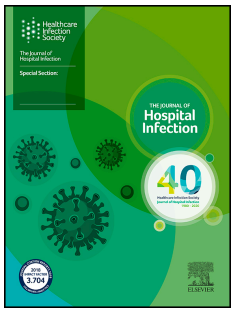

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PII: S0195-6701(20)30313-3

DOI: https://doi.org/10.1016/j.jhin.2020.06.028

Reference: YJHIN 6083

To appear in: *Journal of Hospital Infection*

Received Date: 11 June 2020

Accepted Date: 22 June 2020

Please cite this article as: Martin C, Montesinos I, Dauby N, Gilles C, Dahma H, Van Den Wijngaert S, De Wit S, Delforge M, Clumeck N, Vandenberg O, Dynamic of SARS-CoV-2 RT-PCR positivity and seroprevalence among high-risk health care workers and hospital staff, *Journal of Hospital Infection*, https://doi.org/10.1016/j.jhin.2020.06.028.

Le 31 décembre 2019, les autorités sanitaires de Wuhan (Chine) ont signalé des cas

Dynamic of SARS-CoV-2 RT-PCR positivity and seroprevalence among high-risk health care workers and hospital staff

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Abstract

Staff members from Covid-19 highly exposed units were invited to participate in a six month study of SARS-CoV-2 carriage and seroprevalence.

The results of Day 1 and Day 15 visits show that 41 SARS-CoV-2 infections were confirmed by RT-PCR and/or serology in 326 participants (overall infection rate=12.6%). Having co-morbidity or symptoms at the time of collection was a risk factor for infection but not working as a physician/ nurse. This universal screening in high-risk units irrespective of symptoms allowed asymptomatic and potentially contagious infected workers to be self-isolated during 7 days.

Introduction

The SARS-CoV-2 virus pandemic (causing Covid-19) hit Asia in early 2020 and Europe in February 2020. The epidemiological peak in Belgium was estimated to have occurred around March 31st with 5,759 patients hospitalized on April 6th and occupancy of deployed national hospital intensive care beds at a maximum of 58% (1285 hospitalized patients in intensive care units (ICU) on April 8th[1]). Based on previous experience acquired during the SARS-CoV epidemic, healthcare workers (HCW) are considered as a high risk population for SARS-CoV-2 acquisition. Few studies have been published reporting both current and past infection using RT-PCR and/or serological testing[2,3]. Studies on HCW represent also a unique opportunity to study natural infection in asymptomatic or pauci- symptomatic subjects. High viral loads have been detected in asymptomatic SARS-CoV-2 infected subjects with similar duration of carriage as compared to symptomatic patients [4,5]. Seroconversion is well described in hospitalized patients. It is observed in more than 99% within 19 days and levels of antibodies correlate with severity of COVID-19 [6]. However, less is known about seroconversion rate following asymptomatic infection. The primary objective was to assess the rate and dynamic of SARS-CoV-2 positivity and seroprevalence among high-risk HCW and hospital staff. This report presents the preliminary results at baseline and 2 weeks follow up.

Methods

The Centre Hospitalier Universitaire Saint-Pierre (CHU Saint-Pierre) in Brussels is a tertiary reference hospital for Infectious Diseases and the only reference center for Highly Contagious Respiratory Infectious Diseases in Belgium. At the peak of the first wave of the SARS-CoV-2 pandemic, about 700 persons were working in the Covid-19 Units (7 units with a total of 125 beds), Covid-19 Intensive units (2 units with a total 33 beds) and Emergency Department of CHU Saint-Pierre. Covid-19 Units were reserved for probable or confirmed Covid-19 patients, the latter representing between 50 and 90% of patients. In terms of personal protective equipment (PPE) and infection control, we followed the ECDC recommendations[7]. All staff members working in these Covid-19 highly exposed Units were invited to participate in a six month study of SARS-CoV-2 carriage and seroprevalence on a voluntary basis. Medical and paramedical staff were considered more exposed to SARS-CoV-2 than administrative staff, stretcher-bearers and cleaners and wore FFP2 masks.

Participants were asked at each visit to fill a questionnaire with medical history and recent or current symptoms. Presence of symptoms was not an exclusion criterion. A RT-qPCR (RealStar® SARS-CoV-2 RT-PCR kit 1.0 Altona Diagnostics, Hambourg, Germany) on 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 during 6 months: Day1- Day15- Day30- Month2- Month3- Month6. In accordance with national recommendations, workers with positive nasopharyngeal SARS-CoV-2 RT-qPCR (with or without symptoms) were self-isolated for 7 days.

The results of the two first visits (Day 1 and Day 15) are presented in this preliminary report. The Ethical Committee of CHU Saint-Pierre approved this study (CE/20-04-17) and written informed consent was obtained. We used descriptive statistics to summarize the characteristics of our population. Hypothesis tests for differences between groups were performed using non-parametric Wilcoxon-Mann-Whitney, Kruskal-Wallis tests for continuous variables, and Fisher exact tests for our categorical variables. All our P-values are bilateral and considered statistically significant if <0.05. We used SAS statistical software (version 9,4 SAS institute, Cary North Carolina, USA).

Results

A total of 532 healthcare workers, physicians (n=85), nurses (n=150), paramedical staff (n=60), administrative employees (n=25), stretcher-bearers and cleaners (n= 6), from these Covid-19 highly exposed units agreed to participate in the study. Between April 15th and May 18th, 326 participants completed day1 and day 15 visits.

Fifty-six (17, 1 %) participants reported current symptoms evoking Covid-19 at the time of sampling.

At baseline, the total of SARS-CoV-2 cases confirmed by RT-PCR and/or serology was 37 (11, 3% of overall population). Ten subjects were diagnosed with positive RT-PCR (3%). Among them, 3 had current mild symptoms: cough (n=2), sore throat (n=2), diarrhoea (n=2), headache (n=1) and tiredness (n=2) but none had fever. Eight out of 10 subjects with positive RT-PCR had a previously confirmed COVID-19 diagnostic. Of note, 1 subject with positive RT-PCR had negative IgG.

IgG seroprevalence at baseline was 11% (n=36), with 27 (75%) with negative concomitant RT-PCR. Among these 27 IgG positive/RT-PCR negative subjects, 7 (26%) had concomitant symptoms consisting of dyspnea (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 out of 27 (52%) IgG positive/PCR negative subjects had a previously confirmed COVID-19 diagnosis (mean delay since diagnosis: 29 days).

At day 15, 6 subjects remained positive by RT-PCR and two new infections were detected by RT-PCR (total 2.4%). One presented loss of smell and/or taste at baseline (15 days before) but was negative by RT-PCR at day 15 and the other one was asymptomatic. Both were SARS-CoV-2 IgG negative. Three seroconversions were observed between day1 and day15: one in a participant with positive RT-PCR at baseline. No SARS-CoV-2 was detected by PCR at any time for the other two subjects: one with a previously confirmed COVID-19 diagnostic (53 days earlier) and the other one fully asymptomatic. No seroreversion was observed in this short interval. Evolution of positive SARS-CoV-2 tests between Day1 and Day 15 are summarized in Figure 1.

Overall, 41 SARS-CoV2 infections were confirmed by RT-qPCR and/or serology representing an overall infection rate of 12.6% of the cohort. Three subjects were diagnosed with SARS-CoV-2 pneumonia but none required hospitalization before or during the study. Univariate analysis shows that neither gender, age, being a member of the nursing/medical staff nor working in either unit was a risk factor for infection. However, presence of at least

one comorbidity and symptoms at the time of collection increased the risk of a positive PCR and/or serology test (Table 1). The characteristics of overall, SARS-CoV-2 negative and SARS-CoV-2 positive population confirmed by RT-PCR and/or serology at baseline and follow-up (Day15) visits are summarized in Table 1.

Discussion

Results of the first two visits of this longitudinal study show that the point prevalence of SARS-CoV-2 nasopharyngeal carriage among the staff working in COVID-19 highly exposed units (3% and 2.4 % positive nasopharyngeal RT-PCR at Day 1 and Day 15 respectively) was lower than the rates reported in other studies [2] among not-so highly exposed workers (7,1%). Consistently, the percentage of RT-PCR positive tests among staff members of nursing homes in Belgium was 2% during the same period [1]. In contrast, baseline seroprevalence in our study (11 and 12% at Day 1 and Day 15 respectively) was 2.5 times higher than that of Belgian blood donors at the same period (4.3% on April 14^{th,} Laure Geebelen, Sciensano, personal communication). In comparison, SARS-CoV-2 IgG seroprevalence assessed using the same immunoassay was much lower (1.2%) in a study that included COVID-19 highly exposed healthcare in a German hospital [3]. This could be explained by the fact that this study was performed 2-3 weeks before epidemiological peak while ours was initiated two weeks after the epidemiological peak. This timing might explain the low numbers of positive RT-PCR and the higher seroprevalence rate. Indeed, the phase of the pandemic when these nasopharyngeal carriage and seroprevalence studies are carried out is of crucial importance in comparing numbers.

Healthcare workers in direct contact with infected patients were not at higher risk of infection as compared to other members of the staff suggesting good compliance of personal protective equipment (PPE) measures. Besides direct transmission from COVID-19 patients, indirect transmission via contaminated surfaces is therefore also a plausible hypothesis [9].Universal mask use within all units of the hospital was applied in our institution on April 1st (epidemiological peak) and therefore may also partially explain the high baseline seroprevalence and the plateau afterwards.

In this cohort of young (mean age: 37 years) and healthy (11% of co-morbidities) hospital workers, 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 were asymptomatic. As previously reported[10] screening based solely on symptoms could have resulted in nosocomial spread. At the time of the pandemic, this innovative approach of universal

screening irrespective of symptoms in high-risk units allowed even asymptomatic and potentially contagious infected workers to be screened out and self-isolated for 7 days.
Our results illustrate that epidemiological assessment of SARS-CoV-2 attack rate among hospital staff requires both RT-PCR and IgG evaluation as 62, 5 % of SARS-CoV-2 infections would have been missed if only PCR had been performed.
Our study has some limitations. The different types and timing of lockdown measures carried out in European countries make it difficult to compare data head-to-head. We were not able to define whether overall infection rate was due to nosocomial or community transmission. Phylogenetic studies comparing viral strains between hospital staff and COVID-19 patients could provide insightful information[11], as well as between hospital staff and inanimate surfaces, in order to map the viral spread in hospital.
A major strength is the concomitant testing of nasopharyngeal carriage by PCR and serology, also in the medium and long term (6 months). The persistence of IgG over time will be evaluated, among others in workers with asymptomatic infection, as well as the possibility that some individuals may resume nasopharyngeal carriage of SARS-CoV-2.
In conclusion, transversal screening of all groups of workers in highly exposed COVID-19 Units, not only workers in close contact with patients, is recommended. Combining molecular and serological diagnosis allows a more reliable capture of SARS-CoV-2 infection dynamic 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, we were also able to respond to the workers' anxiety for themselves and their relatives[12].

Acknowledgements and Funding

We warmly thank Philippe Leroy who encouraged us and gave us the human resources to carry out this study. We also thank all the hospital staff who worked hard during the pandemic and without whom this study would not have been possible;

N.D. is a post-doctorate clinical master specialist of the F.R.S.-FNRS. The study was funded partly by the Association Vésale pour la Recherche Médicale. The funder had no role in the study design, collection, analysis and interpretation of the data.

References

[1] Sciensano. COVID-19 BULLETIN EPIDEMIOLOGIQUE DU 10 AVRIL 2020 n.d.
[2] Treibel TA, Manisty C, Burton M, McKnight Á, Lambourne J, Augusto JB, et al. COVID-19: PCR screening of asymptomatic health-care workers at London hospital. The Lancet 2020;395:1608–10. https://doi.org/10.1016/S0140-6736(20)31100-4.
[3] Korth J, Wilde B, Dolff S, Anastasiou OE, Krawczyk A, Jahn M, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. J Clin Virol Off Publ Pan Am Soc Clin Virol 2020;128:104437. https://doi.org/10.1016/j.jcv.2020.104437.
[4] Lin A, He Z-B, Zhang S, Zhang J-G, Zhang X, Yan W-H. Early risk factors for the duration of SARS-CoV-2 viral positivity in COVID-19 patients. Clin Infect Dis 2020. https://doi.org/10.1093/cid/ciaa490.
[5] Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, et al. Viral dynamics in asymptomatic patients with COVID-19. Int J Infect Dis 2020;96:288–90. https://doi.org/10.1016/j.ijid.2020.05.030.
[6] Long Q-X, Liu B-Z, Deng H-J, Wu G-C, Deng K, Chen Y-K, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med 2020. https://doi.org/10.1038/s41591-020-0897-1.
[7] ECDC. Infection prevention and control and preparedness for COVID-19 in healthcare settings - third update. Stockolm: 2020.
[8] LOMBARDI A, Consonni D, Carugno M, Bozzi G, Mangioni D, Muscatello A, et al. Characteristics of 1,573 healthcare workers who underwent nasopharyngeal swab for SARS-CoV-2 in Milano, Lombardy, Italy. medRxiv 2020:2020.05.07.20094276. https://doi.org/10.1101/2020.05.07.20094276.
[9] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect 2020;104:246–51. https://doi.org/10.1016/j.jhin.2020.01.022.
[10] Chow EJ, Schwartz NG, Tobolowsky FA, Zacks RLT, Huntington-Frazier M, Reddy SC, et al. Symptom Screening at Illness Onset of Health Care Personnel With SARS-CoV-2 Infection in King County, Washington. JAMA 2020;323:2087. https://doi.org/10.1001/jama.2020.6637.
[11] Houlihan CF, Frampton D, Ferns RB, Raffle J, Grant P, Reidy M, et al. Use of Whole-Genome Sequencing in the Investigation of a Nosocomial Influenza Virus Outbreak. J Infect Dis 2018;218:1485–9. https://doi.org/10.1093/infdis/jiy335.
[12] Black JRM, Bailey C, Przewrocka J, Dijkstra KK, Swanton C. COVID-19: the case for health-care worker screening to prevent hospital transmission. The Lancet 2020;395:1418–20. https://doi.org/10.1016/S0140-6736(20)30917-X.

Table I: Characteristics of the overall, SARS-CoV-2 negative and positive population confirmed by Rt-PCR and/or serology on day1and day15 visits

	Overall population (n=326)	SARS-CoV-2 negative population (n=285)	SARS-CoV-2 positive population (n=41)	
Age : mean years old and range	37 (21-66)	39 (28-66)	36 (21-59)	*P*=0.1
Sex: women (%)/men (%)	239 (73%)/87 (27%)	208 (73%)/77 (27%)	31 (75,6%)/10 (24,4%)	*P*=0.8
Unit of work				*P*=0,2
COVID-19 units: n (%)	215 (66%)	184 (64,5%)	31 (75,7%)	
COVID-19 ICU units: n (%)	53 (16,2%)	50 (17,2%)	3 (7,3%)	
Emergency Department: n (%)	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 sample: n (%)	56 (17,1%)	46 (16,1%)	10 (24.4%)	***P*=0.07**
Asymptomatic at sample: 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

Figure 1 : Number of symptomatic subjects at the moment of the sample and subjects SARS-CoV-2 positives by Rt-PCR and serology in day one and day 15 visits