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Short Communication

SARS-CoV-2 seroprevalence in a Belgian cohort of patients with cystic fibrosis

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ABSTRACT

Background: In Belgium, COVID-19 epidemy began on February 4, 2020 with a peak on April 10, 2020. Patients with cystic fibrosis (CF) followed in the Cliniques universitaires Saint-Luc were rapidly isolated before the government lockdown.

Methods: After the peak of the epidemy, we measured anti-SARS-CoV-2 IgM and IgG antibodies in 149 patients and collected clinical data.

Results: Only 3 asymptomatic patients presented IgG against the virus. In one patient hospitalized for COVID-19 (positive molecular testing), we did not detect any anti-SARS-CoV-2 antibodies, as in thirty-five other symptomatic patients considered as possible cases.

Conclusions: Even if respiratory symptoms linked to CF are frequent and compatible with COVID-19, anti-SARS-CoV-2 IgG antibodies were detected only in 3 asymptomatic patients. This reassuring study concerning the risk of COVID-19 in patients with CF illustrates the difficulty to distinguish COVID-19 symptoms from respiratory exacerbations and the need of generalized molecular testing to make a precise diagnosis.

1. Introduction

The coronavirus disease 2019 (COVID-19) is a new emerging infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The main risk factors associated with a worse outcome include age and comorbidities such as hypertension, diabetes mellitus or chronic lung disease [1]. Cystic fibrosis (CF) is a multisystemic disorder, responsible for a chronic lung disease. Obstruction of the airways by viscous secretions and the consecutive inflammation induce progressive destruction of the lungs. Several comorbidities are described in CF, including diabetes mellitus and liver disease [2].

Information is lacking on the prevalence and on the clinical impact of COVID-19 among CF patients. In a multinational report, 40 cases have been reported in 8 countries. In contrary with the H1N1 influenza pandemic in 2009–2010 where a significant morbidity was described among affected CF patients [3], the outcomes of COVID-19 in this population seem to be less severe than expected [4]. To our knowledge, no data are available regarding the SARS-CoV-2 seroprevalence among CF patients.

In this monocentric prospective study, we report SARS-CoV-2 seroprevalence of 149 CF patients.

2. Methods

2.1. Study population

CF patients followed in the CF reference center of the Cliniques universitaires Saint-Luc (Brussels), were recruited prospectively by receiving a letter containing an empty tube to test IgM and IgG against SARS-CoV-2. Between April 16, 2020 and May 19, 2020, sera were collected from 149 patients (first case in Belgium on February 4, 2020, peak of the epidemy on April 10, 2020, lockdown for CF patients since March 12, 2020). Blood sampling was performed either in the CF center or in another local center and brought the same day to the CF center through a drive-in system. Patients were contacted by phone to collect the presence and timing of symptoms.

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Table 1
Patient characteristics of the study population.

	Patients
Subjects, n	149
Sex (F/M)	73/76
Smoking history (never/former/current)	0/0/5
F508del/F508del (n/%)	63/42.3
Pancreatic sufficiency (n/%)	26/17.4
Age, yrs	24.9 ± 15
Children/Adults	52/97
BMI, Z-score	−0.39 ± 2.24
FEV1,% predicted (n = 134)	85 ± 25.9
FVC,% predicted (n = 134)	95.8 ± 19.1

All patients respond to the classical definition of CF, defined by Farrell [5]. Clinical data are presented in the Table 1. The local ethical committee stated that no informed consent was needed as the Helsinki declaration was respected, as it was considered as a regular monitoring in this sanitary crisis.

Demographic data, genotype, lung function tests, smoking history are stated for the patients. N is specified when data are missing. Data are means ± standard deviation. Definition of abbreviations: F, female; M, male; yrs, years; BMI, body mass index; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

2.2. Anti-SARS-CoV-2 IgM and IgG detection

Measurements of specific anti-SARS-CoV-2 IgM and IgG antibodies were performed with the Maglumi 2019-nCoV IgG and IgM fully automated quantitative chemiluminescent immunoassays (CLIA). This binding antibody technic detects antibodies against proteins N, S1 and S2 of SARS-CoV-2. Samples were processed according to the manufacturer's instructions on the Maglumi 800 analyzer (Snibe Diagnostic, Shenzhen, China) [6]. These automated immunoassays use magnetic microbeads coated with SARS-CoV-2 recombinant antigens labeled with ABEI, a non-enzyme small molecule with a special molecular formula that enhances stability in acid and alkaline solutions. The threshold of positivity for both IgM and IgG assays is 1.0 arbitrary unit (AU)/mL. The sensitivity and specificity were previously addressed as well as the comparison with anti-SARS-CoV-2 IgA and IgG enzyme-linked immunosorbent assays [7,8].

3. Results

3.1. Possible and confirmed cases

From the 149 patients, 36 (24%) had compatible symptoms. During the lockdown, only hospitalized patients were tested because of the lack of material. One patient was hospitalized for a respiratory exacerbation and SARS-CoV-2 was detected by PCR while two patients hospitalized for other reasons were tested negative. PCR was also negative for two other patients hospitalized for respiratory exacerbations and for one suspected patient tested by his general practitioner.

3.2. Anti-SARS-CoV-2 IgM and IgG in patients with CF

Only 4 patients (2.7%) showed positive serologies against SARS-CoV-2. One asymptomatic patient (0,67%) showed positive anti-SARS-CoV-2 IgM (1.271 AU/ml). He was quarantined for 14 days. A stable IgM level of 1.152 AU/ml was confirmed after 19 days but without appearance of anti-SARS-CoV-2 IgG. Three other asymptomatic patients (2%) had anti-SARS-CoV-2 IgG (4.985, 31.4 and 1.1 AU/ml). Risk factors were found among all of them. One had contact with her sick daughter (compatible symptoms but not tested) and the two others lived with a nurse working in a hospital unit containing COVID-19 patients.

No anti-SARS-CoV-2 antibodies were detected in the blood of the confirmed COVID-19 patient (test repeated trice). The same observation was made for the 35 other possible cases. Mean delay between symptoms onset and realization of the blood test was 44.1 days (± 17.4 days – standard deviation).

4. Discussion

These data suggest that SARS-CoV-2 seroprevalence among CF patients is low (2.7%) and even lower than in the Belgian population in the same period (4.3%) [9]. These results may be partly explained by the early recommendation towards our CF patients to limit the face-to-face contacts, while the directive of social shielding was adopted a few days later by the Belgian government on March 18, 2020. Moreover, CF patients are familiar with protective measures (use of face masks and hand hygiene) while the protective/curative role of azithromycin is still debated [10].

We reported that the presence of anti-SARS-CoV-2 antibodies in CF patients is not always correlated to the clinical presentation. The 3 patients with positive anti-SARS-CoV-2 IgG were asymptomatic. The detection of anti-SARS-CoV-2 IgG among asymptomatic patients has been described in a Chinese control group around 5% [11]. As anti-SARS-CoV-2 IgG assays have been reported to have a great specificity [11,12], the hypothesis of asymptomatic infections seems the most relevant. Moreover, we identified risk factors among positive patients. The detection of anti-SARS-CoV-2 IgG in asymptomatic patients reflects the reality of asymptomatic carriers, an important public health issue that underlines the need of a large scale screening. To our knowledge, the presence of anti-SARS-CoV-2 IgM in asymptomatic patients have not been reported. Therefore and because of the absence of IgG after 19 days, a non-specific antibodies cross-reaction is plausible.

The absence of anti-SARS-CoV-2 antibodies detection in one patient with a positive molecular test 31 days after the onset of the symptoms raises the question of the humoral immunization potential of SARS-CoV-2, essential for vaccine development. However, as recently described, even patients with low serum neutralizing activity have IgG memory B cells that can produce SARS-CoV-2 neutralizing antibodies [13].

The diagnosis of COVID-19 among CF patients can be difficult as symptoms of respiratory exacerbations might be similar. However, most of the patients did not undergo a PCR-based viral RNA detection as they were not eligible for testing. This can lead to an underestimation of the number of infected patients. The mean delay between the onset of the symptoms and the blood test was 44.1 days. The median seroconversion time for IgM and IgG has been reported at day-12 and day-14 respectively [14]. So far, the detection of anti-SARS-CoV-2 IgG has been described for a maximal period of 39 days [15]. The duration of immunoglobulins detection after infection and their protective effect by blocking viral entry into host cells remain unknown. To minimize the false positive rate, it would have been interesting to perform a second serological test in the patients with anti-SARS-CoV-2 IgG.

5. Conclusions

We report the first data on SARS-CoV-2 seroprevalence in a large cohort of CF patients. While possible cases were frequent, antibodies were detected only in a minority of patients, probably reflecting the low incidence of COVID-19 in this population. This study also illustrates the similarity of COVID-19 symptoms and respiratory exacerbations and the need of generalized molecular testing to make a precise diagnosis.

Author contributions

BS wrote the manuscript, VA and GD performed the serologic and molecular tests and revised the manuscript, VA-SC-GM performed the blood tests and collected medical data, GS realized the conception and design of research, performed the analyses and wrote the manuscript.

Declaration of Competing Interest

The authors have declared that no conflict of interest exists.

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