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Low seropositivity for SARS-CoV-2 antibodies among healthcare workers after the first COVID-19 pandemic wave in Greece



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ABSTRACT

Objectives: To estimate the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seropositivity among healthcare workers (HCWs) in Greece and to identify high-risk groups in healthcare facilities.

Study design: The study design used in this study is a nationwide cross-sectional study.

Methods: Data were collected from 1 June to 9 July 2020. HCWs in the Greek National Health System were offered a free SARS-CoV-2 IgG antibody test, regardless of symptoms.

Results: Overall, 379 of 57,418 HCWs (0.66%, 95% confidence interval [CI]: 0.59-0.73) were positive for SARS-CoV-2 antibodies. The adjusted overall seroprevalence was 0.43% (95% CI: 0.35-0.51). We found that HCWs in non-reference hospitals for COVID-19 (odds ratio [OR]: 1.81, 95% CI: 1.23-2.64; P = 0.002) and reference hospitals for COVID-19 (OR: 1.66, 95% CI: 1.06-2.58; P = 0.03) were more likely to be seropositive than HCWs in primary care centres. Regarding professions, nurses (OR: 1.45, 95% CI: 1.07 - 1.98; P = 0.02), physicians (OR: 1.43, 95% CI: 1.06-1.93; P = 0.02), and administrative, cleaning and security staff (OR: 1.50, 95% CI: 1.09-2.06; P = 0.01) had a statistically higher chance of having a positive serology than laboratory employees.

Conclusions: The adjusted overall seroprevalence found in this study indicates a very low prevalence of SARS-CoV-2 among HCWs in Greece. This result is in line with the low incidence of COVID-19 during the first wave of the pandemic and is a direct benefit from the early implementation of lockdown.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which originated from China in late 2019, was declared a pandemic by the World Health Organization on 11 March 2020.¹ Greece underwent a nationwide lockdown during the first phase

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of the pandemic that was gradually lifted from May 2020. At the end of June 2020, a total of 3049 cases and 193 deaths were reported nationwide.² Mortality from COVID-19 in Greece at that point was one of the lowest in the world, with 1.68 deaths per 100,000 population, whereas respective figures for Belgium, Spain, the UK, Italy, the US and Sweden were reported at 93.3, 74.4, 67.2, 61.3, 68.5 and 58.3 deaths per 100,000 population, respectively.³

An increase in transmission of SARS-CoV-2 may lead to an uncontrolled expansion in COVID-19 cases, which can cause a major challenge for national health systems. Countries around the globe have responded in different ways to the pandemic. During the initial stages of the pandemic, Greece developed an efficient crisis management system taking into account the health system characteristics, the available healthcare resources, and surge capacity to face the pandemic. This led to the early implementation of a

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nationwide lockdown in March 2020. This swift response was accompanied by an effort to develop and put in place a number of policies and reforms to meet the population health needs as a result of the pandemic. The strategies implemented were based on an evidence-informed, systematic and comprehensive strategic approach.⁴

Healthcare workers (HCWs) represent a high-risk group for SARS-CoV-2 infection due to their close and frequent contact with COVID-19 patients.^{5,6} Nosocomial transmission of SARS-CoV-2 among HCWs and patients is a major public health problem and represents a significant challenge for healthcare systems. Primary and secondary health services worldwide have been reformed during the COVID-19 pandemic. In particular, reference hospitals for COVID-19 (i.e. hospitals that only care for COVID-19 patients) have been established to provide better health care to these patients and to reduce transmission of the virus in hospitals. In contrast, non-reference hospitals for COVID-19 deal only with patients with chronic diseases and emergency cases and do not admit COVID-19 patients, thus protecting critically ill patients from the virus. The role of primary healthcare centres has been crucial because HCWs in these services can effectively manage COVID-19 patients who have mild symptoms and do not require hospitalisation.^{7,8} In addition, some countries have established specialised COVID-19 health centres, operating 24 h/day, which are solely for the screening and management of mild COVID-19 cases.⁴ Moreover, the role of primary health care in achieving sufficient COVID-19 vaccination coverage as quickly as possible is also essential.⁹

Fortunately, COVID-19 vaccination programmes in the HCW population commenced worldwide in January 2021 and have already shown a positive impact on COVID-19 incidence.^{10–12} However, according to a meta-analysis, the intention of HCWs to receive COVID-19 vaccination is moderate (55.9%) and very variable between countries (27.7%-81.5%).¹³ Moreover, early studies regarding COVID-19 vaccination acceptance among HCWs found contradicting results. In particular, 65% of staff members at University Hospitals of NHS Trust had received COVID-19 vaccination, but ethnic minorities (White HCWs 70.9%; South Asian HCWs 58.5%; and Black HCWs 36.8%) and physicians (57% vs 73% among allied health professionals and administrative/executive staff) were vaccinated in a significantly smaller proportion.¹⁴ A similar COVID-19 vaccination acceptance percentage (73.2%) was found in a dialysis unit in New York.¹⁵ On the other hand, a median of 37.5% of staff members in skilled nursing facilities in the US received ≥ 1 COVID-19 vaccine dose.¹⁰

In addition to the great variability of COVID-19 vaccination acceptance among HCWs in different countries, it is also important to understand which HCWs are at greatest risk, thus determining priority HCW groups for vaccination and targeting information about vaccination programmes and protective measures. Therefore, the aim of the present study was to estimate the prevalence of SARS-CoV-2 seropositivity among HCWs in Greece, to identify high-risk HCW groups in healthcare facilities and to find hotspots of the disease in the different regional units of the country. To the best of our knowledge, this is the first nationwide study in the world to estimate the prevalence of SARS-CoV-2 antibodies among HCWs.

Methods

Study design

A nationwide cross-sectional HCW SARS-CoV-2 seroprevalence study was conducted from 1 June to 9 July 2020. A free SARS-CoV-2 IgG antibody test was offered to all HCWs working in the 110 hospitals and 377 primary healthcare centres throughout the country. The Greek government offered a free SARS-CoV-2 IgG antibody test in all HCWs anytime during the study. At the time of study, a total of 86,421 HCWs and administrative staff were informed about the aims and methods of our study. The test was performed on a voluntary and anonymous basis and was offered irrespective of past history of COVID-19. Blood sampling was organised and performed by the Departments of Clinical Laboratory and Biochemistry in the participating hospitals.

The presence of SARS-CoV-2 IgG antibodies was determined with the EUA-approved and CE-marked Abbott ArchitectTM SARS-CoV-2 IgG assay (ArchitectTM).^{17–19} The assay detects the presence of IgG antibodies against the SARS-CoV-2 nucleocapsid (N) protein. A chemiluminescent microparticle immunoassay was used for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma on the ARCHITECT i System (ARCHITECT i2000SR analyser).²⁰ SARS-CoV-2 IgG antibodies in each sample were determined by comparing its chemiluminescent relative light unit (RLU) to the calibrator RLU (index S/C). The assay is highly sensitive and specific.^{17,21,22} The samples were tested according to the manufacturer instructions.

Ethical approval

The study was performed at the request of the Hellenic Prefectural Health authorities. The Greek National Committee of Public Health against COVID-19 approved the study design (reference number; 44, 27-04-2020) and the Greek Ministry of Health institutional review board approved the use of the database (reference number; 894, 2020).

Statistical analyses

The crude prevalence of antibodies to SARS-CoV-2 (i.e. the proportion of individuals with a positive result) was the outcome. We calculated the crude prevalence as a fraction, dividing the number of individuals with a positive antibody test by the total number of individuals that were tested. In addition, the adjusted prevalence²³ was calculated according to the manufacturer's specification (sensitivity, 100%; specificity, 99.6%) and to the results of a study²² conducted in a sample of the general population in Greece (sensitivity, 84%; specificity, 99.7%). Greece consists of 74 regional administrative units, and we calculated crude and adjusted prevalence for these units.

We investigated associations between seropositivity for SARS-CoV-2 and sex, age, type of healthcare facility (i.e. hospital, reference hospital for COVID-19 or primary healthcare centre), job role (i.e. physician, nurse, administrative, cleaning, security or laboratory staff) and district by creating bivariate and multivariable logistic regression models. First, a bivariate logistic regression of each independent variable (i.e. sex, age, type of healthcare facility, job role and district) was carried out. Then, all independent variables were included in a multivariable logistic regression model with enter method. We performed multivariate analysis to eliminate confounding. Odds ratios (ORs), 95% confidence intervals (CIs), and P-values (two-sided) for seropositivity were estimated. Finally, we performed a post hoc analysis regarding multiple level variables with seropositivity as the dependent variable to give a direct multiple-pairwise comparison. We did not include districts in the post hoc analysis since the number of categories was too many to inference reliable results. IBM SPSS was used for the analysis (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Results

A total of 86,421 HCWs and administrative staff were invited to participate; 57,418 individuals participated, resulting in a 66.4%

response rate. For participating individuals, 50,067 (87.2%) worked in hospitals and 7351 (12.8%) in primary healthcare centres (Table 1). In total, 9060 HCWs worked in a tertiary care hospital, designated as a reference COVID-19 centre according to the COVID-19 national pandemic response plan. The age distribution of participants is shown in Table 1. The 18–59-year-old age groups were equally distributed compared with the \geq 60 years age group (n = 4511, 9%). The mean (standard deviation) age was 46.4 (10.1) years, and the majority of participants were female (40,866 HCWs, 73.5%). With regards to healthcare role, the majority of participating individuals were laboratory staff (n = 16,060, 32.1%), followed by physicians (n = 13,043, 25.7%) and nurses (n = 11,262, 22.2%) (Table 1).

Overall, 379 of 57,418 HCWs (0.66%, 95% CI: 0.59-0.73) were positive for SARS-CoV-2 antibodies. The adjusted overall seroprevalence was 0.43% (95% CI: 0.35-0.51).

According to bivariate logistic regression analysis, there was no significant association between age, gender and prevalence (Table 2). However, healthcare facility, job role and district were related to prevalence. These findings were confirmed by the multivariable adjusted logistic regression model and post hoc analysis (Tables 2 and 3). In particular, our analysis identified that HCWs working in non-reference hospitals for COVID-19 (OR: 1.81, 95% CI: 1.23–2.64; P = 0.002) and reference hospitals for COVID-19 (OR: 1.66, 95% CI: 1.06–2.58; P = 0.03) were more likely to be seropositive than those working in primary care centres. Regarding job roles, nurses (OR: 1.45, 95% CI: 1.07–1.98; P = 0.02), physicians (OR: 1.43, 95% CI: 1.06–1.93; P = 0.02) and administrative, cleaning and security staff (OR: 1.50, 95% CI: 1.09–2.06; P = 0.01) had a statistically higher chance of having a positive SARS-CoV-2 serology than laboratory staff. In geographical terms, prevalence of SARS-CoV-2 antibodies was highest among HCWs in Attica (OR: 5.19, 95% CI: 1.28–21.02; *P* = 0.02) and Western Macedonia (OR: 11.97, 95% CI: 2.85–50.24; P = 0.001). Detailed geographical distribution of SARS-CoV-2 antibodies in HCWs is shown in Table 4 and Fig. 1.

Discussion

To the best of our knowledge, this is the first and largest nationwide study in the world to estimate the prevalence of SARS-CoV-2 antibodies among HCWs. The adjusted overall seroprevalence in this study was 0.43%, indicating a very low prevalence of SARS-CoV-2 among HCWs in Greece, which is consistent with the low burden of COVID-19 in the country during the first wave of the pandemic. This is an important direct benefit of the implementation of the early lockdown. In particular, case fatality rate of COVID-19 in Greece was $1.6\%^{24}$ and the mortality rate was 12.6 per 100,000 population on 20 November 2020.³ The 0.43% seroprevalence in a population of more than 50,000 HWCs and other hospital staff in Greece is lower than previously reported results among 1495 HCWs in two hospitals in Greece (1.07%) during April–May 2020.²⁵ The present study was performed during a period when there was no wide circulation of the virus in Greece, and this could serve as a possible explanation for the very low seroprevalence. In accordance with our results, general Greek population data, as well as recent studies evaluating different populations, also showed low seroprevalence rates for SARS-CoV-2 infection. In particular, Bogogiannidou et al.²² found an even lower seroprevalence (0.25% during April 2020) than our estimation using a non-random and convenience sample from the general population. Moreover, preliminary results for June 2020 from the same study have shown an even lower seroprevalence (0.17%, personal communication). Two studies, one in London²⁶ and one in Stockholm,²⁷ confirm this finding, indicating that the HCW population is at increased risk of being exposed and acquiring SARS-CoV-2 infection. In contrast, the

Table 1

Demographic data for 57,418 healthcare workers voluntarily tested for SARS-CoV-2 antibodies in Greece.

Characteristic	Seropositive for SARS-CoV-2 antibodies? [n/N (%)]			
	No	Yes		
Total	57,039/57,418 (99.34)	379/57,418 (0.66)		
Sex				
Male	14,594/14,700 (99.3)	106/14,700 (0.7)		
Female	40,627/40,866 (99.4)	239/40,866 (0.6)		
Age group (years) ^a				
18-39	12,879/12,957 (99.4)	78/12,957 (0.6)		
40-49	17,734/17,838 (99.4)	104/17,838 (0.6)		
50-59	18,375/18,511 (99.3)	136/18,511 (0.7)		
≥ 60	4511/4534 (99.5)	23/4534 (0.5)		
Healthcare facility				
Hospital	40,716/41,007 (99.3)	291/41,007 (0.7)		
Reference hospital for COVID-19	9001/9060 (99.3)	59/9060 (0.7)		
Primary care centre	7322/7351 (99.6)	29/7351 (0.4)		
Job role	, 522, , 551 (5515)	20,7001 (011)		
Physician	12,951/13,043 (99.3)	92/13,043 (0.7)		
Nurse	11,181/11,262 (99.3)	81/11,262 (0.7)		
Administrative.	10,285/10,362 (99.3)	77/10,362 (0.7)		
cleaning and security staff		,		
Laboratory staff	16,060/16,140 (99.5)	80/16,140 (0.5)		
District				
Attica	18,606/18,754 (99.2)	148/18,754 (0.8)		
Eastern Macedonia and Thrace	2000/2012 (99.4)	12/2012 (0.6)		
Central Macedonia	12,167/12,231 (99.5)	64/12,231 (0.5)		
Western Macedonia	1824/1854 (98.4)	30/1854 (1.6)		
Epirus	4321/4360 (99.1)	39/4360 (0.9)		
Thessaly	3579/3592 (99.6)	13/3592 (0.4)		
Western Greece	2320/2332 (99.5)	12/2332 (0.5)		
Central Greece	1686/1691 (99.7)	5/1691 (0.3)		
Peloponnese	2651/2666 (99.4)	15/2666 (0.6)		
Crete	4733/4751 (99.6)	18/4751 (0.4)		
Ionian	428/428 (100.0)	0/428 (0.0)		
Aegean	1355/1357 (99.9)	2/1355 (0.1)		

^a Mean (standard deviation).

seroprevalence among the personnel and students of the most highly populated university in Greece (National and Kapodistrian University of Athens) was higher (0.93% during June and July 2020) than our estimation.²⁸ This higher seroprevalence might be explained due to the fact that a significant proportion of University personnel are HCWs at COVID-19 reference hospitals, thus representing a high-risk group for SARS-CoV-2 exposure and infection, especially during the first months of the COVID-19 pandemic when knowledge about the virus and appropriate infection control was limited (similar to experiences in other countries).²⁹ In addition, our study population included HCWs from in primary health centres, where seropositivity was lower than HCWs in hospitals.

Worldwide, a wide range of seropositivity has been reported among HCWs. Two meta-analyses^{30,31} found a 7% and 8.7% seroprevalence among HCWs worldwide. In particular, seroprevalence among HCWs in Europe (8.5%) was reportedly lower than HCWs in North America (12.7%) but higher than those in Africa (8.2%) and Asia (4%).³¹ These variabilities, besides the phase of the epidemic, may be attributed to different use of personal protective equipment among HCWs in different countries, different infection prevention and control measures, and different responses of healthcare systems to the COVID-19 pandemic.^{32–35} For example, appropriate training protocols for HWCs results in very low SARS-CoV-2 infection rates, even in highly affected areas, such as Wuhan, China.³⁶

According to our analysis, seropositivity was higher among HCWs in hospitals (both reference and non-reference hospitals for COVID-19) than in primary care centres during the first wave of

Table 2

Bivariate and multivariable logistic regression analysis with seropositivity as the dependent variable (reference category; seropositivity: no).

Variable	Odds ratio (95% confidence	P-value for multivariable model		
	Bivariate	Multivariable		
Sex				
Male	1.24 (0.98-1.55)	1.27 (0.98-1.65)	0.08	
Female	1 [Reference]	1 [Reference]		
Age group (years) ^a				
18-39	1.19 (0.75-1.89)	1.11 (0.67-1.84)	0.68	
40-49	1.15 (0.73-1.81)	1.30 (0.80-2.10)	0.29	
50-59	1.45 (0.93-2.26)	1.51 (0.93-2.43)	0.09	
≥60	1 [Reference]	1 [Reference]		
Healthcare facility				
Hospital	1.81 (1.23-2.64)	1.72 (1.13-2.64)	0.01	
Reference hospital for COVID-19	1.66 (1.06-2.58)	1.34 (0.76-2.37)	0.31	
Primary care centre	1 [Reference]	1 [Reference]		
Job role				
Physician	1.43 (1.06-1.93)	1.31 (0.94-1.83)	0.11	
Nurse	1.45 (1.07-1.98)	1.42 (1.02-1.97)	0.04	
Administrative, cleaning and security staff	1.50 (1.10-2.06)	1.51 (1.09-2.08)	0.01	
Laboratory staff	1 [Reference]	1 [Reference]		
District				
Attica	5.39 (1.33-21.77)	5.19 (1.28-21.02)	0.02	
Eastern Macedonia and Thrace	4.07 (0.91-18.19)	3.59 (0.79-16.25)	0.09	
Central Macedonia	3.56 (0.87-14.58)	3.18 (0.78-13.04)	0.11	
Western Macedonia	11.14 (2.66-46.71)	11.97 (2.85-50.24)	0.001	
Epirus	6.12 (1.48-25.36)	3.01 (0.69-13.05)	0.14	
Thessaly	2.46 (0.56-10.92)	1.36 (0.25-7.44)	0.72	
Western Greece	3.50 (0.78-15.68)	3.04 (0.67-13.73)	0.15	
Central Greece	2.01 (0.39-10.37)	2.09 (0.40-10.84)	0.38	
Peloponnese	3.83 (0.88-16.79)	3.06 (0.65-14.44)	0.16	
Crete	2.58 (0.60-11.12)	2.29 (0.52-10.13)	0.27	
Ionian	NC	NC	NC	
Aegean	1 [Reference]	1 [Reference]		

NC, non-computable.

^a P for trend test = 0.43.

COVID-19 pandemic in Greece, a finding that has been observed in other studies.^{25,37–39} This is indicative of erroneous use of personal protective equipment and has important implications for infection control policies, including training in hospitals at early phases of local epidemics or between phases. Such policies could decrease the risk of SARS-CoV-2 infection.^{37–39} Strict infection control measures in COVID-19 units are especially important. Several studies^{26,27,40} reported that the prevalence of SARS-CoV-2 antibodies was higher among HCWs working in COVID-19 units because HCWs in these settings have a higher exposure risk. In addition, patient-related work is an important factor associated

with seropositivity among HCWs, even in non-COVID-19 units.^{26,27,40} It is possible that HCWs in non-reference hospitals for COVID-19 feel safer and demonstrate lower compliance to prevention and control measures in general (e.g. poor hand hygiene and inappropriate use of personal protective equipment).

In our study, seropositivity was higher among nurses, whereas Plebani et al.⁴¹ and Rudberg et al.²⁷ found that healthcare assistants were the occupational group with the highest seroprevalence. Nurses and healthcare assistants have a high exposure risk due to increased amounts of time with direct patient contact. In addition, administrative, cleaning and security staff were more likely to be

Table 3

Post hoc logistic regression analysis regarding multiple level variables with seropositivity as the dependent variable (reference category; seropositivity: no).

Variable	Odds ratio (95% confidence interval)	P-value	
Age group (years)			
18–39 vs 40–49	1.03 (0.77-1.39)	0.83	
18-39 vs 50-59	0.82 (0.62-1.08)	0.16	
$18-39 \text{ vs} \ge 60$	1.19 (0.75–1.89)	0.47	
40-49 vs 50-59	0.79 (0.61–1.02)	0.08	
$40-49 \text{ vs} \ge 60$	1.15 (0.73–1.81)	0.55	
$50-59 \text{ vs} \ge 60$	1.45 (0.93-2.26)	0.10	
Health care facility			
Hospital vs reference hospital for COVID-19	1.09 (0.82–1.44)	0.55	
Hospitals vs primary care centre	1.81 (1.23-2.64)	0.002	
Reference hospital for COVID-19 vs primary care centre	1.66 (1.06-2.58)	0.03	
Job role			
Physicians vs nurses	0.98 (0.73-1.32)	0.89	
Physicians vs administrative, cleaning and security staff	0.95 (0.70-1.29)	0.74	
Physicians vs laboratory staff	1.43 (1.06–1.93)	0.02	
Nurses vs administrative, cleaning and security staff	0.97 (0.71–1.32)	0.97	
Nurses vs laboratory staff	1.45 (1.07-1.98)	0.02	
Administrative, cleaning and security staff vs laboratory staff	1.50 (1.09-2.06)	0.01	

Prevalence of antibodies to SARS-CoV-2 among healthcare workers in Greece by regional unit	Prevalence of antibodies to 2	SARS-CoV-2 among	healthcare workers	in Greece	by regional un	it.
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Regional Unit	Total	Athens	Piraeus	Drama	Kavala	Rodopi	Evros	Thessaloniki	Imathia
n/N	379/57418	138/17323	10/1431	4/559	3/694	3/496	2/210	48/8347	3/824
Crude prevalence	0.66	0.80	0.70	0.72	0.43	0.6	0.95	0.58	0.36
(95% CI)	(0.59 - 0.73)	(0.67 - 0.94)	(0.34 - 1.28)	(0.2 - 1.82)	(0.09 - 1.26)	(0.12 - 1.76)	(0.12 - 3.4)	(0.42 - 0.76)	(0.08 - 1.06)
Adj. prev. 1	0.26	0.40	0.30	0.32	0.03	0.21	0.55	0.18	Ò
(95% CI)	(0.20 - 0.33)	(0.27 - 0.54)	(0 - 0.88)	(0-1.43)	(0 - 0.86)	(0 - 1.36)	(0 - 3.01)	(0.02 - 0.36)	(0 - 0.66)
Adj. prev. 2	0.43	0.59	0.48	0.5	0.16	0.36	0.78	0.33	0.08
(95% CI)	(0.35-0.51)	(0.44 - 0.77)	(0.04 - 1.17)	(0-1.82)	(0-1.14)	(0-1.74)	(0-3.7)	(0.15-0.55)	(0-0.91)
Regional Unit	Kilkis	Pella	Pieria	Chalkidiki	Kozani	Kastoria	Arta	Thesprotia	loannina
n/N	2/593	5/949	4/737	2/438	11/640	19/351	10/785	1/338	23/2830
Crude prevalence	0.34	0.53	0.54	0.46	1.72	5.41	1.27	0.3	0.81
(95% CI)	(0.04 - 1.21)	(0.17 - 1.23)	(0.15 - 1.38)	(0.06 - 1.64)	(0.86 - 3.05)	(3.29-8.32)	(0.61 - 2.33)	(0.01 - 1.64)	(0.52 - 1.22)
Adj. prev. 1	0	0.13	0.14	0.06	1.32	5.03	0.88	0	0.41
(95% CI)	(0 - 0.82)	(0-0.83)	(0-0.99)	(0-1.24)	(0.46 - 2.67)	(2.9 - 7.96)	(0.21 - 1.94)	(0-1.24)	(0.12 - 0.82)
Adj. prev. 2	0.04	0.27	0.29	0.19	1.70	6.11	1.16	0	0.61
(95% CI)	(0-1.09)	(0-1.11)	(0-1.29)	(0-1.6)	(0.67 - 3.29)	(3.57-9.59)	(0.37-2.43)	(0-1.6)	(0.26-1.1)
Regional Unit	Preveza	Karditsa	Larissa	Magnissia	Achaia	Ilia	Viotia	Evia	Fthiotida
n/N	5/407	1/225	9/1743	3/802	7/1600	5/732	2/485	2/575	1/426
Crude prevalence	1.23	0.44	0.52	0.37	0.44	0.68	0.41	0.35	0.23
(95% CI)	(0.4 - 2.84)	(0.01 - 2.45)	(0.24 - 0.98)	(0.08 - 1.09)	(0.18 - 0.9)	(0.22 - 1.59)	(0.05 - 1.48)	(0.04 - 1.25)	(0.01 - 1.3)
Adj. prev. 1	0.83	0.04	0.12	0	0.04	0.28	0.01	0	0
(95% CI)	(0-2.45)	(0-2.06)	(0-0.58)	(0-0.69)	(0-0.5)	(0-1.19)	(0-1.09)	(0-0.85)	(0-0.9)
Adi prov 2									
Adj. prev. 2	1.11	0.17	0.26	0.09	0.16	0.46	0.13	0.06	0
Adj. prev. 2 (95% CI)	1.11 (0.12–3.04)	0.17 (0–2.57)	0.26 (0-0.81)	0.09 (0-0.94)	0.16 (0-0.72)	0.46 (0-1.54)	0.13 (0–1.41)	0.06 (0-1.14)	0 (0–1.2)
51									0
(95% CI)	(0.12-3.04)	(0-2.57)	(0-0.81)	(0-0.94)	(0-0.72)	(0-1.54)	(0-1.41)	(0-1.14)	(0-1.2)
(95% CI) Regional Unit	(0.12-3.04) Argolida	(0-2.57) Korinthia	(0-0.81) Lakonia	(0-0.94) Messinia	(0-0.72) Iraklio	(0–1.54) Lassithi	(0-1.41) Rethymno	(0-1.14) Chania	(0–1.2) Aigaio
(95% CI) Regional Unit n/N	(0.12–3.04) Argolida 3/695	(0–2.57) Korinthia 3/516	(0-0.81) Lakonia 2/534	(0-0.94) Messinia 7/921	(0-0.72) Iraklio 5/2634	(0–1.54) Lassithi 1/705	(0–1.41) Rethymno 3/422	(0-1.14) Chania 9/990	(0–1.2) Aigaio 2/1357
(95% CI) Regional Unit n/N Crude prevalence	(0.12–3.04) Argolida 3/695 0.43	(0–2.57) Korinthia 3/516 0.58	(0–0.81) Lakonia 2/534 0.37	(0–0.94) Messinia 7/921 0.76	(0–0.72) Iraklio 5/2634 0.19	(0–1.54) Lassithi 1/705 0.14	(0–1.41) Rethymno 3/422 0.71	(0-1.14) Chania 9/990 0.91	(0–1.2) Aigaio 2/1357 0.15
(95% CI) Regional Unit n/N Crude prevalence (95% CI)	(0.12-3.04) Argolida 3/695 0.43 (0.09-1.26)	(0-2.57) Korinthia 3/516 0.58 (0.12-1.69)	(0-0.81) Lakonia 2/534 0.37 (0.05-1.35)	(0-0.94) Messinia 7/921 0.76 (0.31-1.56)	(0-0.72) Iraklio 5/2634 0.19 (0.06-0.44)	(0–1.54) Lassithi 1/705 0.14 (0–0.79)	(0-1.41) Rethymno 3/422 0.71 (0.15-2.06)	(0-1.14) Chania 9/990 0.91 (0.42-1.72)	(0-1.2) Aigaio 2/1357 0.15 (0.02-0.53)
(95% CI) Regional Unit n/N Crude prevalence (95% CI) Adj. prev. 1	(0.12-3.04) Argolida 3/695 0.43 (0.09-1.26) 0.03	(0–2.57) Korinthia 3/516 0.58 (0.12–1.69) 0.18	(0-0.81) Lakonia 2/534 0.37 (0.05-1.35) 0	(0-0.94) Messinia 7/921 0.76 (0.31-1.56) 0.36	(0-0.72) Iraklio 5/2634 0.19 (0.06-0.44) 0	(0-1.54) Lassithi 1/705 0.14 (0-0.79) 0	(0-1.41) Rethymno 3/422 0.71 (0.15-2.06) 0.31	(0-1.14) Chania 9/990 0.91 (0.42-1.72) 0.51	(0–1.2) Aigaio 2/1357 0.15 (0.02–0.53) 0

Adj. prev. 1: adjusted prevalence according to the manufacturer's specification (Se = 100%; Sp = 99.6%).

Adj. prev. 2: adjusted prevalence according to Bogogiannidou et al.²² (Se = 84%; Sp = 99.7%).

Values are expressed as percentages.

CI, confidence interval.

seropositive than HCWs in primary care centres. Administrative, cleaning and security workers have close contact with patients in healthcare facilities, and it is likely that these workers do not apply the appropriate measures of hygiene (e.g. use mask, gloves) because they are not well trained, especially in case of the COVID-19 pandemic.

Regarding geographical distribution of SARS-CoV-2 antibodies in HCWs in Greece, seroprevalence was higher than the overall seroprevalence of 0.43% in 13 of the 74 regional units, with the highest being in Kastoria (6.11%). Kastoria was one of the first hotspots for SARS-CoV-2 virus infection in the country, after introduction of the infection from visitors coming from the Northern Italy epidemic and working in the local fur industry. In addition, seroprevalence was reasonably higher than the overall seroprevalence only in one district (Western Macedonia) and reasonably lower in the Greek islands.

Limitations of this study include the voluntary testing; thus, a selection bias is possible, especially with regard to female HCWs. Nevertheless, only a statistical trend was identified for male gender. It is well known that the virus is associated with more severe disease in males, thus one would expect a higher seroprevalence in men. In addition, we investigated only four potential factors as predictors for positive antibody test, while the cross-sectional nature of the study did not allow for causal inferences. Furthermore, we lacked information on history of infection or symptoms consistent with a SARS-CoV-2 infection or history of contact with a positive case within the household or elsewhere outside the hospital. Case ascertainment may not be a big issue in seroprevalence

studies targeting HCWs, as this population has better access to, and lower clinical thresholds for, laboratory testing for virus presence. The proportion of asymptomatic individuals within the HCW population is largely unknown but is not expected to differ from rates reported from large community studies.⁴² Repeated serology surveys in HCWs would greatly enhance knowledge on transmission dynamics in this vulnerable population, as well as the potential contribution of asymptomatic cases. The specific environment where HCWs work inside the hospital is another potential important factor that may contribute to an increased risk of infection (e.g. HCW working in the Emergency Room or in a designated COVID-19 reference centre or being involved in direct patient care). Information on consistent use of personal protective measures is another important parameter associated with seropositivity to the novel coronavirus²⁹ that was not systematically collected during this study.

In conclusion, the very low prevalence of SARS-CoV-2 antibodies in the present study likely reflects the timely implementation of social distancing measures during the first phase of the COVID-19 pandemic in Greece.⁴³ The swift adoption of a range of measures had a significant impact on the low prevalence of the disease among HCWs, as well as the general population in Greece. The containment measures managed to 'flatten the curve' in a timely manner and therefore minimised exposure risk, severe illness rates and mortality rates for the entire population, including HCWs. Moreover, decision-makers should pay attention to high-risk HCWs who may be impacted by COVID-19 (e.g. HCWs in hospitals, nurses, physicians). Identification of high-risk HCWs is necessary to apply

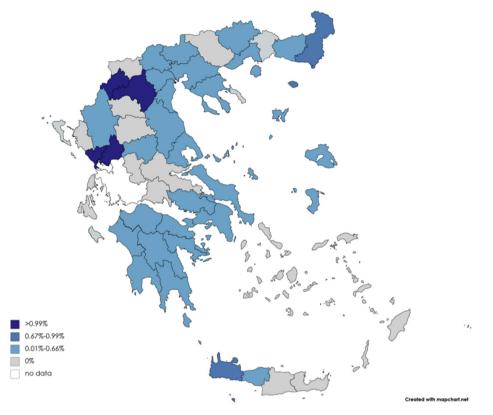


Fig. 1. Geographical distribution of SARS-CoV-2 antibodies in healthcare workers in Greece. Adjusted prevalences according to Bogogiannidou et al.²² are shown.

the appropriate measures, such as extra personal protective equipment, prioritisation for COVID-19 vaccination and appropriate training.

Author statements

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Ethical approval

The study was performed at the request of the Hellenic Prefectural Health authorities. The Greek National Committee of Public Health against COVID-19 approved the study design (reference number; 44, 27-04-2020) and the Greek Ministry of Health institutional review board approved the use of the database (reference number; 894, 2020).

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Competing interests

None to declare.

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