



Early View

Research letter

SARS-CoV-2 infections in people with PCD: neither frequent, nor particularly severe

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SARS-CoV-2 infections in people with PCD: neither frequent, nor particularly severe

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Take home message (220 of 256 characters)

In this longitudinal study of people with PCD followed weekly via online questionnaires, the incidence rate of COVID-19 and the proportion of participants infected were low, and the observed severity mostly mild.

To the editor,

The coronavirus disease 2019 (COVID-19) pandemic caused by SARS-CoV-2 has by March 2021 infected at least 115 million people worldwide and caused over 2.5 million deaths. People with pre-existing chronic health conditions are reportedly at high risk of catching the disease and of having a severe disease course [1-4]. Primary Ciliary Dyskinesia (PCD) is a multisystem, genetic disease which affects about 1 in 10,000 people and leads to chronic upper and lower airway disease, laterality defects, including congenital heart disease, and other health problems [5-8]. In March 2020, PCD patient support groups contacted the paediatric respiratory research group in the University of Bern with the wish to set up a study that generates evidence on the risk and evolution of COVID-19 in people with PCD. This led to the launch of COVID-PCD, a longitudinal online survey of health, shielding behaviours, and quality of life of people with PCD during the pandemic. COVID-PCD is a participatory study that collects data in real-time directly from people with PCD using online questionnaires. This manuscript provides first data on risk and severity of SARS-CoV-2 infections among study participants for the time period between May 30th and March 5th 2021.

A detailed description of the methods has been published [9]. In short, COVID-PCD is an international study advertised through PCD support groups and is open to people of any age with a confirmed or suspected diagnosis of PCD who can complete questionnaires in English, German, Spanish, Italian, or French. The study has been approved by the cantonal ethics committee of Bern (Study ID: 2020-00830), is registered with clinical trials gov (NCT04602481), and is anonymous. PCD support groups from the UK, USA, Switzerland, and Australia helped to develop patient information and questionnaires, and helped to pilot the study before the recruitment started. Since May 30th 2020, participants can register and consent via the study website (www.covid19pcd.ispm.ch) and then receive e-mail links to online questionnaires. A baseline questionnaire collects demographic data, information about the PCD diagnosis and severity using the standardised FOLLOW-PCD questionnaires [10], and information on SARS-CoV-2 infections that had occurred prior to study

entry. One week after completing the baseline questionnaire, and in weekly intervals thereafter, participants receive short follow-up questionnaires about current symptoms, shielding behaviour, and incident SARS-CoV-2 infections. Questions asking about incident SARS-CoV-2 infections refer to the time passed since completing the last follow-up questionnaire, ensuring that all incident SARS-CoV-2 infections are reported, even if a participant fails to complete a weekly questionnaire. Parents complete questionnaires for children under age 13 years.

We described the number and proportion of study participants who received a test for SARS-CoV-2 at any time, summing up antigen tests and antibody tests. We then calculated the proportion of people with a confirmed SARS-CoV-2 infection by dividing the number of those with a positive PCR or antibody test at any time (prior to study entry, or during the observation period) by the study population. Participants were asked how seriously ill they got, with answers categorised as no symptoms, mild symptoms (e.g. mild fever and/or cough), or moderate symptoms (e.g. high fever, cough, headache). We also asked participants if they had been treated in the hospital due to COVID-19 and if yes for how long. We calculated the incidence rate of SARS-CoV-2 infections in those who had been disease-free at study entry (the population at risk). We defined an incident case as a positive SARS-CoV-2 test result reported at least 14 days after study entry. This criterion was set to minimize the risk of selection bias from people registering because of typical symptoms or contact with a case. We defined person-time at risk as time between completing the baseline questionnaire and the latest follow-up among those without SARS-CoV-2 at baseline. Participants who reported a positive test for SARS-CoV-2 remained in the study allowing to detect possible re-infections. For each observation week, we calculated the proportion of study participants who reported behaviours related to shielding such as not leaving the house, visiting grocery stores, going to school or work, and using public transport and then averaged these proportions over all observation weeks.

By March 5th 2021, 640 persons with PCD had registered in COVID-PCD (age range 1 to 85, median age 27 years). 234 (37%) were aged less than 20 years, 299 (47%) were aged 20 to 49 years, and 107

(16%) were older than 49 years (**table 1**). Sixty-one percent were female. The longest time a participant was followed up was 37 weeks (median: 12 weeks, interquartile range: 4-27); 70 participants (11%) only completed the baseline questionnaire. 5 people left the study (one died not due to COVID-19, and 4 did not give a reason). 308 participants (48%) had never been tested for SARS-CoV-2, 173 (27%) had been tested once, and 159 (25%) twice or more. Twenty four participants reported a positive SARS-CoV-2 test either at study entry or during the observation period, corresponding to 3.8% of the study population (95% CI: 2.4-5.5%). Eight cases occurred in those aged under 20, 10 in those 20 to 49 years, and 6 in those 50 years and above. Overall, reported severity in the 24 cases was mild, with five reporting no symptoms, 12 reporting mild symptoms, four reporting moderate symptoms without hospitalization, and three persons reporting hospitalization (one with mild symptoms, hospitalised for 9 days, 2 with moderated symptoms, hospitalised for 7 and 9 days). None needed intensive care or artificial ventilation, and none died from COVID-19. 16 of the 24 infections were reported at the time of registration into the study, and 8 incident infections were observed during follow-up. The total follow-up time was 90,999 days (249 person-years). This resulted in an incidence rate of 3.2 per 100 person years (95% CI 1.6-6.4) – meaning that if 100 participants had been observed for a year, three would have caught COVID-19 during this year. Incidence was highest in adults 50 years or above with 6.0 per 100 person-years (95% CI 0-18) and only one incident case was observed in adults between 20 and 49 years. During the follow-up period, 10% of study participants on average reported not to have left their house during the last 7 days (range: 3 to 17%). 38% had left the house for grocery shopping in the past week (range: 22-46%), 37% had been to school or workplace (range: 16-57%), and 13% had used public transportation (range: 5 to 18%). These proportions varied from week to week and between regions.

Table 1: SARS-CoV-2 infections and shielding behaviour in people with Primary Ciliary Dyskinesia, based on longitudinal data from the COVID-PCD study

	Total N=640 n (%)	Children (0-19 years) N=234 n (%)	Adults (20-49 years) N=299 n (%)	Older adults (>49 years) N=107 n (%)
Male	249 (39)	122 (52)	91 (31)	36 (34)
Female	389 (61)	112 (48)	207 (69)	70 (66)
Tested for SARS-CoV-2				
never	308 (48)	118 (50)	147 (49)	43 (40)
once	173 (27)	70 (30)	73 (24)	30 (28)
twice or more		46 (20)	79 (26)	34 (32)
Confirmed SARS-CoV-2 infections (positive PCR or antibody test at any time during study period, N (%), 95% CI))	24 (3.8, 2.4-5.5)	8 (3.4, 1.5-6.6)	10 (3.3, 1.6-6.1)	6 (6.0, 2.1-11.8)
No symptoms	5 (21)		2	0
Mild symptoms, not hospitalised ^a	12 (50)	3	6	3
Moderate symptoms, not hospitalised ^b	4 (17)	1	1	2
Hospitalised ^c	3 (12)	1	1	1
Very severe symptoms (ICU care, intubation or death)	0	0	0	0
Incident infections reported during follow-up period		4	1	3
Total follow-up time (in person-years)	249	96	103	50
Incidence rate (infections per 100 person years (95% CI))	3.2 (1.6-6.4)	4.2 (1.6-10.9)	1.0 (0.1-6.8)	
Shielding behaviour during the last 7 days (mean proportion (range) per week, ^d during 37 follow-up weeks))				
Did not leave the house	10% (3-17)	10% (1-20)	9% (3-19)	10% (3-19)
Went for grocery shopping	38% (22-46)	18% (6-26)	51% (24-66)	42% (22-60)
Went to workplace/school ^e	37% (16-57)	44% (8-75)	31% (6-49)	34% (19-46)
Used public transportation	13% (5-18)	13% (0-21)	13% (8-22)	13% (5-21)

^aReferred to in the questionnaire as “mild fever or cough” ^bReferred to in the questionnaire as “high fever, cough, headache, etc.” ^cTwo had moderate symptoms (one hospitalised for 7 days, one for 9 days), one had mild symptoms (hospitalised for 9 days) ^dwe calculated the proportion of people in each week, and then averaged this proportion over the 32 weeks of the observation period. ^eAmong those who go to school or work.

In summary, this international longitudinal study of 640 people with PCD found that only 3.8% of the study population had a SARS-CoV-2 infection confirmed by a specific test. This was lower compared to, for example, the overall UK population with a cumulative confirmed number of cases of 6.3%, Italy of 5.0%, and the USA of 8.8% but similar to Germany with 3% (March 5 2021) [11]. We observed one confirmed case in children aged 0-9 years (0.8% of 122 children aged 0-9 years, data not shown) which compares well with national data from Switzerland, where 0.8% of children aged 0-9 years had a laboratory confirmed SARS-CoV-2 infection (March 3, 2021) [12]. An explanation for this may

be that children are more often asymptomatic and SARS-CoV-2 infections therefore stay undetected [13]. We observed fewer cases in participants aged 20-49 (10 of 299; 3.3%) than in the general Swiss population (7.9%) [12]. This suggests that adults with PCD are more careful in shielding themselves because they consider themselves as a high-risk group. Overall, the severity of cases seems to be milder compared to what has been found for cystic fibrosis. For PCD, we found that 3 of 24 (12%) were hospitalised due to COVID-19 and no one was in the ICU. A French study of 7500 CF patients from 47 clinics found that 31 had tested positive for SARS-CoV-2 by June 2020 [12]. Among the 31, 61% had been hospitalized and 13% (4/31) were in the ICU. [12]. The difference between the two studies might partly be explained by a higher degree of detection bias in the hospital-based French study, where mild infections not resulting in hospitalisations might have been missed by the physicians. This bias is less relevant, albeit not absent, for our participatory study with patients themselves reporting weekly on their health. When we compare severity of infections with data from the general population, more people were hospitalised in our study (3 of 24 cases; 12% (95% confidence interval: 2.7-32.4)) compared to data from Switzerland where 23869 of the 554808 confirmed cases (4.3%; 95% CI 4.25-4.36) were hospitalised. However, the severity of COVID-19 is strongly associated with age; most hospitalisations occurred in people aged 70 years or above. The age distribution in our study differs from that of the general Swiss population; the proportion of people aged 49 years or older was 16% in our study but 40% in the general Swiss population. Only 9 participants in our study were 70 years or older. We can therefore not compare severity. The low number of cases and few hospitalisations for COVID-19 is reassuring but also a limitation of this study because it is difficult to draw conclusions about severity based on only 24 cases. Also, in our study, only 52% had been tested for SARS-CoV-2 and it is possible that some participants had an undetected infection. This is also the case in the general population, and we assume that if a SARS-CoV-2 infection was missed, the participant had mild symptoms. Another limitation is the anonymous participation which did not allow to validate hospitalisations and deaths through record

linkage. In return the anonymous online design has allowed to set up the largest international cohort study that collects data directly from people with PCD.

The reassuring results in this study are probably partly explained by the careful shielding behaviour of our study participants – on average, 10% had not left their house in the past week and less than half had gone to school or work. But even so, the study suggests that with careful personal protection, people with PCD do not seem to have an increased risk of infection with SARS-COV-2, nor an especially severe disease course.

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