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Short Communication

SARS-CoV-2 antibodies among people with cystic fibrosis prior to the vaccination campaign: A seroprevalence study in two specialized centres in Northern Italy

Gianfranco Alicandro[a,b], Valeria Daccó[b], Lisa Cariani[c], Martina Contarini[d], Letizia Corinna Morlacchi[d], Chiara Rosazza[a], Calogero Sathya Sciarrabba[b], Federica Ferraro[b], Beatrice Silvia Orena[c], Andrea Gramegna[a,d], Francesco Blasi[a,d], Carla Colombo[a,b,*]

[a] Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy
[b] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Milan, Italy
[c] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Microbiology Unit, Milan, Italy
[d] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Respiratory Unit and Adult Cystic Fibrosis Centre, Milan, Italy

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ABSTRACT

The prevalence of anti-SARS-CoV-2 antibodies in people with cystic fibrosis (CF) is largely unknown. We carried out a cross-sectional study between March and June 2021 with the aim of estimating the seroprevalence of anti-SARS-CoV-2 antibodies in two CF centres in Northern Italy. Total serum anti-SARS-CoV-2 (spike) antibodies levels were measured and values ≥0.8 U/mL were considered positive. Among 434 patients aged >12 years, 64 patients had a positive result (14.7%, 95% CI: 11.5–18.4), 36 (56.3%) without experiencing any COVID-19-related symptoms. Three out of 49 transplanted patients tested positive with an odds ratio for a positive result among transplanted as compared to non-transplanted patients of 0.35 (95% CI: 0.07–1.14). No significant differences were observed between sexes, age groups, socioeconomic status and lung disease severity. In conclusion, SARS-CoV-2 has infected a relatively high proportion of our patients but in most cases the infection was asymptomatic.

1. Introduction

People with cystic fibrosis (pwCF) are considered a clinically vulnerable population at high risk of severe disease in case of infection by SARS-CoV-2. For this reason, since the beginning of the pandemic, CF centres in Milan recommended self-isolation and reinforcement of preventive measures, such as face masks and hand hygiene [1].

Studies on the clinical course of COVID-19 in this population show that most infected patients fully recovered without short-term sequalae, although COVID-19 can be a serious illness in those with severe lung disease and organ transplantation [2–5].

A study within the European CF Registry [2] carried out during the first wave of the pandemic (February-June 2020) estimated a case-fatality ratio of 3.85%, based on 130 COVID-19 cases and 5 deaths. However, this figure is based mostly on symptomatic patients reported by CF centres to national registries, while the real prevalence of SARS-CoV-2 infection in this population remains largely unknown. It is now clear that a relevant number of cases have asymptomatic infections [6] and, in this regard, seroprevalence studies provide important information on the actual spread of the infection and can be used to estimate the infection-fatality ratio, a more useful measure of the risk related to SARS-CoV-2 infection [7].

This study aimed at estimating the seroprevalence of anti-SARS-CoV-2 antibodies in pwCF followed-up at the pediatric and adult Reference Centres for CF of Lombardia, the Italian region most severely hit by the pandemic [1].

2. Methods

All pwCF aged ≥12 years participating in the vaccination campaign against SARS-CoV-2 between March and June 2021, were asked to participate in this cross-sectional study.

* Corresponding author at: Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis centre, Via Della Commenda 9, 20122, Milan, Italy.
E-mail address: carla.colombo@unimi.it (C. Colombo).

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Blood samples for the quantification of total serum anti-SARS-CoV-2 (spike) antibodies levels were collected immediately before the administration of the first dose of the mRNA vaccines (Pfizer-BioNTech or Moderna). Serum antibodies levels were measured using the electrochemiluminescence immunoassay Elecsys Anti-SARS-CoV-2 S (Roche). This serological assay is an in vitro quantitative determination of high affinity antibodies against SARS-CoV-2, which uses a recombinant protein representing the receptor binding domain (RBD) of the spike protein in a one-step double antigen sandwich assay format (sensitivity: 98.8% and specificity: 100%). Values ≥0.8 U/mL were considered positive. All analyses were performed centrally at the Clinical Laboratory of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

Sociodemographic data were collected through a telephone interview carried out by the attending physicians, while clinical data were retrieved from patient medical records. Patients were also asked whether they had experienced symptoms suggestive of COVID-19 before the interview.

Seroprevalence was expressed as number of patients with a positive test divided by the number of patients tested x 100, with 95% confidence intervals computed using the binomial distribution. Seroprevalence was computed across strata of sex, age groups, socioeconomic status (SES), lung disease severity, oxygen therapy, organ transplantation.

SES was determined according to patient's educational attainment for subjects aged ≥25 years, while the highest parental education was used for younger patients. SES was grouped in three categories: low (below high school diploma), intermediate (high school diploma) and high (university degree). Odds ratios (ORs) for a positive test result and corresponding 95% confidence intervals (CIs) were computed across groups and differences were tested using the Fisher's exact test.

The study was approved by the Ethics Committee of the IRCCS, Istituto Nazionale per le Malattie Infettive, Lazzaro Spallanzani, Rome, Italy (protocol number: 354 2020/2021) and patients signed the informed consent before being included in the study.

Group	Positive cases	No. of patients tested	Percentage with positive test [95% CI]	OR for positive result [95% CI]
All	64	434	14.7 [11.5,18.4]	
Sex				
Males	38	229	16.6 [12.0,22.1]	1 [Reference]
Females	26	205	12.7 [8.5,18.0]	0.73 [0.41,1.29]
Age group (years)				
12-17	7	64	10.9 [4.5,21.2]	1 [Reference]
18-24	24	110	21.8 [14.5,30.7]	2.26 [0.87,6.64]
25-39	19	142	13.4 [8.3,20.1]	1.26 [0.47,3.74]
>=40	14	118	11.9 [6.6,19.1]	1.10 [0.39,3.40]
SES				
High	14	108	13.0 [7.3,20.8]	1 [Reference]
Intermediate	38	240	15.8 [11.5,21.1]	1.26 [0.63,2.65]
Low	11	80	13.8 [7.1,23.3]	1.07 [0.41,2.71]
FEV1 (% of predicted)				
>=40	58	400	14.5 [11.2,18.3]	1 [Reference]
<40	2	12	16.7 [2.1,48.4]	1.18 [0.12,5.74]
Oxygen therapy				
No	62	417	14.9 [11.6,18.7]	1 [Reference]
Yes	2	17	11.8 [1.5,36.4]	0.76 [0.08,3.41]
Organ transplantation				
No	61	385	15.8 [12.3,19.9]	1 [Reference]
Yes	3	49	6.1 [1.3,16.9]	0.35 [0.07,1.14]
Positive PCR test				
All patients	21	25	84.0 [63.9,95.5]	
with COVID-19 symptoms	20	23	87.0 [66.4,97.2]	
admitted to hospital	7	9	77.8 [40.0,97.2]	
asymptomatic	1	2	50.0 [1.3,98.7]	

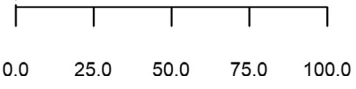

Fig. 1. Seroprevalence of anti-SARS-CoV-2 antibodies in cystic fibrosis prior to the vaccination campaign by sociodemographic, disease severity groups and among patients with a positive PCR test result prior to antibody blood test. Pediatric and adult Reference Centres for Cystic Fibrosis of Lombardia, Italy, March-June 2021.
FEV1: Forced expiratory volume in one second, OR: Odds ratio, PCR: Polymerase chain reaction. SES: Socioeconomic status. Test for differences in proportions of positive test result across groups: sexes ($P = 0.279$), age groups ($P = 0.133$), SES ($P = 0.791$), FEV1 ($P = 0.689$), oxygen therapy ($P = 1.00$), organ transplantation ($P = 0.086$). The 25 patients with a positive PCR test for SARS-CoV-2 included three lung transplant recipients. Four of the 25 patients had undetectable antibodies levels (<0.8 U/mL) with time intervals between PCR test and antibody blood test of 130, 150, 172, 292 days. Missing data: SES was not available for 6 patients, FEV1 was not available for 22 patients.

Table 1
Sociodemographic and clinical characteristics of the study population.

Sex	
Males, n (%)	229 (52.8)
Females, n (%)	205 (47.2)
Age (years)	
Median (IQR)	28 (20–41)
Range	12–81
Socioeconomic status	
High, n (%)	108 (24.9)
Intermediate, n (%)	240 (55.3)
Low, n (%)	80 (18.4)
Not available, n (%)	6 (1.4)
Transplanted organ	
Lung, n (%)	47 (10.8)
Liver, n (%)	2 (0.5)
FEV1 (% of predicted)[a]	
Median (IQR)	92 (72–104)
Range	28–136
Oxygen therapy, n (%)	17 (3.9)

FEV1: Forced expiratory volume in one second, IQR: Interquartile range.
[a] Best FEV1 over the year prior to enrolment in the study (Not available for 22 patients).

3. Results

We tested 434 pwCF for anti-SARS-CoV-2 antibodies, of them 49 patients were transplant recipients. Their sociodemographic and clinical characteristics are shown in Table 1.

Sixty-four patients had a positive test result for SARS-CoV-2 antibodies (14.7%, 11.5–18.4%) with a median antibodies serum concentration of 145 U/mL (IQR: 55–333, range = 3–5112). Thirty-six (56.3%) had been completely asymptomatic, 28 (43.8%) reported they had complained symptoms suggestive of COVID-19 with a median duration of five days (range: 1–30 days). Eight of the 64 patients had been hospitalized (12.5%), three (4.7%) in intensive care units.

Seroprevalence did not significantly differ across all groups considered (Fig. 1). However, a lower proportion of positive test results were observed among transplanted patients (6.1% vs 15.8%, $P = 0.086$).

Twenty-five of the enrolled patients had had a history of positive PCR test for SARS-CoV-2 and the majority ($N = 21$; 84%) had detectable antibodies levels.

Three transplanted patients had virologically-confirmed symptomatic infection, but two of them tested negative after around five months from symptoms onset and one patient had an antibody level of 3.08 U/mL after 50 days. Table 2 describes their main characteristics and the clinical course of SARS-CoV-2 infection.

4. Discussion

Our study provides seroprevalence estimates of anti-SARS-CoV-2 antibodies among a relatively large number of pwCF followed in two specialized centres in Northern Italy. Despite pwCF are supposed to be familiar with measures to prevent respiratory infections, such as mask wearing and hand sanitization, a considerable proportion of our patients got infected by SARS-CoV-2 [1].

Although not statistically significant, the lower prevalence of SARS-CoV-2 antibodies in transplanted compared to non-transplanted pwCF is in line with the figures reported in non-CF transplanted patients [8]. This finding may be related to several factors, including a more cautious attitude towards the risk of infection, the recommendations for self-isolation provided by the CF centres, but also to a possible low seroconversion rate [9,10].

Of note, in contrast to several reports from the general population documenting higher infection rates among less educated than highly educated individuals [11,12], low education was not associated with a higher risk of infection in our CF population. This result may be related to the wide adoption of the preventing measures to avoid infection among patients who are regularly followed-up in specialized care centres.

As recently outlined [13], we cannot exclude a certain degree of underestimation of seroprevalence as a result of: 1) possible, although infrequent, false-negative results; 2) undetectable anti-SARS-CoV-2 antibodies due to their decline over time; 3) lack of humoral response in some infected patients, particularly transplant recipients. In addition, the definition of asymptomatic infection may be affected by recall bias, with mild symptoms potentially confounded with those of CF.

In addition, seroprevalence data are difficult to compare since they vary widely depending on the pandemic period when the blood samples were collected, the region where the study was conducted and the population being studied [14]. Italian data published so far were mostly collected during the first wave showing seroprevalence below 5% among the general population resident in several Italian regions, with data below 1% in most Southern regions and up to 7.5% in Lombardia [15,16]. A study carried out in a North Eastern Italian region including also the last quarter of 2020 (the middle of the second wave in Italy) documented a prevalence up to 16% [17]. In the latter study, a risk reduction of 41% was found in cancer patients, who like patients with CF, are considered a clinically vulnerable population. The only study evaluating

Table 2
Main characteristics, clinical course of COVID-19 and result of the anti-SARS-CoV-2 antibody test among the three transplanted patients with virologically-confirmed symptomatic infection.

	Patient #1	Patient #2	Patient #3
Sex	Female	Male	Female
Age	40	41	26
CFTR mutations	1717–1G->*A*/N1303K	F508del/F508del	F508del/L1077P
Transplanted organ	Lung	Lung	Lung
FEV1 (% of predicted)	88	76	37
Symptoms	Fever, headache, asthenia	Fever, dyspnea	Fever, cough, dyspnea
Duration of symptoms (days)	10	35	60
Time interval between onset of symptoms and antibody blood test (days)	50	172	155
Time interval between PCR test and antibody blood test (days)	50	172	150
Days of hospitalization	30	35	15
ICU admission	Yes	No	No
Additional oxygen therapy	Yes	Yes	Yes
Non-invasive ventilation	No	Yes	Yes
Invasive ventilation	No	No	No
Total anti-SARS-CoV-2 antibodies (U/mL)	3.08	<0.4	<0.4

CFTR: Cystic Fibrosis Transmembrane Conductance Regulator. FEV1: Forced expiratory volume in one second.

the seroprevalence of anti-SARS-CoV-2 antibodies in a CF population was conducted in Belgium [18]. The study found a prevalence of 2% based on 3 positive results among 149 patients tested. However, this figure cannot be compared with our data since the Belgian study was carried out at the beginning of the pandemic (April-May 2020), a year before our study.

In conclusion, prevalence of SARS-CoV-2 antibodies in our CF population was relatively high, and in most cases the infection was asymptomatic.

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Declaration of Competing Interest

None.

CRediT authorship contribution statement

Gianfranco Alicandro: Conceptualization, Methodology, Formal analysis, Data curation, Visualization, Writing – original draft. **Valeria Daccó:** Investigation, Data curation, Writing – review & editing. **Lisa Cariani:** Investigation, Data curation, Writing – review & editing. **Martina Contarini:** Investigation, Data curation. **Letizia Corinna Morlacchi:** Investigation, Data curation. **Chiara Rosazza:** Investigation, Data curation. **Calogero Sathya Sciarrabba:** Investigation, Data curation. **Federica Ferraro:** Investigation, Data curation. **Beatrice Silvia Orena:** Investigation, Data curation. **Andrea Gramegna:** Writing – review & editing. **Francesco Blasi:** Writing – review & editing. **Carla Colombo:** Resources, Project administration, Writing – review & editing, Supervision.

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