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Varicella-zoster virus immunity among health care workers in Catalonia

L. Urbiztondo[a,*], J.M. Bayas[b,c], S. Broner[d], J. Costa[e], M. Esteve[f], M. Campins[g], E. Borrás[a,c,d], A. Domínguez[c,d], the Working Group for the Study of the Immune Status in Healthcare Workers of Catalonia

[a] Public Health Agency, Generalitat of Catalonia, Barcelona, Spain
[b] Adult Vaccination Centre, Hospital Clínic, University of Barcelona, Barcelona, Spain
[c] Department of Public Health, University of Barcelona, Barcelona, Spain
[d] CIBER Epidemiología y Salud pública (CIBERESP), Madrid, Spain
[e] Department of Microbiology, Hospital Clínic, University of Barcelona, Barcelona, Spain
[f] Preventive Medicine and Epidemiology Department, Hospital Germans Trías, Autonomous University of Barcelona, Badalona, Barcelona, Spain
[g] Preventive Medicine and Epidemiology Department, Hospital Vall d' Hebrón, Autonomous University of Barcelona, Barcelona, Spain

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ABSTRACT

Objective: To determine varicella-zoster virus (VZV) immunity among healthcare workers (HCWs). Cross-sectional study. Participants: HCWs attending voluntary periodic health examinations between June 2008 and December 2010. Setting: Six public hospitals and five primary care areas in Catalonia, Spain.
Methods: A self-administered questionnaire was given to eligible HCWs. Variables including age, sex, professional category, type of centre, history of varicella infection, and VZV vaccination were collected. The study was carried out using a convenience sample. The prevalence of antibodies and positive and negative predictive values (PPV and NPV) of the history of clinical VZV infection or vaccination were calculated. Crude and adjusted odds ratios (OR and ORa) and their 95% confidence intervals (CI) were calculated to determine the variables associated with antibody prevalence.
Results: Of 705 HCWs who agreed to participate, 644 were finally included. The overall prevalence of antibodies to varicella was 94.9% (95% CI: 92.9–96.4). Of the variables studied, only age was associated with serological susceptibility to VZV. HCWs aged 25–35 years had the highest serological susceptibility (8.1%, 95% CI: 4.6–13.0). The prevalence of antibodies was 96% in subjects reporting previous VZV infection or vaccination, compared with 93% in subjects who did not report these states or did not know.
Conclusions: The high proportion of serologically-susceptible HCWs found in this study indicates the need to develop for screening and vaccination strategies in Catalonia. Due to the high capacity of propagation of the VZV in health settings and its consequences, VZV vaccination programmes in HCWs should be reinforced.

1. Introduction

Varicella-zoster virus (VZV) is highly contagious, with high secondary attack rates in susceptible people [1]. Varicella is generally benign and self-limiting in immunocompetent children, but is often more severe in adults. Control of varicella is especially important in health care settings because VZV infection is infrequent but potentially serious, as it may affect premature babies, pregnant women, adults and patients who are immunocompromised due to underlying disease or some therapies [2–4]. In these patients, varicella is more severe and has a worse prognosis than in the rest of the population [5–10]. VZV vaccination is included in the measures recommended for all susceptible healthcare workers (HCWs) [11], even when it is not included in the routine immunization schedule [12].

Since 2005, the official immunization schedule of Catalonia, as in most Spanish regions, indicates VZV vaccination (two doses) of susceptible adolescents with no clinical history of VZV infection or previous vaccination (reported by parent or guardian) at 12 years of age [13]. At this age, 90% of subjects have VZV antibodies [14]. An undefined proportion of children of this age are already vaccinated

* Corresponding author. Tel.: +34 93 5513619.
E-mail addresses: luis.urbiztondo@gencat.cat, lup123@gmail.com (L. Urbiztondo).

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by private clinics. Selective vaccination is recommended in people with negative serology belonging to some groups, including HCWs [13].

Both wild-type VZV infection and vaccination induce a humoral and cellular immune response that provides long term protection against varicella in the majority of subjects, although subclinical reinfection is common [12]. Cellular immunity plays a crucial role in defending the infected person from spreading the virus during acute illness and protects persons with latent VZV from developing zoster [15]. It is unclear whether the VZV-specific antibody plays a direct role in protection or if it is simply a surrogate marker of vaccine-elicited T cell responses that accompany seroconversion [16]. Nevertheless, traditionally, immunity to VZV after infection or immunization is assessed by measuring antibody titres [15]. In general, persons with a positive titre in a commercial glycoprotein-based immunoenzyme (gp-ELISA) assay, are thought to be protected from varicella [15]. This is the rationale for serological screening.

Available information on the prevalence of VZV antibodies in Spanish HCWs is scarce. A study carried out in HCW from five hospitals in Catalonia found a prevalence of 96.2% [17].

The aim of this study was to determine the prevalence of VZV antibodies among HCWs from different health care areas in Catalonia.

2. Methods

2.1. Study design and study participants

A cross-sectional study was carried out using a convenience sample. Occupational Risk Prevention (ORP) services from 10 primary healthcare areas and 9 of the leading tertiary hospitals in Catalonia were asked to recruit patients between June 2008 and December 2010. There are an estimated 104,000 HCW in Catalonia, of which 45% belong to the ORP services invited to participate in the study.

HCWs attending voluntary periodic health examinations were informed of the study and were recruited after written informed consent was obtained. ORP services must offer a health examination in order to prevent the specific risks related to HCW at the beginning of the professional relationship and at least every three years thereafter.

The study was approved by the Ethics Committee of the University of Barcelona.

Blood samples were obtained and demographic and epidemiological variables were collected using a self-administered questionnaire (age, sex, type of HCW, type of centre, history of having had varicella infection and vaccination history). If available, the vaccination card was also reviewed.

The presence of VZV IgG antibodies was studied by a gp-ELISA, (Vircell Varicella-Zoster ELISA IgG Kit. Vircell SL. Granada, Spain) using the Tecan Genesis RMP 150 autoanalyser according to the manufacturer's instructions. According to the manufacturer, both the sensitivity and specificity of the method are 96%.

2.2. Statistical analysis

The prevalence of antibodies and their 95% confidence intervals (CI) were calculated by the exact binomial method. Positive and negative predictive values (PPV and NPV) and their 95% CI were calculated using binomial distribution. To determine which variables were associated with antibody prevalence, the odds ratios (OR) and their 95% CI were calculated. Odds ratios were adjusted (ORa) using multiple logistic regression with two additional strategies: full model (i.e. with all candidate variables) and a backward selection procedure. The inclusion and exclusion criteria used were; $p < 0.05$ for model entry and $p > 0.10$ for output, according to Wald statistics. Statistical significance was established assuming an alpha error of 0.05. Data processing and analysis was carried out using the IBM SPSS Statistics for Windows, version 19.0 and R 2.13.0 (R Development Core Team 2011) programs.

3. Results

Five of the 10 primary healthcare ORP and 6 of the 9 hospital ORP invited to participate accepted. The participating centres were located in 5 of the 7 Catalan health regions, representing 87.6% of the population. Very few workers refused to take part in the study (<5% in participating ORP). Of 705 HCWs who agreed to participate, 644 (299 primary and 345 hospital workers) were finally included in the study, of whom 76.5% were female. The distribution by professional category was: 191 (29.8%) physicians, 249 (38.8%) nursing graduates, 86 (13.5%) other health professionals and 115 (17.9%) non-clinical workers. In three workers, the professional category was not recorded.

The overall prevalence of VZV antibodies was 94.9% (95% CI: 92.9–96.4). Table 1 shows the percentages of HCWs seropositive for VZV antibodies according to age, sex, professional category and type of centre. HCWs aged 25–35 years had the highest prevalence of subjects without VZV antibodies (8.1%, 95% CI: 4.6–13.0) and the 36–44 year age group had the lowest frequency of serologically-susceptible HCW (3.0%, 95% CI: 1.0–6.8). There were no statistically significant differences in the prevalence of serological-susceptibility by sex, professional category or type of centre.

Of the study participants, 425 (66%) had a vaccination card. This allowed VZV vaccination to be confirmed in 19 (3%) HCWs, while 445 (69.1%) HCWs reported a clinical history of VZV infection. The prevalence of VZV antibodies in these two groups was 94.7% (95% CI: 74.0–99.9) and 96% (95% CI: 93.7–97.6), respectively.

Neither a history of VZV infection nor VZV vaccination was significantly associated with serological immunity (OR: 1.67, 95% CI: 0.6–4. 64 and OR: 1.00, 95% CI: 0.13–7.92, respectively). Of the 451 HCWs who reported previous VZV infection or VZV vaccination, 432 were seropositive, representing a PPV of 95.8% (95% CI: 93.5–97.4). Of the 193 HCWs who stated they had not suffered VZV infection or received VZV vaccination, or did not know, 14 were seronegative, representing a NPV of 7.3% (95% CI: 4.0–11.9) (Table 2).

4. Discussion

Our results show a high prevalence of VZV antibodies in Catalan HCWs, which helps explain the low frequency of transmission of the VZV virus in healthcare settings in Catalonia. The percentage of HCWs without detectable varicella antibodies observed (5.1%) is slightly higher than the 3.8% found in a previous investigation in Catalonia, which used a similar method of participant selection, but was limited to hospitals [17]. A recently-published study carried out in a hospital in Catalonia found a prevalence of 7.4% [18]. Thus, our results fall between those found by these studies. The multicentre nature of our study, which was carried out in six hospitals and five primary care areas, suggests that our results may be more representative of the reality in our geographical and health setting. This is supported by the fact that the prevalence by age group was almost identical to that observed in a seroepidemiological survey carried out in the general population of Catalonia [14].

The results of seroprevalence studies in HCW in other countries show a wide range of results. In temperate countries, the prevalence of negative results is quite low [19–27]: 9–2.1% in Italy, 5.6–1.5% in Israel, 4.3% in Ireland, 2% in the USA and 1.5% in Belgium. In contrast in warmer or tropical countries, the prevalence of