ORIGINAL PAPER

International Journal of Occupational Medicine and Environmental Health 2022;35(5)
https://doi.org/10.13075/ijomeh.1896.01932

DETERMINANTS OF SEROPOSITIVITY FOR SARS-CoV-2 IN HOSPITAL STAFF IN THE SECOND WAVE OF THE PANDEMIC IN SLOVENIA

MAJA SOCAN[1], KATARINA PROSENC[2], ANDREJA KUKEC[3], LIJANA ZALETEL-KRAGELJ[3], TATJANA REMEC[4], and IRENA GRMEK-KOSNIK[5]

[1] National Institute of Public Health, Ljubljana, Slovenia
Centre for Communicable Diseases
[2] National Laboratory for Health, Food and Environment, Ljubljana, Slovenia
Laboratory for Public Health Virology
[3] University of Ljubljana, Ljubljana, Slovenia
Medical Faculty, Chair for Public Health
[4] Novo Mesto General Hospital, Novo Mesto, Slovenia
Department for Infectious Diseases
[5] National Laboratory for Health, Food and Environment, Kranj, Slovenia
Laboratory for Human Microbiology

Abstract
Objectives: The pandemic caused by the novel coronavirus (SARS-CoV-2) affected a disproportionately high percentage of healthcare workers (HCWs). The aim of the study was to assess the seroprevalence of SARS-CoV-2-specific IgG antibodies in nurses and clinicians working in 2 Slovenian regional hospitals, and to identify the factors associated with seropositivity. **Material and Methods:** The study was designed as a cross-sectional study. Clinicians and nurses were invited to participate in November–December 2020. The respondents (813, 65.8%) completed a questionnaire and consented to provide 10 ml of blood for determining the presence of SARS-CoV-2 IgG antibodies. **Results:** The authors observed a seroprevalence rate of 20.4%. The results of the univariate analysis proved that the age of a nurse or clinician was the factor most strongly associated with seropositivity – in fact, the youngest nurses and clinicians were 8.33 times more likely to be seropositive than those in the oldest age group (p = 0.041). Being in contact with a family/household member who was SARS-CoV-2-positive was also a very important factor. In the work-related factors group, being in the contact with a SARS-CoV-2-positive colleague (OR = 2.35, p = 0.026) or being in contact with a COVID-19 patient (OR = 1.96, p = 0.004) correlated with seropositivity. In the primary work location/department group, the only significant association appeared among those working in surgical, ENT or ophthalmology departments. The results of the multivariate analysis further supported the thesis that the age of nurses and clinicians was the factor most strongly associated with seropositivity. The youngest nurses and clinicians were 12.5 times more likely to be seropositive than those in the oldest age group (p = 0.024). Being in contact with a SARS-CoV-2-positive family/household member remained the second most important factor. **Conclusions:** A significant number of clinicians and nurses working in secondary healthcare were infected in the first 9 months of the pandemic. Int J Occup Med Environ Health. 2022;35(5)

Key words:
seroprevalence, nurse, clinician, healthcare professional, COVID-19, SARS-CoV-2

Funding: this study was supported by National Institute of Public Health (project No. T1/8300/163 entitled "Epidemiological surveillance of SARS-CoV-2 infections in special groups," project manager: Maja Sočan).
Received: October 27, 2021. Accepted: March 30, 2022.
Corresponding author: Maja Sočan, National Institute of Public Health, Centre for Communicable Diseases, Zaloškacesta 29, 1000 Ljubljana, Slovenia (e-mail: maja.socan@nijz.si).

INTRODUCTION

The pandemic caused by the SARS-CoV-2 virus affected people across the world, with a disproportionately high percentage of COVID-19 cases appearing among healthcare workers (HCWs). Systematic reviews and meta-analyses of COVID-19shows that approximately 10% of all confirmed cases were among HCWs [1,2]. A systematic review and meta-analysis of 49 studies published up to August 24, 2020 estimated an overall prevalence of SARS-CoV-2 antibodies among HCWs of 8.7%. The majority of the studies were conducted in Western Europe [3]. At the beginning of the pandemic, a lack of knowledge about the disease and its transmission and a shortage of adequate personal protective equipment (PPE) were important drivers of COVID-19 transmission in healthcare settings. Growing experience and awareness among HCWs, coupled with the availability of PPE and familiarity with its use, led to a substantial reduction in transmission from infected patients to HCWs. Structural and organizational changes (mandatory wearing of face masks in healthcare facilities, health consultations being given more often through indirect communication channels, i.e., via email and telephone rather than face-to-face, screening of patients for SARS-CoV-2 infection before admission, the establishment of wards dedicated exclusively to COVID-19 patients only, etc.) have further reduced healthcare-associated SARS-CoV-2 infections. The higher prevalence of infection among HCWs compared to the general population may be attributed to workplace exposure (colleagues and patients), the more frequent testing that HCWs undergo, and notable community transmission within HCW households [1,4,5]. Seroprevalence studies have shown very different proportions of seropositivity among HCWs, which reflects the timing of the pandemic within specific geographical environments and the type of HCW included in the studies [5].

After the first 2020 pandemic wave, COVID-19 cases surged in Europe in the autumn and winter of 2020/21. The first pandemic wave was modest in Slovenia, with relatively low numbers of COVID-19 cases identified. By contrast, the second wave, with an exponential escalation in the number of cases from mid-September 2020 onwards, contributed to a substantial increase in hospitalizations, an intensification of the burden on the health system and a high pandemic-related mortality rate [6].

The aim of the study was to assess the seroprevalence of SARS-CoV-2-specific IgG antibodies in nurses and clinicians working in 2 Slovenian regional hospitals, and to identify the factors associated with seropositivity.

MATERIAL AND METHODS

Study design

The study was designed as a cross-sectional study. It was conducted at 2 regional hospitals in Slovenia: Novo Mesto General Hospital (NMGH) in the south-east and Jesenice General Hospital (JGH) in the north-west. Serum samples were collected between mid-November and mid-December 2020.

Target populations and sampling

The target population comprised nurses and clinicians providing secondary healthcare at NMGH and JGH. Novo Mesto General Hospital and Jesenice General Hospital deliver healthcare to approx. 143 000 and 260 000 residents, respectively, which is approx. 20% of the Slovenian population. The profiles of the nurses and clinicians invited to take part in the study ranged from nurses with secondary education (secondary school of nursing) to senior consultants. The lists of nurses and clinicians employed at the 2 hospitals were extracted from the Slovenian registry of healthcare workers, which is managed by the National Institute of Public Health (NIPH).

The criterion for inclusion was being currently employed at either hospital, while the criteria for exclusion included absence from the workplace from March 1, 2020 (prolonged sick leave or maternity leave) or being a nursing/

medical student. The invitation to participate in the study was sent to a potential 1235 participants by email and/or telephone text message.

Study instruments and procedures

Laboratory procedure for determining SARS-CoV-2 IgG antibodies

Each participant provided 10–15 ml of blood using the standard venipuncture technique. Whole blood was centrifuged, and serum was separated in the cryotube for archiving after testing. To determine whether SARS-CoV-2 IgG antibodies were present, the authors used the Euroimmun SARS-CoV-2 IgG ELISA test (Euroimmun, Lübeck, Germany), which uses microtiter plate wells coated with the S1 domain of the spike protein as an antigen. The test was performed in accordance with the manufacturer's recommendations. To summarize in brief, sera were diluted 1:101 in a sample buffer, incubated at 37°C for 60 min in a 96-well microtiter plate. This was followed by washing. Conjugate (peroxidase-labelled anti-human IgG) was added and incubated at 37°C for 30 min. This was again followed by washing. The plate with the substrate was incubated at room temperature for 30 min, stop solution was added and optical density (OD) was measured at 450 nm (microplate reader Sunrise, Tecan, Austria). The prescribed controls and calibrator were used. All study sera were tested using the same batch of the kit. The results were evaluated semi-quantitatively by calculating the ratio of the extinction of the control or patient sample over the extinction of the calibrator. The ratio values were calculated and the results interpreted in accordance with the manufacturer's protocol (<0.8 negative, ≥0.8 to <1.0 borderline, ≥1.1 positive). Sera that gave inconclusive (borderline results) were tested again in duplicate and the evaluation resolved. Inter assay coefficient of variability was calculated from positive controls that were used on each plate and it was 6.1%. Intra assay coefficient was calculated from specimens that were run in duplicates and was 1.7%.

Before the study sera were tested, ELISA assays from different producers were studied for their sensitivity and specificity in the literature [7,8]. Reported sensitivity was 100% already 4 days after the positive PCR test and specificity was 97.7%. In addition, Euroimmun SARS-CoV-2 IgG ELISA was tested and validated in-house on 72 sera from patients with a known SARS-CoV-2 infection history. Sensitivity was 100% for sera that were taken ≥14 days after the onset of illness. Sera, 1 sample each, positive for hCoV 229E, hCoV HKU1, hCoV NL63, hCoV OC43, adenovirus, rhinovirus, influenza A and hMPV, were all negative for SARS-CoV-2 IgG, and all sera from asymptomatic PCR negative individuals were negative.

Questionnaire

To obtain information related to COVID-19, a special questionnaire was designed. It comprised 3 groups of questions:
– questions about work-related factors: primary work location, absence from work in weeks, colleague SARS-CoV-2 positivity, frequency of contact with COVID-19 patients (grading from no contact to daily contact);
– questions about personal factors: presence of chronic diseases, pregnancy, smoking;
– questions about family/household factors: SARS-CoV-2 positive family/household member(s).

Acquisition of other data

The date of birth, gender and level of education of participants were extracted from the national registry of healthcare workers.

Data collection procedure

Information about the study was given at departmental meetings, and made available on notice boards and on internal hospital websites. After obtaining written informed consent, HCW completed the questionnaire and a blood sample was taken.

Methods of analysis

The observed outcome was SARS-CoV-2 seropositivity (0 – no, 1 – yes) as confirmed by the Euroimmun SARS-CoV-2 IgG ELISA test. Explanatory factors were classified into 3 groups. The first group consisted of work-related factors:

- health profession group (1 – junior doctors; 2 – consultants; 3 – nurses with college or higher education, with the term 'nurse' used for female and male nurses; 4 – nurses with secondary level of education),
- primary work location/department (1 – emergency; 2 – surgery, otorhinolaryngology, ophthalmology; 3 – internal medicine, infectious diseases; 4 – gynecology and obstetrics; 5 – other), colleague SARS-CoV-2 positive (0 – no; 1 – yes),
- contact with COVID-19 patients (0 – no; 1 – yes).

The second group consisted of personal factors:

- smoking (0 – no; 1 – yes),
- presence of chronic disease (1 – no; 2 – one; 3 – more than one),
- age (1: 21–30 years; 2: 31–40 years; 3: 41–50 years; 4: 51–60 years; 5: 61–65 years),
- gender (1 – male; 2 – female).

The third group consisted of just 1 factor: SARS-CoV-2-positive family/household members (0 – no; 1 – yes).

The association between SARS-CoV-2 seropositivity as the observed outcome and the explanatory factors was assessed univariately and multivariately using binary logistic regression. Dummy variables were created for confounding factors using the simple method (1 group was assigned as the reference group). In multivariate analysis, 3 models were defined. Model 1 consisted of work-related factors, model 2 additionally of personal factors and model 3 additionally of family/household factors. In all statistical tests, a p-value of ≤0.05 was considered significant. IBM SPSS for Windows v. 25.0 software (SPSS Inc., Chicago, IL., USA) was used to conduct the statistical analysis.

Ethical considerations

The study protocol was approved by the National Medical Ethics Commission on July 14, 2020 (reference no 0120-289/2020-3).

RESULTS

Description of the study group

A total of 813 nurses and clinicians consented to participate in the study (65.8% response rate). They comprised 651 women (80.1%) and 162 men (19.9%). They were aged 21–65 years (M±SD 41.5±11 years). The other characteristics of the observed group are shown in Table 1. Serological testing was performed on all 813 participants included in the study, with 166 (20.4%) found to be seropositive for SARS-CoV-2 IgG antibodies. The prevalence of seropositivity within categories of different factors is presented in Table 2.

Results of univariate analysis

The results of the univariate analysis proved that the age of a nurse or clinician was the factor most strongly associated with seropositivity: the youngest age groups were the most exposed and the oldest age groups were the least exposed. Indeed, the youngest nurses and clinicians were 8.33 times more likely to be seropositive than those in the oldest age group (p = 0.041). Being in contact with a family/household member who was SARS-CoV-2-positive played a very important role (Table 2). In the work-related factors group, being in the contact with a SARS-CoV-2-positive colleague proved to be the factor most strongly associated with seropositivity (OR = 2.35, p = 0.026), with strong association also detected between seropositivity and being in contact with a COVID-19 patient (OR = 1.96, p = 0.004). As far as primary work location/department was concerned, the only strong association occurred with surgical, ear, nose and throat (ENT) and ophthalmology departments. Surprisingly, health profession group did not play any important role (Table 2). Among the personal

Table 1. Description of the group of clinicians and nurses from 2 regional hospitals who participated in the study of SARS-CoV-2 seropositivity in Slovenia, 2020

Variable	Participants (N = 813) [n (%)]
Work-related factor	
healthcare workers group (N = 813)	
junior doctors	63 (7.7)
consultants	156 (19.2)
nurses	
with secondary education	276 (33.9)
with college or higher education	318 (39.1)
primary work location (department) (N = 813)	
emergency	120 (14.8)
surgery, otorhinolaryngology (ENT), ophthalmology	233 (28.7)
internal medicine, infectious diseases	190 (23.4)
gynaecology and obstetrics	71 (8.7)
other	199 (24.5)
colleague SARS-CoV-2 positive (N = 810)	
no	77 (9.5)
yes	733 (90.5)
contact with a COVID-19 patient (N = 810)	
no	198 (24.4)
yes	612 (75.6)
Personal factors	
smoking (N = 807)	
no	648 (80.3)
yes	159 (19.7)
the presence of chronic disease (N = 777)	
no	628 (80.8)
1 disease	122 (15.7)
>1 disease	27 (3.5)
age (N = 813)	
21–30 years	156 (19.2)
31–40 years	255 (31.4)
41–50 years	194 (23.9)
51–60 years	187 (23.0)
61–65 years	21 (2.6)
gender (N = 813)	
female	651 (80.1)
male	162 (19.9)
Family/household factor	
family/household member SARS-CoV-2 positive (N = 802)	
no	665 (82.9)
yes	137 (17.1)

factors group, another interesting result was detected: smoking proved to be a protective factor, while non-smokers were twice as likely to be seropositive than smokers. All other details are presented in Table 2.

Results of multivariate analysis

The results of the multivariate analysis were, in many ways, similar to the results of the univariate analysis, but not entirely (Table 3). The multivariate analysis results further supported the thesis that the age of nurses and clinicians was the factor most strongly associated with seropositivity. Again, the youngest age groups were the most exposed and the oldest age groups were the least exposed. In model 3, the youngest nurses and clinicians were 12.5 times more likely to be seropositive than those in the oldest age group (p = 0.024). Being in contact with a SARS-CoV-2-positive family/household member remained the second most important factor. Interestingly in the 2 more complex multivariate models (models 2 and 3), professional group also proved to be an important factor, with nurses with secondary education and consultants being statistically significantly more at risk of SARS-CoV-2 seropositivity. Model 3 also yielded another interesting result, namely that contact with a COVID-19 patient lost a great deal of its power as a factor in SARS-CoV-2 seropositivity. The results are presented in detail in Table 3.

Table 2. Prevalence of SARS-CoV-2 seropositivity within categories of selected factors, and the results of a simple binary logistic regression analysis of the relationship between SARS-CoV-2 seropositivity and selected factors among nurses and clinicians at 2 regional hospitals in Slovenia, 2020

Variable	Participants (N = 813) total [n]	Participants (N = 813) with specific anti-SARS-CoV-2 antibodies [n (%)]	OR (95% CI)	p
Work-related factors				
healthcare worker group (N = 813)				
junior doctors	63	11 (17.5)	1.00	
consultants	156	36 (23.1)	1.42 (0.67–3.00)	0.361
nurses				
with secondary education	276	60 (21.7)	1.31 (0.64–2.67)	0.452
with college or higher education	318	59 (18.6)	1.08 (0.53–2.19)	0.838
primary work location (department) (N = 813)				
emergency	120	19 (15.8)	1.00	
surgery, otorhinolaryngology (ENT), ophthalmology	233	61 (26.2)	1.89 (1.07–3.33)	0.029
infectious diseases, internal medicine	190	38 (20.0)	1.33 (0.72–2.43)	0.357
gynaecology and obstetrics	71	15 (21.1)	1.42 (0.67–3.02)	0.357
other	199	33 (16.6)	1.06 (0.57–1.96)	0.861
colleague SARS-CoV-2 positive (N = 810)				
no	77	8 (10.4)	1.00	
yes	733	157 (21.4)	2.35 (1.11–4.99)	0.026
contact with a COVID-19 patient (N = 810)				
no	198	26 (13.1)	1.00	
yes	612	140 (22.9)	1.96 (1.25–3.09)	0.004
Personal factors				
smoking (N = 807)				
no	648	149 (23.0)	1.00	
yes	159	17 (10.7)	0.40 (0.24–0.69)	0.001
presence of chronic disease (N = 777)				
no	628	131 (20.9)	1.00	
1 disease	122	25 (20.5)	0.98 (0.60–1.58)	0.927
>1 disease	27	5 (18.5)	0.86 (032–2.32)	0.769
age (N = 813)				
21–30 years	156	46 (29.5)	1.00	
31–40 years	255	45 (17.6)	0.51 (0.32–0.82)	0.005
41–50 years	194	44 (22.7)	0.70 (0.43–1.13)	0.148
51–60 years	187	30 (16.0)	0.46 (0.27–0.77)	0.003
61–65 years	21	1 (4.8)	0.12 (0.02–0.92)	0.041

Table 2. Prevalence of SARS-CoV-2 seropositivity within categories of selected factors, and the results of a simple binary logistic regression analysis of the relationship between SARS-CoV-2 seropositivity and selected factors among nurses and clinicians at 2 regional hospitals in Slovenia, 2020 – cont.

Variable	Participants (N = 813) total [n]	Participants (N = 813) with specific anti-SARS-CoV-2 antibodies [n (%)]	OR (95% CI)	p
Personal factors – cont.				
gender (N = 813)				
female	651	131 (20.1)	1.00	
male	162	35 (21.6)	1.09 (0.72–1.67)	0.675
Family/household factor				
family/household members SARS-CoV-2 infection positive (N = 802)				
no	665	100 (15.0)	1.00	
yes	137	66 (48.2)	5.25 (3.53–7.81)	<0.001

Table 3. Results of a multiple binary logistic regression analysis of the relationship between SARS-CoV-2 seropositivity and selected factors among nurses and clinicians at 2 regional hospitals in Slovenia, 2020

Variable	Model 1		Model 2		Model 3	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Work-related factors						
healthcare worker group						
junior doctors	1.00		1.00		1.00	
consultants	1.50 (0.69–3.20)	0.300	2.99 (1.27–7.06)	0.012	2.34 (0.95–5.74)	0.065
nurses						
with secondary education	1.55 (0.75–3.20)	0.234	2.78 (1.24–6.22)	0.013	2.51 (1.09–5.79)	0.031
with college or higher education	1.15 (0.56–2.35)	0.706	1.83 (0.82–4.08)	0.142	1.43 (0.62–3.29)	0.404
primary work location (department)						
emergency	1.00		1.00		1.00	
surgery, otorhinolaryngology (ENT), ophthalmology	1.93 (1.08–3.45)	0.026	2.29 (1.21–4.07)	0.010	2.28 (1.20–4.32)	0.012
infectious diseases, internal medicine	1.42 (0.76–2.62)	0.269	1.64 (0.86–3.13)	0.132	1.66 (0.84–3.27)	0.145
gynaecology and obstetrics	1.76 (0.80–3.86)	0.160	1.95 (0.86–4.42)	0.111	1.59 (0.67–3.76)	0.296
other	1.25 (0.66–3.35)	0.492	1.42 (0.73–2.74)	0.304	1.36 (0.68–2.73)	0.389
colleague SARS-CoV-2 positive						
no	1.00		1.00		1.00	
yes	1.78 (0.81–3.92)	0.154	1.62 (0.72–3.67)	0.243	1.83 (0.77–4.33)	0.171
contact with a COVID-19 patient						
no	1.00		1.00		1.00	
yes	1.93 (1.18–3.15)	0.009	1.85 (1.09–3.13)	0.022	1.60 (0.92–2.77)	0.093

Table 3. Results of a multiple binary logistic regression analysis of the relationship between SARS-CoV-2 seropositivity and selected factors among nurses and clinicians at 2 regional hospitals in Slovenia, 2020 – cont.

Variable	Model 1		Model 2		Model 3	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Personal factors						
smoking						
no			1.00		1.00	
yes			0.37 (0.21–0.64)	<0.001	0.30 (0.17–0.55)	<0.001
presence of chronic disease						
no			1.00		1.00	
1 disease			1.16 (0.69–1.97)	0.573	1.17 (0.67–2.04)	0.579
>1 disease			1.41 (0.48–4.13)	0.526	1.39 (0.44–4.36)	0.570
age						
21–30 years			1.00		1.00	
31–40 years			0.45 (0.27–0.75)	0.002	0.57 (0.29–0.89)	0.018
41–50 years			0.59 (0.34–1.01)	0.057	0.71 (0.39–1.27)	0.246
51–60 years			0.32 (0.17–0.60)	<0.001	0.38 (0.19–0.72)	0.004
61–65 years			0.06 (0.01–0.54)	0.011	0.08 (0.01–0.72)	0.024
gender						
female			1.00		1.00	
male			1.12 (0.68–1.85)	0.656	1.04 (0.61–1.77)	0.886
Family/household factor						
family/household members SARS-CoV-2 infection positive						
no					1.00	
yes					5.67 (3.66–8.80)	<0.001

Model 1 – work-related factors only (N = 808); model 2 – work-related factors and personal factors (N = 773); model 3 – full model including family/household factors (N = 762).

DISCUSSION

The study revealed that there was a medium level of prevalence of seropositivity for SARS-CoV-2 among nurses and clinicians participating in this study. The overall seroprevalence of SARS-CoV-2-specific IgG antibodies was 20.4%, with insignificant differences between professional groups. One of the most important factors contributing to this phenomenon was the age of the nurses and clinicians. The oldest were less likely to have positive SARS-CoV-2 serology compared to their more junior colleagues in both professional groups. Being in contact with a SARS-CoV-2-infected family/household member or colleague or caring for COVID-19 patients was associated with seropositivity. Multiple binary logistic regression analysis revealed a significant relationship between SARS-CoV-2 antibodies and being a nurse with a secondary level of education or being a clinician or nurse working in a surgical, ENT or ophthalmology department. In multiple binary logistic regression, increasing age and current smoking were negatively correlated to SARS-CoV-2 seropositivity.

Different studies show different levels of seroprevalence of positive IgG antibodies against SARS-CoV-2 among HCWs.

Most published studies of SARS-CoV-2 seroprevalence among HCWs were conducted in the spring or early summer of 2020. The first wave of the pandemic affected countries very differently, and there were even differences noted between regions within countries. The high intensity of the pandemic in northern Italy resulted in >12% seroprevalence of specific IgG SARS-CoV-2 antibodies in HCWs in the first few months of the pandemic [9], while in Finland the proportion of seropositive HCWs was significantly lower over the same period [10]. In a systematic review and meta-analysis of seroprevalence studies in healthcare professionals published by August 24, 2020, the average seroprevalence among HCWs was 8.7% [3]. Reasons for the broad range of values for SARS-CoV-2 IgG seropositivity among HCWs include differences in geographical location and cultural background, variances in study design, the use of tests with variable sensitivities and specificities, and differences in the non-pharmaceutical measures applied. The studies originated mostly from Western Europe and North America. As very few seroepidemiological studies have been published from the eastern countries of the EU, no study from these countries was included [3]. A study from Croatia found a 2.7% prevalence rate of SARS-CoV-2 antibodies after the first wave of the pandemic [11]. A high-volume, single-center Hungarian study, including physicians, other HCW and medical students confirmed 1.5%, 1.8% and 0.6% seroprevalence rate during summer 2020 [12]. Three seroepidemiological studies from eastern countries of the EU were conducted among specialist groups of HCWs (2 studies of HCWs in pediatric wards and 1 study of HCWs in gastroenterology units) [13–15]. Staff working in pediatric facilities have been unlikely to face a significant risk of exposure from their patients, with the seroprevalence data reflecting more or less the intensity of transmission in the general community. The results of this study therefore provide insights into the seroepidemiology of SARS-CoV-2 in this geographical area and reflect, above all, the higher intensity of spread in the second wave of the pandemic in Europe.

The results of the studies did not reveal a uniform correlation between age and SARS-CoV-2 IgG seropositivity among HCWs. In some studies, increasing age correlated negatively with the presence of antibodies [16], while other studies have found the reverse [17] or no relationship at all [18,19]. The differences in age-related prevalence are not easy to explain. One possible explanation for the lower seropositivity among older HCWs is that they were more careful when working with patients and followed the recommended rules more strictly, knowing that they were at higher risk of developing severe disease. It is also possible that positive antibodies persist among older HCWs for a shorter period of time after infection. Moreover, younger HCWs tend to socialize more outside healthcare facilities, and might be less careful because they do not recognize and experience COVID-19 as a serious disease. Their antibodies might also persist for a longer period of time [20].

In the majority of publications, gender did not play an important role in the seropositivity rate among HCWs, with men slightly more or equally affected in comparison with their female colleagues [3]. The present study found no difference. Smokers had significantly lower prevalence of anti-SARS-CoV-2 IgG antibodies compared to non-smokers, which has also been observed in other studies. This finding does not indicate that smoking has a protective effect, but it might be the result of lower production or more rapid decline of antibodies in smokers [21–23].

The type of healthcare occupation correlated with seropositivity for SARS-CoV-2 IgG antibodies, with some studies showing that healthcare (or nursing) assistants or nurses were more likely to be seropositive than clinicians or administrators [1,3]. The present study included 2 HCW groups stratified according to level of education. Simple binary logistic regression showed no statistically significant difference when consultants, nurses with a secondary level of education and nurses with college education were compared to non-consultant clinicians. Using multiple binary logistic regression, the seropositivity rate correlated positively with being a nurse with a secondary level of education. This professional profile tends be in very close proximity to patients and exposed for longer periods of time than clinicians, which might explain the difference found in the present study. Clinicians and nurses with higher (college) education are, in general, involved in more administrative work away from patients, which reduces their exposure time.

The primary location of clinical work, including working in a COVID-19 department, did not correlate with increased anti-SARS-CoV-2 seropositivity in some studies, but was a risk factor in others [15,17,24–26]. In the present study, working in a surgical ward posed a higher risk for SARS-CoV-2 IgG seropositivity, as the study conducted by Amendola et al. [27] also found. This finding does not imply that being a surgeon or a nurse in a surgical ward poses a higher risk. It is possible that the higher seropositivity is due to a limited cluster at a super-spreader event or transfer between colleagues within the team. Serological studies involving surgeons and anesthetists failed to reveal a relationship between antibody status and clinical role [28].

Health care workers exposed to COVID-19 patients, especially if the exposure was prolonged (e.g., caring for patients in a COVID-19 ward), were more likely to have positive SARS-CoV-2 antibodies [3]. In the present study, contact with COVID-19 patients in the course of one's professional duties correlated in a statistically significant way with seropositivity in the simple and in the 2 multiple binary logistic regression models (models 1 and 2), but not in model 3. As a number of studies have failed to confirm an association between COVID-19 patient exposure and seropositivity, the question arises as to whether such an association signifies poorer equipment supply or insufficient empowerment of HCWs regarding the proper use of PPE. There was a shortage of personal protective equipment and sub-optimal knowledge of how to use it at the beginning of the pandemic. In the present study, the authors did not explore the shortage of PPE in hospitals included in the study nor have the authors assessed if PPE has been used consistently and according to instructions given. Unavailability of these information is one of the limitation of the study. In the second (autumn-winter) COVID-19 wave in Slovenia, there were enough masks (surgical, FFP2 and FFP3) and other equipment to cover the needs of HCWs. The shortage of PPE might have played a more important role at the beginning of the first wave; the number of COVID-19 cases was much lower, with many patients being treated in dedicated hospitals rather than in the general hospitals included in this study. Personal protective equipment availability in European countries improved during the autumn-winter 2020/21 wave of the pandemic. However, non-pharmaceutical measures within the community were less stringent, at least at the beginning of the second wave. Furthermore, the amount and intensity of exposure is difficult to measure and might be a source of bias.

Few studies have examined the effect of infected colleagues on SARS-CoV-2 seroprevalence in healthcare settings with discrepant results [29,30]. A study from a Belgian tertiary care hospital confirmed that the seropositivity rate was significantly higher among those HCWs who declared having had contact with a SARS-CoV-2-positive colleague. Transmission from an infected colleague might be explained by close, unprotected contact while working in the same room or, even more plausibly, during coffee or meal breaks. In the present study, the authors were able to confirm the correlation between being in contact with a positive colleague and seropositivity by simple logistic regression. This was not the case with by binary logistic regression. Differences between studies may be due to ambiguity regarding the meaning of contact with an infected colleague in terms of proximity, duration, frequency, use of PPE, etc. In this study, the question addressed colleague infection dichotomously (yes or no) without the possibility of describing other circumstances of the contact and the possibility of classifying contact as low, high or medium risk. The authors recognize that this simplistic approach is one of the limitations of the present study.

Contact with a COVID-19-positive household member more consistently showed an association with seropositivity in HCWs [3]. This was confirmed in this study as well. Unmitigated contact with an infected family member in the pre-symptomatic period, when viral load is high and there are no warning signs to dictate social distancing and the need to improve hygiene measures within the family, poses a high risk of infection. At the time of the study, community transmission was very intense in Slovenia. The authors assume that community-acquired SARS-CoV-2 infection is an important driver for positivity in nurses and clinicians. A higher seropositivity rate among HCWs was found in hospitals situated in areas with a high community cumulative incidence of COVID-19 [25,31].

The present study has some limitations. First, only HCW from 2 regional hospitals in Slovenia participated in the study, which means that they might not be representative of clinicians and nurses in Slovenia as a whole, as primary care HCWs and those who worked in hospitals dedicated to COVID-19 patients in the first wave of the pandemic in spring 2020 wave of the pandemic were not included in the study. Second, an inadequate classification of positives or negatives might give distorted results. However, this was considered unlikely because of the high specificity and sensitivity of the ELISA test used in the study. The cross-sectional design of the study is the next limitation. It is possible that some participants had already lost measurable antibodies, especially those in whom the disease was mild or who were almost asymptomatic in the early phase of the pandemic [31]. The magnitude of the first wave of the pandemic in Slovenia was incomparably smaller than that of the second wave. This was due to much stricter non-pharmaceutical measures applied, the willingness of population to follow the rules, and the lower virus transmission potential in the first wave. In the second (autumn) wave, measures were relaxed and the Alpha variant became increasingly dominant. The cumulative number of COVID-19 cases up to June 30, 2020 was 1612. In July 1–December 30, 2020, there were 122 422 cases. This means that infection acquired in the community or in hospital was much more probable in the second wave with the persistence of antibodies detected at the time of the study. One of the limitations of the study was that the acquisition sequence of infection within the family of seropositive HCW was not clearly defined. It might be that the HCW was the inductor of SARS-CoV-2 within the family or vice versa.

CONCLUSIONS

The authors found an overall medium level of seroprevalence of SARS-CoV-2 antibodies among clinicians and nurses working at 2 acute care hospitals during the autumn 2020 wave of the pandemic. The present study gives an insight into the seropositivity of secondary care clinicians and nurses during the intensive community transmission of the Alpha variant of SARS-CoV-2. The study adds to knowledge about the prevalence of infection in a geographical area for which very few studies have been published. It would appear to be important to periodically monitor SARS-CoV-2 serology in HCWs and the determinants of positivity in order to understand the drivers of infection. The knowledge of pre-existent immunity in HCW might gain in importance as vaccination does not confer the same level of protection for Omicron as for previous variants.

REFERENCES

1. Gómez-Ochoa SA, Franco OH, Rojas LZ, Raguindin PF, Roa-Díaz ZM, Wyssmann BM, et al. COVID-19 in Healthcare Workers: A Living Systematic Review and Meta-analysis of Prevalence, Risk Factors, Clinical Characteristics, and Outcomes. Am J Epidemiol. 2021;190(1):161-175. https://doi.org/10.1093/aje/kwaa191.

2. Gholami M, Fawad I, Shadan S, Rowaiee R, Ghanem HA, Khamis AH, et al. COVID-19 and healthcare workers: A systematic review and meta-analysis. Int J Infect Dis. 2021;104:335-346. https://doi.org/10.1016/j.ijid.2021.01.013.
3. Galanis P, Vraka I, Fragkou D, Bilali A, Kaitelidou D. Seroprevalence of SARS-CoV-2 antibodies and associated factors in healthcare workers: a systematic review and meta-analysis. J Hosp Infect. 2021;108:120-134. https://doi.org/10.1016/j.jhin.2020.11.008.
4. Sahu AK, Amrithanand VT, Roshan M, Aggarwal P, Nayer J, Bhoi S. COVID-19 in health care workers – A systematic review and meta-analysis. Am J Emerg Med. 2020; 38(9):1727-1731. https://doi.org/10.1016/j.ajem.2020.05.113.
5. Chou R, Dana T, Buckley DI, Selph S, Fu R, Totten AM. Update Alert 7: Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers. Ann Intern Med. 2021:L21-0034. https://doi.org/10.7326/L21-0034.
6. [National Institute of Public Health (NIJZ) [Internet]. The organization: Ljubljana; 2022 [cited 2022, May 2]. Daily surveillance of SARS-CoV-2 – COVID-19 infections. Available from: https://www.nijz.si/sl/dnevno-spremljanje-okuzb-s-sars-cov-2-COVID-19.
7. Beavis KG, Matushek SM, Abeleda APF, Bethel C, Hunt C, Gillen S, et al. Evaluation of the EUROIMMUN Anti-SARS-CoV-2 ELISA Assay for detection of IgA and IgG antibodies. J Clin Virol. 2020;129:104468. https://doi.org/10.1016/j.jcv.2020.104468.
8. Lassaunière R, Frische A,. Harboe ZB, Nielsen ACB, Nielsen ACY, Fomsgaard A, et al. Evaluation of nine commercial SARS-CoV-2 immunoassays. Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium. medRxiv preprint. https://doi.org/10.1101/2020.04.09.20056325.
9. Poletti P, Tirani M, Cereda D, Guzzetta G, Trentini F, Marziano V, et al. Seroprevalence of and Risk Factors Associated With SARS-CoV-2 Infection in Health Care Workers During the Early COVID-19 Pandemic in Italy. JAMA Netw Open. 2021 1;4(7):e2115699. https://doi.org/10.1001/jamanetworkopen.
10. Kantele A, Lääveri T, Kareinen L, Pakkanen SH, Blomgren K, Mero S, et al. SARS-CoV-2 infections among healthcare workers at Helsinki University Hospital, Finland, spring 2020: Serosurvey, symptoms and risk factors. Travel Med Infect Dis. 2021;39:101949. https://doi.org/10.1016/j.tmaid.2020.101949.
11. Vilibic-Cavlek T, Stevanovic V, Tabain I, Betica-Radic L, Sabadi D, Peric L, et al. Severe acute respiratory syndrome coronavirus 2 seroprevalence among personnel in the healthcare facilities of Croatia, 2020. Rev Soc Bras Med Trop. 2020; 53:e20200458. https://doi.org/10.1590/0037-8682-0458-2020.
12. Kosztin A, Merkely B, Szabó AJ, Blaha B, Varga P, Vásárhelyi B, et al. Acute SARS-CoV-2 infection and seropositivity among healthcare workers and medical students in summer 2020, Hungary. Int J Occup Med Environ Health. 2021;15:141614. https://doi.org/10.13075/ijomeh.1896.01804.
13. Kasztelewicz B, Janiszewska K, Burzyńska J, Szydłowska J, Migdał M, Dzierżanowska-Fangrat K. Prevalence of IgG antibodies against SARS-CoV-2 among healthcare workers in a tertiary pediatric hospital in Poland. PLoS One. 2021;16(4): e0249550. https://doi.org/10.1371/journal.pone.0249550.
14. Malickova K, Kratka Z, Luxova S, Bortlik M, Lukas M. Anti-SARS-CoV-2 antibody testing in IBD healthcare professionals: are we currently able to provide COVID-free IBD clinics? Scand J Gastroenterol 2020;55(8):917-919. https://doi.org/10.1080/00365521.2020.1791244.
15. Goldblatt D, Johnson M, Falup-Pecurariu O, Ivaskeviciene I, Spoulou V, Tamm E, et al. Cross-sectional prevalence of SARS-CoV-2 antibodies in healthcare workers in paediatric facilities in eight countries J Hosp Infect. 2021;110:60-66. https://doi.org/10.1016/j.jhin.2020.12.019.
16. Iversen K, Bundgaard H, Hasselbalch RB, Kristensen JH, Nielsen PB, Pries-Heje M, et al. Risk of COVID-19 in health-care workers in Denmark: an observational cohort study. Lancet Infect Dis. 2020;20(12):1401-1408. https://doi.org/10.1016/S1473-3099(20)30589-2.
17. Xu X, Sun J, Nie S, Li H, Kong Y, Liang M, et al. Seroprevalence of immunoglobulin M and G antibodies against

SARS-CoV-2 in China. Nat Med. 2020;26(8):1193-1195. https://doi.org/10.1038/s41591-020-0949-6.
18. Rudberg AS, Havervall S, Månberg A, Jernbom Falk A, Aguilera K, Ng H, et al. SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. Nat Commun. 2020;11(1):5064. https://doi.org/10.1038/s41467-020-18848-0.
19. Kayı İ, Madran B, Keske Ş, Karanfil Ö, Arribas JR, Pshenichnaya N, et al. The seroprevalence of SARS-CoV-2 antibodies among health care workers before the era of vaccination: a systematic review and meta-analysis. Clin Microbiol Infect. 2021;27(9):1242-1249. https://doi.org/10.1016/j.cmi.2021.05.036.
20. Shrotri M, Navaratnam AMD, Nguyen V, Byrne T, Geismar C, Fragaszy E, et al, Virus Watch Collaborative. Spike-antibody waning after second dose of BNT162b2 or ChAdOx1. Lancet. 2021;398(10298):385-387. https://doi.org/10.1016/S0140-6736(21)01642-1.
21. Lombardi A, Mangioni D, Consonni D, Cariani L, Bono P, Cantù AP, et al. Seroprevalence of anti-SARS-CoV-2 IgG among healthcare workers of a large university hospital in Milan, Lombardy, Italy: a cross-sectional study. BMJ Open. 2021;11(2):e047216. https://doi.org/10.1136/bmjopen-2020-047216.
22. Dobaño C, Ramírez-Morros A, Alonso S, Vidal-Alaball J, Ruiz-Olalla G, Vidal M, et al. Persistence and baseline determinants of seropositivity and reinfection rates in health care workers up to 12.5 months after COVID-19. BMC Med. 2021;19(1):155. https://doi.org/10.1186/s12916-021-02032-2.
23. Watanabe M, Balena A, Tuccinardi D, Tozzi R, Risi R, Masi D, et al. Central obesity, smoking habit, and hypertension are associated with lower antibody titres in response to COVID-19 mRNA vaccine. Diabetes Metab Res Rev. 2021:e3465. https://doi.org/10.1002/dmrr.3465.
24. Moscola J, Sembajwe G, Jarrett M, Farber B, Chang T, McGinn T, et al. Northwell Health COVID-19 Research Consortium. Prevalence of SARS-CoV-2 Antibodies in Health Care Personnel in the New York City Area. JAMA. 2020;324(9):893-895. https://doi.org/10.1001/jama.2020.14765.
25. Self WH, Tenforde MW, Stubblefield WB, Feldstein LR, Steingrub JS, Shapiro NI, et al. CDC COVID-19 Response Team; IVY Network. Seroprevalence of SARS-CoV-2 Among Frontline Health Care Personnel in a Multistate Hospital Network – 13 Academic Medical Centers, April-June 2020. MMWR Morb Mortal Wkly Rep. 2020;69(35):1221-1226. https://doi.org/10.15585/mmwr.mm6935e2.
26. Steensels D, Oris E, Coninx L, Nuyens D, Delforge ML, Vermeersch P, et al. Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium. JAMA. 2020;324(2):195-197. https://doi.org/10.1001/jama.2020.11160.
27. Amendola A, Tanzi E, Folgori L, Barcellini L, Bianchi S, Gori M, et al. Low seroprevalence of SARS-CoV-2 infection among healthcare workers of the largest children hospital in Milan during the pandemic wave. Infect Control Hosp Epidemiol. 2020;41(12):1468-1469. https://doi.org/10.1017/ice.2020.401.
28. Soffin EM, Reisener MJ, Padgett DE, Kelly BT, Sama AA, Zhu J, et al. Coronavirus Disease 2019 Exposure in Surgeons and Anesthesiologists at a New York City Specialty Hospital: A Cross-Sectional Study of Symptoms and SARS-CoV-2 Antibody Status. J Occup Environ Med. 2021;63(6):521-527. https://doi.org/10.1097/JOM.0000000000002182.
29. De Geyter D, Vancutsem E, Van Laere S, Piérard D, Lacor P, Weets I, et al. SARS-COV-2 seroprevalence among employees of a University Hospital in Belgium during the 2020 COVID-19 outbreak (COVEMUZ-study). Epidemiol Infect. 2021;1-24. https://doi.org/10.1017/S0950268821001540.
30. Scohy A, Gruson D, Simon A, Kabamba-Mukadi B, De Greef J, Belkhir L, et al. Seroprevalence of SARS-CoV-2 infection in health care workers of a teaching hospital in Belgium:

self-reported occupational and household risk factors for seropositivity. Diagn Microbiol Infect Dis. 2021;100(4):115414. https://doi.org/10.1016/j.diagmicrobio.2021.115414.
31. Self WH, Tenforde MW, Stubblefield WB, Feldstein LR, Steingrub JS, Shapiro NI et al. CDC COVID-19 Response Team; IVY Network. Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network - 12 States, April-August 2020. MMWR Morb Mortal Wkly Rep. 2020;69(47):1762-1766. https://doi.org/10.15585/mmwr.mm6947a2.