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Title Page

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The Effect of COVID-19 on Anxiety Levels of Children with CF and Healthy Peers

Running Title: THE EFFECT OF COVID-19 ON ANXIETY

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Title Page

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Abstract

Background

Cystic fibrosis (CF) is a chronic disease causing recurrent respiratory tract infections. Viral respiratory tract infections are more severe in CF. The first case of COVID-19 was seen in our country on March 11, 2020 and nationwide school closure and lockdown were implemented. School closure and home confinement might have adverse effects on children's physical and mental health. In this study,

we aimed to compare the effect of COVID-19 pandemic on psychological reactions of CF patients and healthy controls.

Methods

This is a controlled cross-sectional study including 7-18 year-old children with CF. The survey included questions regarding family environment and peer relations, self care and psychological reactions to COVID-19 pandemic. The questionnaire was applied to children via telephone call under parental supervision.

Results

We evaluated 132 CF patients and 135 their healthy peers. Mean age was 11.5 ± 2.9 years in CF group and 11.8 ± 3.2 years in control group ($p=0.98$). There were 55 girls (41.7%) in CF group and 81 girls (60%) in control group ($p=0.027$). The socioeconomic status of families was similar. CF patients were found to be less anxious for family members having the risk of COVID-19, less upset for school closure, less anxious about the COVID-19 pandemic ($p<0.001$, 0.02, 0.01 respectively).

Conclusion

CF patients seem to show more resilience in coping with the pandemic. Appropriate psychological support should be provided to them and resilience strategies in coping with the pandemic should be nurtured.

Key Words: Anxiety, Coping, COVID-19, Cystic Fibrosis

1.INTRODUCTION

Cystic fibrosis (CF) is a chronic, life-shortening disease causing recurrent respiratory tract infections and loss of lung functions [1]. Previous meta-analyses and systematic reviews have shown that adults and children with chronic diseases have higher risk of depression and anxiety compared to community [2,3]. A number of studies reported increased anxiety and depression in CF patients compared to healthy controls [4-6]. Facing a chronic disease such as CF on a daily basis cause significant emotional burden which can be attributed to large number of treatments, hospitalizations, multiple diagnostic procedures, chronic respiratory symptoms, a lower body mass index [6].

Viral respiratory tract infections are more severe in patients with CF compared to general population. Influenza pandemic (H1N1 infection) in 2009, caused significant morbidity in patients with CF and in a subgroup of patients with severe lung disease, H1N1 infection was associated with respiratory deterioration, intensive care admission and even death [7,8]. Coronavirus disease-19 (COVID-19) has emerged in China and been spreading all over the world since December 2019. The first case of COVID-19 infection has been confirmed in our country as of March 11, 2020. In most of the pediatric cases (>90%) the disease is asymptomatic or presented with signs of upper respiratory tract infection symptoms. However in a small number of children (0.6%), the infection may progress into critical disease causing respiratory insufficiency and death [9].

During COVID-19 pandemic people are likely to experience fear of falling sick, dying or feelings of helplessness and a number of studies revealed a wide range of psychosocial impacts on people [4]. In a study by Wang et al, included 1210

respondents, psychological impact of the outbreak was present in 53.8%. Moderate to severe depression, anxiety symptoms and stress levels were present in 16.5%, 28.8% and 8.1% of the participants respectively [10]. Another cross-sectional study in 7143 college students demonstrated that 21.3% had mild and 3.6% had moderate-to-severe anxiety symptoms where economic effects on daily life and delays in academic activities were positively associated with anxiety symptoms [11].

Although children seem to be less vulnerable than adults to COVID-19, initial reports from China indicate that children and adolescents also have been impacted psychologically, manifesting behavioral problem. Previous studies suggested that when children are out of school (eg, weekends and summer holidays), they are physically less active, have longer screen time, irregular sleep patterns, and less favourable feeding habits, resulting in weight gain and a loss of cardiorespiratory fitness [12,13].

Shuang-Jiang Zhou et al conducted a cross-sectional study including 8079 students aged 12–18 years during the COVID-19 pandemic period. The prevalence of depressive symptoms, anxiety symptoms, and a combination of depressive and anxiety symptoms was found 43.7%, 37.4%, and 31.3%, respectively [14]. Home confinement during pandemic appears to be another factor in increasing stress levels in children. In 2013, Sprang et al found that the post-traumatic stress scores of quarantined children was four times higher than those who were not quarantined [15].

Although the mortality of COVID-19 infection was found higher in patients with underlying diseases, until now, there is no evidence suggesting that the course of COVID-19 is more severe in CF patients compared to general population [16].

Clinical features of COVID-19 including dry cough, myalgia, and fever are quite distinct from the symptoms of CF and recognisable. However it is possible that mild

disease might be labelled as within the normal spectrum of symptoms for that individual. Nevertheless COVID-19 infection still might cause more stress and anxiety in CF patients. There is a study from our country evaluating anxiety of CF patients during COVID-19 pandemic. Senkalfa et al compared the anxiety of 45 CF patients with 90 healthy control group and revealed that healthy children, aged 13–18 years had higher state anxiety scores than age-matched children with CF [17].

In this study, our aim was to evaluate the effect of COVID-19 pandemic on family environment and relations, self-care practises and peer relations, psychological reactions including anxiety and coping of CF patients and compare with healthy controls.

2.METHODS

2.1.Study Design and Population

This is a case-control, cross-sectional, single center study including 7-18 year-old CF children who have been followed up in Cystic Fibrosis Center of our hospital and their healthy peers. All 7-18 year-old CF patients undergoing regular follow-up at our CF center were considered for participation. Children on psychiatric treatment for clinical anxiety and/or depression, children with mental problems and children who had been caught COVID-19 or had a family member with COVID-19 were excluded from the study. As a result 27 of 159 CF patients were excluded from the study and 83% participated. We recruited a control group consisting of 135 participants who were contacted from close associations of patients' group like neighbours, children's classmates and friends.

In CF patients, data regarding presence of pancreatic insufficiency, colonisation of *Pseudomonas aeruginosa* and level of forced expiratory volume in 1 second (FEV₁) were collected from patients' medical records. Lung disease was categorised as mild, moderate and severe according to their baseline FEV₁ measurements (FEV₁

70-89% mild lung disease, FEV₁ 40 to 69% moderate lung disease, FEV₁ < 40% severe lung disease) [19].

The data was collected between 30th April, 2020 and 15 th of May, at which time COVID-19 started to peak in our country, schools were closed and education was online. We conducted phone survey by asking questions directly to the children under parental supervision. *Informed consent was obtained from all parents following their agreement to participate the phone survey* and the study was approved by the medical ethics committee of our university.

2.2.Questionnaire

Separate behavioral questionnaires for two different age groups (7-12 years for children and 13-18 years for adolescents), based on the child psychiatry mental health examination references [18], were developed by the authors in Child and Adolescent Psychiatry Department and were not standardized. There were 27 questions in children's questionnaire and 30 questions in adolescents' questionnaire. Twenty six of questions were identical. The only different question in children's questionnaire was about separation anxiety regarding family and siblings during lockdown. The different questions in adolescents' questionnaire included that if they followed the COVID-19 news (if the answer is yes, how many hours per day they spent for it), they had an admission examination for high school or university this year and had a performance anxiety for the exam.

The questionnaire consists of 3 subscales: first family environment and relations, second self-care practises and peer relations during lockdown, and third psychological reactions regarding COVID-19 pandemic. Data regarding presence of a health worker in the family, or a family member diagnosed with COVID-19, current anxiety level, sleep disturbances, change in appetite, activities in order to mitigate their anxiety (any attempt to have a new hobby etc.) and seek for a psychological help were also collected.

2.3. Statistical Analyses

Data were analyzed by using the SPSS Statistical Package for Windows version 23.0. Numerical variables were expressed as mean±standard deviation or median. Categorical variables were compared using the Chi-square test and expressed as numbers and percentages. A p value of less than 0.05 was considered statistically significant.

3. RESULTS

This study included 132 CF patients and 135 healthy peers. The mean age was 11.53±2.86 and 11.76±3.15 years respectively, in CF group and control group (p=0.98).

There were 55 girls (41.7%) in CF group and 81 girls (60%) in control group (p=0.027).

Of the 132 CF patients, 95 (72%) had pancreatic insufficiency, 41 (31.1%) were colonised with *Pseudomonas aeruginosa*, 59 (44.7%) had normal FEV₁ value, 40 (30.3%) had mild, 23 (17.4%) had moderate and 5 (3.8%) of them had severe lung disease. There was no statistically significant difference in terms of severity of the disease and anxiety levels of CF patients (p >0.05). Comparison of psychosocial and psychological findings between CF patients and control group was presented in Table-1. CF patients were found to be less anxious for family members having the risk of COVID-19, less upset for the school closure, less anxious about the COVID-19 pandemic (p<0.001, 0.02, 0.01 respectively). Control group was more overthinking about the pandemic, and feeling sad, lonely or reluctant to have playful time (p=0.03 and 0.02, respectively). Control group also tried to have new hobbies more compared to CF group (p= 0.01).

In CF group 71 (53.8%) of patients were children and 61 (46.2%) were adolescents. Children were feeling more upset for the school closure (p=0.01) and more anxiety about the COVID-19 pandemic (p=0.008), had more appetite changes (p=0.03),

expressed more reluctance of doing homework for online education ($p=0.03$), engaging activities to decrease their anxiety ($p=0.01$) and tried to find new hobbies during lockdown ($p=0.005$) more than adolescents. Although it is not statistically significant, children stated that they needed psychological help more than adolescents ($p=0.059$). Adolescents communicated with their friends via social media more than children ($p=0.005$). Comparison of psychological and psychosocial findings in CF group as children and adolescent was presented in Table-2.

In control group, 79 (58.5%) of them were children and 56 (41.5%) of them were adolescents. Although adolescents communicated with their friends from social media more than children ($p=0.003$), children felt happier for communicating online with their friends ($p=0.02$). Also children engaged new activities more than adolescents ($p=0.008$). Comparison of psychosocial and psychological findings in control group as children and adolescent was presented in Table-3.

In our country examinations for high school and university admission are big stressors for adolescents. Twenty-four (39.4%) of CF and 17 (30.4%) of control group had admission examinations for high school or university. We also asked these adolescents if the pandemic, school closure and online education increased their anxiety. Although it was not statistically significant ($p=0.21$), exam anxiety was higher in control group compared to CF patients (46.4% vs 24.6%).

4.DISCUSSION

The COVID-19 has spread all over the world since the first quarter of 2020 and the uncertainty about the personal and global effects of COVID-19 in addition to psychological effect of quarantine caused fear and anxiety. Previous studies have suggested that the outbreaks can have many psychological effects like anxiety and

depression [20,21]. Although a number of studies evaluated psychological impact of COVID-19 pandemic in children and adults, data regarding the effect of pandemic in patients with chronic disease is scarce [17].

In this study we evaluated the psychological reactions, family and peer relations, self-care practises and coping methods of CF patients during pandemic and compared with healthy controls. Symptoms of anxiety were unexpectedly higher in controls compared to CF patients. Almost 50% of the children in control group and 33% of the CF patients were feeling anxious about the COVID-19 pandemic. Feeling upset for school closure, worries for a family member having the risk of COVID-19 infection, feeling sad, lonely or reluctant to have playful time, overthinking about pandemic are all more common psychological reactions regarding pandemic in control group compared to CF patients.

Consistent to the results of current study, in another study, Senkalfa et al also reported lower anxiety scores regarding COVID-19 pandemic in CF patients compared to age-matched healthy control group [17]. In a 1030-patient study, more than 90% of the patients having a non-pulmonary chronic disease, considerable levels of fear and anxiety were observed in a significant number of patients [22]. Surprisingly lower anxiety scores in CF patients in both of Senkalfa's and our study may be related with a number of factors.

Since the viral respiratory tract infections tend to be more severe in CF patients with an increased risk of complications and a negative impact on lung function, in the first days of pandemic, our patients and their families were more concerned about the possible effect of COVID-19 infection. However until now, only few cases of COVID-19 infection in people with CF were reported, which may probably related with the efforts of families and patients to minimise social contacts [23]. It should also worthwhile to emphasize that reported cases are mainly adult CF patients and

COVID-19 infection does not have an apparent effect on CF disease severity. It is not possible to identify protective factors and we need more data in order to determine the impact of COVID-19 on patients with CF. In cooperation with national registries, European Cystic Fibrosis Society (ECFS) Patient Registry has established an international dataset to identify factors that predict severity of COVID-19. However we assume that low numbers and mild course of COVID-19 infection caused a relieve in CF patients, which may partly explain lower anxiety levels in our patients.

During pandemic, consistent with international guidelines we recommended self-isolation for our CF patients. Recommendations for preventive measures such as using face masks and practising adequate hand hygiene were reinforced. The CF team cancelled routine clinic appointments to prevent unnecessary hospital visits and viral spread. Phone calls and email contacts were used to monitor the clinical condition of patients immediately after the lockdown. In a study from China, presence of psychological problems were negatively associated with the level of awareness of COVID-19 [14]. Wang et al revealed that wearing a mask and practicing hand hygiene decreases the level of anxiety in children older than 12 years old [10]. CF patients are used to follow instructions for infection control guidelines' including wearing masks and avoiding close in-person contact with other CF patients. The awareness regarding respiratory tract infections and familiarity to infection control measurements might be factors which decrease the level of anxiety in CF patients.

Psychosocial maladjustment might be another reason for lower anxiety levels in CF patients. Children with chronic physical disorders have twice the risk of psychosocial maladjustment compared with healthy children [24]. This maladjustment phenomenon might be an explanation for CF patients to give fewer

psychological reactions in our study group in the case of pandemic, as they are already having longer times at home, mostly detached from the school or peer relations.

CF patients are always facing with a serious health problem and have associated anxiety symptoms, however, healthy peers has been encountered fear of disease for the first time in their life during pandemic which can also partly explain relatively lower levels of anxiety in CF patients compared to healthy controls.

Although no significant difference was found between CF and control groups regarding family environment and relations or self care and peer relations, it is important to emphasize that almost half of the children were having appetite changes in both groups and incidence of sleeping problem were 10% in CF patients and 15% in control group. In our country, during disease outbreak, right after the school closure and home confinement, home schooling plan has been implemented. In addition to academic learning, age appropriate and attractive videos may motivate children to have a healthy lifestyle at home by increasing physical activities, having a balanced diet, regular sleep pattern, and good personal hygiene.

Whereas CF patients had a lower tendency to need psychological help compared to control group, children in CF group had more anxiety symptoms compared to adolescents and required more psychological help than adolescents in both groups. During pandemic children are constantly exposed to pandemic-related news, so having direct conversations with children about these issues could alleviate their anxiety. Home confinement, with the right parenting approaches could be a good opportunity to enhance family interactions and improve their self-sufficiency skills of children [25].

Resilience is the ability of properly adapt and react positively to adversity, trauma, individual or society tragedies, including serious health threats [26-27]. Coping

responses mean the behaviours, thoughts and feelings that individuals adopt to avoid being harmed by life stressors [28]. In this study, we found that CF patients seem more resilient and developed adaptive coping strategies with the pandemic. Mental health of children and adolescents constitute the basis for future adult mental health and related to quality of life, productivity, and well-being as well as compliance to treatment in the presence of a chronic health condition. Therefore, it is a vital effort to understand the psychological reactions of CF patients during the unusual period of pandemic, in addition to the chronic illness status.

Current study has several limitations. First and the most important one was the lack of a validated questionnaire. Second, the study design was cross-sectional so causality cannot be interpreted. Third although the CF and control groups are aged-matched, they are not gender-matched. It has been shown that girls experience more anxiety than boys in previous studies [29-30]. However, since the anxiety levels of girls in our study were similar in CF and control groups, we assumed that gender difference has not been an important impact on our results. Forth this was a phone survey and participants were recruited under parental supervision. Since it was a self-report assessment, the indicated levels of anxiety may not always be consistent with the assessment of mental health by a professional. Despite these limitations, there are some strengths of the study. Significant number of subjects were participated in the survey very timely. Psychological reactions regarding the pandemic were tried to be analyzed by COVID-19 specific questions. This study can be a resource for future studies.

Several studies reported increased anxiety and depression in CF patients compared to healthy controls and routine screening is strongly recommended, [4-6]. In a recent unpublished study, before pandemic, we revealed that moderate to severe depression

and moderate anxiety was present in 25.5% and 17.6% of 50 adolescent CF patients respectively in our center.

Current study revealed that CF patients had lower anxiety symptoms and they were more resilient in coping during pandemic than their healthy peers.

In conclusion, although acute events such as pandemics may not seem to increase baseline anxiety and not associated with an important physiological impact in CF patients compared to healthy population, lack of psychological support in routine care may lead to higher levels of anxiety and depression in long term.

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The authors declare no conflict of interests.

Authorship Contribution

Mürüvvet Yanaz performed the questionnaires, collected the data, performed the statistical analysis and wrote the manuscript. Cansu Yilmaz Yegit performed the questionnaires, collected the data, performed the statistical analysis. Almala Pinar Ergenekon performed the statistical analysis and wrote the manuscript. Ayse Toksoy Aksoy contributed to the conception of the study and tables in the manuscript, and collected the data. Gulcin Bilicen performed the questionnaires and collected the data. Yasemin Gökdemir performed study design, conceptualization and statistical analysis, wrote the manuscript and supervised the whole study process. Ela Erdem Eralp performed study design, conceptualization and statistical analysis, wrote the manuscript and supervised the whole study process. Ayşe Rodopman Arman performed study design, conceptualization and supervised the statistical analysis

and the manuscript. Fazilet Karakoc wrote the manuscript and supervised the whole study process. Bulent Karadag performed study design, conceptualization and statistical analysis, wrote the manuscript and supervised the whole study process.

All authors read and approved the final manuscript.

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- Accepted Article
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Tables

Table-1: Comparison of Psychosocial and Psychological Findings Between CF Patients and Control Group

	CF Patients (n=132)	Controls (n=135)	p value
Family Environment and Relations			
Existence of health professionals in the family (n,%)	13 (9.8)	15 (11.1)	0.73
Obligation of separation from mother or father during pandemic (n,%)	10 (7.6)	11 (8.1)	0.86
Feeling of parents spending enough time together (n,%)	125 (94.6)	120 (88.9)	0.12
Self Care and Peer Relations During Lockdown			
Communication with their friends from social media (n,%)	97 (73.4)	106 (78.5)	0.33
Feeling happy for communicating	78 (59.1)	97 (71.9)	1.0

online with friends (n,%)			
Engaging activities to decrease their anxiety (n,%)	111 (84.1)	120 (88.9)	0.25
New hobbies during lockdown (n,%)	32 (24.2)	51 (37.8)	0.01
Psychological Reactions Regarding COVID-19 Pandemic			
Feeling anxious for family members having the risk of COVID-19 (n,%)	31 (23.5)	59 (43.7)	<0.001
Feeling upset for the school closure (n,%)	54 (40.9)	82 (60.7)	0.02
Attentional problems regarding online education (n,%)	26 (19.7)	24 (17.8)	0.7
Reluctance of doing homework for online education (n,%)	6 (4.5)	5 (3.7)	0.67
Feeling anxious about the COVID-19 pandemic (n,%)	44 (33.3)	67 (49.6)	0.01
Having sleep problems (n,%)	13 (9.8)	21 (15.6)	0.09
Having appetite changes (n,%)	65 (49.2)	66 (48.9)	0.95
Overthinking about the pandemic (n,%)	4 (3)	11 (8.1)	0.03
Having somatic complaints of pain, weakness, and fatigue (n,%)	3 (2.3)	4 (3)	0.70
Feeling sad, lonely or reluctant to have playful time (n,%)	1 (0.8)	7 (5.2)	0.02
Need for psychological help (n,%)	24 (18.1)	36 (26.7)	0.11

Table 2. Comparison of Psychological and Psychosocial Findings In CF group as Children and Adolescent

	Children (7-12 years) (n=71)	Adolescent (13-18 years) (n=61)	p value
Family Environment and Relations			
Health professionals in family (n,%)	9 (12.7)	4 (6.6)	0.24
Obligation of separation from mother or father during pandemic (n,%)	5 (7)	5 (8.2)	1.0
Feeling of parents spending enough time together (n,%)	68 (95.8)	57 (93.4)	0.70
Self Care and Peer Relations During Lockdown			
Communication with their friends via social media (n,%)	45 (63.4)	52 (85.2)	0.005
Engaging activities to decrease their anxiety (n,%)	65 (91.5)	46 (75.4)	0.01
New hobbies during lock down (n,%)	24(33.8)	8 (13.1)	0.005
Psychological Reactions Regarding COVID-19 Pandemic			
Feeling anxious for family members having the risk of COVID-19 (n,%)	20 (28.2)	11 (18)	0.76
Feeling upset for the school closure (n,%)	34 (47.9)	20 (32.8)	0.01
Attentional problems regarding online education (n,%)	16 (22.5)	10 (16.4)	0.41
Reluctance of doing homework for online education (n,%)	6 (8.5)	0	0.03
Feeling happy for communicating online with	37 (52.1)	41 (67.2)	0.11

friends (n,%)			
Feeling anxious about the COVID-19 pandemic (n,%)	31 (43.7)	13 (21.3)	0.008
Having sleep problems (n,%)	6 (8.5)	7 (11.5)	0.64
Having appetite changes (n,%)	41 (57.7)	24 (39.3)	0.03
Overthinking about outbreak (n,%)	2 (2.8)	2 (3.3)	0.63
Having somatic complaints of pain, weakness, and fatigue (n,%)	0	3 (4.9)	0.09
Feeling sad, lonely or reluctant to have playful time (n,%)	0	1 (1.6)	0.44
Need for psychological help (n,%)	17 (23.9)	7 (11.5)	0.06

Table-3: Comparison of Psychosocial and Psychological Findings In Control group as Children and Adolescent

	Children (7-12 years) (n=79)	Adolescent (13-18 years) (n=56)	P value
Family Environment and Relations			
Health professionals in family (n,%)	11 (%13.9)	4 (%7.1)	0.21
Obligation of separation from mother or father during	6 (%7.6)	5 (%8.9)	0.76

pandemic (n,%)			
Feeling of parents spending enough time together (n,%)	73 (%92.4)	48 (%85.7)	0.20
Self Care and Peer Relations During Lockdown			
Communication with their friends via social media (n,%)	55 (%69.6)	51 (%91.1)	0.003
Engaging activities to decrease their anxiety (n,%)	75 (94.9)	45 (%80.4)	0.008
New hobbies during lock down (n,%)	35 (%44.9)	16 (%28.6)	0.06
Psychological Reactions Regarding Covid-19 Pandemic			
Feeling anxious for family members having the risk of COVID-19 (n,%)	35 (%44.3)	24 (%42.9)	0.10
Feeling upset for the school closure (n,%)	49 (%62)	33 (%58.9)	0.79
Attentional problems regarding online education (n,%)	15 (%19)	9 (%16.1)	0.87
Reluctance of doing homework for online education (n,%)	2 (%2.5)	3 (%5.4)	0.33
Feeling happy for communicating online with friends (n,%)	59 (%74.7)	38 (%67.9)	0.02
Feeling anxious about the COVID-19 pandemic (n,%)	39 (%49.4)	28 (%50)	0.04
Having sleep problems (n,%)	11 (%13.9)	10 (%17.9)	0.50
Having appetite changes (n,%)	40 (%50.6)	26 (%46.4)	0.63
Overthinking about outbreak (n,%)	6 (%7.6)	5 (%8.9)	1.0
Having somatic complaints of pain, weakness, and fatigue	2 (%2.5)	2 (%3.6)	1.0

(n,%)			
Feeling sad, lonely or reluctant to have playful time (n,%)	3 (%3.8)	4 (%7.1)	0.41
Need for psychological help	25 (%31.6)	11 (%19.6)	0.11