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Short Report

Dynamics of SARS-CoV-2 RT-PCR positivity and seroprevalence among high-risk healthcare workers and hospital staff

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SUMMARY

Staff working in units that were highly exposed to coronavirus disease 2019 were invited to participate in a 6-month study on the carriage and seroprevalence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The results from visits on Day 1 and Day 15 show that 41 cases of SARS-CoV-2 infection were confirmed by reverse transcriptase polymerase chain reaction and/or serology in 326 participants (overall infection rate 12.6%). The presence of comorbidities or symptoms at the time of sample collection was a risk factor for infection, but working as a physician/nurse was not a risk factor. Universal screening in high-risk units, irrespective of symptoms, allowed the identification of asymptomatic and potentially contagious infected workers, enabling them to self-isolate for 7 days.

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, causing coronavirus disease 2019 (COVID-19), hit Asia in early 2020 and Europe in February 2020. The epidemiological peak in Belgium is estimated to have occurred on approximately 31st March 2020, with 5759 patients

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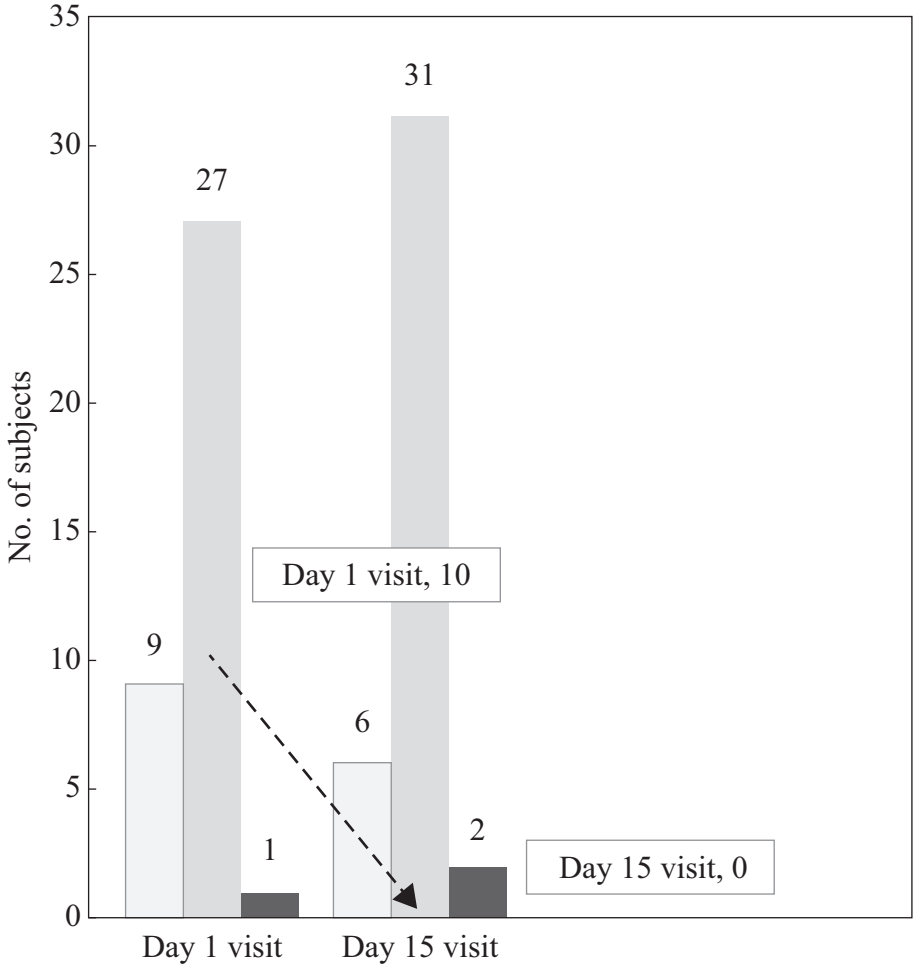

Figure 1. Number of symptomatic subjects at the time of sample collection and subjects testing positive for severe acute respiratory syndrome coronavirus-2 on reverse transcriptase polymerase chain reaction (RT-PCR) and/or serology at Day 1 and Day 15 visits. White bars, positive on both RT-PCR and serology; grey bar, positive on serology; black bar, positive on RT-PCR. Dashed arrow shows cases who were symptomatic at the time of sample collection.

hospitalized on 6th April 2020 and occupancy of deployed national intensive care unit (ICU) beds at a maximum of 58% (1285 hospitalized patients in ICUs on 8th April 2020 [1]). Based on experience gained during the severe acute respiratory syndrome coronavirus epidemic, healthcare workers (HCWs) are considered to be a high-risk population for the acquisition of SARS-CoV-2. Few studies have reported both current and past infection using reverse transcriptase polymerase chain reaction (RT-PCR) and/or serological testing [2,3]. Studies on HCWs represent a unique opportunity to study natural infection in asymptomatic or pauci-symptomatic subjects. High viral loads have been detected in asymptomatic cases of SARS-CoV-2 with a similar duration of carriage compared with symptomatic patients [4,5]. Seroconversion is well described in hospitalized patients. It is observed in more than 99% of cases within 19 days, and the antibody level is correlated with the severity of COVID-19 [6]. However, less is known about the seroconversion rate following asymptomatic infection. The primary objective of this study was to assess the rate and dynamics of SARS-CoV-2 positivity and seroprevalence among high-risk HCWs and hospital staff. This paper presents the preliminary results from baseline and 2-week follow up.

Methods

Centre Hospitalier Universitaire Saint-Pierre (CHU Saint-Pierre) in Brussels is a tertiary reference hospital for infectious diseases, and the only reference centre for highly contagious respiratory infectious diseases in Belgium. At the peak of the first wave of the SARS-CoV-2 pandemic, approximately 700 staff were working in the general COVID-19 units (seven units with a total of 125 beds), COVID-19 intensive care units (two ICUs with a total of 33 beds) and Emergency Department of CHU Saint-Pierre (hereafter 'COVID-19 units'). The COVID-19 units were reserved for probable or confirmed cases of COVID-19, with the latter representing between 50% and 90% of patients. The recommendations of the European Centre for Disease Prevention and Control were followed in terms of personal protective equipment (PPE) and infection control [7]. All staff members working in the COVID-19 units were invited to participate, on a voluntary basis, in a 6-month study on the carriage and seroprevalence of SARS-CoV-2. Medical and paramedical staff were considered to be more exposed to SARS-CoV-2 than administrative staff, stretcher bearers and cleaners, and wore FFP2 masks. At each visit, participants were

Table I
Characteristics of overall, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-negative and -positive populations, confirmed by reverse transcriptase polymerase chain reaction and/or serology on Day 1 and Day 15 visits

	Overall population (*N*=326)	SARS-CoV-2-negative population (*N*=285)	SARS-CoV-2-positive population (*N*=41)	
Age in years, mean (range)	37 (21–66)	39 (28–66)	36 (21–59)	*P*=0.1
Female/male, *N* (%)	239 (73%)/87 (27%)	208 (73%)/77 (27%)	31 (75.6%)/ 10 (24.4%)	*P*=0.8
Work unit, *N* (%)				*P*=0.2
COVID-19 unit	215 (66%)	184 (64.5%)	31 (75.7%)	
COVID-19 ICU	53 (16.2%)	50 (17.2%)	3 (7.3%)	
Emergency Department	58 (17.8%)	51 (18.3%)	7 (17%)	
Type of work, *N* (%)				*P*=0.1
Nursing and medical staff	295 (90%)	257 (90.2%)	38 (92%)	*P*=0.6
Physician	85 (29%)	75 (29.1%)	10 (26.3%)	
Nurse	150(51%)	131 (51%)	19 (50%)	
Care assistant	27 (9%)	23 (8.9%)	4 (10.5%)	
Paramedical staff	33 (11%)	28 (11%)	5 (13.2%)	
Administrative staff	25 (8%)	24 (8.4%)	1 (2.4%)	
Cleaning staff and stretcher bearers	6 (2%)	4 (1.4%)	2 (4.8%)	
Symptomatic at time of sample collection, *N* (%)	56 (17.1%)	46 (16.1%)	10 (24.4%)	*P*=0.07
Asymptomatic at time of sample collection, *N* (%)	270 (82.3%)	239 (83.9%)	31 (75.6%)	*P*=0.07
COVID-19 diagnosis before study	36 (11%)	13 (4.6%)	23 (56%)	
Comorbidities, *N* (%)	38 (11.6%)	29 (10%)	9 (22%)	*P*≤0.05
High blood pressure	16 (4.9%)	12 (4.2%)	4 (9.7%)	*P*=0.12
Diabetes	6 (1.8%)	4 (1.4%)	2 (4.8%)	*P*=0.16
Chronic pulmonary disease	9 (2.7%)	7 (2.4%)	2 (4.8%)	*P*=0.31
Neoplasia	1 (0.3%)	1 (0.3%)	0	
Immunodeficiency	1 (0.3%)	1 (0.3%)	0	
Cardiovascular disease	3 (0.9%)	3 (1%)	0	
Autoimmune disease	3 (0.9%)	3 (1%)	0	
Other	3 (0.9%)	2 (0.7%)	1 (2.4%)	*P*=0.33

COVID-19, coronavirus disease 2019; ICU, intensive care unit.

asked to complete a questionnaire regarding medical history and recent or current symptoms. The presence of symptoms was not an exclusion criterion. RT-PCR (RealStar SARS-CoV-2 RT-PCR kit 1.0 Altona Diagnostics, Hambourg, Germany) of a nasopharyngeal swab sample and a serological test (Euroimmun Anti-SARS-CoV-2 IgG Medizinische Labordiagnostika AG, Luebeck, Germany) were proposed to be carried out at precise time points over the 6-month study period: Day 1 (baseline), Day 15, Day 30, Month 2, Month 3 and Month 6. In accordance with national recommendations, workers with a positive result on RT-qPCR, regardless of the presence or absence of symptoms, self-isolated for 7 days.

The results of the two first visits (Day 1 and Day 15) are presented in this article. The Ethical Committee of CHU Saint-Pierre approved this study (CE/20-04-17) and written informed consent was obtained from the participants. Descriptive statistics were used to summarize the characteristics of the study population. Hypothesis tests for differences between groups were performed using non-parametric Wilcoxon–Mann–Whitney and Kruskal–Wallis tests for continuous variables, and Fisher's exact tests for categorical variables. All *P*-values were two-sided and $P<0.05$ was considered to indicate significance. SAS Version 9.4 (SAS Institute, Cary, NC, USA) was used for statistical analyses.

Results

In total, 532 staff [physicians (*N*=85), nurses (*N*=150), paramedical staff (*N*=60), administrative employees (*N*=25), stretcher bearers and cleaners (*N*=6)] from the COVID-19 units agreed to participate in the study. Between 15th April and 18th May 2020, 326 participants completed the Day 1 and Day 15 visits.

Fifty-six (17.1%) participants reported symptoms suggestive of COVID-19 at the time of sampling.

On Day 1, 37 cases of SARS-CoV-2 were confirmed by RT-PCR and/or serology (11.3% of overall population). Ten subjects were diagnosed based on a positive RT-PCR result (3%). Among them, three patients had current mild symptoms: cough (*N*=2), sore throat (*N*=2), diarrhoea (*N*=2), headache (*N*=1) and tiredness (*N*=2); none of them had fever. Eight of the 10 subjects with a positive RT-PCR result had a previous confirmed COVID-19 diagnosis. Of note, one subject with a positive RT-PCR result tested negative for immunoglobulin G (IgG).

IgG seroprevalence at baseline was 11% (*N*=36); of these subjects, 27 (75%) had a negative RT-PCR result. Among these 27 IgG-positive/RT-PCR-negative subjects, seven (26%) had concomitant symptoms: dyspnoea (*N*=2), fever (*N*=1), cough (*N*=5), sore throat (*N*=2), headache (*N*=2), diarrhoea (*N*=1),

myalgia (*N*=1), conjunctivitis (*N*=1), loss of smell and/or taste (*N*=1), and tiredness (*N*=1). Fourteen of the 27 (52%) IgG-positive/RT-PCR-negative subjects had a previous confirmed COVID-19 diagnosis (mean delay since diagnosis 29 days).

On Day 15, six subjects remained positive on RT-PCR and two new cases were detected by RT-PCR (total 2.4%). One presented with loss of smell and/or taste at baseline (15 days previously) but was negative on RT-PCR, and the other case was asymptomatic. Both subjects tested negative for IgG. Three cases of seroconversion were observed between Day 1 and Day 15, one of which was in a participant with a positive RT-PCR result on Day 1. No cases of SARS-CoV-2 were detected by RT-PCR at any time for the other two subjects: one had a previous confirmed COVID-19 diagnosis (53 days previously), and the other was fully asymptomatic. No seroreversion was observed in this short interval. Evolution of positive SARS-CoV-2 tests between Day 1 and Day is summarized in Figure 1.

Overall, 41 cases of SARS-CoV-2 infection were confirmed by RT-PCR and/or serology, representing an overall infection rate of 12.6%. Three subjects were diagnosed with SARS-CoV-2 pneumonia but none of them required hospitalization before or during the study. Univariate analysis showed that gender, age, working as a physician/nurse, and work unit (general COVID-19 unit, COVID-19 ICU or Emergency Department) were not risk factors for infection. However, the presence of at least one comorbidity and symptoms at the time of sample collection increased the risk of a positive RT-PCR and/or serology test (Table I). The characteristics of the SARS-CoV-2-negative and -positive populations confirmed by RT-PCR and/or serology on Day 1 and Day 15 are summarized in Table I.

Discussion

The results from the first two visits in this longitudinal study show that the point prevalence of SARS-CoV-2 nasopharyngeal carriage among staff working in COVID-19 units (3% and 2.4% positive RT-PCR on Day 1 and Day 15, respectively) was lower than the rates reported in other studies [2] among less-exposed workers (7.1%). The percentage of RT-PCR-positive results among staff members of nursing homes in Belgium was consistently 2% during the same period [1]. In contrast, baseline seroprevalence in this study (11% and 12% on Day 1 and Day 15, respectively) was 2.5 times higher than that of Belgian blood donors during the same period (4.3% on 14th April 2020; Laure Geebelen, Sciensano, personal communication). In comparison, IgG seroprevalence assessed using the same immunoassay was much lower (1.2%) in a study that included HCWs who had been highly exposed to COVID-19 in a German hospital [3]. This could be explained by the fact that the German study was performed 2–3 weeks before the epidemiological peak, whereas the present study was initiated 2 weeks after the epidemiological peak. This timing might explain the low number of positive RT-PCR results and the higher seroprevalence rate. Indeed, the phase of the pandemic when nasopharyngeal carriage and seroprevalence studies are carried out is of crucial importance when comparing numbers.

HCWs in direct contact with infected patients were not at higher risk of infection compared with other members of staff, suggesting good compliance with PPE measures. In addition to direct transmission from patients with COVID-19, indirect transmission via contaminated surfaces is another plausible hypothesis [9]. Universal use of face masks in all hospital units was applied at CHU Saint-Pierre on 1st April 2020 (epidemiological peak), and may explain, in part, the high baseline seroprevalence and the subsequent plateau.

In this cohort of young (mean age 37 years), healthy (11% comorbidities) HCWs, SARS-CoV-2 infection was mild in the vast majority of cases and fever was rarely reported. Importantly, 75% of participants with a positive RT-PCR result were asymptomatic. As reported previously [10], screening based solely on symptoms could have resulted in nosocomial spread. At the time of the pandemic, this innovative approach – universal screening irrespective of symptoms in high-risk units – allowed the identification of asymptomatic and potentially contagious infected HCWs, enabling them to self-isolate for 7 days.

These results show that epidemiological assessment of SARS-CoV-2 among HCWs requires both RT-PCR and IgG evaluation, as 62.5% of cases of SARS-CoV-2 infection would have been missed if RT-PCR alone had been performed.

This study has some limitations. The different types and timings of lockdown measures carried out in European countries make it difficult to compare data. The authors were not able to define whether the overall infection rate was due to nosocomial or community transmission. Phylogenetic studies comparing viral strains between hospital staff and patients with COVID-19 could provide insightful information [11], as well as between hospital staff and inanimate surfaces, in order to map viral spread in hospitals.

A major strength of this study is the concomitant testing of nasopharyngeal carriage by RT-PCR and serology, which will be continued in the medium and long term (6 months). The persistence of IgG over time will be evaluated in HCWs with asymptomatic infection, as well as the possibility that some individuals may resume nasopharyngeal carriage of SARS-CoV-2.

In conclusion, screening of all groups of HCWs in highly exposed COVID-19 units, not just those HCWs who are in close contact with patients, is recommended. Combining molecular and serological diagnosis allows more reliable capture of information on SARS-CoV-2 infection dynamics in a highly exposed population. This type of longitudinal cohort study will help to answer key questions, such as the characterization of asymptomatic infections in highly exposed patients, and post-infection immunity. Finally, through this study, the authors were able to respond to the HCWs' anxiety for themselves and their relatives [12].

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Conflict of interest statement
None declared.

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