8%) in HCW from 9 hospitals in northern Italy. Turkish studies by Alp et al.,²⁷ Aypak et al.,²⁵ and Celikbas et al.,²⁸ found a prevalence of antibodies in HCW of 97%, 97.5%, and 98.3%, respectively. Alp et al.²⁷ suggested that working in a high risk-department is associated with immunity (OR: 2.7, 95% CI 1.4–5.2).

As in the study by Aypak et al.,²⁵ we found fewer immune subjects among young HCW (94.5% in HCW aged <30 y vs. 97.2% for all participants). The prevalence of rubella antibodies was lower in HCW aged <30 y than those aged 30–44 y (adjusted OR 3.92). A possible explanation may be that rubella incidence has been low in Catalonia in recent years, with small, very-limited outbreaks in specific population groups^{11,29} and therefore booster effects due to contact with the wild virus are scarce for younger HCW. In contrast, in HCW aged 30–44 y, the prevalence of rubella antibodies may reflect not only the vaccination status but previous infection or a booster effect by the wild virus. In any case, the lower prevalence of antibodies in HCW aged <30 y suggests that vaccination should be reinforced in this age group.

No differences were observed in the prevalence of antibodies in HCW with and without a recorded history of vaccination. The fact that the prevalence of rubella antibodies was similar in HCW aged <30 y with and without a history of vaccination suggests that, at least in our study, a history of vaccination is not a good predictor of the rubella immune status. In fact, the vast majority of HCW aged <30 y without a recorded history of

Table 2. Prevalence of rubella antibodies in healthcare workers by study variables

Variable	Number	Prevalence (95% CI)	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Age						
<30 y	128	94.5(89.1–97.8)	reference		reference	
30–44 y	254	98.4(96.0–99.6)	3.62 (1.04–12.59)	0.043	3.92 (1.04–14.85)	0.044
45–54 y	169	96.4 (92.4–98.7)	1.57 (0.52–4.80)	0.427	1.31 (0.36–4.78)	0.684
≥55 y	91	98.9 (94.0–100)	5.21 (0.63–43.07)	0.126	4.02 (0.44–36.91)	0.219
All	642	97.2 (95.6–98.3)				
Sex						
Male	151	97.4 (93.4–99.3)	1.08 (0.35–3.33)	0.895	1.34 (0.41–4.39)	0.627
Female	491	97.1(95.3–98.4)	reference		reference	
Professional group						
Physician	191	97.9 (94.7–99.4)	2.92 (0.76–11.17)	0.117	2.89 (0.73–11.51)	0.138
Nurse	248	98.8 (96.5–99.7)	5.1(1.19–21.83)	0.028	5.57(1.21–25.59)	0.027
Other clinical workers	85	94.1(86.8–98.1)	reference		reference	
Non-clinical workers	115	94.8 (89.0–98.1)	1.14 (0.33–3.85)	0.839	1.08 (0.30–3.90)	0.904
Type of center						
Primary health	299	97.7 (95.2–99.1)	1.38 (0.53–3.61)	0.509	1.27 (0.45–3.52)	0.651
Hospital	343	96.8 (94.3–98.4)	reference		reference	
History of vaccination						
Yes	95	96.8 (91.0–99.3)	reference		reference	
No	547	97.3 (95.5–98.5)	1.15 (0.33–4.07)	0.821	0.90 (0.22–3.75)	0.890

vaccination but with rubella antibodies (94.7%) very likely had been vaccinated, even if the vaccination was not recorded.

The risk perception of HCW to vaccine-preventable diseases is 78% with respect to hepatitis according to Dinelli et al.³⁰ but there are no estimates for rubella. However, the lack of vaccination in HCW may be of importance, as shown by a recent outbreak of rubella in India that affected 23 workers.³¹ HCW should be vaccinated against preventable diseases because they have a greater risk than the general population and because infectious diseases can spread to the patients they care for, other HCW, and their families. Due to the nature of the disease, rubella vaccination is essential in some services, such as obstetrics and pediatrics, where infections can have serious repercussions.

Another important factor in favor of rubella vaccination is that the cost of vaccination is lower than the cost of the disease³² since the appearance of the disease implies precautionary measures that have higher health care costs. The mean cost of a hospital stay varies with the severity of the case, but ranges between €2082 and 4832.³³ Therefore, it is important to emphasize prevention strategies and infection control in the workplace, either through strict measures such as obliging new workers to be vaccinated^{34,35} or through specific seroprevalence surveys to determine the situation and develop strategies to improve the immune status of HCW. It would also be desirable to facilitate maximum access to occupational health services and make catch-up campaigns.

The main strengths of this study are the large sample size and the inclusion of both hospital and primary health workers from various Catalan regions, which allowed a true picture of rubella infection in Catalan HCW. A main shortcomings of the study is that data on vaccination were collected retrospectively from the vaccination cards of participants and not all vaccinated HCW have the vaccinations received well recorded. However, because the main objective of the study was to determine the immune status of HCW against rubella, and IgG antibodies can demonstrate this, we believe our conclusions about immunity may be valid. Another limitation is that we used a convenience sample, which may not be representative of all HCW in Catalonia. However, as noted before, the large sample size, which included hospital and primary health workers from 5 of the 7 Catalan regions, and the fact that less than 5% of HCW invited to participate refused, suggest that our results may reflect the true situation in many healthcare centers.

In conclusion, our results show that the prevalence of immunity to rubella in HCW in Catalonia is high, but is lower in younger HCW, which could cause outbreaks in susceptible people and make the aims of eliminating endemic rubella and preventing CRS more difficult. Rubella vaccination should be reinforced in HCW aged <30 y to prevent nosocomial cases and cases of CRS. If vaccination coverage increases, the proportion of protected HCW in this age group will increase and consequently,

Table 3. Distribution of prevalence of rubella antibodies according to recorded history of vaccination in the variables studied

Variable	Recorded history of vaccination		No recorded history of vaccination		OR	P
	Number	Prevalence (95% CI)	Number	Prevalence (95% CI)		
Age						
<30 y	53	94.3 (84.3–98.8)	75	94.7 (86.9–98.5)	0.94 (0.20–4.38)	1
30 – 44 y	38	100 (90.7–100)	216	98.1 (95.3–99.5)	NC	1
45 – 54 y	4	100 (39.8–100)	165	96.4 (92.3–98.7)	NC	1
≥55 y	0		91	98.9 (94.0–100)	NC	1
All	95	96.8 (91.0–99.3)	547	97.3 (95.5–98.5)	0.86 (0.25–3.05)	0.739
Sex						
Male	20	90.0 (68.3–98.8)	131	98.5 (94.6–99.8)	0.14 (0.02–1.05)	0.085
Female	75	98.7 (92.8–100)	416	96.9 (94.7–98.3)	2.39 (0.31–18.52)	0.706
Professional group						
Physician	37	94.6 (81.8–99.3)	154	98.7 (95.4–99.8)	0.23 (0.03–1.69)	0.170
Nurse	38	100 (90.7–100)	210	98.6 (95.9–99.7)	NC	1
Other clinical workers	12	91.7 (61.5–99.8)	73	94.5 (86.6–98.5)	0.64 (0.07–6.25)	0.542
Non-clinical workers	8	100 (63.1–100)	107	94.4 (88.2–97.9)	NC	1
Type of center						
Primary health	31	100 (88.8–100)	268	97.4 (94.7–98.9)	NC	1
Hospital	64	95.3 (86.9–99)	279	97.1 (94.4–98.8)	0.60 (0.15–2.33)	0.437

NC, Not calculable.

the risk of being infected and spreading the infection to the patients they take care of will decrease.

Materials and Methods

We performed a seroprevalence study of rubella antibodies in HCW in Catalonia using a convenience sample. Six public tertiary hospitals and five Primary Care Basic Prevention Units from different provinces of Catalonia (a region in the northeast of Spain with 7.5 million inhabitants) participated in the study.

In 2009, HCW of the participating centers were asked to complete a self-administered questionnaire during the routine health examination performed by the corresponding Occupational Health Unit, and to provide a blood sample. All subjects were informed of the nature of the study and gave written informed consent. The questionnaire collected the following variables: date of birth, sex, professional category (physician, nurse, other clinical workers, and non-clinical workers), type of center (hospital or primary care), history of having had rubella disease and vaccination history.

Blood samples were obtained by venipuncture. Sera were separated by centrifugation at 3000 rpm for 10 min and stored frozen at –40 °C until analysis.

Levels of rubella IgG antibodies were determined using the ADVIA® Centaur G™ Rubella Assay (Siemens Healthcare Diagnostics Inc.) IgG antibody capture microparticle direct chemiluminometric assay according to the manufacturer's instructions. Samples with values ≥10 IU/mL were considered positive¹⁸ and those <5.0 IU/mL, negative. Samples with values between 5.0 and 9.9 IU/mL were considered indeterminate and repeated. Replicated results which were <10 IU/mL were considered negative. According to the manufacturer, the sensitivity and specificity of the method are 97.2% and 99.5% respectively. The intra-assay and interassay coefficients are less than 5% and 6.1%, respectively.

We calculated the prevalence, odds ratios (OR) and 95% confidence intervals (CI). To determine which variables were independently associated with antibody prevalence, crude odds ratios were calculated for different variables. For each variable studied, we took the group with the lowest prevalence of rubella antibodies as the reference group. Odds ratios were adjusted using multiple logistic regression analysis. Statistical significance was established assuming an α error of 0.05.

The data and statistical analyses were processed using the Statistical Package for Social Sciences (SPSS 19.0 for Windows) and R 2.13.0 (R Development Core Team 2011).

All data collected were treated as a confidential, in strict observance of legislation on observational studies. The study was approved by the Ethic Committee of the University of Barcelona. Written information consent was obtained from all subjects included in the study.

Disclosure of Potential Conflict of Interest

No potential conflicts of interest were disclosed.

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