RESEARCH ARTICLE

Check for updates

Seroprevalence of SARS-CoV-2 antibodies among primary healthcare workers in the Republic of Srpska, Bosnia & Herzegovina: A cross-sectional study

DARIJA KNEŽEVIĆ[1*], MIROSLAV PETKOVIĆ[1], LJILJANA BOŽIĆ[1], NATAŠA MILJUŠ[1], BILJANA MIJOVIĆ[2], JELA AĆIMOVIĆ[3], JELENA DJAKOVIĆ-DEVIĆ[3], DRAGANA PUHALO-SLADOJE[4], SRDJAN MAŠIĆ[2], DRAGAN SPAIĆ[2], NEVENA TODOROVIĆ[5], NATAŠA PILIPOVIĆ-BROĆETA[5], VERICA PETROVIĆ[5], DEJAN BOKONJIĆ[6], MILOŠ P. STOJILJKOVIĆ[1] and RANKO ŠKRBIĆ[1]

[1] University of Banja Luka, Faculty of Medicine, Centre for Biomedical Research, Banja Luka, The Republic of Srpska, Bosnia and Herzegovina

[2] University of East Sarajevo, Faculty of Medicine, Department of Primary Health Care and Public Health, Foča, The Republic of Srpska, Bosnia and Herzegovina

[3] Public Health Institute of the Republic of Srpska, Banja Luka, The Republic of Srpska, Bosnia and Herzegovina

[4] University of East Sarajevo, Faculty of Medicine, Centre for Biomedical Research, Foča, The Republic of Srpska, Bosnia and Herzegovina

[5] University of Banja Luka, Faculty of Medicine, Department for Family Medicine, Banja Luka, The Republic of Srpska, Bosnia and Herzegovina

[6] University of East Sarajevo, Faculty of Medicine, Department of Paediatrics, Foča, The Republic of Srpska, Bosnia and Herzegovina

*Corresponding author.
E-mail: darija.a.knezevic@med.unibl.org

AKJournals

ABSTRACT

Healthcare workers (HCW) in primary healthcare centres in the Republic of Srpska, Bosnia and Herzegovina, are on the first combat line with COVID-19. This study aimed to assess the seroprevalence of SARS-CoV-2 among HCW at the primary healthcare centres and to analyse the risk exposure to COVID-19, clinical signs and vaccination status. A cross-sectional study was conducted among HCW at the selected primary healthcare centres between 19 March and 30 April 2021. Antibodies against the SARS-CoV-2 virus were detected by enzyme-linked immunosorbent assay (ELISA). A total of 1,023 HCW (mean age 45 years; 71% female) were included in the study. The anti-SARS-CoV-2 antibodies were detected in 69.5% of all participants. There was a significant difference in seropositivity among primary healthcare centres from different geographical regions. As many as 432 (42%) of all participants had confirmed COVID-19 symptoms before the study and, 84.8% of them were seropositive. This study showed that 702 primary HCW were vaccinated with any of these vaccines: Sputnik V, Sinopharm, Pfizer/Biontech. High titre of SARS-CoV-2 antibodies was found amongst those who received one (92.6%) or both (97.2%) doses of vaccines. In this study, we report high prevalence of SARS-CoV-2 antibody among HCW in primary healthcare in the Republic of Srpska, Bosnia and Herzegovina during the third pandemic wave.

KEYWORDS

SARS-CoV-2, COVID-19, seroprevalence, healthcare workers, primary healthcare

INTRODUCTION

Healthcare workers (HCW) are at higher risk of getting infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) than the general population [1, 2]. A meta-analysis that encompassed 11 studies found that the proportion of HCW among all patients with coronavirus disease-19 (COVID-19) was 10.1%. The incidence of severe or critical disease and COVID-19-related mortality among HCW was lower compared to other patients with COVID-19 [3]. Studies of seroprevalence in HCW could provide important information about the levels of exposure, identification of high-risk departments in hospitals with COVID-19, the success of interventions and understanding the transmission of SARS-CoV-2 in healthcare institutions. The studies found a higher seroprevalence among HCW in North America (12.7%) than in Europe (8.5%), Africa (8.2%) and Asia (4%) [4]. The most common risk factors related to the higher rate of seroprevalence are ethnicity, male sex and exposure of HCW to the contacts outside the healthcare centres [5]. It is not yet known how long the anti-SARS-CoV-2 antibodies will last. The titre of the corresponding antibodies appears to be proportional to the age and severity of the disease [6]. Asymptomatic infections are the main obstacle for the infection's containment, which could explain the very fast spreading of the COVID-19 pandemic. Information on the seroprevalence of SARS-CoV-2 IgG antibodies in different geographic regions before the vaccination is essential for the development of herd immunity [7, 8]. The efficiency of COVID-19 vaccination programmes depends on mass participation, the higher the number of vaccinated people, the lower is the risk of COVID-19 infection in the population [9]. The studies that compared HCW who received at least one dose of the Pfizer-BioNTech BNT16 vaccine to those who were not vaccinated in one centre in Tel Aviv, Israel, showed an association of the former group with a significantly lower incidence of symptomatic and asymptomatic infection with SARS-CoV-2 [10]. Israel was one of the first countries globally that started with anti-COVID 19 vaccination and, HCW were in priority immunisation programms. Results of studies conducted by Lustig et al. showed that 96.5% and 99.9% of HCW got neutralising and IgG antibodies 14 days after the first and the second dose of the vaccine, respectively [11]. The COVID-19 pandemic still endangers the health and lives of HCW. Rapid implementation of new or changes in the existing public health policies, education programms and various infection control measures could significantly decrease the risks of infection [12]. As the world is moving through the era of vaccination, studies of SARS-CoV-2 seroprevalence are very important for tracking infection spreading, identifying the disproportionally affected groups and measuring the progress of collective immunity [13].

HCW in primary healthcare centres in the Republic of Srpska are on the first combat line with COVID-19. The vaccination process in our country started on 12 February 2021, and vaccination of the HCW has got the highest priority. This study aimed to evaluate the seroprevalence of SARS-CoV-2 among HCW at the primary healthcare level in the Republic of Srpska and to assess the risk exposure to COVID-19, clinical signs and the potential differences related to their vaccination status.

MATERIALS AND METHODS

Study design and participants

A cross-sectional study was conducted among HCW at the selected primary healthcare centres in the Republic of Srpska between 19 March and 30 April 2021. The study was led by the Centre for Biomedical Research, Faculty of Medicine, University of Banja Luka and the Faculty of Medicine Foča, University of East Sarajevo.

For this study, 11 largest primary health centres were selected from the area that gravitates towards the headquarter of the national Institute of Public Health located in Banja Luka, as well as seven health centres located in or near the regional Public Health centres located in cities of Doboj, Zvornik, East Sarajevo, Foča and Trebinje. The study included the HCW in selected primary healthcentres present at the workplace on the study day and who agreed to participate in the study. Among a total of 3,519 HCW in the selected primary healthcare centres, 1,023 medical and non-medical staff signed informed consent and were included in the study, resulting in a 29.07% response rate. All study participants voluntarily signed the informed consent and completed the questionnaire designed for this study. Trained medical technicians sampled 5 mL of venous blood from each participant needed for serological testing. After coagulation, the samples were centrifuged at 3,000 rpm for 5 min and the sera were transferred to the research laboratories in compliance with the coldchain protocol.

Detection of SARS-CoV-2 antibodies

Antibodies on the SARS-CoV-2 virus were detected using the automated "Sandwich" enzyme-linked immunosorbent assay (ELISA) method with Euroimmun ELISA Analyser I-2P (EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany). The samples were tested using WANTAI SARS-CoV-2 Ab ELISA assay to detect total antibodies in human serum. Serological testing was performed within 1–3 days after sampling. According to the manufacturer's performance characteristics, the test sensitivity and specificity were 94.36% and 100%, respectively. All samples with a cutoff value higher than 1.0 were considered positive.

Statistical analysis

Descriptive statistics were used for baseline participants' characteristics, symptoms and COVID-19 testing, as well as vaccination. Categorical data were presented as absolute numbers (n) and percentages (%). Seroprevalence was determined as a proportion of individuals with a positive test result for total Ig antibodies. Pearson Chi-square test was

used to determine the differences between categorical variables. Statistical hypotheses were tested at the significance level (alpha) of $P \leq 0.05$. Statistical analysis was done using IBM SPSS Statistics 26 software.

RESULTS

A total of 1,023 HCW from 18 primary healthcare centres in the Republic of Srpska participated in this study. The anti-SARS-CoV-2 antibodies were detected in 69.5% of all participants. The average age of participants was 45 years (SD = 11.6). The youngest participant was 19 and the oldest 65 years old. Out of all participants, 158 (15.4%) were male and, 865 (84.6%) were female. The participants were classified as follows: physicians (n = 303), nurses (n = 547), technical staff (n = 103), administrative staff (n = 26) and others (n = 44). For better evaluation of the individual risk rate, three categories were identified: occupations with high-risk exposure for those working at the frontline, including physicians and nurses; occupations with medium-risk exposure, which included laboratory, radiology and other technicians, as well as healthcare support services; and the low-risk exposure occupations, covering administrative staff and others who had minimal chances of exposure. However, there were no statistical differences in sex, age or exposure risk between seropositive and seronegative participants (Table 1).

There were significant differences in seropositivity among primary healthcare centres from different geographical regions (Chi-square = 141.072, $P \leq 0.001$). The highest seropositivity (70–90%) was found in five primary healthcare centres (Banja Luka, Čelinac, Prnjavor, Srbac, Gradiška), and the lowest seropositivity (30–50%) was detected in three centres (Laktaši, Kotor Varoš, Derventa). In most centres (10), the seropositivity was close to the average value of 69.5% (Table 2).

As many as 432 (42%) of all participants had confirmed COVID-19 symptoms before the study, and among them, 84.8% were seropositive. Among those who had serious clinical symptoms of COVID-19 and needed hospitalisation (29 or 6.7% of those who experienced COVID-19 symptoms), the seropositivity was confirmed in 89.7% of participants.

In total, 605 (59.1%) of participants confirmed positive PCR test for COVID-19 during the pandemic, and 471 (77.9%) were seropositive. The majority (96.9%) of 254 participants who had positive PCR tests any time before the study were seropositive; only 8 were seronegative (3.1%) (Table 3).

In total, 325 (31.8%) of all participants received at least one dose of vaccine against COVID-19 one to three months before the study. Among them, 92.6% were seropositive. However, among 698 participants who were not vaccinated, only 58.7% were seropositive ($P \leq 0.001$). The second dose of vaccine had received 249 participants (24.3%), and 242 of them were seropositive (97.2%) (Table 4).

The majority of participants vaccinated with at least one dose (250 out of 325) received Sputnik V vaccine, 62 participants received Sinopharm vaccine, while the lowest number of participants (13) were vaccinated with Pfizer-BioNTech BNT16 vaccine. The percentage of seropositive participants vaccinated with Sputnik V was 91.2, with Sinopharm 95.2 and all of 13 participants who received Pfizer-BioNTech BNT16 vaccine were seropositive (Table 5).

Table 1. Demographical characteristics of study participants and SARS-CoV-2 seroprevalence

| Characteristics | Total | | SARS-CoV-2 serology test result | | | |
| | | | Positive | | Negative | |
	n = 1,023	(%)	n = 711	69.5%	n = 312	30.5%
Age, years						
19–29	119	11.6	81	68.1	38	31.9
30–39	234	22.9	163	69.7	71	30.3
40–49	276	27	194	70.3	82	29.7
50–65	388	37.9	267	68.8	121	31.2
No data	6	0.6	6	100	0	0
Sex						
Male	158	15.4	117	74.1	41	25.9
Female	865	84.6	594	68.7	271	31.3
Occupation						
Physicians	303	29.6	223	73.6	80	26.4
Nurses	547	53.5	367	67.1	180	32.9
Technical staff	103	10.1	69	67.0	34	33.0
Administrative staff	26	2.5	21	80.8	5	19.2
Other*	44	4.3	31	70.5	13	29.5
Exposure risk						
High-risk exposure	850	83.1	590	69.4	260	30.6
Medium-risk exposure	103	10.1	69	67.0	34	33.0
Low-risk exposure	70	6.8	52	74.3	18	25.7

*Other: cleaning personnel, patient transporters, housekeeping.

Table 2. SARS-CoV-2 seroprevalence among HCW in primary health centers (PHC)

Municipality	Number of cases	COVID-19 Cumulative incidence rate/ 100.000 inhabitants	Seroprevalence in PHC
Novi Grad	244	1,042	53.3%
Prijedor	1,383	1,766	63.0%
Srbac	398	2,456	90.0%
Derventa	653	2,596	50.0%
Doboj	1,588	2,655	74.0%
Zvornik	1,630	3,059	67.6%
Prnjavor	1,053	3,193	90.0%
Kotor Varoš	635	3,535	45.0%
Istočno Sarajevo	2,508	4,171	56.0%
Kozarska Dubica	854	4,443	65.0%
Čelinac	680	4,590	80.0%
Laktaši	1,633	4,672	33.0%
Mrkonjić Grad	699	4,706	70.0%
Bijeljina	4,963	4,775	68.2%
Foča	829	4,934	71.4%
Gradiška	3,001	6,319	80.0%
Banja Luka	12,679	6,859	78.7%
Trebinje	2,515	8,864	57.1%

Out of 769 participants who were not PCR tested or tested as PCR negative, 251 (32.6%) received at least one dose of vaccine, and among them, 227 (90.4%) were seropositive. Of 518 participants who were not PCR tested or tested negative and not vaccinated, 237 (45.8%) were seropositive. The difference in seropositivity between these two groups was statistically significant (Chi-square = 141.072, $P \leq 0.001$) (Table 6).

A significant difference was found between SARS-CoV-2 seropositive vaccinated and non-vaccinated participants in relation to COVID-19 symptoms. Among 702 seropositive participants, 334 (47.6%) did not experience any COVID-19 symptom before the study and out of the 190 (63.5%) have been vaccinated (Table 7).

DISCUSSION

The first case of COVID-19 in the Republic of Srpska was recorded on 5 March 2020. When this study was conducted, between 19 March and 30 April 2021, the third wave of the COVID-19 epidemic was ongoing in the Republic of Srpska. Until 19 March, a total of 48,783 PCR confirmed cases of COVID-19 were recorded, out of 219,118 tested. The cumulative incidence rate was 4,270 per 100,000. The total number of notified deaths due to COVID-19 was 2,442, and the cumulative mortality rate was 214 per 100,000 [14]. This study found that the seroprevalence of total SARS-CoV-2 antibodies among 1,023 HCW of the selected primary health care centres was 69.5%. The obtained results showed that employees from primary health centres have crossed over the 67% herd immunity threshold, estimated an R0 of 3 for SARS-CoV-2 [15]. According to the SARS-CoV-2 seroprevalence study in the Republic of Srpska conducted in December 2020, the overall seroprevalence rate in the general population in the Republic of Srpska, at the end of the second wave and before the vaccination against COVID-19 started, was 40.3% (unpublished data).

The data from other analyses were mainly focused on the burden of SARS-CoV-2 infection among the hospital HCW. However, since the beginning of the SARS-CoV-2 pandemic in early 2020, the role of primary HCW have become substantial [16]. Primary HCW were at the front line for most

Table 3. Relationship between SARS-CoV-2 seroprevalence and previous SARS-CoV-2 infection

Questions	Total		SARS-CoV-2 serology test result				P-value
			Positive		Negative		
	n	%	n	%	n	%	
Symptoms of COVID-19							
Yes	432	42.2	368	85.2	64	14.8	≤0.001*
No	575	56.2	334	58.1	241	41.9	
No data	16	1.6	9	56.3	7	43.7	
Hospitalised due to COVID 19							
Yes	29	2.8	26	89.7	3	10.3	≤0.05
No	977	95.5	677	69.3	300	30.7	
No data	17	1.7	8	47.1	9	52.9	
Tested with RT-PCR on COVID-19							
Yes	605	59.1	471	77.9	134	22.1	≤0.001
No	418	40.9	240	57.4	178	42.6	
Positive RT-PCR test							
Yes	254	42	246	96.9	8	3.1	≤0.001
No	351	58	224	63.8	127	36.2	

*The values refer to the Chi-square test; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus; RT-PCR: real-time polymerase chain reaction.

Table 4. SARS-CoV-2 seroprevalence in vaccinated participants

	Total		Positive		Negative		
Questions	n	%	n	%	n	%	P-value
Vaccinated with 1st dose							
Yes	325	31.8	301	92.6	24	7.4	≤0.001*
No	698	68.2	410	58.7	288	41.3	
Vaccinated with 2nd dose							
Yes	249	24.3	242	97.2	7	2.8	≤0.001*
No	774	75.7	469	66.6	305	39.4	

*The values refer to the Chi-square test.

Table 5. SARS-CoV-2 seroprevalence in participants relative to the type of vaccine

	Total		Positive		Negative		
Type of vaccine	n = 325	(%)	n = 300	92.3%	n = 25	7.7%	P-value
Sputnik V	250	76.9	228	91.2	22	8.8	≤0.001*
Sinopharm	62	19.1	59	95.2	3	4.8	
Pfizer-BioNTech	13	4	13	100.0	0	0	

*The values refer to the Chi-square test.

Table 6. SARS-CoV-2 seropositivity in participants with negative PCR test or no PCR testing in relation to vaccination status

	No PCR test or negative PCR test		Positive		Negative		
Vaccination status	n = 769	(%)	n = 300	92.3%	n = 25	7.7%	P-value
Yes	251	32.6	227	90.4	24	9.6	≤0.001*
No	518	67.4	237	45.8	281	54.2	

*The values refer to the Chi-square test.

Table 7. Vaccination status of seropositive participants who had COVID-19 symptoms

	Total		Yes		No		
Vaccination status	n = 702	(%)	n = 368	52.4%	n = 334	47.6%	P-value
Vaccinated	299	42.6	109	36.5	190	63.5	≤0.001*
Non-vaccinated	403	57.4	259	64.3	144	35.7	

*The values refer to the Chi-square test.

COVID-19 patients, for which they organised special care. Primary healthcare centres in the Republic of Srpska rearranged their organisation structure according to the epidemiological situation. By the recommendation of the Public Health Institute and Ministry of Health, formed outpatient clinics for patients with symptoms of acute respiratory infections (ARI), the so called ARI ambulances. Depending on clinical symptoms, they organised clinical examination of these patients, PCR sampling, therapy, and referred COVID-19 patients to home or hospital treatment based on their clinical status. Analysis of several studies suggested that front line HCW are at higher risk to be infected with SARS-CoV-2 because of the direct contact with COVID-19 [17,18]. In the study performed in Sweden between 14 April and 8 May 2020, the seroprevalence of IgG antibodies against SARS-CoV-2 was 19.1% among the 2,149 healthcare workers recruited, which was higher than the reported regional seroprevalence during the same period. The seroprevalence was significantly higher in the HCW with patient contact than in those without patient contact. The seroprevalence among the HCW without patient contact was in line with that reported in the general population of Stockholm, using the same serological test during the same period [19].

Poletti et al. analysed seroprevalence for of IgG antibodies against SARS-CoV-2 targeting all individuals employed in the healthcare sector in Lombardy, and they found a 12% seroprevalence by the end of May 2020 [20]. Spain had one of the highest infection rates of COVID-19 in the world. In the study conducted after the first pandemic wave in Barcelona, from 4 May to 22 May 2020, 10.3% of HCW were positive on anti-SARS-CoV-2 IgG. There were no statistically significant differences between those who worked in the primary healthcare centres or at the referral hospital [21]. In the study carried out in HCW from 17 hospitals across four regions in Spain, between April and June 2020, 11% of HCW were positive for anti-SARS-CoV-2 IgG antibodies [22].

The overall seroprevalence of 0.66% was found in a nationwide cross-sectional HCW SARS-CoV-2 seroprevalence study, conducted among 57,418 HCW in Greece after the first wave, from 1 June to 9 July 2020, indicating a very low prevalence of SARS-CoV-2 among HCW. In that study, HCW working in COVID-19 hospitals were more likely to be seropositive than HCW in the primary care centres [23].This result is in line with the low incidence of COVID-19 during the first wave of the pandemic and reflects the direct benefits from the early implementation of lockdown.

The study that investigated the seroprevalence of SARS-CoV-2 in HCW in the northern part of Italy between 28 March and 7 August 2020 discovered that HCW with a higher risk of exposure to SARS-CoV-2 were often seropositive, as compared to those with medium or low risk [24]. Moreover, HCW who were in direct contact with patients, regardless of the COVID-19 status of patients, had a higher seroprevalence of anti-SARS-CoV-2 IgG antibodies than those who were not in direct contact, as shown in a study conducted in Sweden [19].

In the present study, there was no significant difference in the seroprevalence of anti-SARS-CoV-2 antibodies between the front line HCW in primary care and employees of primary healthcare centres working in other settings. The seroprevalence was slightly higher among the administrative staff than among the HCW and in low-risk exposure staff than high-risk exposure staff. The HCW in the Republic of Srpska were using recommended personal protective equipment (PPE) from the very beginning of the epidemic, especially if they cared for patients with ARI and patients with confirmed COVID-19. Employees of primary healthcare centres with low-risk exposure probably were less cautious in c0mplying with protective measures at the workplace. Since incidence rates in the Republic of Srpska suggest high transmission rates, the HCW and other employees probably were highly exposed in their families and social contacts and contacts with colleagues at the workplace, similarly as the general population.

Several seroprevalence studies among HCW found a higher risk of infection among men than women [25, 26]. In our study, there was no statistically significant difference in seropositivity regarding the gender or age of participants.

In general, HCW is at the highest risk to be infected with SARS-CoV-2 [27]. A few studies noted a rather low prevalence of seroconversion among HCW [28, 29]. Most studies reported a significant incidence of infection among HCW who were taking care of patients infected with SARS-CoV-2 [30]. Infection prevention and control, as well as appropriate and precise diagnosis of COVID-19 in HCW, are essential to keep hospital operations up and running. It has been reported that HCW accounted for a high proportion of infections early in the SARS-CoV-2 outbreak, because of a sudden increase in the spread of the SARS-CoV-2 infection, lack of adequate PPE and recommendation for its use [31, 32, 33].

The present study showed significant differences in seropositivity of HCW in primary healthcare centres from different geographical regions, ranging from 33.3% to 90%. The obtained spatial variability of seroprevalence in primary healthcare centres may be associated with the different infection rates throughout different geographical regions and the spatiotemporal spread of SARS-CoV-2 during the initial pandemic phase. Studies in Italy and Spain found similar regional differences [20, 22]. The HCW had a higher chance for infection in those geographical areas where the infection rate was higher, and because of that, they had more contacts with the infected persons. Given the fact that data from the Public Health Institute of the Republic of Srpska related to the cumulative incidence rates in municipalities at the same period are not entirely in line with the findings of the study, it is assumed that differences in compliance with the infection prevention and control measures among different healthcare centres could be an additional cause for different seroprevalence rates.

SARS-CoV-2 infection can be presented through a spectrum of clinical presentations, from asymptomatic infection, mild symptoms, influenza-like symptoms (eg. fever, myalgia) to severe respiratory disease with dyspnoea and pneumonia [34, 35]. One year after the beginning of the pandemic, 43% of all participants in this study reported that they experienced some of the COVID-19 symptoms. Lackermair et al. showed that 72% of primary HCW had symptoms compatible with COVID-19, while 25% had fever [36]. Testing of HCW was mainly reserved for persons reporting consistent symptoms [37]. In the present study, 85.2% of seropositive participants confirmed that they had experienced symptoms associated with COVID-19. In addition, out of 245 participants with positive PCR tests at any time during the pandemic, 96.1% were seropositive. Similarly, in a study by Grant et al., 73% of HCW in the seropositive group reported a typical symptom of COVID-19. Of those who were RT-PCR positive, most had detectable antibodies [38].

Vaccination against COVID-19 in the Republic of Srpska started on 12 March 2021, and at the time of the completio of the present study, most vaccinated people received the Sputnik V vaccine. Our study found a high seroprevalence of anti-SARS-CoV-2 antibodies amongst HCW who received one (92.6%) or both (97.2%) doses of vaccines. The prospective longitudinal study in Turkey showed that after the first dose of the inactive Sinovac vaccine, antibodies on SARS-CoV-2 were detected in 77.8% of HCW. After the

second dose of the vaccine, 99.6% of HCW had detectable antibodies [39]. Similar results were found in the study in Oxfordshire, UK, where 98.9% of HCW were seropositive after the first dose of the Pfizer-BioNTech or Oxford-AstraZeneca vaccine and all HCW who have been tested after the second dose of the vaccine were seropositive. It has been shown that natural immunity and two vaccination doses provide similar protection against symptomatic infection [40]. The study from Argentina reported that the seropositivity of HCW was 94% after the first dose of the vaccine. A single dose of the Sputnik V vaccine produced a fast and robust immune response in seropositive participants with neutralising titres exceeding those found in seronegative participants who received two doses [41]. Efficacy of Pfizer-BioNTech vaccine in HCW was similar to the studies in Israel 96.5% [11], Greece 99.82% [42] and France 94.6% [43]. Xia et al. confirmed that humoral immune response against SARS-CoV-2 was identified in all people who received Sinopharm vaccine 42 days before testing [44]. The present study evaluated seropositivity in HCW in primary healthcare centres that were vaccinated with Sputnik V, Sinopharm or Pfizer-BioNTech vaccine. The percentage of seropositivity among those vaccinated with Sputnik V was 91.2%, with Sinopharm vaccine 95.2% and with Pfizer-BioNTech vaccine 100%. The high seropositivity of vaccinated HCW obtained in the present study suggests that the vaccination is the most effective measure of protection against SARS-CoV-2. In the longitudinal study, Morgat et al. followed the anti-SARS-COV-2 IgG seroprevalence in a nationally representative cohort of HCW in 850 hospitals in Belgium and showed that the seroprevalence varied from about 8% to 20% [45]. Beneson et al. reported that vaccination of HCW with two doses of vaccine reduced the incidence of new COVID-19 infections. Since the beginning of vaccination, the incidence of COVID-19 in HCW has decreased significantly [46].

The serological analysis is becoming increasingly important in understanding the extent to which COVID-19 is disseminating in the population and detecting immunised individuals. According to the estimates from 2020, it is considered that 40–45% of all SARS-CoV-2 infections are asymptomatic, although this estimate is still uncertain [47]. In our study, the incidence of seropositive participants who had no COVID-19 symptoms and were not vaccinated was 35.7%. These findings are not consistent with reports of Damluji et al., who demonstrated that the incidence of seropositivity in asymptomatic HCW was 1.15% [48].

CONCLUSIONS

High seroprevalence of SARS-CoV-2 in HCW in primary healthcare centres in the Republic of Srpska during the third pandemic wave was found. Almost all HCW who received the first or second dose of vaccine were seropositive. Results of this study are very important in terms of the protection of HCW who are on the front line of defence against COVID-19. Since vaccination is ongoing, a future study is necessary to

follow-up titres of antibodies in HCW of primary healthcare centres after achieving greater vaccination coverage.

ACKNOWLEDGEMENTS

REFERENCES

1. Nguyen LH, Drew DA, Graham MS, Joshi AD, Guo CG, Ma W, et al. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health 2020; 5(9): e475–83. https://doi.org/10.1016/S2468-2667(20)30164-X.

2. McCauley L, Hayes R. Taking responsibility for front-line health-care workers. Lancet Public Health 2020; 5: e461–2. https://doi.org/10.1016/S2468-2667(20)30179-1.

3. Sahu AK, Amrithanand VT, Mathew R, Aggarwal P, Nayer J, Bhoi S. COVID-19 in health care workers - a systematic review and meta-analysis. Am J Emerg Med 2020; 38: 1727–31. https://doi.org/10.1016/j.ajem.2020.05.113.

4. Galanis P, Vraka I, Fragkou D, Bilali A, Kaitelidou D. Seroprevalence of SARS-CoV-2 antibodies and associated factors in health-care workers: a systematic review and meta-analysis. J Hosp Infect 2021; 108: 120–34. https://doi.org/10.1016/j.jhin.2020.11.008.

5. 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; S1198-743X(21): 00284–6. https://doi.org/10.1016/j.cmi.2021.05.036.

6. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV- 2 in patients of novel coronavirus disease 2019. Clin Infect Dis 2020; 71: 2027–34. https://doi.org/10.1093/cid/ciaa344.

7. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann Intern Med 2020; 173: 362–7. https://doi.org/10.7326/M20-3012.

8. Hossain A, Nasrullah SM, Tasnim Z, Hasan MK, Hasan MM. Seroprevalence of SARS-CoV-2 IgG antibodies among health care workers before vaccine administration in Europe, the USA and East Asia: a systematic review and meta-analysis. EClinicalMedicine 2021; 33: 100770. https://doi.org/10.1016/j.eclinm.2021.100770.

9. Freeman D, Sheng LB, Yu LM, Freeman J, Chadwick A, Vaccari C, et al. Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): a single-blind, parallel-group, randomised controlled trial. Lancet Public Health 2021; 6: e416–27. https://doi.org/10.1016/S2468-2667(21)00096-7.

10. Angel Y, Spitzer A, Henig O, Saiag E, Sprecher E, Padova H, et al. Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers. JAMA 2021; 325: 2457–65. https://doi.org/10.1001/jama.2021.7152.

11. Lustig Y, Sapir E, Regev-Yochay G, Cohen C, Fluss R, Olmer L, et al. BNT162b2 COVID-19 vaccine and correlates of humoral immune responses and dynamics: a prospective, single-centre, longitudinal cohort study in health-care workers. Lancet Respir Med 2021; 2. https://doi.org/10.1016/S2213-2600(21)00220-4.

12. Moey PKS, Ang ATW, Ee AGL, Ng DCC, Ng MCW, Teo SSH, et al. What are the measures taken to prevent COVID-19 infection among healthcare workers? A retrospective study in a cluster of primary care clinics in Singapore. BMJ Open 2021; 11: e049190. https://doi.org/10.1136/bmjopen-2021-049190.

13. Bobrovitz N, Arora RK, Cao C, Boucher E, Liu M, Donnici C, et al. Global seroprevalence of SARS-CoV-2 antibodies: a systematic review and meta-analysis. PLoS One 2021; 16, e0252617. https://doi.org/10.1371/journal.pone.0252617.

14. Institut za javno zdravstvo Republike Srpske. COVID-19: epidemiološka situacija u Republici Srpskoj. Available from: https://www.phi.rs.ba/pdf/sadrzaj/COVID%2019%20%20Epidemioloska%2019%2003%202021.pdf.

15. Randolph HE, Barreiro LB. Herd immunity: understanding COVID-19. Immunity 2020; 52: 737–41. https://doi.org/10.1016/j.immuni.2020.04.012.

16. Pouquet M, Decarreaux D, Prévot-Monsacré P, Hervé C, Werner A, Grosgogeat B, et al. A. Nationwide seroprevalence of SARS-CoV-2 IgG antibodies among four groups of primary health-care workers and their household contacts 6 Months after the initiation of the COVID-19 vaccination campaign in France: SeroPRIM study protocol. Pathogens 2021; 10: 911. https://doi.org/10.3390/pathogens10070911.

17. Fukuda H, Seyama K, Ito K, Ai T, Nojiri S, Hori S, et al. SARS-CoV-2 seroprevalence in healthcare workers at a frontline hospital in Tokyo. Sci Rep 2021; 11: 8380. https://doi.org/10.1038/s41598-021-87688-9.

18. Grant JJ, Wilmore SMS, McCann NS, Donnelly O, Lai RWL, Kinsella MJ, et al. Seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a London NHS Trust. Infect Control Hosp Epidemiol 2021; 42: 212–4. https://doi.org/10.1017/ice.2020.402.

19. Rudberg AS, Havervall S, Månberg A, Jernbom FA, Aguilera K, Ng H, et al. SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. Nat Commun 2020; 11: 5064. https://doi.org/10.1038/s41467-020-18848-0.

20. 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; 4: e2115699. https://doi.org/10.1001/jamanetworkopen.2021.15699.

21. Barallat J, Fernández-Rivas G, Quirant-Sánchez B, González V, Doladé M, Martinez-Caceres E, et al. Seroprevalence of SARS-CoV-2 IgG specific antibodies among healthcare workers in the Northern Metropolitan Area of Barcelona, Spain, after the first pandemic wave. PLoS One 2020; 15: e0244348. https://doi.org/10.1371/journal.pone.0244348.

22. Varona JF, Madurga R, Peñalver F, Abarca E, Almirall C, Cruz M, et al. Seroprevalence of SARS-CoV-2 antibodies in over 6000 healthcare workers in Spain. Int J Epidemiol 2021; 50: 400–9. https://doi.org/10.1093/ije/dyaa277.

23. Galanis P, Kaitelidou D, Prezerakos P, Kotsiopoulos I, Siskou O, Konstantakopoulou O, et al. Low seropositivity for SARS-CoV-2 antibodies among healthcare workers after the first COVID-19 pandemic wave in Greece. Public Health 2021; 198: 223–9. https://doi.org/10.1016/j.puhe.2021.07.029.

24. Airoldi C, Patrucco F, Milano F, Alessi D, Sarro A, Rossi MA, Cena T, et al. High seroprevalence of SARS-CoV-2 among healthcare workers in a North Italy hospital. Int J Environ Res Public Health 2021; 18: 3343. https://doi.org/10.3390/ijerph18073343.

25. Lidström AK, Sund F, Albinsson B, Lindbäck J, Westman G. Work at inpatient care units is associated with an increased risk of SARS-CoV-2 infection; a cross-sectional study of 8679 healthcare workers in Sweden. Ups J Med Sci 2020; 125: 305–10. https://doi.org/10.1080/03009734.2020.1793039.

26. Eyre DW, Lumley SF, O'Donnell D, Campbell M, Sims E, Lawson E, et al. Differential occupational risks to healthcare workers from SARS-CoV-2 observed during a prospective observational study. Elife 2020; 9: e60675. https://doi.org/10.7554/eLife.60675.

27. Chou R, Dana T, Buckley DI, Selph S, Fu R, Totten AM. Epidemiology of and risk factors for coronavirus infection in health care workers: a living rapid review. Ann Intern Med 2020; 173: 120–36. https://doi.org/10.7326/M20-1632.

28. Rashid-Abdi M, Krifors A, Sälléber A, Eriksson J, Månsson E. Low rate of COVID-19 seroconversion in health-care workers at a Department of Infectious Diseases in Sweden during the later phase of the first wave; a prospective longitudinal seroepidemiological study. Infect Dis (Lond) 2021; 53: 169–75. https://doi.org/10.1080/23744235.2020.1849787.

29. 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: 1401–8. https://doi.org/10.1016/S1473-3099(20)30589-2.

30. Schmitz D, Vos M, Stolmeijer R, Lameijer H, Schönberger T, Gaakeer MI, et al. Association between personal protective equipment and SARS-CoV-2 infection risk in emergency department healthcare workers. Eur J Emerg Med 2021;28: 202–9. https://doi.org/10.1097/MEJ.0000000000000766.

31. Lai X, Wang M, Qin C, Tan L, Ran L, Chen D, et al. Coronavirus disease 2019 (COVID-2019) infection among health care workers and implications for prevention measures in a tertiary hospital in Wuhan, China. JAMA Netw Open 2020; 3: e209666. https://doi.org/10.1001/jamanetworkopen.2020.9666.

32. Kluytmans-van den Bergh MFQ, Buiting AGM, Pas SD, Bentvelsen RG, van den Bijllaardt W, van Oudheusden AJG, et al. Prevalence and clinical presentation of health care workers with symptoms of coronavirus disease 2019 in 2 Dutch hospitals during an early phase of the pandemic. JAMA Netw Open 2020; 3: e209673. https://doi.org/10.1001/jamanetworkopen.2020.9673.

33. Cheng VC, Wong S, Yuen K. Estimating coronavirus disease 2019 infection risk in health care workers. JAMA Netw Open 2020; 3: e209687. https://doi.org/10.1001/jamanetworkopen.

34. Lan FY, Filler R, Mathew S, Buley J, Iliaki E, Bruno-Murtha LA, et al. COVID-19 symptoms predictive of healthcare workers' SARS-CoV-2 PCR results. PLoS One 2020; 15: e0235460. https://doi.org/10.1371/journal.pone.0235460.

35. Cordova E, Bacelar B, Nieto F, Garibaldi F, Aguirre V, Machuca M, et al. SARS-CoV-2 IgG response in symptomatic and asymptomatic COVID-19-infected healthcare workers. Occup Med (Lond) 2021; 19: kqab061. https://doi.org/10.1093/occmed/kqab061.

36. Lackermair K, William F, Grzanna N, Lehmann E, Fichtner S, Kucher HB, et al. Infection with SARS-CoV-2 in primary care health care workers assessed by antibody testing. Fam Pract 2021; 38: 76–9. https://doi.org/10.1093/fampra/cmaa078.

37. Centers for Disease Control and Prevention (CDC). Interim U.S. Guidance for risk assessment and public health management of healthcare personnel with potential exposure in a healthcare setting to patients with coronavirus disease (COVID-19); 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html.

38. Grant JJ, Wilmore SMS, McCann NS, Donnelly O, Lai RWL, Kinsella MJ, et al. Seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a London NHS Trust. Infect Control Hosp Epidemiol 2021; 42: 212–4. https://doi.org/10.1017/ice.2020.402.

39. Bayram A, Demirbakan H, Günel KP, Erdoğan M, Koçer I. Quantitation of antibodies against SARS-CoV-2 spike protein after two doses of CoronaVac in healthcare workers. J Med Virol 2021; 93: 5560–7. https://doi.org/10.1002/jmv.27098.

40. Lumley SF, Rodger G, Constantinides B, Sanderson N, Chau KK, Street TL, et al. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. Clin Infect Dis 2021: ciab608. https://doi.org/10.1093/cid/ciab608.

41. Rossi AH, Ojeda DS, Varese A, Sanchez L, Gonzalez L, Ledesma MM, Mazzitelli I, et al. Sputnik V vaccine elicits seroconversion and neutralizing capacity to SARS-CoV-2 after a single dose. Cell Rep Med 2021; 2: 100359. https://doi.org/10.1016/j.xcrm.2021.100359.

42. Kontou E, Ranellou K, Zoulas D, Bletsa A, Rompola E, Piperaki ET, et al. Antibody response following a two-dose mRNA vaccination regimen, in health care workers of a tertiary hospital in Athens, Greece. J Pers Med 2021; 11: 576. https://doi.org/10.3390/jpm11060576.

43. Paris C, Perrin S, Hamonic S, Bourget B, Roué C, Brassard O, et al. Effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19 vaccines against COVID-19 in healthcare workers: an observational study using surveillance data. Clin Microbiol Infect 2021; 13. https://doi.org/10.1016/j.cmi.2021.06.043.

44. Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao G, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial. Lancet Infect Dis 2021; 21: 39–51. https://doi.org/10.1016/S1473-3099(20)30831-8.

45. Mortgat L, Verdonck K, Hutse V, Thomas I, Barbezange C, Heyndrickx L, et al. Prevalence and incidence of anti-SARS-CoV-2 antibodies among healthcare workers in Belgian hospitals before vaccination: a prospective cohort study. BMJ Open 2021; 11: e050824. https://doi.org/10.1136/bmjopen-2021-050824.

46. Benenson S, Oster Y, Cohen MJ, Nir-Paz R. BNT162b2 mRNA covid-19 vaccine effectiveness among health care workers. N Engl J Med 2021; 384: 1775–7. https://doi.org/10.1056/NEJMc2101951.

47. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection. Ann Intern Med 2020; 173: 362–7. https://doi.org/10.7326/M20-3012.

48. Damluji AA, Wei S, Bruce SA, Haymond A, Petricoin EF, Liotta L, et al. Seropositivity of COVID-19 among asymptomatic healthcare workers: a multi-site prospective cohort study from Northern Virginia, United States. Lancet Reg Health Am 2021; 29: 100030. https://doi.org/10.1016/j.lana.2021.100030.