



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

SARS-CoV-2 seroprevalence among 7950 healthcare workers in the Region of Southern Denmark

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ARTICLE INFO

Article history:

Received 3 May 2021

Revised 6 September 2021

Accepted 13 September 2021

Keywords:

SARS-CoV-2

COVID-19

Healthcare workers

Seroprevalence

Antibodies

Epidemiology

ABSTRACT

Objective: Healthcare workers (HCWs) carry a pronounced risk of acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The aim of this study was to determine the seroprevalence and potential risk factors of SARS-CoV-2 infection among HCWs in the Region of Southern Denmark after the first pandemic wave in the spring of 2020.

Methods: This was an observational study conducted between May and June 2020. SARS-CoV-2 IgG and IgM antibodies were measured in plasma. Participants were asked to complete a questionnaire consisting of demographic information, risk factors, and COVID-19-related symptoms.

Results: A total of 7950 HCWs participated. The seroprevalence of SARS-CoV-2 antibodies was 2.1% (95% confidence interval (CI) 1.8–2.4%). Seropositive participants were significantly older (mean age 48.9 years vs 46.7 years in seronegative participants, $P = 0.022$) and a higher percentage had experienced at least one symptom of COVID-19 ($P < 0.001$). The seroprevalence was significantly higher among HCWs working on dedicated COVID-19 wards (3.5%; OR 2.02, 95% CI 1.44–2.84). Seroprevalence was significantly related to 11–50 close physical contacts per day outside work (OR 1.54, 95% CI 1.07–2.22).

Conclusions: The prevalence of SARS-CoV-2 antibodies was low in HCWs. However, the occupational risk of contracting the infection was found to be higher for those working on dedicated COVID-19 wards. Further, the results imply that attention should be paid to occupational risk factors in planning pandemic preparedness.

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1. Introduction

Coronavirus disease 2019 (COVID-19) surged as an ongoing worldwide pandemic throughout 2020 (Park et al., 2020; Siorchia, 2020). The first Danish cases were reported in late February 2020, and the initial spread of infection most likely originated from ski tourists returning from Northern Italy and Austria (Madsen et al., 2021). The first epidemic wave in Denmark peaked in late March and early April, with 9.2 patients admitted to hospital per 100 000 population (Madsen et al., 2021; Statens Serum Institut 2021).

Several studies have demonstrated that healthcare workers (HCWs) have a significantly increased risk of contracting COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Galanis et al., 2021; Gomez-Ochoa et al., 2021). Current knowledge suggests that working as a healthcare professional poses an occupational risk of infection, and further raises concern about the occupational safety of HCWs. Previous studies have demonstrated a moderate-to-high risk of COVID-19 among HCWs throughout the world, including Italy (Felice et al., 2020), Spain (Suarez-Garcia et al., 2020), the Netherlands (Sikkema et al., 2020), Belgium (Schoy et al., 2021), Sweden (Rudberg et al., 2020), Norway (Molvik et al., 2021), Switzerland (Piccoli et al., 2021), France (Davido et al., 2021), Brazil (Toniasso et al., 2021), the USA (Barrett et al., 2020), and the UK (Nguyen et al., 2020). Furthermore, HCWs have been found to have a higher prevalence of antibodies against SARS-CoV-2 compared to the general population (Galanis et al., 2021; Gomez-Ochoa et al., 2021). Previous studies from Denmark found seroprevalence rates of SARS-CoV-2 among HCWs ranging from 3.4% to 4.04% (Iversen et al., 2020; Jespersen et al., 2020).

In general, the highest seroprevalence rates among HCWs are found in countries and regions with widespread community infection and large numbers of COVID-19 patients admitted to the hospital (Barrett et al., 2020; Nguyen et al., 2020; Rudberg et al., 2020). Further, it has been demonstrated that disease severity and mortality among HCWs is generally lower than among patients (Sahu et al., 2020). Compared to other professions, HCWs face a challenging task of wearing correct protective equipment while having close contact with COVID-19 patients, and are often working in limited workspaces in close contact with colleagues (Agius et al., 2020).

Knowledge of the SARS-CoV-2 seroprevalence among HCWs is important in order to determine the occupational risk and to understand and prevent the spread of SARS-CoV-2 in healthcare facilities, including hospitals. It is not known to what extent HCWs acquire SARS-CoV-2 from contacts outside the hospital, and subsequently introduce SARS-CoV-2 to the wards, giving rise to in-hospital spread to patients and between colleagues. Due to the nature of COVID-19, including the risk of serious illness and debilitating long-term sequelae, it is important to continue monitoring the prevalence among HCWs.

In this study, information was specifically collected on general risk factors that are known to pose a risk of contracting COVID-19 (Elmore et al., 2020). Further, the aim was to describe the prevalence of SARS-CoV-2 antibodies and potential risk markers for seroconversion among HCWs and administrative staff, with special focus on travel history, the extent of social contacts, and other potential risk behaviours.

2. Methods

2.1. Study design

The Region of Southern Denmark covers approximately 12 000 km² and is inhabited by 1.2 million people (Region of South-

ern Denmark 2021). The Region is administratively responsible for healthcare services and runs 13 somatic hospitals and 12 psychiatric hospitals (Region of Southern Denmark 2021). HCWs and administrative staff in the Region of Southern Denmark ($n = 30\,490$ at the present time) were invited to participate in the study on a voluntary basis. HCWs and administrative staff included staff employed in somatic and psychiatric wards, prehospital staff, and staff employed in general practice. The project was announced on the local intranets, and invitations to participate were sent online to the employee's state-provided personal and password-protected e-mail system (e-Boks). Invitations were sent out in May 2020, and participants were allowed to accept participation until June 2020. All participants were asked to fill out a corresponding questionnaire, as described below. All employees were offered serological testing, regardless of their participation in the questionnaire.

The project was registered with the Danish Data Protection Authorities (Ref. No. 20/20627). The Regional Committees on Health Research Ethics for the Region of Southern Denmark evaluated the project and found that further registration and ethical permission was not necessary.

The study was initiated by a group of senior scientists and supported by the national organization Danske Regioner ("Danish Regions").

2.2. Serological testing

Blood sampling was performed at the local hospital laboratory in designated ethylenediaminetetraacetic acid (EDTA) blood collection tubes. SARS-CoV-2 IgG and IgM were measured in plasma with the lateral flow assay Livzon IgM/IgG LFT – Diagnostic Kit for IgM/IgG Antibody to Corona Virus (Zhuhai Livzon Diagnostics, Inc., Zhuhai, China). The test is CE-IVD approved, and uses a colloidal gold immunochromatography technology to detect either IgM or IgG SARS-CoV-2 antibodies. The assay was performed according to the manufacturer's instructions, as described by Nilsson et al. (Nilsson et al., 2021). The result of the assay was read by visual inspection by trained laboratory personnel 15 minutes after application of the test material (one observer per test, but tests were performed by multiple laboratory technicians). Only tests in which the control line was visible were regarded as valid. If the control line was not visible, the test was repeated. If no control line was visible when the test was repeated, the test was considered negative. If a line for IgM and/or IgG was observed, the test was defined as positive for that isotype of antibody.

Two batch numbers (CK2004150410 and CK2003100410) were used for the study. The batches were validated using a test panel of 600 blood donor samples from February 2018 and February 2019 (negative controls) and 150 samples from patients who had previously tested PCR-positive for SARS-CoV-2 (positive controls). The sensitivity was 77.3% for batch CK2004150410 and 78% for batch CK2003100410, and the specificity was 99.3% for CK2004150410 and 98.7% for CK2003100410.

Data on seroprevalence in healthy blood donors inhabiting the same geographical area as the study participants (Region of Southern Denmark) were used in order to compare the results with the general population, as described by Erikstrup et al. (Erikstrup et al., 2021) and further personal communication with the authors.

2.3. Questionnaire

All participants were asked to complete an online questionnaire in Danish on a secured platform. The questionnaire contained questions regarding employment data, demographics, information on chronic illness, travel history, and symptoms of infection. The questionnaire was designed by the author group, with inspiration from the questionnaire applied by Iversen et al. (Iversen et al.,

Table 1
Baseline characteristics of the study participants.

	Seronegative, n (%)	Seropositive, n (%)	OR (95% CI)	P-value
Total	7784 (97.8%)	166 (2.1%)		
Age (years), mean ± SD	46.7 ± 11.9	48.9 ± 11.9	1.016 (1.002; 1.029)	0.022
Sex				
Female	6803 (98.0%)	142 (2.0%)	1.00 (Ref.)	0.477
Male	981 (97.6%)	24 (2.4%)	1.17 (0.76; 1.82)	
Body mass index (kg/m ²)				
<25	4137 (98.2%)	74 (1.8%)	1.00 (Ref.)	0.078
25–30	2290 (97.4%)	61 (2.6%)	1.49 (1.06; 2.10)	
≥30	1255 (97.9%)	27 (2.1%)	1.20 (0.77; 1.88)	
PCR tested for SARS-CoV-2	1511 (95.2%)	76 (4.8%)	3.61 (2.64; 4.94)	<0.001
≥1 symptom of COVID-19	5419 (97.4%)	143 (2.6%)	2.71 (1.74; 4.23)	<0.001
No symptoms	2271 (99.1%)	20 (0.9%)	0.33 (0.21; 0.53)	<0.001
Professional group				
Administrative staff	1058 (97.9%)	23 (2.1%)	1.00 (Ref.)	
Assisting nurse	435 (97.3%)	12 (2.7%)	1.27 (0.63; 2.57)	0.509
Laboratory technician	516 (99.0%)	5 (1.0%)	0.45 (0.17; 1.18)	0.104
Logistics staff	253 (96.6%)	9 (3.4%)	1.64 (0.75; 3.58)	0.218
Medical doctor	950 (97.4%)	25 (2.6%)	1.21 (0.68; 2.15)	0.513
Medical student	100 (100.0%)	0 (0.0%)	-	-
Nurse	2845 (97.6%)	69 (2.4%)	1.12 (0.69; 1.80)	0.653
Nursing student	107 (100.0%)	0 (0.0%)	-	-
Other staff with patient contact	740 (98.7%)	10 (1.3%)	0.62 (0.29; 1.31)	0.213
Other staff without patient contact	599 (98.2%)	11 (1.8%)	0.84 (0.41; 1.74)	0.649
PhD student	31 (100.0%)	0 (0.0%)	-	-
Prehospital staff	70 (100.0%)	0 (0.0%)	-	-

OR, odds ratio; CI, confidence interval; SD, standard deviation.

2020), and was based on known risk factors for COVID-19 and other viral diseases. The questionnaire was proofread by both laymen and HCWs not involved in the study. The complete questionnaire in Danish and translated into English is available in the **Supplementary Material**.

2.4. Data handling and statistical analyses

The online questionnaires were archived on a secured online REDCap-based system provided by OPEN (Open Patient Data Explorative Network) (Harris et al., 2019; Harris et al., 2009). Serological data were merged with questionnaire data through the participants' social security numbers. Anonymized data were extracted by a dedicated data manager, who was not involved in the analysis and interpretation of the results.

The outcome investigated was seroprevalence reported as counts and proportions with exact binomial 95% confidence intervals (CI). The overall seroprevalence estimates were adjusted to mean test sensitivity and specificity of the two batches using the method suggested by Rogan and Gladen (Rogan and Gladen, 1978), and reported with Wald confidence intervals.

Associations with possible risk factors were investigated by univariate logistic regression, reporting the odds ratios (OR) with 95% CI and *P*-values for absence of association.

All analyses were performed in Stata 16.1. *P*-values below 0.05 were considered statistically significant.

3. Results

3.1. Characteristics of the study participants

In May 2020, all HCWs and administrative staff employed by the Region of Southern Denmark were invited to participate in the study. A total of 20 510 persons provided blood for serological testing. Of these, 7950 (38.8%) provided questionnaire data. Only individuals with both serological and questionnaire data were included in the study.

The mean age of the participants was 46.7 years (standard deviation 11.9 years, range 18–76 years); 87.4% were female and

12.6% were male (Table 1). Participants were from all professional groups, both with and without direct patient contact, and included 37% nurses, 12% medical doctors, 13% administrative staff, etc. (Table 1). No significant differences between the different professional groups were found regarding seropositivity.

3.2. Prevalence of SARS-CoV-2 antibodies

In total, 166 (2.1%, 95% CI 1.8–2.4%) participants were found to have antibodies (either IgG, IgM, or IgG and IgM) against SARS-CoV-2. Adjusting for sensitivity and specificity of the applied antibody test, this prevalence corresponds to an estimated true-positive rate of 1.4% (95% CI 1.0–1.8%). Of the 166 positive samples, 143 (86.1%) were IgG-positive, 111 (66.7%) were IgM-positive, and 88 (53.0%) were both IgG and IgM-positive. There were no inconclusive test results.

The baseline characteristics stratified by antibody response are shown in Table 1. The seropositive participants were significantly older (mean age 48.9 years vs 46.7 years in seronegative participants). There was no significant difference according to sex (*P* = 0.477) or body mass index between the two groups (*P* = 0.078). Among the seropositive participants, a higher percentage had been PCR tested for SARS-CoV-2 when compared to seronegative participants.

3.3. Self-reported symptoms

The association between self-reported symptoms and SARS-CoV-2 seroprevalence is reported in Table 1 and shown in detail, including all reported symptoms, in **Supplementary Material** Table S1. Displaying at least one symptom of COVID-19 significantly increased the odds of having SARS-CoV-2 antibodies (OR 2.71, 95% CI 1.74–4.23).

Nearly all symptoms were significantly associated with an increased OR for SARS-CoV-2 seropositivity, except nasal discharge or congestion, sore throat, conjunctivitis, and abdominal pain. The most pronounced symptoms were found to be loss of taste or smell (OR 15.22, 95% CI 10.73–21.58, *P* < 0.001) and loss of appetite (OR 9.27, 95% CI 6.38–13.47, *P* < 0.001). Further, fever (OR 6.02, 95% CI

Table 2
Frequencies of positive antibody tests stratified according to type of work

	Seronegative, n (%)	Seropositive, n (%)	OR (95% CI)	P-value
Work without direct patient contact	1658 (97.8%)	37 (2.2%)	1.00 (Ref.)	0.750
Work involving direct patient contact	6044 (97.9%)	127 (2.1%)	0.94 (0.65; 1.36)	
Does not work on dedicated COVID-19 wards	3393 (96.7%)	116 (3.3%)	1.00 (Ref.)	<0.001
Work on dedicated COVID-19 wards	1309 (96.5%)	48 (3.5%)	2.02 (1.44; 2.84)	
Does not work in COVID-19 testing facilities	6393 (98.2%)	116 (1.8%)	1.00 (Ref.)	0.697
Work in COVID-19 testing facilities	284 (97.6%)	7 (2.4%)	1.16 (0.54; 2.51)	

OR, odds ratio; CI, confidence interval.

4.40–8.23, $P < 0.001$), chills (OR 5.34, 95% CI 3.72–7.68, $P < 0.001$), chest pain (OR 4.59, 95% CI 2.88–7.31, $P < 0.001$), coughing (OR 3.67, 95% CI 2.69–4.99, $P < 0.001$), and shortness of breath (OR 3.47, 95% CI 2.29–5.27, $P < 0.001$) were strongly associated with SARS-CoV-2 seropositivity. Reporting no symptoms was associated with a decreased OR of 0.33 (95% CI 0.21–0.53, $P < 0.001$). Just over twelve percent (12.3%, 20/163) of the participants with SARS-CoV-2 antibodies reported no symptoms prior to testing.

3.4. Reported type of work and occupational COVID-19 exposure

Table 2 describes the frequencies of positive antibody tests according to self-reported type of work, including work with direct patient contact. It was found that working on dedicated COVID-19 wards was associated with a significantly increased risk of being seropositive when compared to those who did not work on dedicated wards (OR 2.02, 95% CI 1.44–2.84, $P < 0.001$).

3.5. Number of close physical contacts, travel history, and work from home

Self-reported potential work-related and personal risk factors for COVID-19 are shown in Table 3. Seroprevalence was only significantly related to 11–50 close physical contacts outside work per day (OR 1.54, 95% CI 1.07–2.22, $P = 0.021$), suggesting that crowding and multiple close contacts increase the risk of COVID-19. No association was found between working from home and a decreased prevalence of SARS-CoV-2 antibodies. Furthermore, the data do not support a history of travel during the first months of 2020, prior to the first pandemic wave and corresponding lockdown, either within or outside Europe, as being associated with an increased risk of COVID-19 (Table 3).

3.6. Geographical influence of SARS-CoV-2 seroprevalence

The geographical workplace and residence of participants are shown in Table 3. It was found that working in Southern Jutland significantly decreased the risk of SARS-CoV-2 seropositivity (OR 0.37, 95% CI 0.17–0.81, $P = 0.013$) when compared to working on the island of Funen (two hospitals; Odense University Hospital Odense and Svendborg). None of the other geographical workplaces included in this study were associated with an increased or decreased risk.

The area of residence of the participants did not seem to influence the risk of SARS-CoV-2 seropositivity.

The seroprevalence at the different hospital sites is shown in **Supplementary Material** Table S2. The seroprevalence rates in the larger hospitals (Odense University Hospital, Hospital of South West Jutland, and Hospital of Lillebælt) were comparable, ranging from 2.1% to 2.8%. The SARS-CoV-2 seroprevalence in psychiatric departments was comparable to that in the larger somatic hospitals (2.4%). An overall low prevalence was found in Hospital Sønderjylland (0.4%), among general and specialist practitioners (0.0% and 0.9%, respectively) and prehospital staff (1.3%).

3.7. Alcohol and tobacco consumption, chronic comorbidities, and SARS-CoV-2 seroprevalence

The associations between SARS-CoV-2 seroprevalence and self-reported chronic diseases are depicted in Table 4. No association was found between any chronic disease and SARS-CoV-2 seropositivity. Furthermore, alcohol and tobacco consumption did not seem to be associated with SARS-CoV-2 seropositivity.

4. Discussion

The purpose of this study was to investigate the prevalence of SARS-CoV-2 antibodies in HCWs in the Region of Southern Denmark after the first pandemic wave of COVID-19 in the spring of 2020, and to identify potential risk factors for infection. Among the 7950 participating HCWs, 2.1% (estimated true-positive rate adjusted to test sensitivity and specificity, 1.4%) were found to have SARS-CoV-2 antibodies. The study results suggest that working in dedicated COVID-19 wards poses an occupational risk of SARS-CoV-2 infection. In addition, the seropositive HCWs were significantly older. It was also found that having a larger number of physically close contacts outside work increased the odds of seropositivity. Furthermore, the study findings support those of previous studies regarding symptoms (Casella et al., 2021; Hu et al., 2021), suggesting that displaying one or more symptoms of COVID-19 increased the odds of seropositivity.

Participants who were PCR tested for SARS-CoV-2 were found to have increased odds of seropositivity. Unfortunately, the results of the PCR tests were not available, but in a setting with only limited access to PCR test for SARS-CoV-2, it was presumed that the participants had displayed symptoms of COVID-19.

The seroprevalence among HCWs and administrative staff in the Region of Southern Denmark in this study is lower than those found in the Capital Region and the Central Denmark Region, where the seroprevalence was 4.04% and 3.4%, respectively (Iversen et al., 2020; Jespersen et al., 2020). This might reflect the distribution of the epidemic in Denmark, as the Region of Southern Denmark experienced one of the lowest overall prevalence rates of COVID-19. Furthermore, as the total number of infected persons and individuals admitted to the hospital in the other regions was larger than that of the Region of Southern Denmark, the risk of infection among HCWs was higher in the other regions.

As described previously, the prevalence of SARS-CoV-2 antibodies among healthy blood donors in Denmark varied between different regions (Erikstrup et al., 2021), reflecting the overall regional variances in prevalence of COVID-19. In the Region of Southern Denmark during March and April 2020, the seroprevalence among blood donors was 1.74% (95% CI 0.43–2.16%), based on 4952 antibody tests. In the present study, it was found that the seroprevalence in HCWs and administrative staff was a little higher than in blood donors during the same period of time, which suggests that HCWs at the time were at increased risk of COVID-19 when compared to the general population. This finding has been con-

Table 3
Frequencies of positive antibody tests stratified according to exposure

	Seronegative, n (%)	Seropositive, n (%)	OR (95% CI)	P-value
Number of close physical contacts per day outside work				
<10	2515 (98.5%)	39 (1.5%)	1.00 (Ref.)	
11–50	4855 (97.7%)	116 (2.3%)	1.54 (1.07; 2.22)	0.021
51–100	309 (97.5%)	8 (2.5%)	1.67 (0.77; 3.61)	0.192
>100	36 (94.7%)	2 (5.3%)	3.58 (0.83; 15.40)	0.086
Working from home 4 weeks up to answered questionnaire				
No	6607 (97.8%)	146 (2.2%)	1.00 (Ref.)	
Yes, mainly	456 (98.9%)	5 (1.1%)	0.50 (0.20; 1.22)	0.125
Yes, partly	634 (98.1%)	12 (1.9%)	0.86 (0.47; 1.55)	0.609
Working from home in the period from mid-March to mid-April 2020				
No	6128 (97.8%)	135 (2.2%)	1.00 (Ref.)	
Yes, mainly	752 (98.7%)	10 (1.3%)	0.60 (0.32; 1.15)	0.126
Yes, partly	817 (97.8%)	18 (2.2%)	1.00 (0.61; 1.64)	1.000
Any travel history 2020				
No	5071 (98.0%)	102 (2.0%)	1.00 (Ref.)	
Yes	2713 (97.7%)	64 (2.3%)	1.17 (0.86; 1.61)	0.323
Any travel history 2020 (within Europe)				
No	5382 (98.0%)	110 (2.0%)	1.00 (Ref.)	
Yes	2402 (97.7%)	56 (2.3%)	1.14 (0.82; 1.58)	0.428
Travel history within 2020, but before serological testing				
Italy	138 (97.2%)	4 (2.8%)	1.37 (0.50; 3.74)	0.542
Austria	484 (98.2%)	9 (1.8%)	0.86 (0.44; 1.70)	0.674
Spain	308 (98.7%)	4 (1.3%)	0.60 (0.22; 1.63)	0.315
France	118 (99.2%)	1 (0.8%)	0.39 (0.05; 2.84)	0.355
Belgium	8 (80.0%)	2 (20.0%)	11.85 (2.50; 56.25)	0.002
Netherlands	42 (100.0%)	0 (0.0%)	-	-
Great Britain	88 (96.7%)	3 (3.3%)	1.61 (0.50; 5.14)	0.422
Other European countries	1575 (97.8%)	35 (2.2%)	1.05 (0.72; 1.54)	0.787
China	5 (100.0%)	0 (0.0%)	-	-
Iran	1 (100.0%)	0 (0.0%)	-	-
Asia (except China and Iran)	209 (98.6%)	3 (1.4%)	0.67 (0.21; 2.11)	0.490
Australia	20 (95.2%)	1 (4.8%)	2.35 (0.31; 17.63)	0.405
Africa	75 (97.4%)	2 (2.6%)	1.25 (0.31; 5.15)	0.754
North America	69 (100.0%)	0 (0.0%)	-	-
South America	27 (93.1%)	2 (6.9%)	3.50 (0.83; 14.86)	0.089
None of the above	5004 (98.0%)	101 (2.0%)	0.86 (0.63; 1.18)	0.360
Geographical workplace				
Funen	3484 (97.9%)	74 (2.1%)	1.00 (Ref.)	
Lillebælt	2152 (97.6%)	53 (2.4%)	1.16 (0.81; 1.66)	0.416
Southern Jutland	888 (99.2%)	7 (0.8%)	0.37 (0.17; 0.81)	0.013
South West Jutland	918 (97.2%)	26 (2.8%)	1.33 (0.85; 2.10)	0.213
Other	342 (98.3%)	6 (1.7%)	0.83 (0.36; 1.91)	0.655
Area of residence				
Funen	3621 (97.8%)	83 (2.2%)	1.00 (Ref.)	
South Jutland	3746 (98.1%)	73 (1.9%)	0.85 (0.62; 1.17)	0.317
Region Central Jutland	281 (97.9%)	6 (2.1%)	0.93 (0.40; 2.15)	0.868
Region Northern Jutland	3 (100.0%)	0 (0.0%)	-	-
Region Zealand	18 (100.0%)	0 (0.0%)	-	-
Capital Region	24 (92.3%)	2 (7.7%)	3.64 (0.85; 15.64)	0.083
Outside Denmark	25 (96.2%)	1 (3.8%)	1.75 (0.23; 13.03)	0.587
Unknown	66 (98.5%)	1 (1.5%)	0.66 (0.09; 4.82)	0.683

OR, odds ratio; CI, confidence interval.

firmed in other countries previously (Galanis et al., 2021; Gomez-Ochoa et al., 2021).

It is well established that HCWs are at greater risk of contracting SARS-CoV-2 infection when compared to the general population (Grant et al., 2021; Rudberg et al., 2020) and that HCWs are prone to the transmission of viral infection (Canova et al., 2020; McMichael et al., 2020; Ooi and Low, 2020; Oran and Topol, 2020; Ran et al., 2020; Riediker and Tsai, 2020; Sakurai et al., 2020; Wilson et al., 2020; Yu and Yang, 2020). Furthermore, it has been demonstrated that HCWs are prone to infection despite vaccination (Bergwerk et al., 2021) and are able to transmit SARS-CoV-2 despite correct usage of personal protective equipment (Klompas et al., 2021).

Previous studies have suggested that SARS-CoV-2 seropositivity is higher in HCWs performing patient-related work, in front-line HCWs, and in HCWs working on dedicated COVID-19 wards

(Grant et al., 2021; Iversen et al., 2020; Rudberg et al., 2020). The findings of the present study are in line with this observation; however, only a significantly increased risk for HCWs working on dedicated COVID-19 wards was observed, and no difference between HCWs with and without direct patient contact.

It is well established that asymptomatic carriers are able to spread infection (Ooi and Low, 2020; Rasmussen and Popescu, 2021). In an observational study from Canada, symptomatic SARS-CoV-2 infection in HCWs was found to be more common than asymptomatic, and only 0.50% of the asymptomatic participants were PCR-positive (Ferreira et al., 2021). In the present study, 12.3% of seropositive HCWs did not report any symptoms, highlighting that although asymptomatic infections are infrequent, they may cause outbreaks among both patients and co-workers.

The main reported symptoms in this study were mild and included fever, nasal congestion, lethargy, and headache. All reported

Table 4
Frequencies of positive antibody tests stratified according to self-reported chronic diseases, smoking and alcohol consumption

	Seronegative, n (%)	Seropositive, n (%)	OR (95% CI)	P-value
Self-reported chronic diseases				
Any chronic disease	1739 (97.9%)	37 (2.1%)	1.00 (0.69; 1.44)	0.987
Asthma	552 (97.9%)	12 (2.1%)	1.02 (0.56; 1.85)	0.946
Heart disease	117 (96.7%)	4 (3.3%)	1.62 (0.59; 4.44)	0.350
Hypertension	846 (98.0%)	17 (2.0%)	0.94 (0.56; 1.55)	0.797
COPD	61 (95.3%)	3 (4.7%)	2.33 (0.72; 7.50)	0.156
Kidney disease	27 (100.0%)	0 (0.0%)	-	-
Diabetes mellitus	139 (97.9%)	3 (2.1%)	1.01 (0.32; 3.21)	0.983
Immune deficiency	179 (96.8%)	6 (3.2%)	1.59 (0.70; 3.65)	0.270
Abdominal disease	156 (98.7%)	2 (1.3%)	0.60 (0.15; 2.43)	0.470
Alcohol consumption				
0 units/week	2665 (98.0%)	55 (2.0%)	1.00 (Ref.)	-
1–7 units/week	4439 (97.9%)	95 (2.1%)	1.04 (0.74; 1.45)	0.832
8–14 units/week	507 (97.7%)	12 (2.3%)	1.15 (0.61; 2.16)	0.671
≥15 units/week	51 (100.0%)	0 (0.0%)	-	-
No answer provided	21 (100.0%)	0 (0.0%)	-	-
Tobacco use				
No, never	4755 (97.9%)	103 (2.1%)	1.00 (Ref.)	-
No, previous smoker	2174 (97.8%)	49 (2.2%)	1.04 (0.74; 1.47)	0.821
Yes, sometimes	319 (98.5%)	5 (1.5%)	0.72 (0.29; 1.79)	0.483
Yes, daily, <10 cigarettes/day	230 (98.3%)	4 (1.7%)	0.80 (0.29; 2.20)	0.669
Yes, daily, >10 cigarettes/day	184 (99.5%)	1 (0.5%)	0.25 (0.03; 1.81)	0.170
No answer provided	21 (100.0%)	0 (0.0%)	-	-

OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

symptoms were in line with previous publications and indistinguishable from those of other viral infections. This may partly explain the increased prevalence among HCWs compared to the general population; at the beginning of the epidemic, HCWs were less aware of the potential transmission of SARS-CoV-2 between colleagues and perhaps attended work with mild symptoms. Furthermore, the PCR test capacity was limited during the first wave, and mild symptoms were not an indication for a SARS-CoV-2 PCR test.

Previous studies reported that healthcare assistants had a higher prevalence of SARS-CoV-2 antibodies compared to other groups of HCWs, as these professional groups have the most close-patient contact (Plebani et al., 2020; Rudberg et al., 2020). In the present study, no particular professional group had a higher seroprevalence. This could suggest that viral transmission was not from patient to HCW, but rather between HCWs. As personal protective equipment was not worn outside of separate patient rooms in Denmark during the first pandemic wave in the spring of 2020, transmission between HCWs is very likely to have occurred.

There are some limitations to this study that need to be taken into account. The sensitivity of the applied antibody test was rather low, increasing the risk of false-negative results. However, the overall seroprevalence was adjusted according to the test sensitivity and specificity.

The study setup allowed participants to have antibody testing performed without providing questionnaire data. This led to a large number of participants not providing questionnaire data. As a result, a possible selection bias could have been introduced, which cannot be determined as we have no information on the non-responders. Further, the questionnaire was designed so that questions could be left unanswered, which resulted in some missing data.

Not all potentially important risk factors were considered in the questionnaire. Knowledge on risk behaviour both inside and outside healthcare facilities, including compliance with personal protective equipment, hand sanitation habits, and number of physical colleagues at work, would have been of value.

In conclusion, low seroprevalence of SARS-CoV-2 was found among HCWs in the Region of Southern Denmark. However, working in dedicated COVID-19 wards posed a significantly higher occu-

pational risk of SARS-CoV-2 infection. The majority of the seropositive HCWs had been symptomatic, which underlines the need for increased routine screening of HCWs in order to minimize the spread of the infection. Finally, increased attention should be paid to larger numbers of physically close contacts among HCWs during a pandemic.

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Acknowledgements

The authors wish to thank all of the personnel involved in the serological analyses, including blood collection, handling, and analysis. Further, we wish to thank all of the study participants, and thank the hospital administrations and the Region of Southern Denmark for financial support.

Funding source: This work was financially supported by Danish Regions (Danske Regioner) and the Region of Southern Denmark (Region Syddanmark). The funding sources were not involved in the study design, data collection, analysis, and interpretation, writing of the manuscript, or decision to publish.

Data availability: An anonymized dataset containing all data to obtain the results described in the present paper is available from the corresponding author on reasonable request.

Conflict of interest: None of the authors have any conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2021.09.023.

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