BRIEF REPORT

Transmission Routes of Severe Acute Respiratory Syndrome Coronavirus 2 Among Healthcare Workers of a French University Hospital in Paris, France

Adrien Contejean,[1,2,a,] Jérémie Leporrier,[3,a] Etienne Canouï,[2] Jacques Fourgeaud,[4,5] Alice-Andrée Mariaggi,[6] Fanny Alby-Laurent,[1,3] Emmanuel Lafont,[1,3] Lauren Beaudeau,[2] Claire Rouzaud,[3] Fabienne Lecieux,[7] Agnès Greffet,[8] Anne-Sophie L'Honneur,[9,10,11] Jean-Marc Tréluyer,[9,10,11] Fanny Lanternier,[1,3] Anne Casetta,[12] Pierre Frange,[5,13,] Marianne Leruez-Ville,[4,5] Flore Rozenberg,[6,14] Olivier Lortholary,[1,3,15] and Solen Kernéis[2,16,17]

[1]Université de Paris, Faculté de Médecine, Paris, France, [2]Equipe Mobile d'Infectiologie, AP-HP, Hôpital Cochin, Paris, France, [3]Service de maladies Infectieuses et Tropicales, AP-HP, IHU Imagine, Hôpital Necker-Enfants malades, Paris, France, [4]Laboratoire de Virologie, AP-HP, Hôpital Necker-Enfants malades, Paris, France, [5]EHU 7328 PACT, Institut Imagine, Université de Paris, Faculté de Médecine, Paris, France, [6]Département de Virologie, AP-HP, Hôpital Cochin, Paris, France, [7]Service de Santé au Travail, AP-HP, Hôpital Cochin, Paris, France, [8]Service de Santé au Travail, AP-HP, Hôpital Necker-Enfants malades, Paris, France, [9]Département de Soins Intensifs Pédiatriques, AP-HP, Hôpital Necker-Enfants malades, Paris, France, [10]Pharmacology and Drug Evaluation in Children and Pregnant Women EA7323, Université de Paris, Faculté de Médecine, Paris, France, [11]Département de Pharmacologie Clinique AP-HP, Hôpital Cochin, Paris, France, [12]Equipe opérationnelle d'hygiène Hospitalière, AP-HP, Hôpital Cochin, Paris, France, [13]Laboratoire de Microbiologie Clinique, AP-HP, Hôpital Necker-Enfants malades, Paris, France, [14]Université de Paris, Institut Cochin, INSERM U1016, CNRS UMR8104, Paris, France, [15]Institut Pasteur, Molecular Mycology Unit, National Reference Centre for Invasive Mycoses and Antifungals, CNRS UMR 2000, Paris, France, [16]Université de Paris, INSERM, IAME, Paris, France, [17]Institut Pasteur, Epidemiology and Modelling of Antibiotic Evasion (EMAE), Paris, France

In this case-control study on 564 healthcare workers of a university hospital in Paris (France), contacts without protection with coronavirus disease 2019 (COVID-19) patients or with colleagues were associated with infection with severe acute respiratory syndrome coronavirus 2, whereas working in a COVID-dedicated unit and having children kept in childcare facilities were not.

Keywords. case-control study; COVID-19; determinants; healthcare workers; SARS-CoV-2.

Effective protection of healthcare workers (HCWs) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) requires assessment of transmission routes in this at high-risk population, both inside and outside healthcare.

We previously published an observational multicenter cohort study on HCWs during the first French coronavirus disease 2019 (COVID-19) breakthrough [1]. Only 20% of HCWs infected with SARS-CoV-2 reported close contact with suspected or confirmed COVID-19 patients, and 78% were not regularly posted in COVID-19-dedicated units. In contrast, 54% declared frequent close contacts with colleagues without protection. However, we were unable to compare our cohort to a robust control group of HCWs not infected with SARS-CoV-2. Diagnosis sensitivity of reverse-transcriptase polymerase chain reaction (rtPCR) on nasopharyngeal swab for COVID-19 is imperfect [2], and serological assessment was not available at this time. Immunoglobulin (Ig)G serological test has since been proven to be reliably associated with a COVID-19 past infection [3]. In this study, we present a case-control study that compared COVID-19-positive and COVID-19-negative HCWs regarding their occupational activity, symptoms, and in-hospital and out-of-hospital exposures to SARS-CoV-2.

MATERIAL AND METHODS

Patients and Design

This study was led among HCWs at a 2100-bed tertiary care university hospital (Assistance Publique-Hôpitaux de Paris Centre, Université de Paris) located in central Paris, France, employing 13 278 personnel. From February 24 to 10 April 10, 2020, symptomatic staff were referred to dedicated onsite testing centers where trained medical staff collected a nasopharyngeal swab for SARS-CoV-2 rtPCR. The HCWs who tested positive were included as cases. For each confirmed case, we included a control symptomatic HCW tested on the same day, with a negative rtPCR and a negative serological assessment performed at least 1 month after symptoms onset. Immediately after testing, both cases and controls were questioned on their professional activity, symptoms, occupational exposures (eg, average daily number of close contacts with COVID-19 patients with and without personal protective equipment [PPE], compliance to infection prevention protocols, contacts with colleagues during meal breaks, meetings, etc), and nonoccupational exposures to SARS-CoV-2 (eg, frequentation of public transports, contacts inside and outside the household) [1]. All schools and childcare facilities closed on March 12, 2020 in France, except for children of hospital staff, and a nationwide lockdown started on March 17, 2020. Lift of containment measures occurred on May 11, 2020.

Virology Methods

The SARS-CoV-2 rtPCR technique has been described elsewhere [1]. The SARS-CoV-2 serology was determined by

the Abbott SARS-CoV-2 IgG assay, a chemiluminescent microparticle immunoassay for qualitative detection of IgG antibodies to SARS-CoV-2.

Statistical Analysis

Continuous variables are presented as median (interquartile range), and categorical variables are presented as number (percentage). Fisher exact tests were used for comparisons of qualitative variables, and Mann-Whitney tests were used for quantitative variables. All tests were 2-sided with a .05 value for significance. Factors associated with SARS-CoV-2 infection were assessed using multivariate logistic regression models. To account for the impact of lockdown on exposures, we considered 2 periods before and after March 22, 2020 (March 17, 2020 [date of national lockdown] + mean incubation period of 5 days). For each period, we first entered all exposures with a $P < .40$ in a multivariate model then used a backward stepwise selection procedure (removal criteria: $P > .05$) to build the final model. Statistical analyses were performed using R-software (version 3.3.2; R Foundation for Statistical Computing, Vienna, Austria).

Patient Consent Statement

This study was approved by the Ethical Review Committee for publications of the Cochin University Hospital (number AAA-2020-08012). According to French policy, a nonopposition statement was obtained for all participants, meaning that all had received written detailed information on the objectives of the study and were free to request withdrawal of their data at any time.

RESULTS

Between February 24 and April 10, 2020, 1344 symptomatic HCWs were screened for SARS-CoV-2 by rtPCR on a nasopharyngeal swab. Among them, 373 had positive rtPCR results (28%), 336 (90%) completed the questionnaire, and were included as cases. Among 338 matched HCWs with negative rtPCR, 247 (73%) had a serological assessment, and 228 (92%) tested negative. This group of 228 HCWs with both negative rtPCR and serology constituted the control group.

Cases and controls were comparable in terms of age, sex, and professional category (Table 1). Cases presented more frequently with anosmia, ageusia, asthenia, fever, muscle pain, dyspnea, and headaches. Frequency of diarrhea, cough, or rhinorrhea did not differ between groups. Among cases, 3 were hospitalized and no death was reported.

Univariate and multivariate analyses are displayed in the Table 1. In brief, patient-facing activities and assignment to a COVID-19-dedicated unit were not associated with infection in both periods. Before lockdown, wearing a mask at all times outside home and limiting contacts with colleagues were independently protective. During lockdown, only close contacts

with suspected or confirmed COVID-19 patients without PPE were independently associated with infection in HCWs. In both periods, contacts with children kept outside of the household were not associated with infection in HCWs.

DISCUSSION

Our results confirm that COVID-19 infection in HCWs is associated with risky behavior both inside and outside healthcare, as already shown by others [4, 5]. Most previous reports focused on occupational exposures [5] or did not use PCR testing or serologic assessment to formally confirm or exclude the diagnosis of COVID-19 [6, 7]. Other strengths of our study are the evaluation of multiple sources of infection, both inside and outside care, in particular contacts with children at home, and data collection through a direct investigator-to-respondent interview.

Our study took place during first wave of the pandemic, and occupational risk factors for COVID-19 were dominated by exposure to suspected or confirmed COVID-19 patients without PPE, as described elsewhere [5]. However, it is interesting to note that direct patient care in COVID-19-dedicated wards was not associated with infection in HCWs in our cohort. The PPE supplies were immediately and fully available in our center, which was not the case in all French healthcare settings. Compliance to protective measures may also have been higher among highly trained HCWs in dedicated units, as suggested by others [4, 5]. In a recent report, a large cohort study on 99 795 HCWs suggested that frontline HCWs may be at increased risk of COVID-19 compared with community individuals, especially in case of exposition to patients with inadequate PPE [6]. Our results also underline the role of transmission outside care, through exposure to colleagues without protection. Indeed, SARS-CoV-2 infectiousness starts up to 2 days before symptoms onset [8], thus strict compliance to universal masking and social distancing measures at hospital are critical to prevent SARS-CoV-2 transmissions from asymptomatic individuals.

Analysis of nonoccupational exposures suggest that wearing a mask outside the home may provide protection against COVID-19. In Hong Kong, a study suggested that the number of COVID-19 clusters were reduced when universal masking was recommended [9], and a study conducted in the United States concluded that mandatory mask wearing reduced daily COVID-19 growth rates [10]. However, to our knowledge, no study with high level of evidence has been published yet on that question. Of note, HCWs who reported to wear a mask outside home in our cohort (17%) were also probably more cautious regarding social activities and other suspected sources of SARS-CoV-2, which were not assessed in the questionnaire.

One important result is that HCWs who reported to have children kept outside the family home did not have a higher risk of COVID-19 infection, as suggested in our first report [1]. This question of SARS-CoV-2 transmission from children is highly

Table 1. Cases and Controls Comparisons Regarding Demography, Profession, Symptoms, and Occupational or Out-of-Hospital Exposures

Variable	Overall n = 564	Controls (HCW−) n = 228	Cases (HCW+) n = 336	Prelockdown Period		Lockdown Period	
				Univariate Analysis OR [95% CI]	Multivariate Analysis OR [95% CI]	Univariate Analysis OR [95% CI]	Multivariate Analysis OR [95% CI]
Median age (IQR), years	40 (31–53)	41 (33–52)	40 (30–53)	1.00 [0.98–1.02]		0.99 [0.97–1.01]	
Sex (female)	448 (79)	183 (80)	265 (79)	0.79 [0.44–1.39]		1.32 [0.63–2.72]	
Professional Category[a]							
Physicians	155 (28)	64 (28)	91 (27)	ref		ref	
Paramedic staff (nurses, care assistants. . .)	331 (59)	126 (55)	205 (61)	0.98 [0.60–1.60]		1.49 [0.75–2.93]	
Administrative staff (secretaries)	56 (10)	28 (12)	28 (8)	0.85 [0.39–1.84]		0.56 [0.19–1.59]	
Other employees (housekeepers. . .)	22 (4)	10 (4)	12 (4)	0.71 [0.21–2.42]		1.02 [0.26–4.44]	
Symptoms							
Headaches	420 (75)	158 (69)	262 (78)	1.19 [0.70–2.02]		1.99 [1.01–3.89]	
Asthenia	405 (72)	133 (58)	272 (81)	3.03 [1.78–5.22]		2.66 [1.40–5.08]	
Fever (measured or reported)	369 (65)	123 (54)	246 (73)	3.17 [1.93–5.26]		1.35 [0.73–2.47]	
Cough	363 (64)	136 (60)	227 (68)	1.23 [0.75–1.99]		1.55 [0.85–2.83]	
Muscle pain	323 (57)	103 (45)	220 (66)	2.11 [1.32–3.39]		2.46 [1.36–4.49]	
Rhinorrhea	284 (50)	113 (49)	171 (51)	0.89 [0.55–1.37]		1.32 [0.74–2.38]	
Anosmia	244 (43)	15 (7)	229 (68)	16.3 [8.45–34.0]		118 [29.1–1032]	
Ageusia	233 (41)	18 (8)	215 (64)	21.7 [10.5–49.5]		172 [7.50–44.7]	
Diarrhea	197 (35)	68 (30)	129 (38)	1.24 [0.77–2.02]		1.73 [0.92–3.34]	
Dyspnea	187 (33)	61 (27)	126 (38)	1.69 [1.03–2.80]		1.53 [0.82–2.94]	
Exposures							
In-hospital exposures							
Exposure to patients							
Occupational activities with direct patient facing	388 (69)	154 (68)	234 (70)	0.86 [0.53–1.40]		1.47 [0.76–2.82]c	-
Regularly posted in a unit dedicated to COVID-19 patients	123 (22)	48 (21)	75 (22)	0.59 [0.28–1.25]c	-	1.53 [0.82–2.88]c	-
Had on average ≥1/day close contact with suspected or confirmed COVID-19 patients without PPE[b]	100 (18)	28 (12)	72 (21)	1.22 [0.64–2.38]		3.85 [1.59–10.8]d	**3.87 [1.73–9.89]**
Had on average ≥1/day close contact with suspected or confirmed COVID-19 patients with PPE	204 (38)	93 (45)	111 (34)	0.28 [0.16–0.51]d	-	1.04 [0.56–1.92]	
Exposure to Colleagues							
Wears a medical mask always/most of the time at hospital	372 (67)	163 (73)	209 (63)	0.45 [0.28–0.72]d	-	0.99 [0.34–2.63]	
Spends on average >1 hour/day with colleagues without mask	153 (31)	42 (24)	111 (34)	2.77 [1.63–4.77]d	-	0.52 [0.20–1.43]c	-
Had on average >10 close contacts/day with colleagues without mask	101 (18)	26 (12)	75 (23)	2.80 [1.57–5.16]d	**2.58 [1.49–4.60]**	1.36 [0.42–5.13]	
Out-of-Hospital Exposure							
Uses public transports	328 (58)	127 (56)	201 (60)	0.92 [0.57–1.47]		1.86 [1.03–3.37]d	-
Systematically wears a mask outside home	96 (17)	50 (22)	46 (14)	0.40 [0.19–0.83]d	**0.43 [0.21–0.85]**	0.69 [0.35–1.35]c	-
Systematically washes hands when back home	509 (91)	210 (92)	299 (90)	1.01 [0.47–2.13]		0.31 [0.03–1.46]c	-
Leaves home on average ≥1 times a week	495 (88)	205 (90)	290 (86)	0.81 [0.33–1.88]		0.62 [0.25–1.42]c	-

Table 1.   Continued

Variable	Overall n = 564	Controls (HCW−) n = 228	Cases (HCW+) n = 336	Prelockdown Period		Lockdown Period	
				Univariate Analysis OR [95% CI]	Multivariate Analysis OR [95% CI]	Univariate Analysis OR [95% CI]	Multivariate Analysis OR [95% CI]
Lives with ≥2 additional household members	281 (50)	109 (48)	172 (51)	0.88 [0.56–1.40]		1.58 [0.88–2.87]c	-
Lives with ≥1 child aged 0–4 years	82 (15)	35 (15)	47 (14)	0.86 [0.44–1.67]		0.83 [0.37–1.94]	
Lives with ≥1 child aged 5–15 years	138 (25)	60 (26)	78 (23)	0.61 [0.36–1.04]c	-	1.37 [0.69–2.82]	
Lives with ≥1 adult aged 70+ years	12 (3)	6 (3)	6 (2)	0.55 [0.08–3.31]		1.67 [0.13–89.3]	
Has ≥1 child kept outside the household (school, nursery)	105 (19)	45 (20)	60 (18)	1.02 [0.60–1.75]		0.65 [0.23–1.88]	
Nursery	31/105 (30)	13/45 (29)	18/60 (30)	1.19 [0.40–3.63]		0.72 [0.08–6.10]	
School	70/105 (67)	28/45 (62)	42/60 (70)	1.37 [0.46–4.03]		1.62 [0.20–15.6]	
Children kept in a facility with >5 other children	89/100 (89)	35/41 (85)	54/59 (92)	3.16 [0.42–372]c	-	0.89 [0.06–10.7]	

Bold text show OR [95% CI] for variables significantly associated with COVID-19 (HCW+) in a multivariable analysis.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HCW, healthcare workers; IQR, interquartile range; OR, odds ratio; PPE, personal protective equipment; ref, reference.

aProfessions were as follows: medical doctors or surgeons (n = 81), psychiatrists (n = 3), pharmacists (n = 3), biologists (n = 9), midwives (n = 10), residents (n = 32), nurses (n = 140), students (n = 19), healthcare assistants (n = 99), head nurses (n = 33), laboratory technicians (n = 18), radiology technicians (n = 9), physiotherapists (n = 5), secretaries (n = 20), support functions employees (n = 32), other (n = 51).

bPPE, including gowns, gloves, eye protections, and either medical masks for standard care or FFP2 masks during airway aerosol-generating procedures.

cVariables with P < .40 in the univariate model, which were included in the multivariable analysis.

dVariables with P < .05 in the univariable model.

debated since the start of the pandemic, but accumulating data suggest that children are not significant drivers for COVID-19 pandemic [11]. It is interesting to note that childcare facilities that remained open for HCWs' children during French national lockdown gathered a limited number of children simultaneously (<10). Therefore, our results suggest that keeping small-sized childcare facilities open for essential workers would be acceptable especially in case of further lockdown, when HCWs should be fully available at hospital.

We were not surprised to find that symptoms were significantly different between cases and controls. Anosmia and ageusia appeared to be strongly associated to SARS-CoV-2 infection as reported elsewhere [12, 13], whereas cough or rhinorrhea were not.

We acknowledge several limitations, in particular recall bias, but cases and controls were interrogated prospectively and shortly after PCR assay. In addition, our questionnaire might not have fully explored all sources of SARS-CoV-2.

CONCLUSIONS

In conclusion, more than 10 daily contacts with colleagues without protection or close contacts with suspected or confirmed COVID-19 patients without PPE were associated with COVID-19 infection in our cohort of HCWs, whereas profession category, assignment to a COVID-19-dedicated unit, and having children kept in childcare facilities were not. Adherence to PPE in healthcare, irrespective of patient profile, seems critical to prevent COVID-19, as well as strict compliance with social distancing measures with colleagues.

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