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Original article

COVID-19 exposure in SARS-CoV-2-seropositive hospital staff members during the first pandemic wave at Strasbourg University Hospital, France

Aurélie Velay[a,b,*], Floriane Gallais[a,b], Marie-Josée Wendling[a], Sophie Bayer[c], Nathalie Reix[c], Anne Schneider[d], Ludovic Glady[c], Nicolas Collongues[e], Jean-Marc Lessinger[c], Yves Hansmann[f], Laurence Kling-Pillitteri[g], Jérome De Sèze[e], Maria Gonzalez[g,h], Catherine Schmidt-Mutter[e], Nicolas Meyer[i], Samira Fafi-Kremer[a,b]

[a] Virology Laboratory and INSERM UMR_S 1109, Strasbourg University Hospital, 3, rue Koeberlé, 67000 Strasbourg, France
[b] Strasbourg University, INSERM, IRM UMR-S 1109, 67000 Strasbourg, France
[c] CHU de Strasbourg, Laboratoire de Biochimie Clinique et Biologie Moléculaire, 67091 Strasbourg, France
[d] CHU de Strasbourg, Département de Génétique Moléculaire du cancer, 67091 Strasbourg, France
[e] Centre d'investigation Clinique INSERM 1434, CHU Strasbourg, Strasbourg, France
[f] CHU de Strasbourg, Service des maladies infectieuses et tropicales, 67091 Strasbourg, France
[g] CHU de Strasbourg, Service de santé au travail du personnel hospitalier, 67091 Strasbourg, France
[h] CHU de Strasbourg, Service de Pathologies Professionnelles, Strasbourg, France
[i] CHU de Strasbourg, Service de santé Publique, GMRC, 67091 Strasbourg, France

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ABSTRACT

Objectives: Strasbourg University Hospital faced an important COVID-19 first wave from early March 2020. We performed a longitudinal prospective cohort study to describe clinical and virological data, exposure history to COVID-19, and adherence to strict hygiene standards during the first pandemic wave in 1497 workers undergoing a SARS-CoV-2 serological test at our hospital, with a follow up of serology result three months later.
Patients and Methods: A total of 1497 patients were enrolled from April 6 to May 7, 2020. Antibody response to SARS-CoV-2 was measured, and COVID-19 exposure routes were analyzed according to SARS-CoV-2 serological status.
Results: A total of 515 patients (34.4%) were seropositive, mainly medical students (13.2%) and assistant nurses (12.0%). A history of COVID-19 exposure in a professional and/or private setting was mentioned by 83.1% of seropositive subjects ($P < 0.05$; odds ratio [OR]: 2.5; 95% confidence interval [CI]: 1.8–3.4). COVID-19 exposure factors associated with seropositive status were non-professional exposure (OR: 1.9, 95% CI: 1.3–2.7), especially outside the immediate family circle (OR: 2.2, 95% CI: 1.2–3.9) and contact with a COVID-19 patient (OR: 1.6; 95% CI: 1.1–2.2). Among professionally exposed workers, systematic adherence to strict hygiene standards was well observed, except for the use of a surgical mask ($P < 0.05$, OR: 1.9, 95% CI: 1.3–2.8). Of those who reported occasionally or never wearing a surgical mask, nurses (25.7%), assistant nurses (16.2%), and medical students (11.7%) were predominant.
Conclusion: Infection of staff members during the first pandemic wave in our hospital occurred after both professional and private COVID-19 exposure, underlining the importance of continuous training in strict hygiene standards.

1. Introduction

In early December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in the city of Wuhan, in China's Hubei Province. This highly contagious virus, mainly transmitted via droplets, is the causative agent of the Coronavirus Disease 2019 (COVID-19) [1]. Given the current COVID-19 pandemic, infection of medical and nursing staff is a common occurrence. Shortly after the first wave of the pandemic, the occupational risk of contamination among healthcare workers (HCWs) was well identified [2–4], with contamination rates ranging from 3.5% to 29% amongst hospitals in Wuhan [5].

* Corresponding author at: Virology Laboratory and INSERM UMR_S 1109, Strasbourg University Hospital, 3, rue Koeberlé, 67000 Strasbourg, France.
E-mail address: aurelie.velay@chru-strasbourg.fr (A. Velay).

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Whilst RT-PCR tests were mostly performed in symptomatic patients, especially during the first wave, the mass testing, which followed, revealed the predominance of asymptomatic forms of this infection. Since viral replication, and therefore contamination, can take place before symptoms appear, or even in the absence of symptoms, those in contact with COVID-19-positive cases, such as hospital staff, also constitute a population of potentially infected people. Antibodies to SARS-CoV-2 are detectable from around 15 days after symptom onset and seem to persist for at least 6 months [6]. Serological tools could provide precious information by detecting antibodies induced by previous SARS-CoV-2 infection, especially among populations, which are highly exposed to the virus such as HCWs.

At the end of February 2020, a cluster of SARS-CoV-2 infections was detected following an annual religious gathering attended by more than 2,000 people in Mulhouse, eastern France. Infected individuals were admitted to regional hospitals. Strasbourg University Hospital (SUH) (2,566 beds including 97 in the intensive care unit [ICU]) faced this early first wave of COVID-19, which was of high intensity compared to other areas in France. All hospital staffs were at high risk of SARS-CoV-2 exposure, both occupationally and outside the hospital. The occurrence of the early epidemic wave in our hospital represented an opportunity to study the SARS-CoV-2 antibody response in staff members, and to identify risk factors for SARS-CoV-2 infection at a time when knowledge about COVID-19 remained sparse.

We performed a longitudinal prospective cohort study to describe clinical and virological data, exposure history to COVID-19, and adherence to strict hygiene standards during the first pandemic wave in 1497 workers undergoing a SARS-CoV-2 serological test at our hospital, with a follow up of serology result 3 months later. The effectiveness of prevention measures for first-line and non-first-line workers in the hospital setting is also discussed.

2. Methods

2.1. Study design

Participants were randomly selected among the entire SUH staff members by the occupational health department and invited by phone call to participate in this study. Individuals were enrolled in the study from April 6 to May 7, 2020 (Visit 0, V0) and followed up 3 months later (V1). A SARS-CoV-2 serological test was performed both at V0 (inclusion visit) and V1 (follow-up visit) (Fig. 1). At enrollment (V0), written informed consent was collected and participants completed a questionnaire that covered sociodemographic characteristics, clinical data (medical history, COVID-19 symptoms), and virological finding history of SARS-CoV-2 RT-PCR testing, including results and date of testing. Collected information also included exposure history to COVID-19, medical practice and extent of adherence to strict hygiene standards (hand hygiene and proper personal protective equipment [PPE]). COVID-19 exposure was defined as exposure to an individual positive for COVID-19 confirmed by RT-PCR. This article follows the STROBE statement for reporting of cohort studies.

2.2. Serological response measurement

All serum samples were tested using two commercial assays:

- the Biosynex® (COVID-19 BSS IgG/IgM) immunochromatographic Lateral Flow Assay (LFA) detecting IgM and IgG against the Receptor Binding Domain (RBD) of the SARS-CoV-2 spike protein (specificity 99.4%, and sensitivity 95.6% [7]);
- the EDI™ Novel coronavirus COVID-19 IgG ELISA assay detecting the anti-nucleocapsid protein (N) IgG antibodies. Seropositivity was defined as the presence of detectable anti-SARS-CoV-2 IgM and/or IgG antibodies with at least one of the two serological assays.

2.3. Statistical analysis

Categorical data were described as frequencies and proportions. Quantitative data were described by the median and interquartile range (IQR). Seronegative and seropositive subjects were included using a complex survey design, stratified by the 35 hospital sectors. Data were analyzed using the sampling weight with either a chi-square test for contingency tables or a logistic regression. Data are described with raw values in tables, but *p*-values were calculated including the sampling design. A value of $P < 0.05$ was considered significant. Categorical variables are presented as proportions, and reported as odds ratio (OR) and 95% confidence intervals (95% CI). Subjects for whom data was not completed were excluded from the statistical analysis. Computations were carried out using the survey package in R 3.5.2.

2.4. Ethical statement

This study was registered in ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT04441684). The protocol was approved by the institutional review board of CPP Sud Méditerranée III. All participants provided written informed consent.

3. Results

3.1. Baseline sociodemographic characteristics

The study population demographics, corresponding to 1497 subjects is shown in Table 1. Ages ranged from 19 to 73 years with a median of 37 years (IQR: 29–49). Women were predominantly represented (76.6%), which reflects the sex distribution of staff members in our hospital. The median body mass index was 23.5 (IQR: 21.2-26.8). The blood group distribution showed a predominance of group A (36.4%) and group O (36.1%) (Table 1).

In the entire cohort, 74.5% of workers experienced COVID-19 symptoms (Table 1). Among them, only 20 were hospitalized for moderate disease. Concerning occupation distribution, nurses (28.3%) and clinicians (16.4%) were the most represented professional categories (Table 1).

3.2. SARS-CoV-2 serological status among workers

Serological results are displayed in Table 1 and Table 2. Among the entire cohort, 515 (34.4%) subjects were SARS-CoV-2 seropositive at V0. Among them, 453 (88.0%) had a molecular diagnosis performed by RT-PCR and 389 (75.5%) had a positive RT-PCR result. The SARS-CoV-2 serological status did not differ according to sex ($P = 0.48$) or age ($P = 0.82$).

COVID-19 symptoms were reported by 95.7% of seropositive individuals and by 74.8% of seronegative workers, respectively (Table 1). Each symptom was more frequently observed in seropositive subjects (Table 1), especially in those who were previously detected positive by RT-PCR (Fig. 2). However, the difference was far more significantly marked for anosmia and dysgeusia (OR: 21.2, 95% CI: 15.2–29.5) (Fig. 3).

Serological results at V1 were available for 1230 subjects. Among the 444 seropositive subjects at V0 who were followed at V1, 87.8% (390/444) were still seropositive at V1. Those who were previously tested positive for the presence of SARS-CoV-2 by RT-PCR mainly

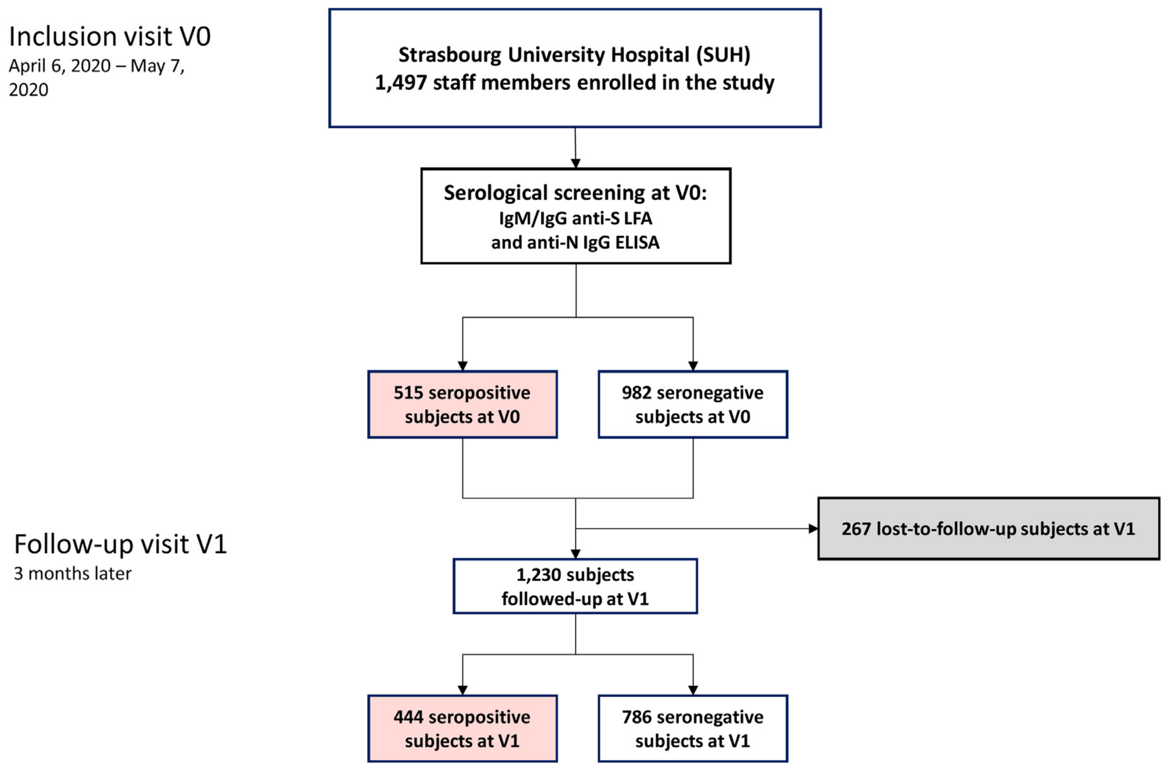

Fig. 1. Flow chart of survey recruitment and serum sampling among staff members at Strasbourg University Hospital. Serological screening was performed using two commercial assays: the Biosynex® (COVID-19 BSS IgG/IgM) Lateral Flow Assay (LFA) detecting anti-Spike (S) antibodies and the EDI™ Novel coronavirus COVID-19 IgG ELISA assay detecting the anti-Nucleocapsid protein (N) IgG. Serological testing was first performed between April 6 and May 7, 2020 (V0) and then 3 months later (V1). Anti-S: anti-spike protein; Anti-N: anti-nucleocapsid protein; ELISA: Enzyme-linked immunosorbent assay; HCW: Healthcare workers; LFA: Lateral flow assay.

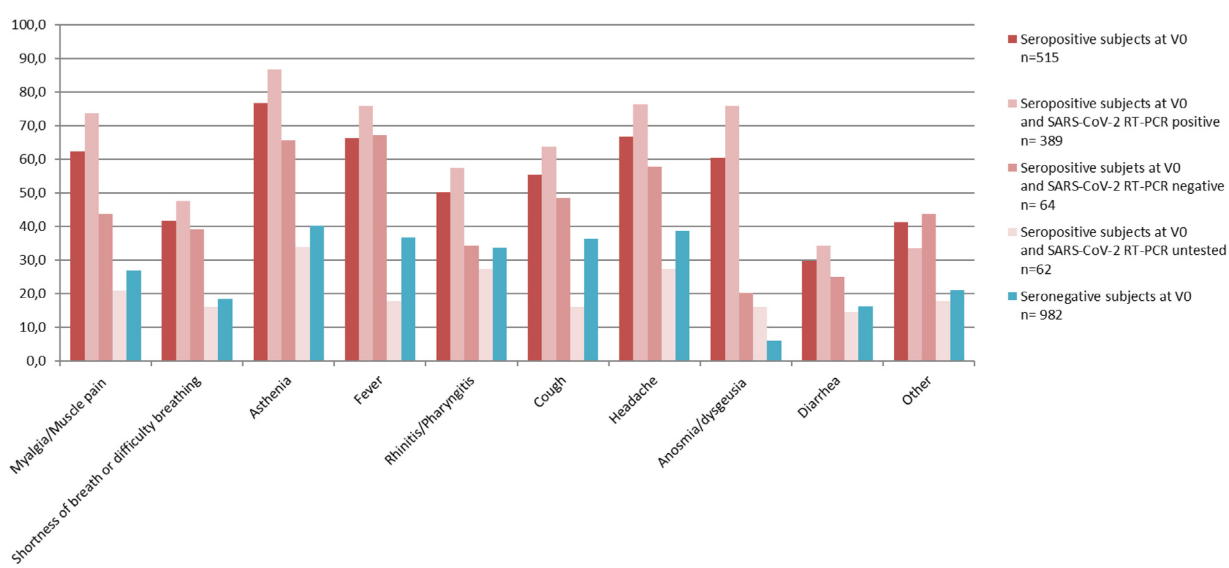

Fig. 2. Distribution of COVID-19-associated symptoms according to serological status at V0 and SARS-CoV-2 RT-PCR status (positive, negative, or untested). Percentage of subjects of each category reporting each COVID-19-associated symptom. Seropositive and seronegative subjects at V0 are represented by red bars and blue bars, respectively. Within those workers seropositive at V0, individual percentages for those who were SARS-CoV-2-positive, negative by RT-PCR or untested are shown as differing shades of red.

still had antibodies at V1 (320/331; 96.7%), while those previously tested negative by RT-PCR or who were not previously tested by RT-PCR were more likely to present with antibody decrease with 57.9% (33/57) and 66.1% (37/56) of them still seropositive at V1, respectively (Table 2). A total of 754 workers were still seronegative at V1, and 484 of them reported mild COVID-19 symptoms, including five individuals who reported a positive SARS-CoV-2 RT-PCR.

3.3. COVID-19 contact history among hospital staff members

A history of COVID-19 exposure in a professional and/or private setting (overall exposure) was mentioned by 83.1% of seropositive subjects and 66.4% of seronegative subjects at V0 ($P < 0.05$; OR: 2.5; 95% CI: 1.8–3.4) (Figs. 4 and 5; Table 3).

We first considered the occurrence of non-professional exposure to COVID-19 among participants, outside of the hospital

Table 1
Characteristics of seropositive and seronegative subjects at V0.

	Total cohort n = 1497	Seropositive subjects at V0 n = 515	Seronegative subjects at V0 n = 982	P-value/ OR (95%CI)
Male (%)/Female (%)	351 (23.4)/1146 (76.6)	129 (25.0)/386 (75.0)	222 (22.6)/760 (77.4)	P = 0.48
Age (years), median (IQR)	37 (29–49)	38 (28–49)	37 (29–49)	P = 0.82
BMI, median (IQR)	23.5 (21.2–26.8)	23.6 (21.3–26.8)	23.5 (21.1–26.9)	P = 0.78
Blood group				
A, n (%)	544 (36.4)	203 (39.4)	341 (34.7)	P = 0.38
AB, n (%)	66 (4.4)	23 (4.5)	43 (4.4)	
B, n (%)	130 (8.7)	40 (7.8)	90 (9.2)	
O, n (%)	540 (36.1)	173 (33.6)	367 (37.4)	
Unknown, n (%)	217 (14.4)	76 (14.7)	141 (14.3)	
Occupation (medical and non-medical professions)				
Clinician, n (%)	246 (16.4)	87 (16.9)	159 (16.2)	P = 0.23
Medical student, n (%)	161 (10.8)	68 (13.2)	93 (9.5)	
Nurse, n (%)	424 (28.3)	143 (27.7)	281 (28.6)	
Nursing assistant, n (%)	159 (10.6)	62 (12.0)	97 (9.9)	
Other healthcare staff*, n (%)	49 (3.3)	16 (3.1)	33 (3.4)	
Admin. staff, n (%)	153 (10.2)	49 (9.5)	104 (10.6)	
Cleaning staff, n (%)	52 (3.5)	17 (3.3)	35 (3.6)	
Psychologist, social worker, n (%)	25 (1.7)	8 (1.5)	17 (1.7)	
Technical staff, n (%)	90 (6.0)	21 (4.1)	69 (7.0)	
Other occupation, n (%)	138 (9.2)	45 (8.7)	93 (9.5)	
Previous SARS-CoV-2 RT-PCR testing				
Positive, n (%)	400 (26.7)	389 (75.5)	11 (1.1)	P < 0.05
Negative, n (%)	531 (35.5)	64 (12.4)	467(47.6)	
Untested, n (%)	566 (37.8)	62 (12.1)	504 (51.3)	
COVID-19 history				
COVID-19 symptoms, n (%)	1115 (74.5)	486 (94.4)	629 (64.1)	OR: 9.4 (6.3–14.5)
Myalgia/muscle pain, n (%)	587 (52.6)	322 (62.5)	265 (27.0)	OR: 4.3 (3.4–5.4)
Shortness of breath or difficulty breathing, n (%)	397 (35.6)	215 (41.8)	182 (18.5)	OR: 3.0 (2.4–3.9)
Asthenia, n (%)	790 (70.9)	395 (76.7)	395 (40.2)	OR: 4.4 (3.4–5.7)
Fever, n (%)	703 (63)	342 (66.4)	361 (36.8)	OR: 3.3 (2.6–4.2)
Rhinitis/pharyngitis, n (%)	590 (52.9)	259 (50.3)	331 (33.7)	OR: 2 (1.6–2.5)
Cough, n (%)	642 (57.6)	286 (55.5)	356 (36.3)	OR: 2.1 (1.7–2.6)
Headache, n (%)	725 (65%)	344 (66.8)	381 (38.8)	OR: 2.9 (2.3–3.7)
Anosmia/dysgeusia, n (%)	370 (33.2)	311 (60.4)	59 (6.0)	OR: 21.2 (15.2–29.5)
Diarrhea, n (%)	314 (28.2)	154 (29.9)	160 (16.3)	OR: 2.1 (1.7–2.8)
Other, n (%)	421 (37.8)	213 (41.4)	208 (21.2)	OR: 2.4 (1.9–3.1)
Mean time between symptom onset and V0 serology (days after symptom onset) (range)	38 (2–122) n = 1039	32 (6–96) n = 475	42 (2–122) n = 564	P < 0.05
Hospitalization due to COVID-19, n (%)	20 (1.3)	17 (3.3)	3 (0.3)	P < 0.05
Asymptomatic subjects, n (%)	382 (25.5)	30 (5.8)	352 (35.8)	OR: 0.1 (0.1–0.2)
Serological test result at V1				
Positive, n (%)	422 (28.2)	390 (75.7)	32 (3.2)	P < 0.05
Negative, n (%)	808 (54.0)	54 (10.5)	754 (76.8)	
Untested, n (%)	267 (17.8)	71 (14.8)	196 (20.0)	
Mean time between symptom onset and V1 serology (days after symptom onset) (range)	124 (69–214) n = 859	110 (78–191) n = 408	131 (69–214) n = 451	P < 0.05

Admin.: administrative. n is the total number of patients with available data.
* Dentists, midwives, physiotherapists, hospital porters.

Table 2
Seropositive rates at V0 and V1 according to SARS-CoV-2 RT-PCR status (positive, negative, or untested).

	Seropositive subjects at V0, n (%)	Seropositive subjects at V0 and tested at V1, n (%)	Subjects still seropositive at V1, n (%)
SARS-CoV-2 RT-PCR-positive subjects	389/515 (75.5)	331/389 (85.1)	320/331 (96.7)
SARS-CoV-2 RT-PCR-negative subjects	64/515 (12.4)	57/64 (89.1)	33/57 (57.9)
SARS-CoV-2 RT-PCR-untested subjects	62/515 (12.0)	56/62 (90.3)	37/56 (66.1)
Total	515	444/515 (86.2)	390/444 (87.8)

setting. Non-professional COVID-19 exposure (family and other personal contacts) was significantly more often reported by seropositive subjects at V0 (21.1%) than seronegative subjects (12.5%) ($P < 0.05$; OR: 1.9, 95% CI: 1.3–2.7), especially outside the immediate family circle (OR: 2.2, 95% CI: 1.2–3.9) (Fig. 5 and Table 3). Among extra-professionally exposed workers, 79.2% of seropositive subjects and 42.1% of seronegative subjects at V0 could date their exposure precisely. The median time between presumed contact and onset of first symptoms was 5 days in both groups of participants.

Occupational COVID-19 exposure analysis showed that professional exposure to COVID-19 (patients and/or colleagues) was reported in 54.2% of seropositive workers and in 42.6% of seronegative workers at V0 (OR: 1.6; 95%CI: 1.2–2.1). The distribution of seropositive and seronegative subjects between different professional categories was equivalent at V0, except for medical

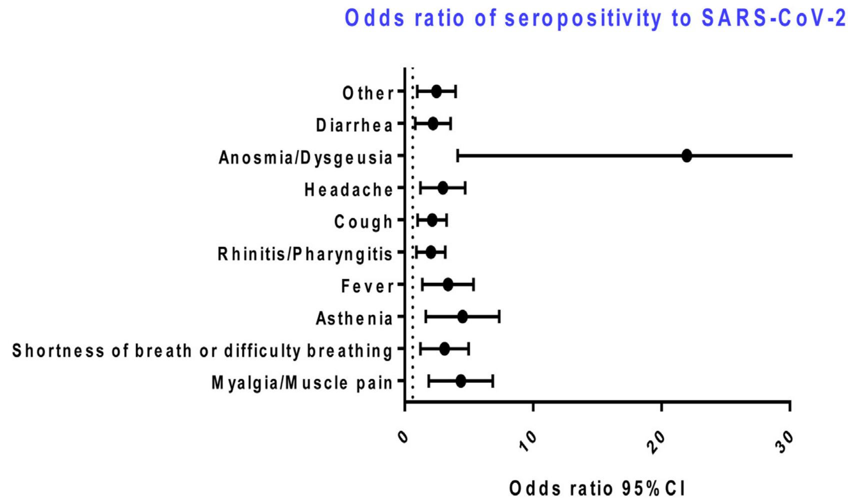

Fig. 3. Associations between prior COVID-19 symptoms and SARS-CoV-2 serological status. Odds ratio of seropositivity for individually reported symptoms. Data are depicted as odds ratios (black circle) and 95% confidence intervals (bars either side). A total of 1227 participants reported COVID-19 symptoms. Among them, 493 were seropositive at V0, while 734 were seronegative at V0. Symptoms included in the survey were: myalgia, shortness of breath or difficulty breathing, fever, asthenia, rhinitis/pharyngitis, cough, headache, anosmia/dysgeusia, diarrhea, other.

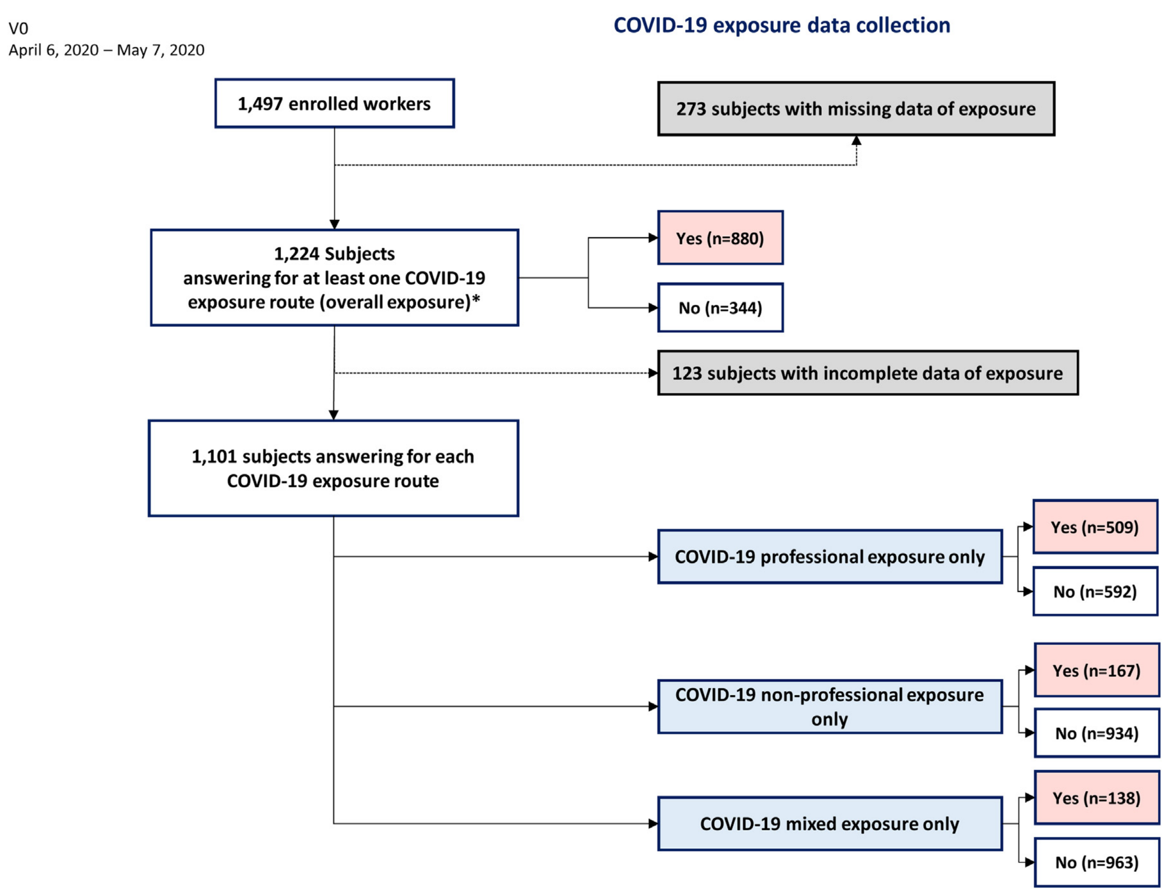

Fig. 4. COVID-19 exposure data collection. Among the 1497 workers enrolled in the study, 1224 subjects answered to at least one COVID-19 exposure route (overall exposure). Among them, 1101 subjects answered for each exposure route: COVID-19 professional exposure only (patients or colleagues), COVID-19 non-professional exposure only (family or other exposure in the private sphere), and COVID-19 mixed exposure (both professional and non-professional exposure).

students (13.2% versus 9.5%, respectively) and assistant nurses (12.0% versus 9.9%, respectively). Regardless of serological status, professional exposure and more specifically, COVID-19 patient exposure were predominantly reported in nurses (35.0% and 33.0%, respectively), clinicians (16.0% and 14.2%), and assistant nurses (16.0% and 12.8%). Seropositive subjects at V0 were significantly more exposed to COVID-19 patients than those who were seronegative at V0 ($P < 0.05$; OR: 1.6; 95% CI: 1.1–2.2), whereas exposure to COVID-19 colleagues was equivalent between the two groups ($P = 0.35$). Among professionally exposed staff members, only 42.2% of seropositive workers and 24.1% of seronegative workers at V0 were able to provide a precise date of exposure. For those reporting a precise date of exposure, the median time between supposed contact and onset of initial symptoms was 5.5 days (range:

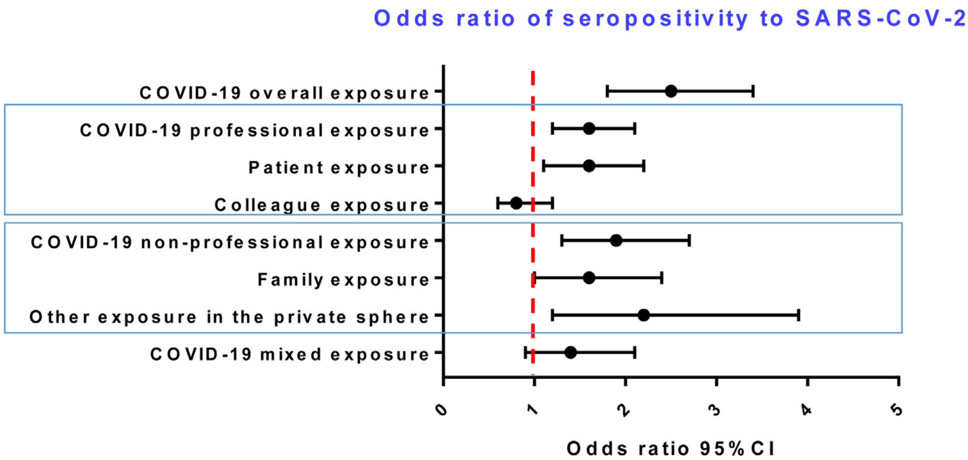

Fig. 5. Associations between COVID-19 exposure and SARS-CoV-2 serological status. Odds ratio of seropositivity following COVID-19 exposure, according to the type of exposure (professional, patient, colleague, non-professional, family, other non-professional exposures), compared to no COVID-19 exposure. Data are depicted as odds ratios (black point) and 95% confidence intervals (bars either side).

Table 3
SARS-CoV-2 seroprevalence among workers at V0 according to contact history.

	Total	Seropositive subjects at V0	Seronegative subjects at V0	*P*-value/ OR (95%CI)
Overall exposure*, *n* (%)	880/1,224 (71.9)	334/402 (83.1)	546/822 (66.4)	$P < 0.05$ OR: 2.5 (1.8–3.4)
Professional exposure only, *n* (%)	509/1,101 (46.2)	185/341 (54.2)	324/760 (42.6)	$P < 0.05$ OR: 1.6 (1.2–2.1)
Patient exposure, *n* (%)	206/947 (21.7)	69/247 (27.9)	137/700 (19.6)	$P < 0.05$ OR: 1.6 (1.1–2.2)
Colleague exposure, *n* (%)	185/947 (19.5)	43/247 (17.4)	142/700 (20.3)	$P = 0.35$ OR: 0.8 (0.6–1.2)
Median time between supposed COVID-19 exposure and symptom onset, days (range)**	6.5 (0–30)	5.5 (0–30)	7.0 (0–30)	$P = 0.36$
Non-professional exposure only, *n* (%)	167/1,101 (15.2)	72/341 (21.1)	95/760 (12.5)	$P < 0.05$ OR: 1.9 (1.3–2.7)
Family exposure, *n* (%)	111/1,101 (10.1)	45/341 (13.2)	66/760 (8.7)	$P < 0.05$ OR: 1.6 (1.0–2.4)
Other exposure in the private sphere, *n* (%)	56/1,101 (5.1)	27/341 (25.0)	29/760 (3.8)	$P < 0.05$ OR: 2.2 (1.2–3.9)
Median time between supposed COVID-19 exposure and symptom onset, days (range)***	5 (0–24)	5 (0–18)	5 (0–24)	$P = 0.68$
Mixed exposure****, *n* (%)	138/1,101 (12.5)	52/341 (15.2)	86/760 (11.3)	$P = 0.07$ OR: 1.4 (0.9–2.1)

Subjects for whom data was not completed were excluded from the analysis.
* Participants reporting at least one COVID-19 exposure route.
** Median time estimated when a precise date of professional exposure (excluding mixed exposure) was reported (78 [42.2%] seropositive subjects and 78 [24.1%] seronegative subjects at V0).
*** Median time estimated when a precise date of non-professional exposure (excluding mixed exposure) was reported (57 [79.2%] seropositive subjects and 40 [40.1%] seronegative subjects at V0).
**** Participants reporting both a professional and a non-professional COVID-19 exposure.

0–30) for seropositive workers at V0 and 7 days (0–30) for workers seronegative at V0. Neither the initial ward of occupation ($P = 0.05$), nor a change of ward ($P = 0.17$) due to hospital reorganization during the pandemic, were found to impact SARS-CoV-2 serological status of staff members. A total of 138 (12.5%) participants reported COVID-19 exposure in both professional and private settings – this proportion did not differ between seropositive and seronegative subjects.

3.4. Adherence to strict hygiene standards among COVID-19 professionally exposed subjects

We analyzed the extent of systematic adherence to strict hygiene standards among occupationally exposed participants, according to their serological status (Table 4). Participants were asked about their systematic use of hand hygiene by alcohol-based hand sanitizer, surgical masks, FFP2 masks, gloves, protective glasses, isolation gowns, and head caps. Among all PPE reported, only the use of a surgical mask was significantly less frequently reported by seropositive subjects than seronegative subjects at V0 ($P = 0.0007$, OR: 1.9 [95% CI: 1.3–2.8]). Among the 136 professionally exposed workers who reported occasionally ($n = 39$) or never ($n = 97$) wearing a surgical mask, nurses (25.7%; $n = 35$), assistant nurses (16.2%; $n = 22$), and medical students (11.7%; $n = 16$) were predominant. Looking in further detail at virological data for these workers, 17 (48.6%) of these nurses and 11 (50.0%) of these assistant nurses were seropositive at V0. Whilst 13 of these nurses reported a RT-PCR-confirmed SARS-CoV-2 infection, all seropositive assistant nurses were previously diagnosed as COVID-19-positive by RT-PCR. Only one of these assistant nurses mentioned any

Table 4
PPE used among professionally exposed subjects, according to SARS-CoV-2 serological status at V0.

		Seropositive subjects at V0, professionally exposed n = 262	Seronegative subjects at V0, professionally exposed n = 450	P-value/ OR (95%CI)
Systematic adherence to strict hygiene standards, n (%)	Hand hygiene with alcohol-based hand sanitizer	244 (93.1)	434 (96.4)	$P = 0.22$ OR: 1.7 (0.8–3.5)
	Surgical masks	190 (72.5)	380 (84.4)	$P < 0.05$ OR: 1.9 (1.3–2.8)
	FFP2 masks	58 (22.1)	108 (24.0)	$P = 0.71$ OR: 1.1 (0.8–1.6)
	Gloves	164 (62.6)	263 (58.4)	$P = 0.20$ OR: 0.8 (0.6–1.1)
	Protective glasses	78 (29.8)	128 (28.4)	$P = 0.61$ OR: 0.9 (0.7–1.3)
	Isolation gown	103 (39.3)	183 (40.7)	$P = 0.94$ OR: 1.0 (0.8–1.4)
	Head cap	113 (43.1)	208 (46.2)	$P = 0.53$ OR: 1.1 (0.8–1.5)

non-professional exposure to COVID-19. Interestingly, among the 16 medical students concerned, 10 (62.5%) were seropositive at V0, nine of them had a history of SARS-CoV-2-positive RT-PCR and the remaining student did not report any RT-PCR testing subsequent to his professional exposure. Eight of them (80%) did not report any non-professional exposure to COVID-19.

4. Discussion

This large serological and COVID-19 exposure investigation enrolled 1497 hospital staff members during the first wave of COVID-19, including members of medical, non-medical, and administrative staff, which is an accurate representation of the general distribution of SUH staff. A total of 515 subjects (34.4%) were found SARS-CoV-2 seropositive at V0. A total of 484 individuals without circulating SARS-CoV-2 antibodies detected at V0 nor at V1, reported mild COVID-19 symptoms including five individuals who reported a positive SARS-CoV-2 RT-PCR. These individuals may have developed very low levels of antibodies that were not detected by the serological assays that we used [8] or may have developed symptoms in response to another respiratory disease, such as the flu, which was circulating at the same time.

Defining the immunity status among HCWs is of particular interest to health authorities to estimate the exposure risk, and to distinguish potential chains of infection in clinical settings from those due to COVID-19 contacts in the household or private spheres. It has long been established that exposure in settings with personal contacts greatly increases the potential for SARS-CoV-2 transmission, and dramatically hinders any slowdown of the pandemic [9]. In a small cohort of 58 HCWs, Paderno et al. showed that the predominant risk of infection was related to out-of-hospital personal contacts, implying close and prolonged interactions with less cautious use of PPE [10]. In our study, seropositive status was associated with non-professional exposure (family and other contacts in a personal setting), as well as with COVID-19 patient exposure (OR: 1.9, 95% CI: 1.3–2.7 and OR: 1.6; 95% CI: 1.1–2.2, respectively). No association was observed with exposure to COVID-19-positive colleagues. In theory, HCWs may be an important source of transmission to other HCWs within the hospital setting, but our results are consistent with those reported by Brandstetter et al., who showed that exposure to COVID-19-positive co-workers in a hospital setting does not lead to the development of measurable immune responses in a significant proportion of asymptomatic COVID-19 contacts [11].

Irrespective of the serological status, clinicians, nurses, and assistant nurses were those who predominantly reported professional exposure, in particular COVID-19 patient exposure. These observations are consistent with those reported by others [12,13]. However, we found that medical students and assistant nurses were more represented among seropositive subjects. Neither the initial department of occupation, nor a change of department due to hospital reorganization appeared to impact SARS-CoV-2 serological status of the workers. We therefore carried out a further analysis regarding the appropriate use of PPE and respect of strict hygiene standards among professionally exposed workers. Except for the systematic use of a surgical mask ($P < 0.05$, OR: 1.9, 95% CI: 1.3–2.8), systematic adherence to strict hygiene standards was similar between seropositive and seronegative subjects. Among those who reported occasionally or never wearing a surgical mask, nurses, assistant nurses, and medical students were predominant, despite the fact that these professional categories were precisely those most frequently exposed to COVID-19 patients. In many countries, a major issue during the first wave of the pandemic was sufficient access to appropriate PPE by hospital staff members. During this critical period, SUH did not face such a shortage of PPE, and surgical masks were always available for hospital staff. A possible explanation of these findings could be the misunderstanding or unawareness of the transmission risks among some professional categories such as assistant nurses and medical students. Our data showed that no non-professional exposure was reported for a large part of these medical students and assistant nurses who were SARS-CoV-2-seropositive and COVID-19-positive confirmed by RT-PCR. In these subjects, SARS-CoV-2 transmission could most likely have been avoided by the simple act of systematically wearing a surgical mask [14,15].

The main limitation of this study is its single-center setting, potentially leading to a selection bias. SUH was particularly impacted by the first wave of the COVID-19 pandemic and our results may probably differ from other less severely affected French hospitals during the same period. In addition, the retrospective use of declarative information collected from enrolled workers could affect the accuracy of certain data, such as the identification of a precise date of exposure. Although serological interpretation may be impacted by the varying sensitivities of SARS-CoV-2 serological tools, we chose to associate two different assays in order to limit this source of potential bias [7].

5. Conclusion

Our results not only support an occupational risk of SARS-CoV-2 transmission to SUH staff members from COVID-19 patient contact, but also, and to a similar extent, in their private sphere, not only household contacts but also, and especially, outside the immediate family circle. Concerning COVID-19 professional exposure, it seems imperative to regularly ensure awareness of good practice and respect of strict hygiene standards.

This study will provide valuable public health information, which should facilitate discussion and put into context the exposure risk of hospital staff. Equally, these results indicate the importance of educating healthcare workers, in particular, medical students and assistant nurses, with regard to the importance of strictly respecting stringent hygiene standards.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

Ethical statement

This study was registered in ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT04441684). The protocol was approved by the institutional review board of CPP Sud Méditerranée III. All participants provided a written informed consent.

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Contribution of authors

SFK, NM, CSM, MG, YH, and JDS conceived and designed the study. CSM, JDS, NC, LKP, and MG recruited participants. SB, NR, AS, LG, and JML carried out LFA experiments. AV, FG, and MJW analyzed the data. NM performed the statistical analyses. SFK, AV, and FG wrote the manuscript with substantial input from all co-authors.

Disclosure of interest

The authors declare that they have no competing interest.

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