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SARS-CoV-2 seroprevalence in hospital healthcare workers in Western Switzerland at the end of the second pandemic wave

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Abstract

Introduction. In early January 2020, the pandemic of COVID-19 (coronavirus disease 2019) rapidly spread from China and caused a worldwide pandemic.

Hypothesis. Healthcare workers represent a high-risk group for acquiring COVID-19 and for nosocomial transmission of severe acute respiratory coronavirus 2 (SARS-CoV-2).

Aim. We aimed to investigate over a 1 year period, across two pandemic waves, the SARS-CoV-2 seroprevalence in employees at a Western Switzerland public hospital.

Methodology. A prospective observational SARS-CoV-2 seroprevalence study was proposed to all hospital employees who enrolled on a voluntary basis.

Results. Out of 594 participants recruited on a voluntary basis, 269 volunteers (45.3%) had anti-SARS-CoV-2 antibodies: this seroprevalence was twice higher than that reported in the local community. Healthcare workers with prolonged exposure to patients with COVID-19 showed a significantly higher odds ratio (OR) of having a positive SARS-CoV-2 serology [OR 3.19, 95% confidence interval (CI) 2.16–4.74]. Symptoms showing the highest association with a positive serology were anosmia (OR 11.9, 95% CI 5.58–30.9) and ageusia (OR 10.3, 95% CI 4.8–26.3). A total of 17.1% (95% CI 12.2–21.1%) of SARS-CoV-2 seropositive volunteers did not report a suspicion of COVID-19 in their personal history.

Conclusion. Overall, we observed that the impact of the second SARS-CoV-2 pandemic wave was considerable and significantly affected healthcare workers with prolonged exposure to patients with COVID-19.

INTRODUCTION

In early January 2020, the pandemic of COVID-19 (coronavirus disease 2019) caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) started in Wuhan City, China, then rapidly spread to other regions in China and caused a worldwide pandemic. Switzerland experienced two epidemic waves, the first between February and June 2020, while the second started in October, peaked in November 2020 and slowly decreased up to May 2021 [1–3]. In addition to constraining measures in the community, such as social distancing, limitation of public gatherings and a ban of travelling, employers drastically limited the number of active persons at the workplace. In contrast, hospitals represent potential hotspots for SARS-CoV-2 transmission

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Abbreviations: CHUV, Centre Hospitalier Universitaire Vaudois; CI, confidence interval; COVID-19, coronavirus disease 2019; EHC, Ensemble Hospitalier de la Côte'; ICU, intensive care unit; RAT, rapid antigenic testing; RT-PCR, reverse-transcriptase PCR; SARS-CoV-2, severe acute respiratory coronavirus 2.
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for healthcare staff and patients with COVID-19. Serological population-based investigations are sensitive tools for estimating retrospectively the number of infected individuals [4]. Such an approach can identify asymptomatic individuals at high risk of COVID-19 transmission [5] and those with flu-like symptoms or SARS-CoV-2 positive contacts who were self-quarantined without diagnostic investigation with reverse-transcriptase PCR (RT-PCR) or rapid antigenic testing (RAT). In a study including 4726 hospital healthcare workers in Southern Switzerland during the first wave in April 2020, those with direct exposure to patients with COVID-19 presented a higher absolute risk [odds ratio (OR) 1.75, confidence interval (CI) 1.28–2.40] of having a SARS-CoV-2 positive serology compared to those working in low-risk-exposure hospital areas [6]. Another study at the Lausanne University Hospital, Switzerland, at the end of the first wave (May to June 2020), reported no association between direct exposure to patients with COVID-19 and seropositivity (10.3% in exposed vs 9.6% in unexposed individuals, respectively) [7]. Most SARS-CoV-2 seroprevalence studies performed were limited to the first pandemic wave [8–12], and showed seroprevalence rates ranging from 0 to 45.3%, mean 8.7% [9]. These important discrepancies are linked to variable diagnostic performances of serological methods, study designs, periods of sample collection, local lockdown and quarantine measures, and SARS-CoV-2 local seroprevalences in the general population.

We investigated over a 1 year period, across two pandemic waves, the SARS-CoV-2 seroprevalence in employees at the Ensemble Hospitalier de la Côte (EHC), a public hospital with 1800 employees in Western Switzerland, with 240 acute beds and 85 post-acute beds. This professional population presented very different risk profiles for exposure to SARS-CoV-2. We aimed to identify groups at increased risk for anti-SARS-CoV-2 seropositivity in and outside the professional environment.

METHODS

Study design

A prospective observational study was proposed to all employees of the EHC, Morges, Switzerland (n=1800). Participants (n=594) were included on a voluntary basis. Persons vaccinated against SARS-CoV-2 were excluded. All participants who signed an informed consent were recruited between February 24 and March 19, 2021.

Questionnaire

All participants filled in a questionnaire with data on demographics, clinical characteristics, history of professional and extra-professional SARS-CoV-2 exposure, COVID-19 symptoms and diagnosis, including the diagnostic method used, i.e. RT-PCR or RAT (File S1, available with the online version of this article). Questionnaires were manually digitalized. Some volunteers did not fully answer the questionnaire. Volunteers with incomplete questionnaires were not included in the specific groups if the related question was missing. This explains why the total number of volunteers is not always recorded as 594.

Serum sampling

Blood was obtained at the inclusion visit (using a 10 ml Monovette without anticoagulant) and processed as previously described [13].

Serological method

The samples were analysed for IgG anti-spike SARS-CoV-2 antibodies using the Luminex system at the Laboratory of the Institute of Immunology, Lausanne University Hospital, Switzerland [13]. An antibody ratio between the sample and the control signal ≥6 defined seropositivity. A ratio <4 was interpreted as negative. A ratio of ≥4 and <6 was considered as undetermined. In this case, a second blood sampling was scheduled 2–4 weeks later. Serological results that remained undetermined after the second blood sampling were excluded from the statistical analysis (n=5). The same serological assay was used for a national population study in Switzerland [14] and for a study in healthcare workers at the Lausanne University Hospital [7].

Statistical analysis

All analyses were performed with R version 3.6.2. The 95% CIs were calculated using the Clopper–Pearson CI for a binomial proportion (exactci). The Wilcoxon–Mann–Whitney test was used to compare the distribution of antibody ratios between the two pandemic waves (wilcox.test). Fisher's exact test was used to compare the SARS-CoV-2 seroprevalence between groups and to calculate ORs (fisher.test). The P values are two-sided with a significance level set at 5%.

RESULTS

Demographics of study volunteers and SARS-CoV-2 seroprevalence

A total of 594 unvaccinated volunteers participated in this prospective observational study, representing 33% of the 1800 hospital employees (155, 8.6%, were vaccinated and not eligible for inclusion). The majority of study participants were women (81%) and the median age was 42 years (Q1 32 – Q3 51). Overall, 45.3% (95% CI 41.2–49.3%) of volunteers had a positive SARS-CoV-2

Table 1. SARS-CoV-2 antibody positivity in hospital employees according to gender, exposure to patients with COVID-19 and personal history of previous COVID-19

The *n* values represent the number of participants in each category.

Participants		SARS-CoV-2 serology	
	All (*n*)	Negative (%), 95% CI (%)	Positive (%), 95% CI (%)
All	594	54.7, 50.6–58.7	45.3, 41.2–49.3
Female	487	54.5, 49.8–58.9	45.5, 41.0–50.1
Male	107	56.1, 46.1–65.6	43.9, 34.3–53.8
With patient contacts	413	46.3, 41.3–51.1	53.7, 48.8–58.6
Without patient contacts	170	74.8, 67.4–81.0	25.2, 18.9–32.5
Absence of protected contacts at work	243	67.1, 60.9–72.6	32.9, 27.3–39.0
Protected contacts at work	346	46.3, 41.0–51.5	53.7, 48.4–58.9
Occasional protected contacts at work	112	58.5, 49.4–66.9	41.5, 33.0–50.5
Frequent protected contacts at work	234	38.9, 32.8–45.2	61.1, 54.7–67.1
SARS-CoV-2 positive RT-PCR or RAT	186	2.7, 0.8–6.1	97.2, 91.7–98.1
SARS-CoV-2 unknown or negative RT-PCR or RAT	408	78.2, 73.8–82.0	21.8, 17.9–26.1

serology. No correlation was observed between seropositivity and gender or age (Table 1, Fig. S1A, B). Positive anti-spike IgG antibody ratios (≥6) showed a broad distribution with a median of 36.6 (Q1 23.7 – Q3 61.7) (Fig. S1C). According to the participant self-reported date of positive RT-PCR or RAT, the date of seroconversion was retrospectively estimated. The median antibody ratio did not significantly change over a 1 year period (Fig. 1a). In total, 19 cases of COVID-19 (3.2% of 594 participants) were diagnosed by RT-PCR or RAT during the first pandemic wave (February–June 2020), while 166 infections (27.9% of participants) occurred during the second wave (July 2020–March 2021). This significantly increasing proportion of hospital employees with COVID-19 is comparable to the magnitude of the second wave in Switzerland. It reflected the growing number of COVID-19 diagnoses in the local community (Fig. 1b). As expected, COVID-19-associated absenteeism of employees peaked early during the second wave (Fig. 1c).

Self-reported work-related exposure to patients with COVID-19

Although the present cohort included a majority of nursing personnel, bedside auxiliary personnel and physicians, 174 volunteers (29.5%) had no or very infrequent contacts with patients (Fig. 2a, Table S1). People with roles without patient contact displayed a low seroprevalence, particularly in the hospital administration, logistics, pharmacy or laboratory, whereas bedside auxiliary personnel presented a high risk of SARS-CoV-2 seropositivity. Stratification of functions according to absence or presence of direct contacts with hospitalized patients for COVID-19 showed a seroprevalence of 25.2% (95% CI 18.9–32.5%) and 53.7% (95% CI 48.8–58.6%), respectively, with a corresponding OR of 3.1 for persons directly exposed (95% CI 2.09–4.70) (Fig. 2b). As the classification by professional function is only an assumption to an exposition to COVID-19 patients, we investigated the self-reported type of professional contacts with COVID-19 patients, protected or non-protected, as well as their frequency to verify data robustness. A non-protected contact was defined as a contact with a COVID-19 infected individual without a mask at a distance of less than 1.5 m for more than 15 min. Very few employees reported non-protected contacts and no statistical difference was observed between the two groups (Fig. 2c). Volunteers not involved in patient care showed a SARS-CoV-2 seroprevalence of 32.9% (95% CI 27.3–39.0%), whereas those with protected patient contacts showed a seroprevalence of 53.7% (95% CI 48.4–58.9%) (Fig. 2d). Among volunteers reporting protected contacts with COVID-19 patients, no difference was observed between occasional exposure (<10 reported protected contacts) and no exposure with an OR of 1.44 (95% CI 0.89–2.33). In sharp contrast, the seroprevalence of healthcare workers reporting frequent and prolonged exposure (≥10 reported protected contacts) was 61.1% (95% CI 54.7–67.1%) with an OR of 3.19 (95% CI 2.16–4.74) (Fig. 2d). This suggests that the protective measures were sufficient for occasional exposures, while the risk of being seropositive increased significantly with frequent and prolonged exposures in hospital areas dedicated to care of patients with COVID-19. Accordingly, healthcare workers of the Department of Medicine were at the highest risk of seropositivity (Fig. 2e, Table S2).

Self-reported symptoms of COVID-19

Among the symptoms reported by the participants, a strong association with positive anti-SARS-CoV-2 antibodies was observed for alteration of smell (OR 11.91, 95% CI 5.58–30.39) and taste (OR 10.29, 95% CI 4.80–26.30). Asthenia and chest pain showed

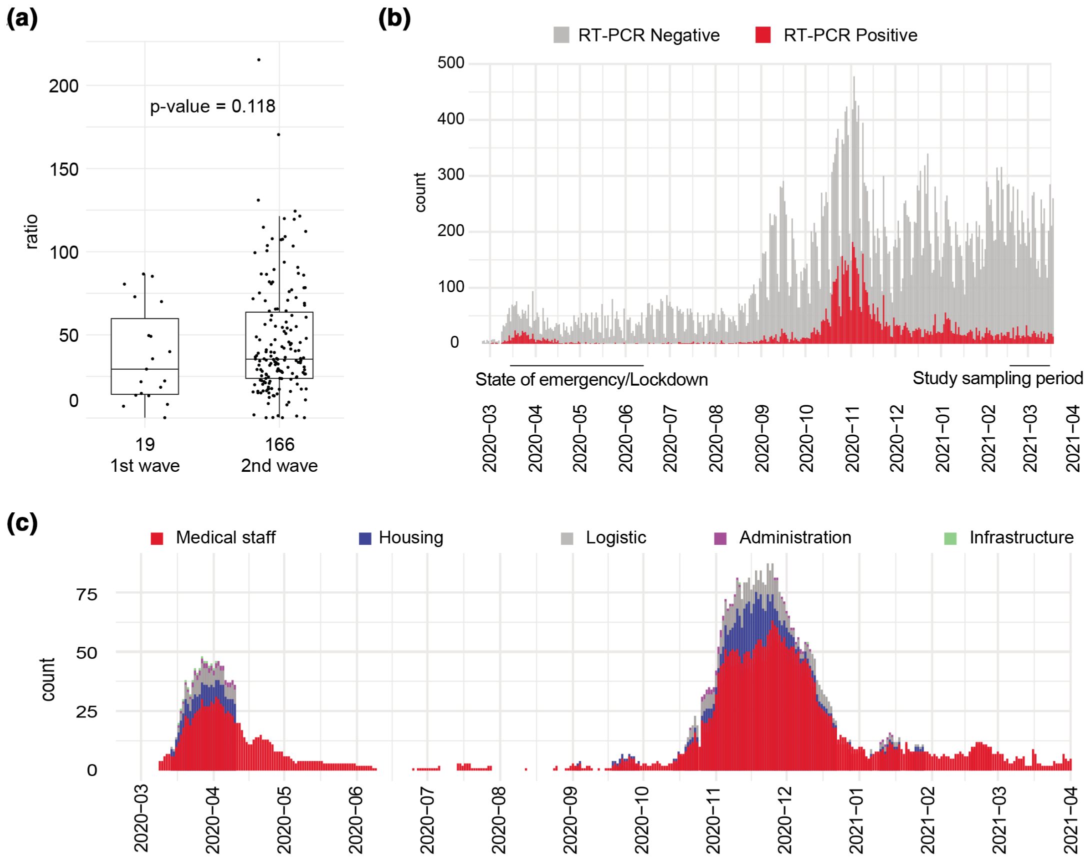

Fig. 1. (a) Distribution of anti-spike antibody ratios in the two epidemic waves. Positive RT-PCR or RAT results were used to retrospectively estimate the timing of SARS-CoV-2 seroconversion. No significant (Wilcoxon–Mann–Whitney test) decline of antibody ratios was observed between the two waves (first wave February–July 2020, second wave July 2020–March 2021). (b) SARS-CoV-2 testing performed at the COVID-19 outpatient diagnostic centre at the EHC. These results represent the magnitude of the epidemic waves in the local community. The lockdown and sampling periods are depicted on the graph. (c) Absenteeism of hospital employees associated with COVID-19 according to department during the 1 year study period.

a weak association with COVID-19 seropositivity, while cough, sore throat and gastrointestinal symptoms showed a negative association (Fig. 3a–c, Table S3). No SARS-CoV-2 reinfection was observed and two volunteers reported having been hospitalized for COVID-19.

Seroconversion in volunteers with asymptomatic COVID-19

Out of the 186 participants who self-reported a positive RT-PCR or RAT, 177 (97.2%, 95% CI 91.7–98.1%) had a positive serology for SARS-CoV-2 (Table 1). The absence of antibodies in five participants (2.8%) was not related to recent diagnosis of COVID-19 and their self-reported symptoms were compatible with COVID-19 or another flu-like illness (Table S4). They had all been tested by RT-PCR with cycle thresholds between 34 and 37 corresponding to low viral loads (1000–7000 copies ml^{-1}). The absence of seroconversion in 2.8% of persons with documented COVID-19 was within the range of seronegativity reported in other studies [15, 16]. To evaluate the number of individuals with asymptomatic infection in our cohort, all participants were also asked whether they suspected having suffered from COVID-19. Out of 289 volunteers who were not suspecting previous COVID-19, 49 (17.1 %, 95 CI 12.2–21.1%) had a positive serology (Fig. 4a). No correlation was found with their hospital function, nor the type of diagnostic test (RT-PCR or RAT) that was used for ruling out COVID-19 [17]. Among these individuals, no antibody ratios close to the threshold for seropositivity, which may represent a false-positive result, were observed (Table S5). Self-reported symptoms included mostly sore throat or cough, while six volunteers reported flu-like symptoms (Table S5).

Self-reported community-related exposure to COVID-19

Non-protected or protected contact with COVID-19 infected individuals within the household and in the community had no significant impact on SARS-CoV-2 seropositivity (Fig. 4b). As expected, volunteers assigned to home office showed a negative association with detection of SARS-CoV-2 antibodies (Fig. 4c). Of note, those working at the hospital mostly included health-care workers caring for patients with COVID-19, which likely explains the negative association of home-based work. Public

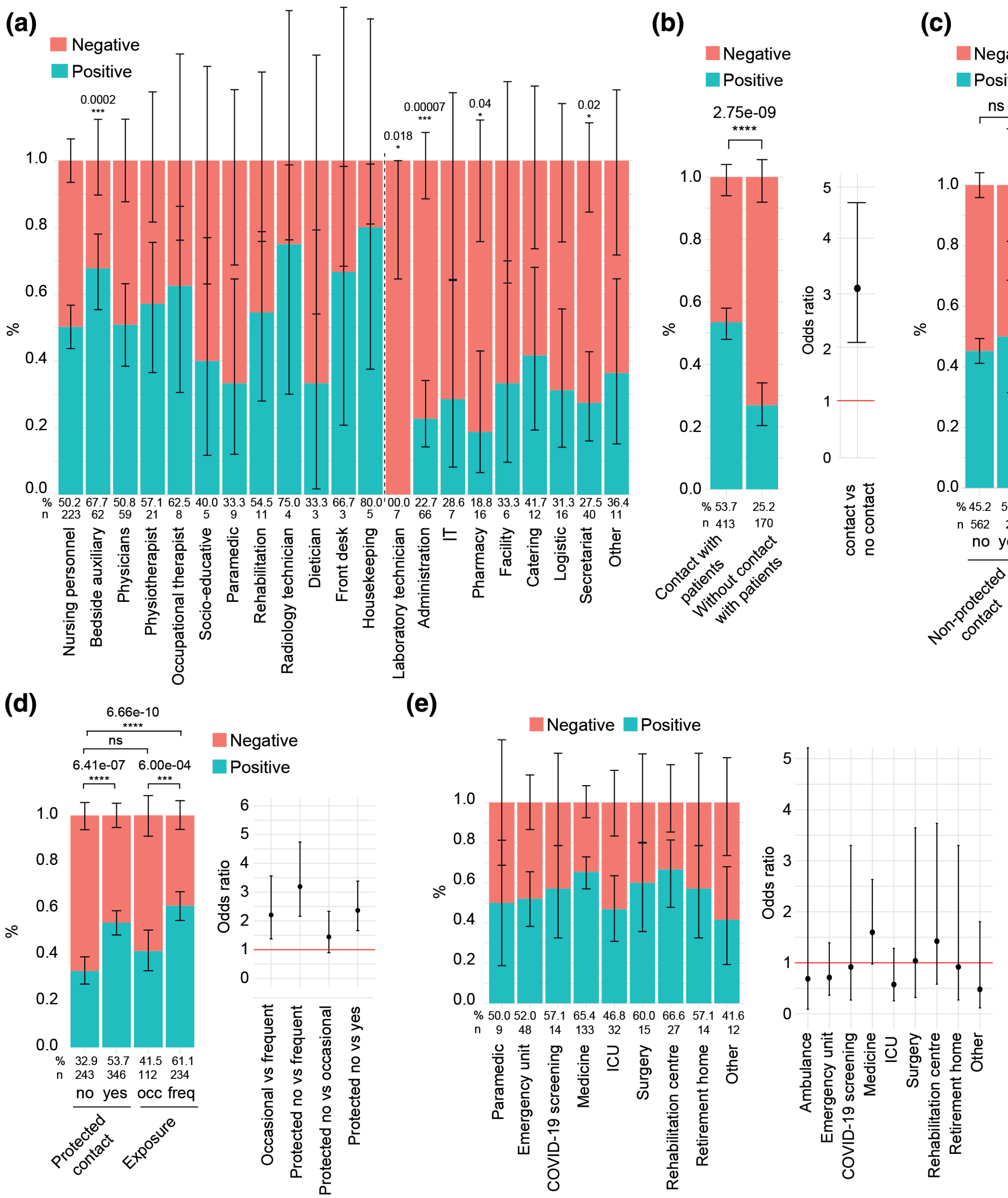

Fig. 2. (a) SARS-CoV-2 seroprevalence comparing functions in the hospital. The dashed line separates functions with (on the left) or without (on the right) contact with COVID-19 patients. (b) Seropositivity rates according to functions with or without exposure to patients with COVID-19. Healthcare workers with patient contacts showed a significantly higher risk for a positive SARS-CoV-2 serology. A total of 11 volunteers, labelled 'other' in (a), reported no professional occupation and, therefore, were not represented (413+170=583 out of 594). (c) Reported non-protected professional exposures to patients with COVID-19 (yes/no). These few exposures had no significant impact on SARS-CoV-2 serology. A total of eight participants did not answer the related question in the questionnaire and were not represented (562+24=586 out of 594). (d) Seroprevalence of SARS-CoV-2 antibodies in employees according to frequency of protected exposure to patients with COVID-19. No statistical difference was observed between participants who declared no protected contact or only occasional contacts with COVID-19 patients, while frequent exposure (≥10 occasions) significantly increased the risk for a positive SARS-CoV-2 serology. Out of the 346 volunteers who reported protected contacts, 112 reported frequent and 234 occasional contacts with COVID-19 patients (112+234=346). Out of the 594 volunteers, 243 reported no contact, while 346 reported protected contacts with COVID-19 patients (243+346=589). Five volunteers failed to answer the related question in the questionnaire and were not included. (e) Seroprevalence of SARS-CoV-2 antibodies in employees according to hospital departments. While no significant differences were observed, employees from medicine and rehabilitation departments showed the highest ORs for a positive SARS-CoV-2 serology. Significance was assessed using Fisher's exact test by comparing each individual group to the hospital cohort. Data are presented with 95% CIs. The percentages indicate the positive SARS-CoV-2 serology rates, the *n* values represent the total number of participants per group. The *P* values are indicated in the graphs: *P*>0.05, *; *P*≤0.001, ***; *P*≤0.0001, ****; not displayed or 'ns', non-statistically significant. The red line indicates an OR of 1.

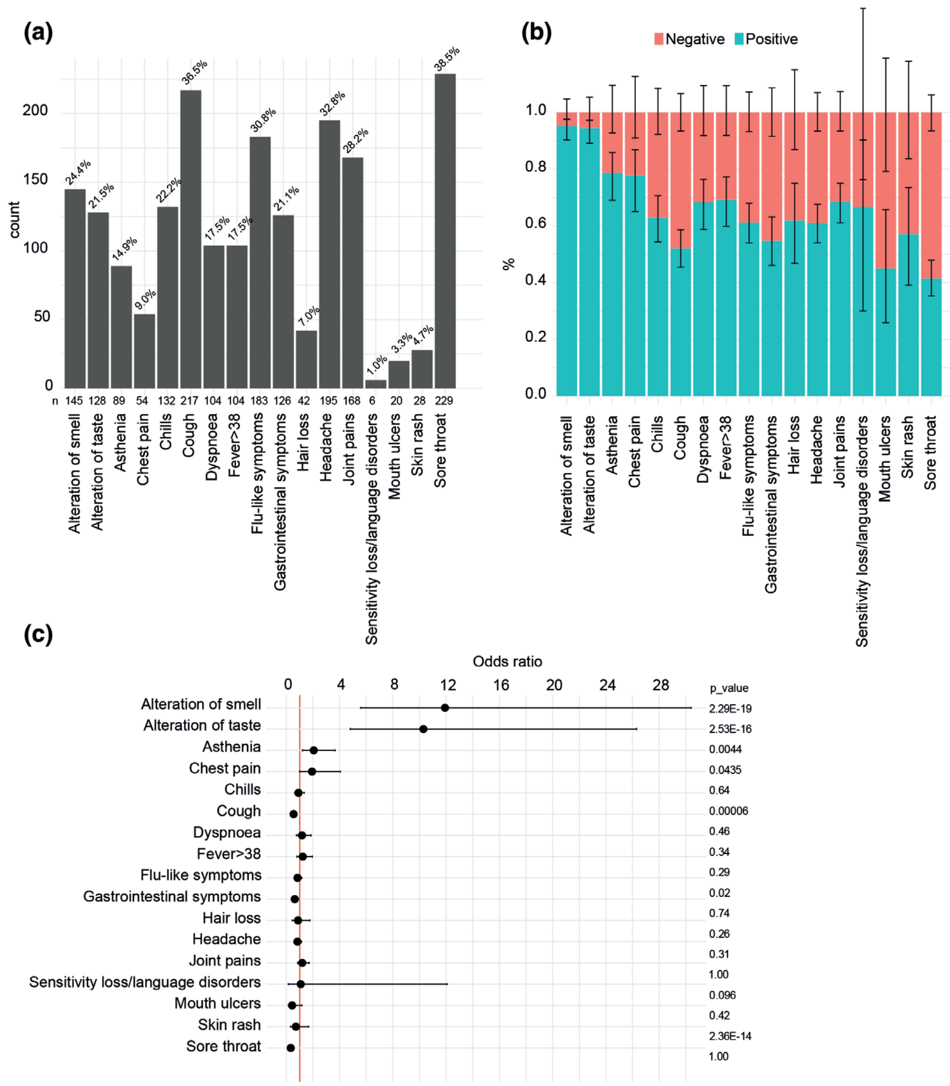

Fig. 3. (a) List of self-reported symptoms in participants regardless of the SARS-CoV-2 serology result. Percentages represent the rates of participants who reported a specific symptom, the *n* values correspond to the total number of participants reporting a specific symptom. (b, c) Association between presence of a specific symptom and a positive SARS-CoV-2 serology. The red line corresponds to an OR of 1. Data are presented with 95% CIs. Significance was assessed using Fisher's exact test with *P* values reported in the graphs.

transportation to work and its duration were not associated with a higher SARS-CoV-2 seroprevalence (Fig. 4d, e). Holidaying abroad, mainly during summer 2020, had no significant association with SARS-CoV-2 seropositivity (Fig. 4f).

DISCUSSION

The present study investigated the seroprevalence of anti-SARS-CoV-2 antibodies among employees of a public hospital in Western Switzerland during the first and second pandemic waves. We showed that median antibody levels were similar among those individuals infected during the first wave and those infected during the second wave. With a time gap of more than 10 months between the serology and infection, those infected in the first wave could have exhibited a sharper antibody decline with an initial higher ratio. However, in both waves, participants have been infected with the wild-type Wuhan variant and, therefore, we do not expect that the ratio between the two groups would be different if the serology was assessed closer to the time of infection. Therefore, this rather suggests a relative long-term persistence of SARS-CoV-2 antibodies [18, 19].

The first wave accounted for the minority of COVID-19 diagnoses among study participants, compared to infections occurring during the second wave. This suggests that the data published so far, mostly focusing on the first months of the pandemic, likely underestimate the impact of COVID-19 in healthcare workers. Data from USA healthcare personnel (August 30 2020) showed

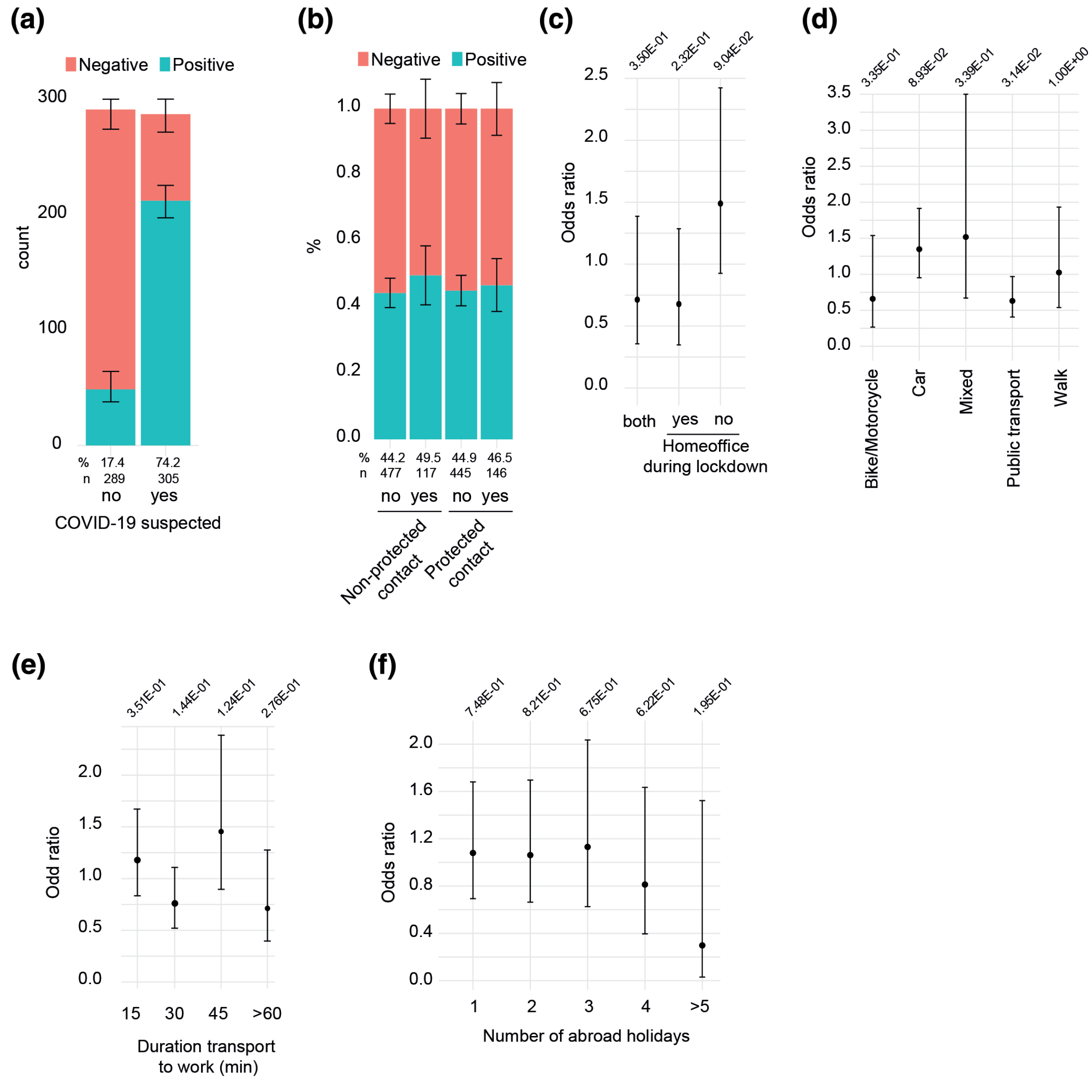

Fig. 4. (a) SARS-CoV-2 seroprevalence according to suspected COVID-19 as self-reported in personal history by participants. Data are presented as numbers with 95% CIs. The percentages correspond to the rates of positive SARS-CoV-2 serology. In total, 47 individuals (17.4%) had a positive serology without having experienced any symptoms suggestive of COVID-19. (b) SARS-CoV-2 seroprevalence according to reported contacts. Participants were asked to report protected (yes/no) or non-protected (yes/no) contact with SARS-CoV-2 infected individuals within the household or in the community. The percentages represent the rates of positive SARS-CoV-2 serology with 95% CIs, the *n* values represent the total number of participants per group. No statistical differences were observed between the groups. (c, d, e and f) ORs for a positive SARS-CoV-2 serology in participants according to home office work during the first pandemic wave (c), mode of transportation to work (d), duration of transport to work (e) and holiday stay abroad (f). Data are presented with corresponding 95% CIs. Significance was assessed using Fisher's exact test with *P* values reported in the graphs.

that community rather than workplace exposures were associated with SARS-CoV-2 seropositivity [20]. In contrast, studies in Sweden (May 8 2020) and the UK (25 April 2020) showed an occupational risk for SARS-CoV-2 infection among healthcare workers [11] and reported significant numbers of asymptomatic seroconversions [12]. The present study encompasses the longest possible period between the start of the pandemic and before the vaccination era that would have complicated the interpretation of the serological results. Here, we found that healthcare workers with prolonged direct exposure to patients hospitalized with COVID-19 showed an OR of 3.19 for a positive anti-SARS-CoV-2 serology when compared with employees at low risk of hospital exposure (care for patients without COVID-19, logistic and administrative tasks). The seroprevalence rate of 25% observed in these low-risk hospital activities was close to that observed in a national seroprevalence study conducted in the local community. The study, with 30 000 volunteers enrolled across Switzerland, reported an estimated seroprevalence of about 25% in the Vaud Canton state [14, 21]. This study used the same serological assay along with a comparable timing of sera collection (February–March 2021).

Among participants reporting daily direct contacts with patients hospitalized for COVID-19, the highest seroprevalence rate was observed in healthcare workers in medicine wards (65%), while seroprevalence was lower in the intensive care unit (ICU) (47%). This is possibly related to a stricter adherence to the use of personal protective equipment and to a better infrastructure and logistics in the ICU staff working spaces. The decreasing viral loads in the later stages of COVID-19 when the patients develop inflammatory lung complications might also have contributed to lower transmission rates in the ICU [22, 23].

Out of 289 volunteers not self-reporting a suspicion of COVID-19 based in their personal history, 49 (17%) had a positive serology, in full agreement with the estimated seroprevalence rate of 17% reported in asymptomatic individuals by a recent systematic review and meta-analysis [5]. Adjusted to the total number of hospital employees, this represents 150 persons with asymptomatic COVID-19 at risk of undetected hospital transmission to staff and patients. Therefore, a diagnostic screening strategy in healthcare workers driven by the presence of symptoms/signs of infection might miss one-sixth of COVID-19 cases. This would argue, in particular during periods of high COVID-19 incidence, in favour of a universal screening strategy in all exposed non-vaccinated employees irrespective of the presence of symptoms in order to minimize the risk of nosocomial transmission [24]. Vaccination is the most effective measure to reduce the risk of SARS-CoV-2 transmission within the hospital. In total, 344 study participants (58%, 95% CI 53.8–61.9%) declared to be willing to get vaccinated and 36 (6%, 95% CI 4.4–8.5%) declared being undecided. A recent seroprevalence study in the population of the Geneva region of Switzerland showed that 67% of participants had developed antibodies, with half of them after natural infection and the other half after vaccination [25]. Altogether, these data confirm that a significant proportion of employees with daily patient contacts will remain at high risk for hospital-acquired infection and transmission.

Limitations of the present study cohort are the self-enrolment of participants on a voluntary basis, which may have represented a selection bias, in particular because previously infected individuals and those with daily exposure to infected patients might have been more prone to participate. Moreover, 155 healthcare workers in charge of front-line care of infected patients – all without history of previous COVID-19 (whose majority were, thus, probably seronegative) – had priority for anti-SARS-CoV-2 vaccination at the time of starting the present study and, thus, were excluded. These two potential recruitment biases might have resulted in an overestimate of the SARS-CoV-2 seroprevalence among hospital employees.

In conclusion, we observed that the second SARS-CoV-2 pandemic wave significantly affected healthcare workers and in particular those who had prolonged contacts with COVID-19 patients. Since persons with asymptomatic COVID-19 represent about a sixth of infected individuals, accelerating vaccination campaigns combined with screening of non-vaccinated asymptomatic personnel might constitute a dual strategy to optimize patients' and hospital staff's safety by minimizing the risk of nosocomial transmissions.

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Conflicts of interest

G.G. is a medical advisor of Resistell, a start-up active in the development of a new instrument for faster antibiotic-susceptibility results. G.G. has a research agreement with Becton Dickinson (USA) and Resistell (Switzerland), both unrelated to the present work. G.G. is the co-director of JeuPro, a start-up distributing games on microbes (Krobs and MyKrobs). The other authors declare that they have no conflicts of interest.

Ethical statement

The Cantonal Ethical Review Board for Human Research (CER-VD, Commission Cantonale d'Éthique de la Recherche sur l'Être Humain) approved the study protocol (authorization no. 2020-02300).

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