

Is Quarantine for COVID-19 Pandemic Associated with Psychological Burden in Primary Ciliary Dyskinesia? A Prospective Study.

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Research

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Abstract

Background: Primary ciliary dyskinesia (PCD) is a rare disorder with variable disease progression. Information on the psychological impact of the Coronavirus Disease 2019 (COVID-19) quarantine in PCD, a condition with characteristics of personal and familiar increased stress due to frequent pulmonary exacerbations and high risk of lung function deterioration, is lacking. We designed a prospective study to assess the psychological burden and parental stress during the COVID-19 lockdown in Italy in a PCD population.

Methods: Questionnaires assessing psychological well-being were administered to 10 PCD patients <15 years-old's mothers (Group A: Parenting Stress Index-Short Form), to 17 PCD patients \geq 15 years-old (Group B: Psychological General Well-Being Index) and to 27 controls. We compared the PCD pulmonary exacerbations from the beginning of the outbreak and the frequency of weekly chest physiotherapy sessions during quarantine to the same period in 2019.

Results: Seventy percent of Group A cases did not present parental stress levels. Ninety percent of Group B subjects did not show scores indicating distress. Groups A and B showed no significant difference versus controls in parental stress and psychological well-being, respectively. In the whole PCD population pulmonary exacerbations from the beginning of outbreak were less than in the same period of 2019 ($p < 0.05$), and weekly chest physiotherapy sessions significantly increased during the quarantine compared to the same period of 2019 ($p < 0.05$).

Conclusions: We found that during COVID-19 quarantine, a PCD population in Italy neither developed psychological distress nor had a psychological burden significantly different than controls. We speculate that the low pulmonary exacerbation rate, explained by lower exposure to infectious triggers or by improved compliance to weekly chest physiotherapy, likely contributes to the psychological well-being of PCD patients and their families. The evaluation of the psychological burden and parental stress is a valuable tool for measuring the emotional impact of PCD and ultimately improving the medical care to PCD patients and their families, especially when exceptional events such as a pandemic occur.

Background

Originating in December 2019 as a cluster of unexplained pneumonia in China, the novel severe acute respiratory syndrome due to coronavirus 2 (SARS-CoV-2) designated as Coronavirus Disease 2019 (COVID-19) rapidly reached the level of a global pandemic ^[1]. The clinical spectrum of adult COVID-19 ranges from pauci- or asymptomatic forms to acute respiratory distress syndrome, and in several cases multi-organ failure and death have been described ^[2]. Incidence of paediatric COVID-19 is lower than adult disease, with less critical cases and very few deaths ^[3].

Having a pre-existing chronic condition might pose a threat to severe COVID-19 ^[4]. However, data are heterogeneous as the risk is increased in adult chronic obstructive pulmonary disease or non-allergic

asthma (5, 6), while in patients with cystic fibrosis (CF) the COVID-19 course was not significantly different from the general population [7].

Primary ciliary dyskinesia (PCD; MIM244400), a rare genetic disorder, is characterized by impaired mucociliary clearance and recurrent-to-chronic respiratory infections [8]. Development of bronchiectasis with progressive loss of pulmonary function, fertility issues, and *situs viscerum inversus* in 50% of cases (Kartagener syndrome) are the hallmarks of the condition [9]. Yet in adolescence or young adulthood PCD lung disease may progressively deteriorate and therefore PCD is considered a chronic entity [8]. There are no reports on COVID-19 in PCD.

Because of the massive outbreak of COVID-19 reported in Italy since last February [10], the Government adopted a plan of preventive measures to contain the viral spread [11]. According to the decree of the President of the Council of Ministers, the whole population was placed under lockdown and strict social isolation was imposed from March 8, 2020 up to May 4, 2020 [12].

Isolation has a considerable psychological impact on either subjects who are infected or those who keep distance for preventing infection [13]. In addition to concerns associated with the diffusion of the outbreak, limited access to hospital facilities during the quarantine period could make patients with chronic disorders more susceptible to psychological stress. As respiratory exacerbations result in PCD increased morbidity [9], concerns on COVID-19 are expected to impact on patients' psychological well-being, but information is lacking on this. The primary aim of our study was to assess prospectively the PCD patients psychological burden and parental stress level compared to healthy people during the lockdown period in Italy.

Methods

We performed a prospective study of a PCD population including either patients with PCD or the mothers of patients with PCD who were compared to sex- and age-matched healthy subjects. Signed informed consent was obtained from all participants. The study was performed in accordance with the Declaration of Helsinki for Human Research and approved by the Ethical Committee, Federico II University, Naples (protocol n° 275/20).

Patients

At the Department of Translational Medical Science, University "Federico II", Naples, Italy, a specialized centre that provides care to children and adults with PCD was instituted in 1993. Patients are followed through scheduled ambulatory visits which also include sputum culture, spirometry and chest imaging (when needed), and hospital admission for intravenous antibiotic administration and/or treatment of medical/surgical complications. At our centre, treatment of PCD consists of *a)* airway clearance techniques at least twice in a day aimed to facilitate clearance of mucus from the airways, i.e. nebulised hypertonic saline followed by chest physiotherapy (including percussion and vibration and/or postural

drainage and/or autogenic drainage and/or active cycle breathing, with or without the aid of positive expiratory pressure devices and mechanical cough assist); *b*) antibiotic treatment in case of airway exacerbation.

As soon as the notice of the President of the Council of Ministers that imposed the quarantine in Italy was received (March 8, 2020) ^[12], we modified our policy of care to PCD patients. According to our hospital board, we switched from regular hospital visits scheduled on a three-monthly basis to home-based management of PCD patients through remote assistance service in telemedicine. This consisted of weekly telephone or email contacts between patients and PCD physicians. Treatment of PCD was confirmed and/or modified on the basis of each patient's needs. Patients could not access the hospital unless urgent consultations were required.

During the quarantine (March 8, 2020- May 4, 2020), after a telephone contact we remotely enrolled 27 PCD patients. Inclusion criteria were: PCD diagnosis according to the European Respiratory Society guidelines ^[14]; active follow-up for at least 12 months; and adherence to the study protocol after informed consent signature. Exclusion criteria were: confirmed or suspected COVID-19 infection; PCD diagnosis made in 2020; concomitant chronic diseases or psychiatric/neurodevelopmental disorders; incomplete information availability; inability to give informed consent.

Study design

The enrolled PCD patients or their parents received by email a questionnaire aimed to assess their psychological stress level in the quarantine period. We divided the PCD population in two age-based groups, < 15 (Group A) and \geq 15 years-old (Group B), respectively. The age limit was set at 15 years as we used a questionnaire on the self-perceived evaluation of psychological well-being that has been previously validated in subjects above 15 years ^[15].

In Group A patients, we assessed their parents stress through the Italian version of the Parenting Stress Index- Short Form questionnaire (PSI-SF) ^[16]. The PSI-SF is a standardized self-report tool that explores the stress levels of parents or caregivers of children ^[16, 17]. It has 36 items, each graded on a 5-point Likert scale. The PSI-SF is organized in 4 subscales: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), Difficult Child (DC), Defensive Responding (DEF, which indicates likely response bias). It also provides a total stress score index. Higher scores indicated higher perceived stress in the parents. The PSI-SF provides both raw and percentile scores. Classes of percentile were defined according to age as follows: a) >85th percentile: "High stress level"; b) between 50th and 85th percentile: "Symptomatic stress" (but not clinically relevant condition); c) <50th percentile: "Non-pathological stress levels". The PSI-SF validity has been established in parents of children with PCD and other chronic medical conditions such as diabetes or asthma ^[18, 19]. In the current study, the PSI-SF was administered only to the mother, as the parent who usually spends more time with the children.

In Group B patients, psychological well-being was assessed by administering the Italian version of the Psychological General Well-Being Index (PGWBI) questionnaire [20]. The PGWBI is a self-administered questionnaire that measures the level of subjective psychological well-being in subjects older than 15 years [15]. It assesses the self-representations of intrapersonal affective or emotional states reflecting a sense of subjective well-being or distress and thus captures what we could call a subjective perception of well-being. It consists of 22 standardized items organized in 6 subscales: Anxiety, Depression, Well-being, Self-control, General Health, and Vitality. Responses for each item are evaluated on a six-point Likert scale ranging from 0 to 5. Higher scores indicate better well-being. The subscales sum provides a global index score for subjective well-being (range 0–110). Considering “distress” as the reverse of well-being, a total score <60 suggests “Severe Distress”, while the “Moderate Distress” and “No Distress” categories are defined with a global score of 60 to 72, and >72, respectively. The PGWBI provides both raw and percentile scores. Classes of percentile were defined for subscales and global scores, according to gender and age, as follows: a) <25th percentile: “severe distress”; b) between 25th and 50th percentile: “moderate distress”; c) between 50th and 75th percentile: “No distress”; d) >75th percentile: “positive well-being” [20]. The PGWBI and the PSI-SF have been previously validated in Italian [16, 20].

When we designed the study protocol, we decided to assess also *a*) the PCD respiratory exacerbations rate occurring in our PCD patients from the beginning of the outbreak in Italy. According to a recent publication, we resolved in advance to concentrate on those occurring in the lower airways [21]. The PCD pulmonary exacerbations occurring from February 1 to May 4, 2020 were compared to those registered in the medical records over the same period of the previous year (2019); *b*) the number of chest physiotherapy per week performed by each patient during the quarantine period, which was compared to the number registered in the medical records in the same period of the previous year (2019). Data referring to 2020 were obtained by email or telephone interview to PCD patients or PCD mothers.

We administered the PGWBI and the PSI-SF questionnaires also to twenty-seven age- and sex-matched controls, including 17 healthy subjects aged over 15 years and the mothers of 10 healthy subjects aged less than 15 years, respectively.

Adherence to the measures imposed by the Government was evaluated by administering the following questions to *a*) adult workers (either PCD patients or controls): “During the lockdown period did you adopt the smart working model?”; *b*) subjects with PCD or controls either attending school or university: “During the lockdown period did you/your kid stop attending school or university courses?”.

Statistical Analysis

Analyses were made with Graphpad Software, version 8.0.0 (San Diego, California USA). The Kolmogorov-Smirnov Test was used to evaluate normality distribution of data. Data were presented as mean [standard deviation (SD)] or median [interquartile range (IQR)], and categorical variables as frequency (%). The exact Fisher, T-student and Mann-Whitney tests were used to compare patients and

control groups and data of PCD patients between the two study periods (2019 and 2020). A two-sided $p < 0.05$ was considered significant.

Results

None of the patients had confirmed or suspected COVID-19, or had undergone medical consultations related to COVID-19. Demographic and clinical characteristics of PCD patients including 10 subjects aged < 15 years and 17 cases older than 15 years are summarized in Table 1. In the control group of seventeen healthy subjects older than 15 years (65% males), mean age was 34.5 years (SD 12.6), while the 10 healthy subjects younger than 15 years (70% males) whose mothers were administered the PSI-SF questionnaire had a mean age 10.3 years (SD 3). All participants, including PCD patients, mothers and controls sent back the questionnaires on May 5, 2020.

Table 1
Demographic and clinical characteristics of patients with primary ciliary dyskinesia.

	Total (n = 27)	Group A (n = 10)	Group B (n = 17)
Male, n. (%)	15 (56)	6 (60)	9 (53)
Age, years* (SD)	22.6 (12.3)	12.8 (2.4)	28.4 (12.1)
Age at diagnosis, years* (SD)	7.7 (10.3)	2.6 (3.9)	10.8 (11.7)
Patients with laterality defect, n. (%)	22 (81)	7 (70)	15 (88)
Patients with bi-allelic mutation, n. (%)	23 (85)	8 (80)	15 (88)
Patients with abnormal TEM, n. (%)	17 (63)	6 (60)	11 (65)
FVC, % predicted* (SD)	94.7 (17.4)	96.1 (14.8)	94 (19)
FEV₁, % predicted* (SD)	84.7 (21.6)	88.6 (21)	82.9 (22.3)
Patients with bronchiectasis, n. (%)	15 (56)	4 (40)	11 (65)
Monolateral, n. (%)	7 (26)	1 (10)	6 (35)
Bilateral, n. (%)	8 (30)	3 (30)	5 (29)
Patients with PA colonization, n. (%)	8 (30)	2 (20)	6 (35)

Patients and families with PCD, as well as controls and their families strictly observed the stringent preventive measures ordered by the Government as either all the adults entering the study adopted the smart working model or all students attended online school or university courses at home.

Results of the PSI-SF questionnaire administered to PCD mothers showed that in 7 of 10 cases (70%), the total scores were below the 50th percentile and, therefore, did not suggest a stress condition (Table 2).

Only in 3 PCD mothers (30%) the total scores fell above the 50th percentile, indicating parental stress. In the mothers of control group, only 1 case (10%) had a total score between the 50th and 85th percentile, in the remaining cases (90%) the total scores were below the 50th percentile. The percentage of PCD and control group mothers with different categories of stress level (high; symptomatic stress; non-pathological stress) were not significantly different ($p > 0.05$). PSI-SF mean scores related to total stress and subscales (PD, P-CDI, DC, DEF) in PCD patients' mothers (Group A) were not significantly different than those in controls' mothers (Table 2). However, 3 PCD mothers (30%), and only 1 mother in the control group (10%), had a DC score equal to or higher than 85th percentile (Fig. 1).

Table 2
Results of PSI-SF questionnaire to the mothers of Group A patients and controls.

	Group A (n = 10)	Healthy controls (n = 10)	P
Male	6 (60) †	7 (70) †	1.0
Age, years	12.8 (2.4) *	10.3 (3) *	0.56
PSI-SF categories			
High stress level (s > 85th percentile)	2 (20) †	0 (0) †	0.47
Symptomatic stress (50th > s < 85th percentile)	1 (10) †	1(10) †	1.00
Non-pathological stress (s < 50th percentile)	7 (70) †	9 (90) †	1.00
PSI-SF scores			
PD	23.8 (7.8) *	20.1 (6.0) *	0.12
PCD-I	20.3 (10.3) *	16.3 (4.4) *	0.27
DC	26.1 (9.6) *	19.8 (5.2) *	0.08
DEF	14.9 (3.7) *	13.0 (3.5) *	0.25
Total stress index	67.3 (23.0) *	53.9 (13.8) *	0.13
Abbreviations: s, score; PD, parental distress domain; P-CDI, parent-children dysfunctional interaction domain; DC, difficult child subscale; DEF, defensive responding. †Expressed as number of patients or controls and percentage in parenthesis * Expressed as mean and Standard Deviation in parenthesis			

As shown in Table 3, results of the PGWBI questionnaire showed that 13 of 17 cases (76%) of Group B patients did not present total scores indicating distress. In 3 subjects (18%), the total score indicated "Moderate distress" and only in 1 subject (6%) "Severe distress". In the control group, 12 of 17 subjects (70%) did not present total scores indicating distress, while 3 (18%) and 2 (12%) of the remaining cases showed a total score of moderate and severe distress, respectively. Percentages of patients and controls with different categories of PGWBI (i.e. severe; moderate; no distress) were not significantly different ($p > 0.05$). Compared to controls, in PCD subjects older than 15 years no significant differences of raw scores

of anxiety, depression, well-being, self-control, general health, vitality and PGWBI total index were found ($p > 0.05$; Fig. 2). We did not find any significant difference between the number of PCD patients and controls with subscale scores < 25 th percentile (indicating severe distress) (Fig. 3a-f). However, less PCD subjects than controls reported anxiety, depression, difficulties relating well-being or vitality feelings (Fig. 3a, b, c, f), while more difficulties associated with self-control and general health were found in a higher proportion of PCD cases than controls (Fig. 3d, e).

Table 3
Results of the PGWBI questionnaire to Group B and controls.

	Group B (n = 17)	Healthy controls (n = 17)	P
Male	9 (53) †	11 (65) †	0.73
Age, years	28.4 (12.1) *	34.5 (12.6) *	0.16
PGWBI categories			
Severe distress (s < 60)	1 (6) †	2 (12) †	1.00
Moderate distress (60 > s < 72)	3 (18) †	3 (18) †	1.00
NO distress (s > 72)	13 (76) †	12 (70) †	1.00
PGWBI scores			
Anxiety	17.5 (3.5) *	17.1 (3.5) *	0.77
Depression	12.8 (1.3) *	12.1 (1.4) *	0.11
Well-being	11.5 (3.0) *	10.8 (2.7) *	0.48
Self-control	11.8 (2.3) *	12 (2.2) *	0.82
Health	11.3 (1.5) *	11.8 (2.2) *	0.42
Vitality	14.3 (2.8) *	13.4 (2.6) *	0.32
PGWBI total score	79.2 (11.5) *	77.2 (12.2) *	0.62
Abbreviations: s, score. †Expressed as number of patients or controls and percentage in parenthesis * Expressed as mean and Standard Deviation in parenthesis			

Compared to the rate in the same period of the current year (2020), the pulmonary exacerbation rate was higher in the period February-May 4, 2019 in the whole PCD study population, ($p = 0.03$), and in PCD subjects younger ($p = 0.02$) or older than 15 years ($p = 0.04$), respectively (Table 4). The mean number of chest physiotherapy sessions per week performed by each PCD patient significantly increased during the quarantine period (i.e. from March 8, to May 4, 2020) compared to the same period in the previous year (12 *versus* 8 sessions/week per patient, respectively; $p = 0.04$).

Table 4

Pulmonary exacerbations in PCD patients during COVID-19 outbreak compared to the same period of 2019.

	February – May 2019	February – May 2020	<i>P</i>
Total patients (n = 27)	1 (0–1)	0 (0–0)	0.03
Number of exacerbations (IQR)			
Patients with at least one exacerbation, n (%)	16 (59)	3 (11)	0.00
Patients aged < 15 years (n = 10)	1 (0–1)	0 (0–0)	0.02
Number of exacerbations (IQR)			
Patients with at least one exacerbation, n (%)	7 (70)	1 (10)	0.02
Patients aged > 15 years (n = 17)	1 (0–1)	0 (0–0)	0.04
Number of exacerbations (IQR)			
Patients with at least one exacerbation, n (%)	9 (53)	2 (12)	0.02
Abbreviations: n, number; IQR, interquartile range.			

Discussion

To our knowledge, this is the first prospective study on the levels of psychological burden in a PCD population compared to healthy subjects during the imposed lockdown period for COVID-19 in Italy. This study was designed starting from the assumption that PCD is a chronic disorder with potential psychological effects also on the intra-familial relationships because of patients' frequent need of medical consultations, their own perception of being sick, and the possible effects of denial and rejection of the disease by patients and/or parents. Our main finding is that, overall, during the COVID-19 quarantine, PCD patients did not show scores indicating distress, and only some of them reported more difficulties related to self-control and general health. Among PCD parents, only 20% had high levels of stress. Finally, when compared to healthy subjects, the current PCD population did not show significantly different psychological burden or parental stress level during the quarantine. Patients with PCD and their families, as well as controls, strictly observed the stringent preventive measures ordered by the Italian Government. We speculate that the quarantine, avoiding the risk of exposure to SARS-CoV-2, gave PCD patients a great sense of security. Despite the access to the healthcare service was fairly limited, the telemedicine facility at our hospital warranted a continuous medical surveillance through the remote contact.

Some data from the current study deserve a comment. The finding of less PCD lung exacerbations during the COVID-19 quarantine period imposed in Italy, quite novel to the best of our knowledge, is not surprising, and might be likely explained by the strict adherence to the preventive measures for reducing

viral transmission. These consisted of *a*) social distancing with avoidance behaviours; *b*) the adoption of the smart working model that allowed workers to work at home with a flexible time schedule; *c*) schools closure for limiting contacts with or among kids and their teachers; *d*) education to frequent handwashing; *e*) respiratory (especially, while coughing or sneezing) and environmental hygiene measures [22]. Since health care institutions are major foci of disease, and the nosocomial SARS-CoV-2 transmission is a concrete possibility, several hospitals, also including our, imposed to patients to limit the access to healthcare services during the quarantine unless urgent or serious problems were claimed by emails or telephone calls. The detection of respiratory pathogens in the PCD lower airways is associated with frequent exacerbations, and fuels the vicious cycle of infection, inflammation and lung damage that further increases bacterial growth [9]. Therefore, the absence of stress perception during the quarantine found in the vast majority of our study population might be related to less symptoms or signs of pulmonary exacerbation. As our patients during the COVID-19 quarantine period had a lot more free time, we speculate that the smart working model or school closure likely resulted in improved compliance to chest physiotherapy. This could represent an additional reason for explaining, at least in part, the reduced number of lung infections [23].

In PCD, retention of airways mucus and growth of biofilms caused by abnormal ciliary structure and/or function result in early recurrent airways infection. These are, indeed, a common issue also in non-PCD subjects [9]. The diagnostic delay and delayed start of PCD treatment may eventually result in patients' uncertainty or anxiety about their disease outcome. This, combined with the need of continued care, may negatively impact on patients' emotional status and place them and their families at risk for impaired psychosocial functioning. Research on well-being and psychological issues of PCD has focused on the emotional burden of the condition, including patients' concern about current and future health [24]. Several studies have highlighted that PCD patients of any age are at risk of experiencing anxiety or depression, or reduced self-esteem, even though ultimately they may not present worse rates of psychological well-being than healthy peers [25-27].

The primary goal of public health measures for controlling a pandemic is to prevent person-to-person spread of the infection by separating people. Isolation is an unpleasant experience, and individuals report not only boredom or sense of frustration, but also feelings such as sadness, fear, or nervousness due to reduced social contacts and loss of daily tasks [28]. During disease outbreaks, anxiety can also rise following repeated media reporting on everyday rate of new cases or deaths. In addition to this, being unable to get regular medical care and prescriptions may be a matter of concern, especially for patients with chronic disorders [29]. In PCD patients and their families the uncertainty about the future, combined with the fear that a respiratory exacerbation or any additional medical problem could occur and not be addressed because hospital visits were blocked, might increase patients' or parents' level of anxiety. However, social distancing likely halted the transmission of all respiratory pathogens also including SARS-CoV-2, and this might have a beneficial effect on PCD patients and family well-being.

We chose to evaluate the stress levels of a parent of a PCD patient younger than 15 years rather than the patient him/herself. In fact, we believe that remote assessment of the psychological state in younger subjects could result unreliable because of the difficulties of self-monitoring and self-awareness at that age. Actually, PCD parents may exhibit a great emotional and stress load (27) which, conversely, during COVID-19 quarantine did not appear increased compared to healthy peers. Nevertheless, in the current PCD mothers' group, the PSI-SF total score and the scores of other subscales appeared higher than the control group score, although the difference was not statistically significant. The data suggest that in Italy the emergency condition associated with COVID-19 increased the stress levels in the general population, reducing the gap with subjects with an underlying chronic condition such as PCD. Actually, greater care, greater hygiene and staying at home might represent a protective factor for people with chronic respiratory diseases, paradoxically affecting the levels of psychological well-being in their parents. Comparing the scores obtained in each subscale, we found that the percentage of subjects with clinically relevant scores of the "Difficult Child" subscale, was greater in the group of PCD mothers than in the control group. Moreover, 30% of PCD mothers had T-scores above 85th pc in the subscale relating to DC. The DC subscale represents the perception that a parent has of his/her own child, seen as a "difficult child" for any problematic behaviour. High scores on this scale indicate the presence of characteristics which may make it difficult for parents to play their role. This finding suggests that some of our mothers felt themselves more stressed during the quarantine period in the daily management of their kids when compared to healthy kids.

Also in the group of PCD patients older than 15 years, the evaluation of the psychological impact of the COVID-19 quarantine did not reveal clinically significant differences *versus* the control group. Nevertheless, when we compared the scores obtained in each subscale, we found that the percentage of subjects with clinically relevant scores associated to "Anxiety", "Depression", "Positivity and well-being" and "Vitality", was greater in the control group than in PCD patients. Conversely, more PCD subjects showed clinically significant scores in the subscales related to "Self-control" and "General health". These data indicate that in the healthy controls anxiety and depression levels were increased because of the concerns of the outbreak, with a consequent reduction in the perception of well-being and vitality, as recently reported [30]. In PCD patients, on the other hand, self-control was decreased, perhaps because of the fear of getting infected. The general sense of health might be perceived as more precarious, but stress levels, mood and perception of anxiety were stable.

Our study has strengths and limitations. First, we provided the novel information of the psychological effects of quarantining patients with PCD that was lacking in the literature. An additional strength is the availability of detailed medical records from a well-defined cohort of PCD patients. This allowed to compare the data collected during the COVID-19 lockdown period to the same period of the previous year. Moreover, we designed a prospective, observational study with a control group who adhered strictly to the isolation preventive measures as well as PCD patients. Yet, the study has some limitations. First, due to the unexpected nature of the COVID-19 outbreak we could not evaluate the psychological burden in the previous year and thus ignore the level of emotional stress in the pre-COVID-19 period both in PCD

patients and controls. Second, the study population from a single-centre in Southern Italy was small. Actually, designing a study of a large and homogeneous population of patients with a rare condition like PCD is not easy. However, these findings should be hopefully confirmed by data from larger PCD population in countries with even different sociocultural background.

Conclusions

In conclusion, this study provides the novel information that patients with PCD, a chronic condition with pre-existing potential characteristics of personal and familiar increased stress, during COVID-19 quarantine neither developed psychological distress nor had a psychological burden significantly different than controls. Similar multicentre, longitudinal studies in patients with underlying chronic respiratory disorders would increase the understanding of COVID-19 outbreak, likely the most dramatic ever lived by humans over the last century.

List Of Abbreviations

PCD: Primary Ciliary Dyskinesia; SARS-CoV-2: severe acute respiratory syndrome due to coronavirus 2; COVID-19: Coronavirus Disease 2019; PSI-SF: Parenting Stress Index- Short Form; PD: Parental Distress; P-CDI: Parent-Child Dysfunctional Interaction; DC: Difficult Child; DEF: Defensive Responding; PGWBI: Psychological General Well-Being Index; TEM: transmission electron microscopy; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 second; PA: *Pseudomonas aeruginosa*.

Declarations

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Authors' contributions

MPR, MB, MTF and MDB designed the study. MPR, MB, MTF, and MDB drafted the manuscript. MTF and MDB collected and provided the patient data. MP performed the statistical analysis. The whole scheme was planned and supervised by FS, MB and CB. FS and MB critically revised the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration for Human Research and was approved by the Ethical Committee, Federico II University, Naples (protocol n^o 275/20).

Consent for publication

Signed informed consent was obtained from all participants by email.

Competing interests

All authors declare that they have no conflict of interest.

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References

1. Park M, Cook AR, Lim JT, Sun Y, Dickens BL. A Systematic Review of COVID-19 Epidemiology Based on Current Evidence. *J Clin Med*. 2020;9(4):967. doi:10.3390/jcm9040967
2. Lupia T, Scabini S, Mornese Pinna S, Di Perri G, De Rosa FG, Corcione S. 2019 novel coronavirus (2019-nCoV) outbreak: A new challenge. *J Glob Antimicrob Resist*. 2020;21:22-27. doi:10.1016/j.jgar.2020.02.021
3. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med*. 2020;26(4):502-505. doi:10.1038/s41591-020-0817-4
4. Adams ML, Katz DL, Grandpre J. Updated Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States. *Emerg Infect Dis*. 2020;26:10.3201/eid2609.202117. doi:10.3201/eid2609.202117
5. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med*. 2020;167:105941. doi:10.1016/j.rmed.2020.105941
6. Zhu Z, Hasegawa K, Ma B, Fujiogi M, Camargo CA Jr, Liang L. Association of asthma and its genetic predisposition with the risk of severe COVID-19. *J Allergy Clin Immunol*. 2020;S0091-6749 30806-X. doi:10.1016/j.jaci.2020.06.001
7. Cosgriff R, Ahern S, Bell SC, Brownlee K, Burgel PR, Bymes C, et al. A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis. *J Cyst Fibros*. 2020;19:355-358.

doi:10.1016/j.jcf.2020.04.012

8. Damseh N, Quercia N, Rumman N, Dell SD, Kim RH. Primary ciliary dyskinesia: mechanisms and management. *Appl Clin Genet*. 2017;10:67-74. doi:10.2147/TACG.S127129
9. Mirra V, Werner C, Santamaria F. Primary Ciliary Dyskinesia: An Update on Clinical Aspects, Genetics, Diagnosis, and Future Treatment Strategies. *Front Pediatr*. 2017;5:135. doi:10.3389/fped.2017.00135
10. Romagnani P, Gnone G, Guzzi F, Negrini S, Guastalla A, Annunziato F, et al. The COVID-19 infection: lessons from the Italian experience. *J Public Health Policy*. 2020;1-7. doi:10.1057/s41271-020-00229-y
11. Istituto Superiore di Sanità. Epicentro. Coronavirus. Available on: <https://www.epicentro.iss.it/coronavirus/> (**Date of update:** 29 July 2020)
12. Decree of the President of the Council of Ministers. Available on: http://www.governo.it/sites/new.governo.it/files/Dpcm_20200410.pdf (accessed on June 30, 2020).
13. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020;395:912-920. doi:10.1016/S0140-6736(20)30460-8
14. Lucas JS, Barbato A, Collins SA, Goutaki M, Behan L, Caudri D, et al. ERS Task Force guideline for the diagnosis of primary ciliary dyskinesia. *Eur Respir J*. 2017 Jan 4;49:1601090.
15. Grossi E, Groth N, Mosconi P, Cerutti R, Pace F, Compare A, et al. Development and validation of the short version of the Psychological General Well-Being Index (PGWB-S). *Health Qual Life Outcomes*. 2006;4:88. doi:10.1186/1477-7525-4-88
16. Abidin RR. Parenting stress index, 3rd ed: professional manual. Lutz: Psychological Assessment Resources Inc, 1995: 53-71.
17. Abidin RR. Parenting stress index: a measure of the parent-child system. In: Zalaquett CP, Wood R, eds. *Evaluating stress-a book of resources*. Lanham: Scarecrow Press, 1997: 277-291.
18. Carson DK, Schauer RW. Mothers of children with asthma: perceptions of parenting stress and the mother-child relationship. *Psychol Rep*. 1992;71:1139-1148. doi:10.2466/pr0.1992.71.3f.1139
19. Tynan WD. Adjustment to diabetes mellitus in preschoolers and their mothers. *Diabetes Care*. 1990;13:456-457. doi:10.2337/diacare.13.4.456
20. Grossi E, Mosconi P, Groth N, Niero M, Apolone G. Questionario Psychological General Well-Being Index. Versione Italiana. Istituto di ricerche farmacologiche "Mario Negri" Milano, Maggio 2002
21. Lucas JS, Gahleitner F, Amorim A, Boon M, Brown P, Constant C, et al. Pulmonary exacerbations in patients with primary ciliary dyskinesia: an expert consensus definition for use in clinical trials. *ERJ Open Res*. 2019;5:00147-2018. doi:10.1183/23120541.00147-2018
22. Sjödin H, Wilder-Smith A, Osman S, Farooq Z, Rocklöv J. Only strict quarantine measures can curb the coronavirus disease (COVID-19) outbreak in Italy, 2020. *Euro Surveill*. 2020;25:2000280. doi:10.2807/1560-7917.ES.2020.25.13.2000280

23. Hill AT, Barker AF, Bolser DC, Davenport P, Ireland B, Chang AB, et al. Treating Cough Due to Non-CF and CF Bronchiectasis With Nonpharmacological Airway Clearance: CHEST Expert Panel Report. *Chest*. 2018; 153:986-993
24. Whalley S, McManus IC. Living with primary ciliary dyskinesia: a prospective qualitative study of knowledge sharing, symptom concealment, embarrassment, mistrust, and stigma. *BMC Pulm Med*. 2006;6:25. doi:10.1186/1471-2466-6-25
25. Zengin Akkus P, Gharibzadeh Hizal M, Ilter Bahadur E, Ozmert EN, Eryilmaz Polat S, Ozdemir G, et al. Developmental and behavioral problems in preschool-aged primary ciliary dyskinesia patients. *Eur J Pediatr*. 2019;178:995-1003. doi:10.1007/s00431-019-03382-z
26. Behan L, Rubbo B, Lucas JS, Dunn Galvin A. The patient's experience of primary ciliary dyskinesia: a systematic review. *Qual Life Res*. 2017;26:2265-2285. doi:10.1007/s11136-017-1564-y
27. Carotenuto M, Esposito M, Di Pasquale F, De Stefano S, Santamaria F. Psychological, cognitive and maternal stress assessment in children with primary ciliary dyskinesia. *World J Pediatr*. 2013;9:312-317. doi:10.1007/s12519-013-0441-1
28. Rubin GJ, Wessely S. The psychological effects of quarantining a city. *BMJ*. 2020;368:m313. doi:10.1136/bmj.m313
29. Blendon RJ, Benson JM, DesRoches CM, Raleigh E, Taylor-Clark K. The public's response to severe acute respiratory syndrome in Toronto and the United States. *Clin Infect Dis*. 2004;38:925-931. doi:10.1086/382355
30. Wang C, Pan R, Wan X, Wan X, Tan IY, Xu L, et al. Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. *Int J Environ Res Public Health*. 2020;17:1729. doi:10.3390/ijerph1705172

Figures

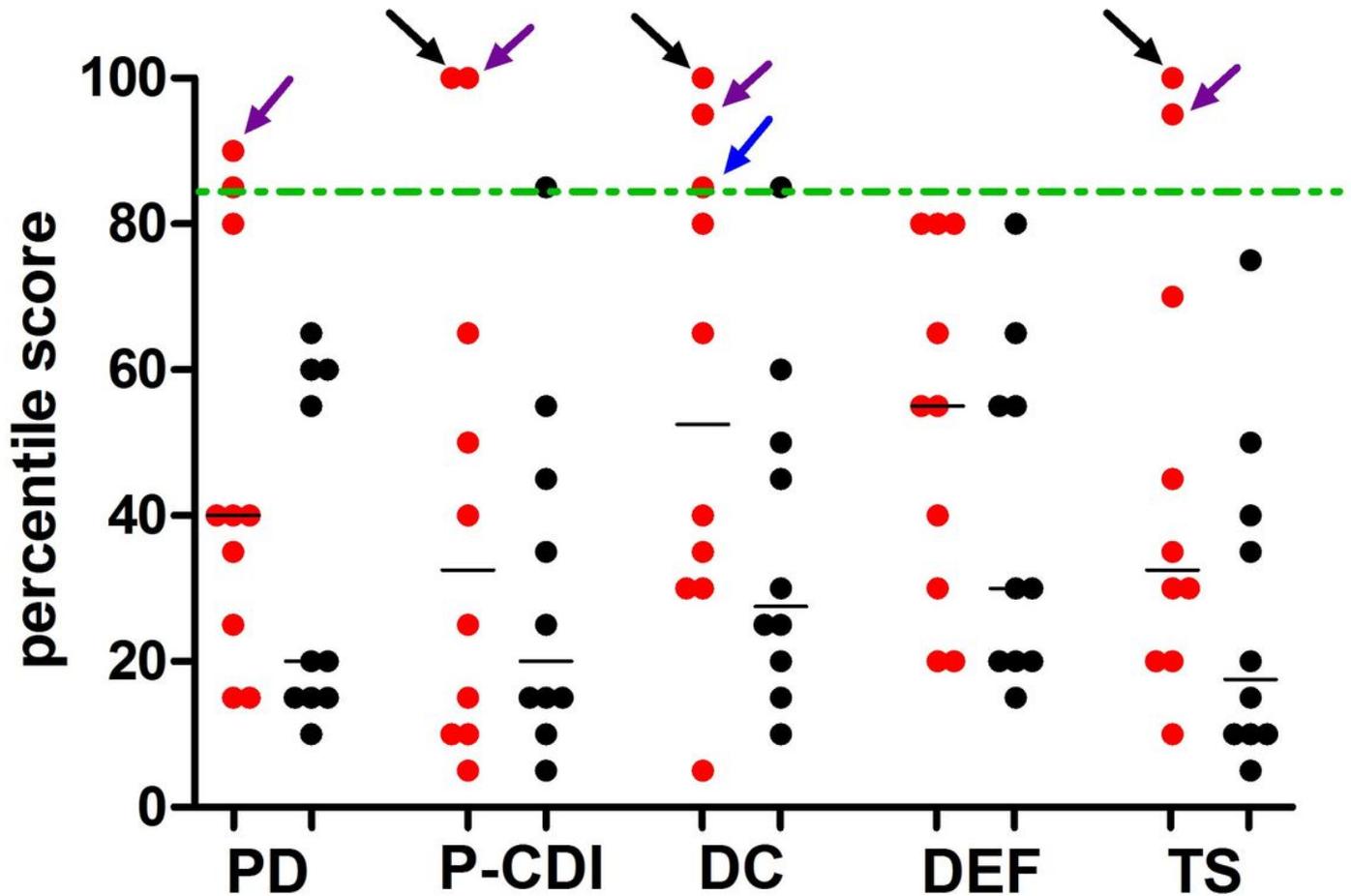


Figure 1

Distribution of PSI-SF percentile scores of subscales and total score from PCD mothers and controls. The stress levels were explored by Parenting Stress Index- Short Form questionnaire (PSI-SF) in the mothers of PCD patients (n=10) and of healthy controls (n=10) younger than 15 years. The PSI-SF is organized in 4 subscales: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), Difficult Child (DC), Defensive Responding (DEF). Each point (red and black for PCD patients and controls, respectively) represents the percentile score taken from a single subject. Horizontal bars represent the median values. Dashed line indicates the 85th percentile (high stress level). Only 3 PCD mothers presented a pathologic percentile score: one (purple arrow) in PD, P-CDI and DC subscales and in total score (TS); one (black arrow) in score in P-CDI, DC and TS and one (blue arrow) presented a score equal to 85th percentile only in DC subscale. In each subscale and in the total score the percentile scores were not significantly different between patients and healthy controls ($p > 0.05$).

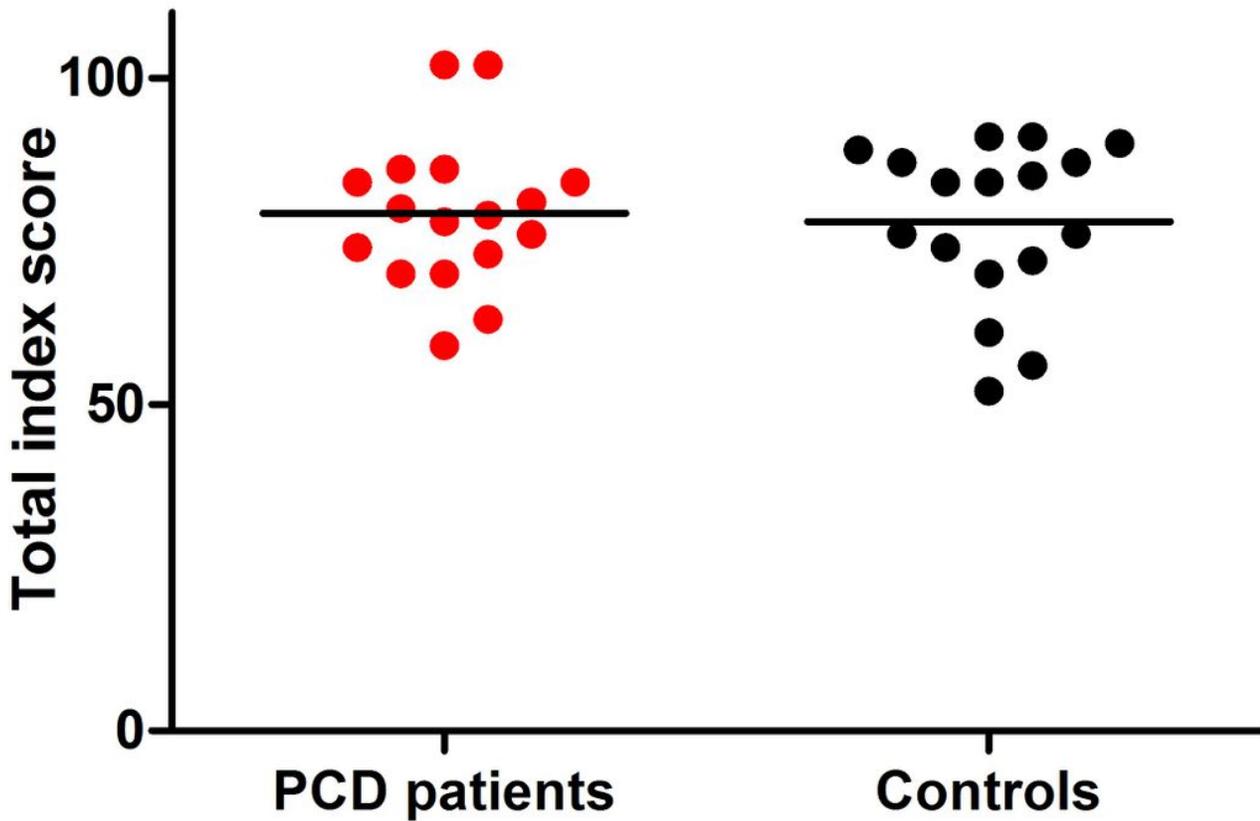


Figure 2

Distribution of PSGWBI total index score from PCD patients and controls. It was assessed by administering the Psychological General Well-Being Index (PSGWBI) questionnaire in PCD patients (n=17) and healthy controls (n=17) older than 15 years. The PSGWBI is organized in subscales, the subscales sum provides a total index score for subjective well-being (range 0–110). Considering “distress” as the reverse of well-being, a total score <60 suggests “Severe Distress”, while the “Moderate Distress” and “No Distress” categories are defined with a total score between 60 and 72, and >72, respectively. Each point (red and black for PCD patients and controls, respectively) represents the total index score obtained by a single subject. Horizontal bars represent the mean values. The dashed line represents the total index score of 60. Only one PCD patient and two controls presented pathological scores. There were no significant differences of total index score between PCD patients and healthy controls ($p > 0.05$).

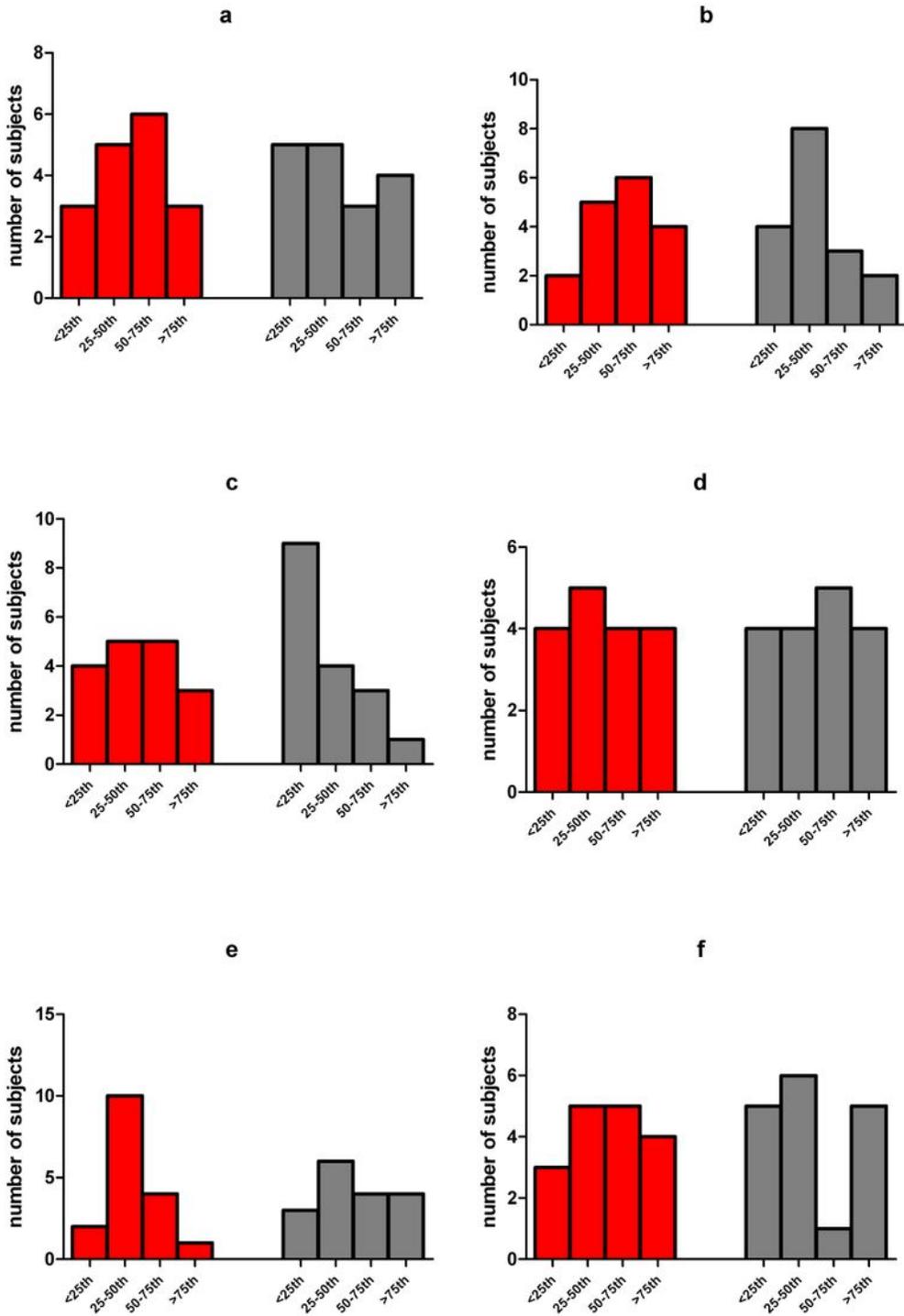


Figure 3

a-f. Distribution of PCD patients and controls in the classes of percentile of PSGWBI subscales. The Psychological General Well-Being Index (PSGWBI) questionnaire was administered to PCD patients (n=17) and healthy controls (n=17) older than 15 years. The PSGWBI is organized in 6 subscales: (a) anxiety; (b) depression; (c) well-being; (d) self-control; (e) general health; (f) vitality. Classes of percentile were defined for subscales, according to gender and age, as follows: <25th pc: “severe distress”; between

25th and 50th percentile: "moderate distress"; between 50th and 75th percentile: "No distress"; >75th percentile: "positive well-being". Red columns indicate PCD patients and grey columns indicate healthy controls. No significant difference between the number of PCD patients and controls with subscale scores <25th percentile was found (a-f). Less PCD subjects than controls reported anxiety (a), depression (b), difficulties relating well-being (c) or vitality feelings (f), while more difficulties associated with self-control (d) and general health (e) were found in a higher proportion of PCD cases than controls.