Transmission routes of SARS-CoV-2 among healthcare workers of a French university hospital in Paris, France

Adrien Contejean[1,2]*, Jérémie Leporrier[3]*, 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[6], 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], Solen Kernéis[2,16,17]

*Contributed equally

[1] Université de Paris, Faculté de Médecine, F-75006 Paris, France
[2] Equipe Mobile d'Infectiologie, AP-HP, Hôpital Cochin, F-75014 Paris, France
[3] Service de maladies infectieuses et tropicales, AP-HP, IHU Imagine, Hôpital Necker-Enfants malades, F-75015 Paris, France
[4] Laboratoire de virologie, AP-HP, Hôpital Necker-Enfants malades, F-75015 Paris, France
[5] EHU 7328 PACT, Institut Imagine, Université de Paris, Faculté de Médecine, F-75006 Paris, France
[6] Département de virologie, AP-HP, Hôpital Cochin, F-75014 Paris, France
[7] Service de santé au travail, AP-HP, Hôpital Cochin, F-75014 Paris, France
[8] Service de santé au travail, AP-HP, Hôpital Necker-Enfants malades, F-75015 Paris, France
[9] Département de soins intensifs pédiatriques, AP-HP, Hôpital Necker-Enfants malades, F-75015 Paris, France
[10] Pharmacology and Drug Evaluation in Children and Pregnant Women EA7323, Université de Paris, Faculté de Médecine, F-75006 Paris, France
[11] Département de pharmacologie clinique AP-HP, Hôpital Cochin, F-75014 Paris, France
[12] Equipe opérationnelle d'hygiène hospitalière, AP-HP, Hôpital Cochin, F-75014 Paris, France
[13] Laboratoire de microbiologie clinique, AP-HP, Hôpital Necker-Enfants malades, F-75015 Paris,
[14] Université de Paris, Institut Cochin, INSERM U1016, CNRS UMR8104, F-75006 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, F-75018 Paris, France
[17] Institut Pasteur, Epidemiology and Modelling of Antibiotic Evasion (EMAE), F-75015 Paris, France

Corresponding author:
Solen Kernéis
Equipe Mobile d'Infectiologie, Hôpital Cochin, 27, rue du Faubourg Saint Jacques, 75014, Paris, France
Phone: +33158414111
Mail: solen.kerneis@aphp.fr

Alternate corresponding author:
Adrien Contejean
Equipe Mobile d'Infectiologie, Hôpital Cochin, 27, rue du Faubourg Saint Jacques, 75014, Paris, France
Phone: +33158414111
Mail: adrien.contejean@aphp.fr

Abstract

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

Key words: COVID-19, SARS-CoV-2, Healthcare Workers, Determinants, Case-Control study

Introduction

Effective protection of healthcare workers (HCW) 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 HCW during the first French coronavirus disease-19 (COVID-19) breakthrough[1]. Only 20% of HCW infected with SARS-CoV-2 reported close contact with suspected or confirmed COVID19 patients, and 78% were not regularly posted in COVID-19-dedicated units. Conversely, 54% declared frequent close contacts with colleagues without protection. We were however unable to compare our cohort to a robust control group of HCW 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. IgG serological test has since been proven to be reliably associated with a COVID-19 past-infection[3]. We present here a case-control study which aimed to compare COVID-19 positive and negative HCW 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 HCW of a 2,100-bed tertiary-care university hospital (AP-HP. Centre, Université de Paris) located in central Paris, France, employing 13,278 personnel. From 24th February, to 10th April 2020, symptomatic staff were referred to dedicated on-site testing centers where trained medical staff collected a nasopharyngeal swab for SARS-CoV-2 rtPCR. HCW 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 (e.g., 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 non-occupational exposures to SARS-CoV-2 (e.g., frequentation of public transports, contacts inside and

outside the household)[1]. All schools and childcare facilities closed on March 12th in France, except for children of hospital staff, and a nationwide lockdown started on March 17th. Lift of containment measures occurred on May 11th.

Virology methods

SARS-CoV-2 rtPCR technique has been described elsewhere[1]. 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 as number (percentage). Fisher exact tests were used for comparisons of qualitative variables and Mann-Whitney tests 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 two periods before and after March 22nd, 2020 (March 17th [date of national lockdown] + mean incubation period of 5 days). For each period, we first entered all exposures with a p-value < 0.40 in a multivariate model then used a backward stepwise selection procedure (removal criteria: $p > 0.05$) to build the final model. Statistical analyses were performed using R-software (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 non-opposition 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 24th and April 10th, 2020, 1344 symptomatic HCW 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 HCW with

negative rtPCR, 247 (73%) had a serological assessment, and 228 (92%) tested negative. This group of 228 HCW with both negative rtPCR and serology constituted the control group.

Cases and controls where comparable in terms of age, sex and professional category (table). 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. Briefly, 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 HCW. In both periods, contacts with children kept outside of the household were not associated with infection in HCW.

Discussion

Our results confirm that COVID-19 infection in HCW 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]. But interestingly, direct patient care in COVID-19-dedicated wards was not associated with infection in HCW in our cohort. 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 HCW in dedicated units, as suggested by others[4,5]. Recently, a large cohort study on 99,795 HCW suggested that frontline HCW may be at increased risk of COVID-19 compared to 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 two 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 non-occupational exposures suggest that wearing a mask outside 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 USA 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, HCW 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 HCW 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 debated since the start of the pandemic, but accumulating data suggest that children are not significant drivers for COVID-19 pandemic[11]. Of note that childcare facilities that remained open for HCW's children during French national lockdown gathered a limited number of children simultaneously (<10). Then, our results suggest that keeping small-sized childcare facilities open for essential workers would be acceptable especially in case of further lockdown, when HCW should be fully available at hospital.

Unsurprisingly, 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. Additionally, our questionnaire might not have fully explored every sources of SARS-CoV-2.

In conclusion, more than ten 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 HCW, while 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.

Authors' Contributions

AC, JL, OL and SK designed the study and drafted the paper. AC, JL, ML, FR, OL and SK contributed to data analysis and interpretation. All authors critically revised the manuscript for important intellectual content and gave final approval for the version to be published. SK had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Conflicts of Interests

All authors declare no conflict of interest in relation with the submitted work

Role of the funding source

This study had no funding source or sponsor implicated in the study design, in the collection, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

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Table: Cases and controls comparisons regarding demography, profession, symptoms and occupational or out-of-hospital exposures.

	Overall n=564	Controls (HCW-) n=228	Cases (HCW+) n=336	Pre-lockdown 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[#]							
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]		17.2 [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]*	-
Regularly posted in a unit dedicated to COVID19-patients	123 (22)	48 (21)	75 (22)	0.59 [0.28-1.25]*	-	1.53 [0.82-2.88]*	-
Had on average ≥1/day close contact with suspected or confirmed COVID-19 patients without PPE[##]	100 (18)	28 (12)	72 (21)	1.22 [0.64-2.38]		3.85 [1.59-10.8]**	**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]**	-	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]**	-	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]**	-	0.52 [0.20-1.43]*	-
Had on average >10 close contacts/day with colleagues without mask	101 (18)	26 (12)	75 (23)	2.80 [1.57-5.16]**	**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]**	-
Systematically wears a mask outside home	96 (17)	50 (22)	46 (14)	0.40 [0.19-0.83]**	**0.43 [0.21-0.85]**	0.69 [0.35-1.35]*	-
Systematically washes hands when back home	509 (91)	210 (92)	299 (90)	1.01 [0.47-2.13]		0.31 [0.03-1.46]*	-
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]*	-
Lives with ≥ 2 additional household members	281 (50)	109 (48)	172 (51)	0.88 [0.56-1.40]		1.58 [0.88-2.87]*	-
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]*	-	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	42/60	1.37 [0.46-4.03]		1.62 [0.20-15.6]	

Children kept in a facility with >5 other children	89/100 (89)	(62) 35/41 (85)	(70) 54/59 (92)	3.16 [0.42-37.2]*	-	0.89 [0.06-10.7]

[#] Professions were: 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), health care 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).

[##] PPE: Personal Protective Equipment, including gowns, gloves, eye protections, and either medical masks for standard care or FFP2 masks during airway aerosol-generating procedures.

*variables with p-value < 0.40 in the univariable model, which were included in the multivariable analysis

**variables with p-value < 0.05 in the univariable model